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GENETICS AND THE ORIGIN OF SPECIES

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GENETICS AND THE ORIGIN OF SPECIES

BY

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Preface to the Third Edition

TEN YEARS have elapsed since the publication of the second edition of this book. This decade witnessed the convulsion of the War and the gloom of the postwar reaction. And yet, it has proved to be the most fruitful decade in the history of evolutionary thought since the appearance of Darwin's classic in 1859.

The earlier conclusions reached by the different biological disciplines bearing on evolution had often seemed inconsistent with each other. There seemed to be no common language spoken by geneticists, systematists, paleontologists, ecologists, embryologists and comparative anatomists interested in evolutionary problems. This is no longer the case. Mayr's *Systematics and the Origin of Species* (1941) and Stebbins's *Variation and Evolution in Plants* (1950) showed that the findings of animal and plant systematics are wholly compatible with the theory of the mechanisms of evolution developed by geneticists. Simpson's *Tempo and Mode in Evolution* (1944) and *Meaning of Evolution* (1949) ended the belief which used to have a surprisingly wide currency, that paleontology has discovered some mysterious "macroevolution" which is inexplicable in the light of the known principles of genetics. The long pageant of evolution extending over one billion years appears to have been brought about by fundamental causes which are still in operation and which can be experimented with today. Rensch (1947) and Schmalhausen (1949) generalized the facts of comparative morphology and comparative and experimental embryology, and integrated them with genetics. A similar integration of the findings of ecology and natural history was given by Huxley (1942), Lack (1947), and Emerson (in Allee et al., 1949), and of cytology by White (1945). Only the fields of physiology and biochemistry still remain relatively little influenced by the evolutionary approach. However that may be, instead of the varied theories of evolution which arose in different branches of biology, we are now witnessing the emergence of a

new science of life unified by the great evolutionary idea. It is quite possible to analyze and to describe the processes of life one by one. But biology is becoming more than a branch of technology concerned with organic materials and processes. It aspires towards understanding life and man. Such an understanding requires knowledge of the organism as a part of the constantly changing and developing pattern of nature. Evolutionary biology is a study of the dynamics of life.

The amount of new data bearing on evolution published in recent years is very large. In preparing a third edition of the present book it has been even more necessary than in the past to avoid submerging the fundamental principles of the evolutionary thought in a review of the current literature. In numerous instances this has meant that some valuable papers could not be adequately discussed or even mentioned. More than in the first two editions the economy of space required that the presentation be made assertive rather than polemic.

This book owes much to the critical reading of the manuscript by my colleagues and friends Drs. A. B. da Cunha, M. Demerec, L. C. Dunn, E. Mayr, J. A. Moore, and T. Prout. My greatest appreciation goes to Mrs. N. P. Sivertzev-Dobzhansky for her advice, criticism, and her help in the preparation of the manuscript and in reading the proofs. The adroit editorial pencil of Miss Elizabeth Adams, of the Columbia University Press, has efficiently removed numerous rough spots in the original manuscript.

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Contents

I. ORGANIC DIVERSITY 3

II. HEREDITY AND MUTATION 19

III. MUTATION IN POPULATIONS 50

IV. SELECTION 76

V. ADAPTIVE POLYMORPHISM 108

VI. RACE FORMATION 135

VII. ISOLATING MECHANISMS 179

VIII. HYBRID STERILITY 212

IX. SPECIES AS NATURAL UNITS 254

X. PATTERNS OF EVOLUTION 276

LITERATURE 313

INDEX 343

GENETICS AND THE ORIGIN OF SPECIES

I : Organic Diversity

DIVERSITY AND ADAPTEDNESS

MAN HAS ALWAYS been fascinated by the great diversity of organisms which live in the world around him. Many attempts have been made to understand the meaning of this diversity and the causes that bring it about. To many minds this problem possesses an irresistible aesthetic appeal. Inasmuch as scientific inquiry is a form of aesthetic endeavor, biology owes its existence in part to this appeal.

Organisms are amazingly varied in the gross and in the microscopic structure of their bodies. They are equally varied in their ways of life. Several generations of morphologists and anatomists have worked to describe the structures of recent organisms, and the end of this work is not yet in sight. Paleontologists keep discovering a tremendous variety of fossils. Ecologists have only begun to explore the multiform relationships between organisms and their environments. The extent of the diversity of physiological and biochemical traits in living beings is still quite imperfectly known.

All this diversity is at first sight staggering and bewildering. The greatest achievement of biological science to date is the demonstration that the diversity is not fortuitous. It has not arisen from a whim or caprice of some deity. It is a product of evolution, an outcome of a long historical process of development, the duration of which is surmised to be of the order of two billion years (Simpson 1949). Biology cannot fathom whether life may be a part of some Cosmic Design. But biology does show that the evolution of life on earth is governed by causes that can be understood by human reason. Darwin was the first to infer that organic diversity is a response of the living matter to the diversity of environments on our planet.

The adaptedness of organisms to their environments is striking. The structures, functions, and modes of life of every species are at least tolerably consonant with the demands of its environment. Every organism is adjusted to occupy and to exploit certain habitats. But

habitats vary in space. Evolution has, accordingly, brought about the diversity of allopatric organisms, which inhabit different territories. Diverse habitats occur also within territories which are accessible to an individual organism in its wanderings during its lifetime, or in which the sex cells or seeds of an individual are dispersed. Adaptation to such local diversities of habitats brings about the diversity of sympatric organisms. Finally, the habitats change with time, and the inhabitants often change hand in hand with the environmental changes. The evolutionary changes not only enable life to endure the shocks emanating from the environment; they permit life to conquer ever new habitats, and to establish progressively firmer control of the older ones.

DISCONTINUITY

Organic diversity is an observational fact more or less familiar to everyone. It is perceived by us as something apart from ourselves, independent of the working of our mind. Experience shows that every person whom one meets differs from all met before. Every human individual is unique, different from all others who live or lived. This is probably true also of individuals of organisms other than man.

The uniqueness and unrepeatability of individuals are aspects falling primarily within the province of philosophers and artists. Although individuals, limited in existence to only a short interval of time, are the prime reality with which a biologist is confronted, a more intimate acquaintance with the living world discloses a fact almost as striking as the diversity itself. This is the discontinuity of the variation among organisms. If we assemble as many individuals living at a given time as we can, we notice at once that the observed variation does not form any kind of continuous distribution. Instead, a multitude of separate, discrete, distributions are found. The living world is not a single array in which any two variants are connected by unbroken series of intergrades, but an array of more or less distinctly separate arrays, intermediates between which are absent or at least rare. Each array is a cluster of individuals which possess some common characteristics. Small clusters are grouped together into larger secondary ones, these into still larger ones, and so on in an hierarchical order.

Biologists have exploited the discontinuity of variation to devise a scientific classification of organisms. The hierarchical nature of the observed discontinuity evidently lends itself admirably to this purpose. For the sake of convenience the discrete clusters are designated races, species, genera, families, and so forth. The classification thus arrived at is to some extent an artificial one, because it is a matter of convenience and convention which cluster is to be designated a genus, family, or order. But the clusters themselves, and the discontinuities observed between them, are not, as sometimes contended, abstractions or inventions of the classifier. Classification is natural and not artificial, in so far as it reflects the objectively ascertainable discontinuity of variation, and in so far as the dividing lines between species, genera, and other categories are made to correspond to the gaps between the discrete clusters of living forms. Biological classification is simultaneously a man-made system of pigeonholes, devised for the pragmatic purpose of recording observations in a convenient manner, and an acknowledgment of the fact of organic discontinuity. A single example will suffice to illustrate the point.

Any two cats are individually distinguishable, and this is probably equally true of any two lions. And yet no individual has ever been seen about which there could be a doubt as to whether it belongs to the species of cats (*Felis domestica*) or to the species of lions (*Felis leo*). The two species are discrete because of the absence of intermediates. Therefore, one may safely affirm that any cat is different from any lion. Any difficulty which may arise in defining the species *Felis domestica* and *Felis leo*, respectively, is due not to the artificiality of these species themselves, but to the fact that in common as well as in scientific parlance the words "cat" and "lion" frequently refer neither to individual animals nor to all existing individuals of these species, but to certain modal, or average, cats and lions. These modes and averages are statistical abstractions which have no existence apart from the mind of the observer. The species *Felis domestica* and *Felis leo* are evidently independent of any abstract modal points which we may contrive to make. No matter how great may be the difficulties encountered in finding the modal "cats" and "lions," the discreteness of these species is not thereby impaired.

In organisms which reproduce sexually and by cross-fertilization, the reality of species as biological units can also be demonstrated by a quite different method. If mating and procreation are observed, it will soon be found that organisms form usually quite discrete reproductive communities. These communities consist of individuals united by the bonds of sexual unions, as well as of common descent and common parenthood. It will doubtless be discovered that one of these reproductive communities consists of animals which, on the basis of previous morphological study, were called cats, while another community will consist of lions. No lion cub is ever born to a pair of cats, nor is the converse ever observed. A species is, consequently, not merely a group and a category of classification. It is also a supraindividual biological entity, which, in principle, can be arrived at regardless of the possession of common morphological characteristics.

What has been said above with respect to the species *Felis domestica* and *Felis leo* holds for innumerable other pairs of species. Discrete groups are encountered among animals as well as plants, among structurally simple as well as among very complex ones. Formation of discrete groups is so nearly universal that it must be regarded as a fundamental characteristic of organic diversity. An adequate solution of the problem of organic diversity must consequently include, first, a description of the extent, nature, and origin of the differences between living beings, and, second, an analysis of the nature and the origin of the discrete groups into which the living world is differentiated.

The true extent of organic diversity can only be surmised at present. In 1758 Linnaeus knew 4,235 species of animals. How many species are known at present, and how many remain to be discovered, can be estimated only very roughly. According to Mayr (1946a), 8,616 species of birds have been described, and it seems doubtful that even as many as 100 remain to be discovered. The systematics of birds is, however, known better than that of any other group of comparable size, not only because collections have been made in most parts of the world but also because the evaluation of the taxonomic status of the described forms as species or as races and subspecies has acquired a fair degree of reliability and internal consistency. In other groups—notably among insects—many new species are described

every year, large additions may be expected in the future, and some forms now regarded as species will be eventually reduced to subspecific status and vice versa. The estimates of numbers of species known have, therefore, quite different margins of error in different groups. They are relatively more reliable for the vertebrates, for which Mayr gives the following figures:

Mammals	3,500
Birds	8,600
Reptiles and Amphibians	5,500
Fishes	18,000
Total Vertebrates	35,600

Mayr's estimates for the phyla of the animal kingdom are:

Vertebrates	35,600
Tunicates and Prochordates	1,700
Echinoderms	4,700
Arthropods	815,000
Mollusks	88,000
Worms and related groups	25,000
Coelenterates and Ctenophores	10,000
Sponges	5,000
Protozoans	15,000
Total	1,000,000

Among the estimated 815,000 known arthropod species, some 750,000 are insects. These numbers are growing rapidly, and may eventually be more than doubled. The number of plant species is smaller than that of animals. The following estimates have been kindly furnished by Professor Carl Epling:

Angiosperms	150,000
Fungi	70,000
Mosses	15,000
Algae	14,000
Pteridophytes	10,000
Liverworts	6,000
Gymnosperms	500
Total	265,500

A million and a half species of animals and plants combined is, therefore, a minimal estimate of the number now living on earth.

ADAPTIVE PEAKS

Organic diversity and discontinuity of organic variation are perceived by direct observation. Similarly, we recognize, through observation and experiment, that living beings with different body structures occur in different habitats, and that they possess organs, traits, and forms of behavior which permit them to secure food, shelter, protection from enemies, and to care for the offspring in countless different ways. It is a natural surmise as well as a profitable working hypothesis, that the diversity and discontinuity on one hand, and the adaptation to the environment on the other, are causally related. The present book is devoted to an inquiry into the nature of this relationship. It may, however, be useful at the outset, as an aid in arriving at clear-cut statements of the problems involved, to consider a symbolic picture of the relations between the organism and the environment devised by Wright (1932).

Every organism may be conceived as possessing a certain combination of organs or traits, and of genes which condition the development of these traits. Different organisms possess some genes in common with others and some genes which are different. The number of conceivable combinations of genes present in different organisms is, of course, immense. The actually existing combinations amount to only an infinitesimal fraction of the potentially possible, or at least conceivable, ones. All these combinations may be thought of as forming a multi-dimensional space within which every existing or possible organism may be said to have its place.[1]

The existing and the possible combinations may now be graded with respect to their fitness to survive in the environments that exist in the world. Some of the conceivable combinations, indeed a vast majority of them, are discordant and unfit for survival in any environment. Others are suitable for occupation of certain habitats and ecological niches. Related gene combinations are, on the whole, similar in adaptive value. The field of gene combinations may, then, be visualized most simply in a form of a topographic map, in which the

[1] A more precise and realistic version of Wright's symbolic picture will be given in chapter X of this book.

"contours" symbolize the adaptive values of various combinations (Fig. 1). Groups of related combinations of genes, which make the organisms that possess them able to occupy certain ecological niches, are then, represented by the "adaptive peaks" situated in different parts of the field (plus signs in Fig. 1). The unfavorable combinations of genes which make their carriers unfit to live in any existing environment are represented by the "adaptive valleys" which lie between the peaks (minus signs in Fig. 1).

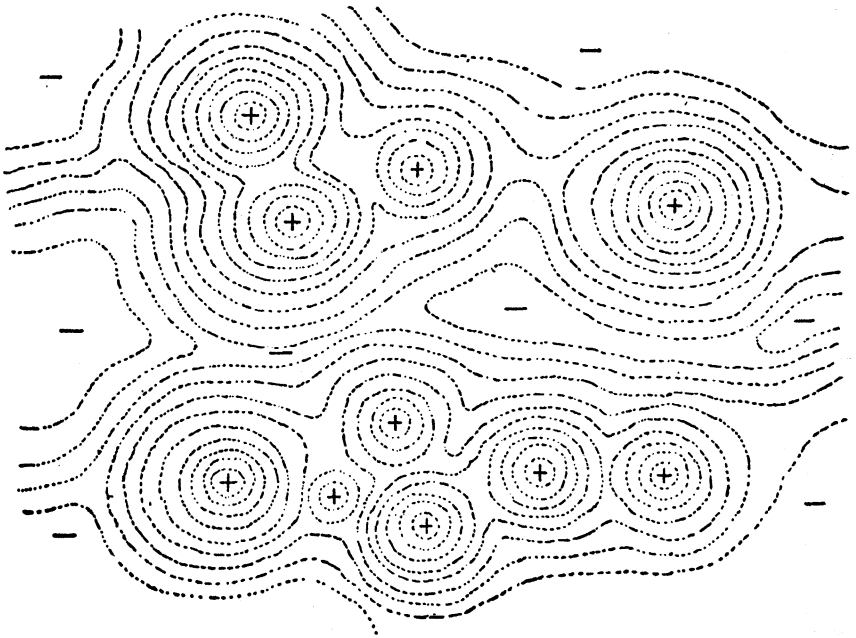


FIG. 1. The "adaptive peaks" and "adaptive valleys" in the field of gene combinations. The contour lines symbolize the adaptive value (Darwinian fitness) of the genotypes. (After Wright.)

The enormous diversity of organisms may be envisaged as correlated with the immense variety of environments and of ecological niches which exist on earth. But the variety of ecological niches is not only immense, it is also discontinuous. One species of insect may feed on, for example, oak leaves, and another species on pine needles; an insect that would require food intermediate between oak and pine would probably starve to death. Hence, the living world is not a

formless mass of randomly combining genes and traits, but a great array of families of related gene combinations, which are clustered on a large but finite number of adaptive peaks. Each living species may be thought of as occupying one of the available peaks in the field of gene combinations. The adaptive valleys are deserted and empty.

Furthermore, the adaptive peaks and valleys are not interspersed at random. "Adjacent" adaptive peaks are arranged in groups, which may be likened to mountain ranges in which the separate pinnacles are divided by relatively shallow notches. Thus, the ecological niche occupied by the species "lion" is relatively much closer to those occupied by tiger, puma, and leopard than to those occupied by wolf, coyote, and jackal. The feline adaptive peaks form a group different from the group of the canine "peaks". But the feline, canine, ursine, musteline, and certain other groups of peaks form together the adaptive "range" of carnivores, which is separated by deep adaptive valleys from the "ranges" of rodents, bats, ungulates, primates, and others. In turn, these "ranges" are again members of the adaptive system of mammals, which are ecologically and biologically segregated, as a group, from the adaptive systems of birds, reptiles, etc. The hierarchic nature of the biological classification reflects the objectively ascertainable discontinuity of adaptive niches, in other words the discontinuity of ways and means by which organisms that inhabit the world derive their livelihood from the environment.

EVOLUTION

Scientific study of the organic diversity and adaptation begins of necessity with description and classification. At the beginning of its existence as a science, biology was forced to reduce to a rational system the seemingly boundless variety of living things. In the eighteenth and nineteenth centuries systematics and morphology, two predominantly descriptive disciplines, took precedence among biological sciences. But description is only the first step in scientific inquiry. However great may be the satisfaction which an investigator derives from observation and accurate recording of facts, sooner or later he feels a desire to inquire into the causal connections between the phenomena observed. The theory of evolution arose in the nineteenth century through generalization and inference from a body of

predominantly systematic and morphological data. It has furnished a rational framework for biological thought.

The theory of evolution asserts that (1) the beings now living have descended from different beings which lived in the past; (2) the evolutionary changes were more or less gradual, so that if we could assemble all the individuals which have ever inhabited the earth, a fairly continuous array of forms would emerge; (3) the changes were predominantly divergent, so that the ancestors of the now living forms were on the whole less different from each other than these forms themselves are; (4) all these changes have arisen from causes which now continue to be in operation, and which therefore can be studied experimentally.

Evolutionists of the nineteenth century were interested primarily in demonstrating that evolution has actually taken place. They succeeded eminently well. Evolution as a historical process is established as thoroughly and completely as science can establish facts of the past witnessed by no human eyes. At present, an informed and reasonable person can hardly doubt the validity of the evolution theory, in the sense that evolution has occurred. The very rare exceptions (such as Marsh 1947) prove only that some people have emotional biases and preconception strong enough to make them reject even completely established scientific findings. However that may be, the mass of evidence which can be adduced to show that evolution has indeed taken place in the history of the earth does not concern us in this book; we take it for granted.

Two distinct approaches to evolutionary problems became crystallized rather early in the development of evolution theory. The first concentrated on unraveling and describing the actual course which the evolutionary process took in the history of the earth, and which has led to the status of the organic world which we find at our time level. The historical process, phylogeny, is the central theme for the exponents of this approach, while their methods are mainly those of systematics, comparative morphology, comparative embryology, and paleontology. The second approach emphasizes studies on the mechanisms that bring about evolution, causal rather than historical problems, phenomena that can be studied experimentally rather than events which happened in the past. In general, the phylogenetic

approach to evolutionary problems was predominant during the second half of the nineteenth century, while in the twentieth century the attention shifted toward the causal aspects, which were taken up by genetics and related biological disciplines. In fact, Darwin was one of the very few nineteenth-century evolutionists whose major interests lay in studies on the mechanisms of evolution, in the causal rather than the historical problems. In this sense, genetics and not evolutionary morphology is heir to the Darwinian traditions. Finally, the most recent developments indicate a trend toward synthesis of what were often divergent historical and causal approaches, and toward emergence of a unified evolutionary biology.

GENETICS AND EVOLUTION

Genetics as a discipline is not synonymous with the evolution theory, nor is the evolution theory synonymous with any subdivision of genetics. Nevertheless, genetics has so profound a bearing on the problem of the mechanisms of evolution that any evolution theory which disregards the established genetic principles is faulty at its source. Every individual resembles its parents in some respects but differs from them in others. Every succeeding generation of a species resembles but is never a replica of the preceding generation. Evolution is the development of dissimilarities between the ancestral and the descendant populations. The mechanisms which determine the similarities and dissimilarities between parents and offspring constitute the subject matter of genetics. Genetics is the physiology of inheritance and variation.

The signal successes of genetics to date have been in studies on the mechanisms of the transmission of hereditary characteristics from parents to offspring, that is, on the architectonics of the germ plasm of the sex cells. The germ plasm has been shown to be composed of discrete particles known as genes. Chromosomes as carriers of genes have been studied in detail. The transmission of hereditary characters has been brought under human control, in the sense that in organisms which have been well studied genetically the characteristics of the offspring are frequently predictable, with a rather high degree of accuracy, from a knowledge of the characteristics of the parents.

The elegance and precision of methods devised by genetics to control the results of experiments which involve crosses of individuals

differing in many hereditary characteristics have led to claims that the problem of heredity has been solved. Although a large amount of work still remains to be done in this field, it is indeed fair to say that the laws of the transmission of hereditary characters are, by and large, understood now. But the problem of heredity is much wider. Between the genes of a fertilized egg and the characters of the adult organism which arises from it there lies the whole of individual development during which the genes exert their determining action. The mechanisms of gene action in development constitute the central problem of the second major subdivision of genetics; this has been variously labeled genetics of realization of hereditary characters, phenogenetics, or developmental genetics.

The problem of gene action is as yet unsolved, although much important work has been done in this field by geneticists and biochemists in recent years (see Beadle 1945, 1946, 1947, 1949, Wright 1941b, 1945, and Horowitz 1950 for reviews). The only possible way in which genes could influence the development of an organism is through physiological, and ultimately chemical, processes in the living body. Indeed, it is known in several instances that the formation of adult characteristics involves chains of chemical reactions, at least some of which are controlled by genes. The remarkable work of Beadle's school on the biochemistry of metabolism in the fungus *Neurospora* has disclosed that mutation of some genes blocks certain reactions at specific points in the reaction chains, and causes accumulation in the cells of substances which normally exist only as intermediate products.

Despite the great interest of these findings for chemical physiology, rather little insight has so far been gained into the gene action proper. Beadle and his colleagues have supposed that the "normal" alleles of the genes studied by them in *Neurospora* produce enzymes which mediate specific reactions, and that mutation (or destruction) of these genes causes nonproduction of the enzymes and blockage of the reactions. They further implied that every gene produces one and only one enzyme which catalyzes a specific reaction. This supposition is temptingly simple, and it has so far vindicated itself as a stimulating working hypothesis. Yet, there is no compelling evidence in favor of the one gene—one enzyme assumption, and the postulated enzymes have rarely been identified. A brilliantly conceived attempt

in this direction by Caspari (1946) in the moth, *Ephestia kühniella*, and by Wagner and Guirard (1948) and Wagner (1949) in *Neurospora*, have led to ambiguous results.

A gene is a particle of molecular dimensions. It is located in a chromosome in the cell nucleus (or in the cytoplasm, in the case of plasmagenes). How can such particles bring about the often very striking macroscopic changes in living bodies? Gene action must of necessity start with intracellular processes, which may subsequently be translated into chains of reactions that culminate in the appearance of visible characters. Little is known regarding these intracellular processes—interactions between the constituent parts of the chromosomes and their nuclear and cytoplasmic surroundings, although Muller (1947), Rapoport (1947), Mather (1948), and Spiegelman (1948) have advanced interesting hypotheses concerning the possible mechanisms of the gene action in development. Are all genes continually active, or does each gene exert its determining function at a certain period of development and remain quiescent at other periods? Is the gene action merely a by-product of the self-reproduction of the genes in the course of cell division? What are the relations between gene specificity and the specificity of chemical substances, particularly proteins, composing the organism and manifested especially in serological reactions?

Biophysical and biochemical work has revealed a great complexity of cellular organization on the ultramicroscopic level of molecular aggregates. To a geneticist, it seems that genes should be determining agents of this "molecular morphology," and Delbrück (1941) and Emerson (1945) have advanced interesting suggestions which will be helpful in further thinking and experimentation in this important field. According to Emerson, gene specificity resides chiefly in the molecular surface configuration of the gene. This might permit the gene specificity to be transmitted to molecules of different chemical make-up, and some of the latter may in turn serve as "templates" for synthesis of new genes and enzymes (and, hence, for gene reproduction).

GENETICS OF POPULATIONS

Genetics of the transmission of hereditary materials, and genetics of development, are concerned with individuals as units. The former

seeks to find out the rules which govern the formation of gene constellations in individual zygotes, so that the probable distribution of genes in the offspring may be predicted from a knowledge of the genotypes of the parents. The latter studies the mechanisms of gene action in ontogeny. A third subdivision of genetics has as its province the processes which take place in groups of individuals, in populations, and is therefore called genetics of populations.

In a broad sense, a population may be defined as "any single or mixed species association in the laboratory or in nature that presents a closely interacting system which can be studied and expressed with some quantitative rigor" (Park 1942, Allee et al. 1949). Allee et al. argue that a population is not a group concept but a spatiotemporal entity which possesses the following five organismic attributes. (1) A definite structure and composition. (2) "The population is ontogenetic. It exhibits (as does the organism) growth, differentiation and division of labor, maintenance, senescence, and death. (3) The population has a heredity. (4) The population is integrated by both genetic and ecologic factors that operate as interdependent mechanisms. (5) Like the organism, the population is a unit that meets the impact of its environment. This is a reciprocal phenomenon, since the population is altered as a consequence of this impact, and, in time, it alters its effective environment."

Among the different kinds of populations that exist in nature, the organism-like integration is most evident in the breeding associations which are formed in all sexual and cross-fertilizing organisms. The integrating agent in such Mendelian populations is the process of reproduction itself, which establishes mating, parenthood, and progeny bonds between the component individuals. *A Mendelian population is, then, a reproductive community of individuals which share in a common gene pool* (Dobzhansky 1950d).

A Mendelian population may be said to possess a corporate genotype. The population genotype is evidently a function of the genetic constitution of the component individuals, just as the health of an individual body is a function of the soundness of its parts. The rules governing the genetic structure of a population are, nevertheless, distinct from those which govern the genetics of individuals, just as rules of sociology are distinct from physiological ones, although the former are in the last analysis integrated systems of the latter (Novikoff

1945). Suppose for example, that some factors have arisen in the environment which discriminate against too tall or too short individuals of a species. From the standpoint of an individual, some growth genes would have acquired lethal properties, and the effects of these genes might be described adequately by stating the precise nature of the physiological reactions leading to death. From the viewpoint of population genetics, death of this category of individuals initiates a complex chain of consequences: the relative frequencies of homozygotes and heterozygotes for certain growth genes and for genes located in the same chromosomes would be altered; some genetic factors which previously were being eliminated because of their harmfulness might become neutral or even favorable; after some generations the genetic constitution of the whole species may be changed.

Evolution is a change in the genetic composition of populations. The study of mechanisms of evolution falls within the province of population genetics. Of course, changes observed in populations may be of different orders of magnitude ranging from those induced in a herd of domestic animals by the introduction of a new sire to phylogenetic changes leading to the origin of new classes of organisms. The former are obviously trifling in scale compared with the latter. Experience shows, however, that there is no way toward understanding of the mechanisms of macroevolutionary changes, which require time on geological scales, other than through understanding of microevolutionary processes observable within the span of a human lifetime, often controlled by man's will, and sometimes reproducible in laboratory experiments.

Many authors believe that microevolutionary changes are different in principle from macroevolutionary ones, and that while the former can be understood in terms of the known genetic agents (mutation, selection, genetic drift), the latter involve forces that are experimentally unknown or only dimly discerned. Views of this kind have been entertained by few geneticists (among whom there is, however, so eminent a man as Goldschmidt 1940), but they have been popular among those who approach evolutionary problems on the basis of data of paleontology and comparative anatomy. Well-known writers have supposed macroevolutionary changes to be engendered by some directing forces either inherent in the organism itself or act-

ing on it by some inscrutable means from the outside. These guiding forces received a variety of names, including orthogenesis, nomogenesis, aristogenesis, hologenesis, and finalism, but they escaped precise definition which would make them subject to experimental test or to any kind of rigorous proof or disproof (see Simpson 1949).

Methods of experimental genetics apply directly only to forms which can be crossed and which produce hybrids. Genetic analysis is, accordingly, limited to differences on the individual, racial, specific, and at most the generic levels, which are usually regarded the province of microevolution. A geneticist can approach macroevolutionary phenomena only by inference from the known microevolutionary ones. It is obviously impossible to reproduce in the laboratory the evolution of, for example, the horse tribe, or for that matter of the genus *Drosophila.* All that is possible is to examine the evidence bearing on macroevolution which has been accumulated by paleontologists and morphologists, and to attempt to decide whether it agrees with the hypothesis that all evolutionary changes are compounded of microevolutionary ones. This difficult but important task has been brilliantly accomplished in recent years by Simpson (1949) for paleontological and by Schmalhausen (1949) and Rensch (1947) for comparative anatomical and embryological evidence. The three authors find nothing in the known macroevolutionary phenomena that would require other than the known genetic principles for causal explanation. The words "microevolution" and "macroevolution" are relative terms, and have only descriptive meaning; they imply no difference in the underlying causal agencies.

EVOLUTIONARY STATICS AND EVOLUTIONARY DYNAMICS

Evolution is a process of change or movement. Description of any movement may be divided into two parts: statics, which treats of the forces producing a motion and the equilibrium of these forces, and dynamics, which deals with the motion itself and the action of forces producing it. Following this scheme, we shall discuss, first, the factors which bring about changes in the genetic composition of populations (evolutionary statics), and second, the interactions of these forces in race and species formation and disintegration (evolutionary dynamics).

In bare outline, the mechanisms of evolution as seen by a genet-

icist appear as follows. Gene changes, mutations, are the primary source of evolutionary changes and of diversity in general. Next come changes of a grosser mechanical kind, rearrangements of the genic materials within the chromosomes. Such rearrangements at least occasionally entail changes in the functioning of the genes themselves (position effects), since the effects of a gene on the development are determined not only by the structure of that gene but also by its neighbors. Combining chromosome complements of different species to produce a single new one (allopolyploidy) is an important evolutionary method among plants. Finally, there is an insufficiently studied field of changes in extranuclear structures, usually associated with the cytoplasm.

Mutations and chromosomal changes arise in every species and supply the raw materials for evolution. But the origin of mutations and chromosomal changes is only the first stage or level of the evolutionary process. Once produced, mutations are injected into the gene pool of the population, where their further fate is determined by the dynamic regularities of the physiology of populations. The influences of selection, migration, and geographical isolation then mold the genetic structure of populations into new shapes, in conformity with the secular environment and the ecology, especially the breeding habits, of the species. This is the second level of the evolutionary process, on which the impact of the environment produces the historical changes in the living populations.

Finally, the third level is a realm of fixation of the diversity attained on the preceding two levels. Races and species are populations or groups of populations which remain distinct only so long as some cause limits their interbreeding. Unlimited interbreeding of two or more initially different populations results in exchange of genes between them and a consequent fusion of the once distinct groups into a single variable array. A number of reproductive isolating mechanisms encountered in nature (ecological isolation, sexual isolation, hybrid sterility, and others) guard against such a fusion of the discrete arrays and the consequent decay of discontinuous variability. The origin and functioning of the reproductive isolating mechanisms constitute one of the most important problems of the genetics of populations.

II: Heredity and Mutation

HEREDITY AND SELF-REPRODUCTION

ALL ORGANISMS grow and reproduce. Growth occurs through the transformation of materials taken up from the environment into body constituents. The organism reproduces itself in the progeny from food which it consumes and assimilates. The processes whereby this self-reproduction is accomplished are the essence of heredity. The greatest discovery of genetics is that the units of self-reproduction are molecules, or molecular aggregates, called genes. The chemical processes whereby a gene engenders the synthesis of its copies are unknown, but in a most generalized way they may be symbolized as follows:

$$A + B = 2A + C$$

A stands for the gene, B for the materials from which gene replicas are synthesized, and C for the by-products formed in the process. Despite its abstractness, this representation is helpful, because it illustrates a very important point (Dobzhansky 1950b). The genes are doubtless among the chemically most active cellular constituents. In the interval between every two successive cell divisions the genes must undergo transformations which result in their own reduplication. And yet, the genes are by far the most stable of all organic structures. The same genes are transmitted not only to all the cells of the developing body, but also from generation to generation. This singular combination of changeability and stability is possible because the transformations which the genes undergo are cyclic. With few exceptions, these transformations of the genes lead to the production of their replicas. This enables life to preserve its essential autonomy and continuity, and not only to withstand many environmental shocks but even to alter its environment. Self-reproduction is the most basic attribute of life; the appearance in the world of the first

bit of self-reproducing material was the origin of life (Muller 1929, Dobzhansky 1943, Plunkett 1944).

The sum total of genes of an individual or a population constitutes the genotype. The genotype can be transmitted without change to the offspring, and, in asexually reproducing organisms, is potentially able to be carried in any number of individuals. Anderson (1936) and Camp (1945) found large colonies of *Iris* and *Vaccinium* which consisted of genetically identical individuals. Every genotype exerts a "pressure" on its environment; it tends to organize and to transform into its replicas all the materials available in the environment (B in the above scheme) which it can use. All organisms can, however, subsist not in one only but in a certain variety of environments, which may be symbolized as B^1, B^2, B^3, etc. The self-reproduction of the genes gives then:

$$A + B^1 = 2A + C^1$$
$$A + B^2 = 2A + C^2$$
$$A + B^3 = 2A + C^3, \text{ etc.}$$

If the environment of the genes is changed, the genes still continue producing faithful copies of themselves (2A). If, however, the change in the environment is such that the gene copying cannot go on, the genes fail to reproduce altogether. Only very rarely a gene may produce a slightly changed copy, a mutant gene, which reproduces its changed structure. By contrast with this relative stability of the genes, the outcomes of the developmental processes vary in different environments. The resulting bodily forms (C^1, C^2, C^3, etc.) are different phenotypes.

The total range of phenotypes which a given genotype can engender in all possible environments constitutes the norm of reaction of the genotype. The distinction between the genotype and the phenotype, formulated in 1911 by Johannsen, is basic for clear thinking about biological problems. The phenotype is what is perceived by direct observation, the organism's structures and functions, in short, what a living being appears to be to our sense organs. The phenotype of an individual changes continuously from birth to death. The genotype is relatively quite stable, because the genes reproduce themselves. However, the stability of the genotype is certainly not due to

a chemical inertness of the genes, but to the fact that all but a very minute fraction of the altered genes are cast out through failure to reproduce themselves.

The error of the Lamarckian belief in the inheritance of acquired characters is due to a failure to recognize that the phenotype (C) is a by-product of the gene reproduction (A), and not vice versa. Any phenotype that may be formed is necessarily a response of the environment to the activity of a genotype. A genotype is potentially able to engender a multitude of phenotypes, which can be realized if the environments needed to have the potentialities come to light are available or can be created. Whatever change is induced in the phenotype, this change is of necessity within the norm of reaction circumscribed by the genotype; and yet, the genotype is neither unchangeable nor independent of the environment. Genotypic changes do occur in which the environment plays the role of at least a trigger mechanism (induced mutation, see below). Moreover, any genotype is the result of an agelong process of evolutionary development, in which the environment, through natural selection, has been a force of paramount importance. The structure of the genotype, and hence the kind of changes it is capable of producing, are in the last analysis environmentally determined. The "determining environment" is, however, not the one prevailing at the moment, but rather it is the sum of the historical environments to which the organism had been exposed in its phylogeny.

THE NORM OF REACTION

The most general definition of evolution is change in the genotype of a population. Modifications of the phenotype alone, brought about by alterations of the environment, do not constitute evolution, unless they are accompanied by some genotypic changes. Nevertheless, what counts in evolution are the phenotypes which are produced by interaction of the genotypes of the organisms with the environments that are encountered in different parts of the world. It is the phenotype which is adaptive in some environments and unfit in other environments. Infirmity or well being, survival or death of an individual or a population in a given environment are determined, in the last analysis, by the genes which they carry. But the genes act through the de-

velopmental patterns which the organism shows in each environment. What changes in evolution is the norm of reaction of the organism to the environment.

The survival values of the different phenotypes which can arise on the basis of a given genotype are often unequal. The phenotypes which develop in response to environmental influences which recur regularly in the normal habitats of a species are usually adaptive and conducive to survival. The reactions to environmental stimuli which the species encounters rarely or never in its normal habitats are, on the contrary, seldom adaptive (Schmalhausen 1949, Muller 1950a). Schmalhausen calls the former modifications and the latter morphoses. Every norm of reaction includes the potentialities of numerous modifications and of, presumably, even more numerous morphoses. Neither modifications nor morphoses influence the genotype, because they are conditioned by the genotype, while the genotype reproduces itself regardless of what phenotype it happens to evoke in a given instance.

Modifications maintain the normal equilibrium of physiological processes in the body (homeostasis), as well as the harmony between the organism and the external world. Thus, seasonal changes in the reproductive physiology and behavior in many animals and plants are clearly adjusted to the annual climatic cycles in the geographic regions in which the species normally occur. The manifold immunological reactions of the body to invasions by parasites and pathogens are strikingly adaptive. So are the processes of healing of wounds and fractures. The apparent purposefulness of the behavior of a paralyzing wasp providing food for its progeny, or of the different castes in an ant or a termite colony defending or repairing their nests, is quite impressive. The strengthening of organs with use, and weakening with disuse, are classical examples of adaptive modifications. All these physiological reactions and forms of behavior belong, of course, to the phenotypes of the organisms which show them, but it is equally obvious that they are conditioned by the genotypes of these forms. The success or failure of a genotype in evolution is determined by its reaction norm, by the adaptedness of the modifications evolved in response to recurring environmental influences.

The situation is quite different with morphoses. Morphoses are adaptively haphazard, and often harmful. Typical examples of mor-

phoses are the changes which can be induced in a developing organism by chemicals with which the species does not normally come in contact in nature (chemomorphoses), or by X-ray and radium treatments (radiomorphoses). Morphoses are induced also by abnormal intensities of widespread environmental variables, such as temperatures much higher or lower than those which occur in natural habitats. Diseases and breakdowns caused by abnormal strains and exposures can be considered morphoses in genetic sense. According to Schmalhausen (1949), morphoses "arise as new reactions which have not yet attained a historical basis." Adaptive modifications are, on the contrary, forged in the evolutionary development of the species. Lamarck took for granted the adaptive modifications following use and disuse of organs and proposed to explain evolution as a result of such modifications. Actually, it is the ability of organs to react adaptively to the effects of use and disuse that must be explained as an evolutionary achievement.

A complete description of the norm of reaction of a genotype would require experiments placing carriers of this genotype in all possible environments, and observing the resulting phenotypes. Since the number of possible environments is virtually infinite, our knowledge of the reaction norms is at best fragmentary. It is nevertheless plain that some genotypes permit a greater amplitude of modifications and morphoses than others, and that some traits are plastic while others are more rigidly fixed. An often quoted example of traits irrevocably fixed by the genotype are the human blood groups. Carriers of the gene for blood group A will have the A antigen in their bloods in all known environments and regardless of the age and the state of health. The presence of this antigen can be ascertained even in fossil bones, provided that the process of mineralization has not gone too far. Conversely, human intellectual and emotional development is an example of a great plasticity and susceptibility to environmental influences. Environment, upbringing, schooling, associations with other people, and the manifold variations of individual biographies are powerful moulders of human personality. The genotypic determinants of human personality are easily obscured by the environmental ones. The variability of human skin color is genetically less rigidly fixed than the variability of the blood groups, but it is less susceptible to environmental modifications than is the personality development.

The influence of both genetic and environmental factors on human skin color is readily apparent.

It must be emphasized that the fixity or plasticity of a trait with respect to environmental influences is determined by the genotype. The amplitude of the reaction norm is conditioned by the hereditary constitution. Schmalhausen (1949) has especially stressed the homeostatic properties of the genotypes which are adaptively "normal" for the species, i.e., are widespread in the natural habitats. The normal patterns of the developmental processes are so buffered against the influences of recurrent environmental agencies that the outcome of the ontogeny is not unduly variable. Conversely, the phenotypes of mutants which do not normally occur in natural populations are often very unstable. For example, normal, or wild-type, strains of *Drosophila melanogaster* are much less variable than many of its mutants. Temperature, nutritional changes, and most genetic modifiers do not appreciably alter the sexual characteristics of normal males and females, but they produce gross changes in the reproductive organs of triploid intersexes. It is obviously important to the species that the male and female genotypes (which differ usually in the number of X and Y chromosomes) give rise to normally functioning male and female individuals. The developmental reactions of these sexes are, accordingly, stabilized and buffered against deleterious fluctuations. But intersexes are not regular constituents of the species populations; their norms of reaction have not become consolidated in the evolutionary development, and their phenotypes are highly variable.

PHENOCOPIES

It would, nevertheless, be hazardous to classify the traits of an organism, for example of the human species, into those rigidly fixed by the genotype and environmentally plastic ones. Since the norm of reaction of any genotype is only imperfectly known, it is always possible that environmental influences will be discovered which will produce altogether unexpected morphoses. Goldschmidt (1938) pointed out that, theoretically, any change in the phenotype caused by a genotypic change (mutation) may be reproduced as a purely phenotypic modification if a suitable experimental technique is in-

vented. Goldschmidt and others have described special treatments that induce phenotypic variations (phenocopies) in *Drosophila melanogaster* which more or less resemble some of the well-known mutant types of that insect. For example, "normal" strains of *Drosophila melanogaster* have in most known environments a brownish body color, while the mutants yellow and straw are bright yellow in color. However, Rapoport (1939, see also Di Stefano, 1943 and Maas, 1948) discovered that larvae of normal strains give rise to yellow or straw phenocopies if grown on food to which certain silver salts have been added. Chevais (1943) found a converse case: a phenotypic transformation of a mutant into a phenocopy of the normal type. Namely, the mutant Bar, which usually has eyes much reduced in size, may develop normal eyes if an extract of pupae of *Calliphora* flies is added to the larval food (see also Gordon and Sang 1941).

Despite their phenotypic similarities, there exists a fundamental difference between a mutant and a phenocopy. The offspring of a yellow phenocopy are normal in body color if they develop on a culture medium free of silver salts; the offspring of the yellow mutant are yellow regardless of the culture medium on which they grow. The norm of reaction of "normal" *Drosophila melanogaster* is such that in most environments the development results in flies with "normal" traits, but when silver salts are added to the food yellow-bodied flies are produced. The norm of reaction of the yellow mutant engenders a yellow body in all known environments in which the development is possible. Mutations change the norm of reaction, but in a phenocopy the norm of reaction remains unaltered.

DEFINITION OF MUTATION

Owing to the inherent stability of the genotype, heredity is a conservative agent. Evolution is possible only because heredity is counteracted by another process opposite in effect—namely, mutation. The mutation concept has had a tortuous history. Not only has the term changed repeatedly in meaning, but even now it is being used in two different senses. Alternatives to the term "mutation" have been proposed, but all of them have failed of adoption. Many years ago Waagen (1869) designated as mutations the smallest perceptible changes in the temporal series of forms in a species of ammonites;

these changes have a definite direction, and their gradual accumulation with the passage of time leads to the appearance of types progressively more distinct from the progenitor.

The creators of the mutation theory were Korjinsky and De Vries. The latter (De Vries 1901) defines it as follows: "As the theory of mutation I designate the statement that the properties of organisms are built from sharply distinct units.... Intergrades, which are so numerous between the external forms of plants and animals, exist between these units no more than between the molecules of chemistry." A mutation is, then, a change in one of the units which at present are known as genes. Thus far De Vries's statements have a decidedly modern ring. De Vries proceeds, however, to define the distinctions between his mutation theory and Darwin's selectionism: "The latter [selectionism] assumes that the usual or the so-called individual variability is the starting point of the origin of new species. According to the mutation theory the two [individual and mutational variabilities] are completely independent. As I hope to show, the usual variability cannot lead to a real overstepping of the species limits even with a most intense steady selection...." On the other hand, each mutation "sharply and completely separates the new form, as an independent species, from the species from which it arose." Since De Vries's "species" are evidently not identical with the usual, or Linnaean, ones, an attempt was made to introduce the term "elementary species" for the former. This attempt has met with little sympathy, not only because the word species was here used in an entirely new sense, but especially because in sexually reproducing organisms one would have to consider almost every individual an elementary species. Furthermore, it is clear at present that the individual variability, in so far as it is hereditary at all, is due to the fact that the populations of most species are mixtures of types differing from each other in one or in several genes. Finally, the mutants obtained by De Vries in his classical investigations with *Oenothera* proved to be an assemblage of diverse changes, including gene alterations, segregation products due to a hybridity of the initial material, and chromosomal aberrations.

The studies begun by Morgan in 1910 on mutability in the fly *Drosophila melanogaster* constitute a turning point in the history of the mutation theory. Although mutations occur as sudden changes,

in the sense that no gradual passage through genetic conditions intermediate between the original and the mutant types is observed, the distinction which De Vries has attempted to draw between individual and mutational variability does not exist. The amount of change produced by a mutation, as measured by the visible departure from the ancestral condition in the structural and physiological characters, varies greatly. Since mutants which are recognizable even to an untrained eye are most useful in experiments, such mutants are preserved while the slight ones are generally discarded; this has created a false impression among some biologists that all *Drosophila* mutants show striking visible alterations. Slight mutants, falling well within the normal range of individual variability, have been observed by Johannsen (1909) in beans, and Morgan (1918) has repeatedly emphasized that they occur in *Drosophila* as well. Baur (1924) claimed small mutations to be very common in the snapdragon (*Antirrhinum majus*). Small and large mutations are not distinct classes as some writers have implied.

From the very beginning of the work on *Drosophila* it has become clear that most mutations behave as changes in single Mendelian units (Morgan 1911, 1913). Since Mendelian segregation and recombination constitute the twin bases on which the existence of genes is inferred, the conclusion is drawn that most mutations represent gene changes. The nature of these changes is, however, a different problem. If a gene is a self-reproducing unit in a chromosome, alterations which permit the changed particle to retain its autosynthetic functions might be a source of the mutational variability. It would seem reasonable to restrict the term "mutation" to apply to this, and only to this, kind of change. Such a restriction leads, however, to difficulties in practice, since no methods are available for a direct comparison of the chemical structures of the ancestral and the mutated genes. The sole evidence of the occurrence of a change in the gene is the appearance of a phenotypic variant, a mutant, which follows Mendel's law in inheritance. Yet a loss (deficiency) or a reduplication of a part of a chromosome likewise results in phenotypic alterations that show Mendelian inheritance. Similar effects may be produced by rearrangements of the genic materials within the chromosomes (inversion, translocation). Finally, reduplications and losses of whole chromosomes may simulate Mendelian units.

The term mutation subsumes a variety of phenomena. In a wide sense, any change in the genotype which is not due to recombination of Mendelian factors is called mutation. In the narrower sense, it is a presumed change in a single gene, a Mendelian variant which is not known to represent a chromosomal aberration.

CLASSIFICATION OF MUTATIONS

Mutational changes fall into two large classes: those presumably caused by chemical alteration of individual genes (mutation proper), and those of a grosser structural kind, which involve destruction, multiplication, or spatial rearrangement of the genes in the chromosomes (chromosomal aberrations). In turn, several types of chromosomal aberrations can be distinguished:

I. NUMERICAL CHANGES—affecting the number of chromosomes.
   a. HAPLOIDY. Higher organisms are mostly diploid during a major part of the life cycle, that is, they possess two chromosomes of each kind in the nuclei of most cells. Gametes, and gametophytes (in plants), are haploid, and carry one chromosome of each kind. Some diploid organisms have produced under experimental conditions haploid aberrants, which have a single set of chromosomes in the tissues that are normally diploid.
   b. POLYPLOIDY. Normally diploid organisms may give rise to forms with more than two sets of homologous chromosomes. Such forms are known as polyploids.

II. STRUCTURAL CHANGES—affecting the arrangement of genes in the chromosomes.
   A. Changes due to loss or reduplication of some of the genes.
      a. DEFICIENCY (deletion). A section containing one gene or a block of genes is lost from one of the chromosomes. If a normal chromosome carries genes ABCDEFG, the deficient chromosome is ABEFG.
      b. DUPLICATION. A section of a chromosome may be present at its normal location in addition to being present elsewhere. If a normal chromosome has genes ABCDEFG, the duplication may be ABCDECDFG or the like. Studies on chromosomes in salivary gland cells of *Drosophila* and *Sciara* have shown that in the "normal" chromosomes certain sections are represented two or more times in the haploid set. Such "repeats" are duplications which have become established in the phylogeny.
   B. Changes due to an alteration of the normal arrangement of genes.
      a. TRANSLOCATION. Two chromosomes, ABCDEFG and HIJK, may

exchange parts, giving rise to "new" chromosomes ABCDJK and HIEFG.

b. INVERSION. The location of a block of genes within a chromosome may be changed by a rotation through 180°. The resulting chromosome carries the same genes as the original one, but the arrangement of the genes is modified from ABCDEFG to AEDCBFG.

Discrimination of point mutations and chromosomal aberrations is frequently impossible. The direct cytological method, examination of the chromosomes of mutants under the microscope, is more reliable in some materials than in others. Thus, a loss of a chromosome section may be detectable in a species with large and well-differentiated chromosomes, but not in one with small and compact ones. The giant chromosomes in the larval salivary glands of *Drosophila* and of certain other flies unquestionably offer the most favorable material for such studies, but even there one cannot be certain that very small structural changes (for example, losses or additions of single discs) are not overlooked. Stadler (1932, 1941) has correctly emphasized that the so-called gene mutations are merely the residuum left after the elimination of all classes of hereditary changes for which a mechanical basis is detected.

Goldschmidt (1938, 1940) takes the extreme view that all supposed gene mutations are rearrangements in the chromosomal materials. All that one can say regarding this view, is that the postulated mechanical changes have not been shown to exist in most mutants. Admittedly, the inability to detect such changes in any one mutant is not a proof that this particular mutant is caused by a chemical, rather than a mechanical, change, but it remains, nevertheless, probable that many mutants do belong to this class.

TYPES OF CHANGES PRODUCED BY MUTATION

Since all developmental processes are gene controlled, any morphological or physiological trait may be altered by mutation. In *Drosophila melanogaster*, mutations are known that affect the coloration of all external parts of the body, of the eyes, testicular envelope, and Malpighian vessels; the length, diameter, and shape of the bristles—definite bristles or sets of bristles may be absent or reduplicated. Mutations influence the size of the eyes, antennae, and

legs, the form and arrangement of the ommatidia, and the chitinization and arrangement of body sclerites. A very interesting class of mutations cause homeosis, i.e., transformation of some organs into others. Here belong the transformation of the balancers into a second pair of wings, of wings into organs resembling balancers, appearance of a pair of wings on the prothorax (Hexaptera of Herskowitz 1949), of legs in place of antennae, and of the mouth parts of the fly in the direction of those of lower insects. Sexual characters are affected: sexcombs, external male genitalia, spermathecae, number of eggstrings and egg chambers in the ovaries, shape and appearance of the eggs.

The kinds of mutations that one finds depend on the methods of their detection. Since mutations in *Drosophila* have been used chiefly as markers in linkage experiments, emphasis has been laid on easily visible external changes in the adult insect. Although changes in anatomical and physiological traits have rarely been looked for, mutations which affect size and shape of larvae and pupae are known. Changes in the internal organs are observed chiefly in connection with external changes; thus, the brain is changed in mutants which have small eyes or no eyes at all (Power 1943). Purely physiological and behavioral traits may be affected: reactions to light and gravity (McEwen 1918, Barigozzi and Tonissi 1946), viability, longevity, fecundity, duration of developmental stages, number of larval instars, sex-determining factors. Mutations are known with tumorlike growths in various organs in larvae and in adults.

The only conceivable way in which a gene can influence the development of an organism is through physiological, and ultimately biochemical, processes. Mutations which alter the course of such processes must occur. This *a priori* expectation has been brilliantly confirmed particularly by the work of Beadle and his school on the fungus *Neurospora* and more recently on bacteria (reviews in Beadle 1947, 1949, Horowitz 1950, Lederberg 1949). Wild-type strains of these microorganisms can grow on certain "minimal" media. Mutant strains often require more "complete" media, which differ from the minimal by addition of certain vitamins, amino acids, or other substances. Analysis of the mutants usually permits identification of the particular metabolic reaction which is mediated by the normal alleles of the mutated genes.

One thing no single mutation has done is to produce a new species, genus, or family. This is because species and supraspecific categories differ always in many genes, and hence arise by summation of many mutational steps. A four-winged mutant of *Drosophila melanogaster* still belongs to that species, although the presence of one pair of wings and a pair of balancers is a character which distinguishes the order of flies (Diptera) from most other insect orders (see Heitz 1944 and Stubbe and Wettstein 1941). This fact has in the past given rise to the contention that mutations affect only "superficial" but not "fundamental" traits. This contention is meaningless because the words "superficial" and "fundamental" are not defined. Mutations exist that produce radical changes in embryonic processes, such as cleavage, gastrulation, and organ formation (Poulson 1940, 1945, Gloor 1945, Hadorn 1945, 1948).

EXTENT OF CHANGES PRODUCED BY MUTATION

De Vries thought that mutations produce sharply discontinuous changes. It is known at present that mutations form a spectrum, ranging from drastic changes lethal in early development stages to changes so minute that their detection presents serious technical problems. The relative frequencies of large, medium, and small mutations are of much interest to evolutionists. Unfortunately, to determine the relative frequencies of different types of mutations is not easy. The greater the phenotypical change, the easier the detection of a mutation. Since striking mutations are more valuable as chromosome markers than the weak ones, the former are picked out and studied. The published descriptions of mutations give a grossly distorted picture of the characteristics of the mutation process.

Timofeeff-Ressovsky (1934c, 1935b), and Kerkis (1938) have done pioneering work to clarify the situation. They treated with X rays wild-type males of *Drosophila melanogaster* from a thoroughly inbred strain, and crossed them to ClB females which previously had been repeatedly outcrossed to the same inbred strain. (The ClB females have in one of their X chromosomes a lethal gene, a marker producing a visible effect [Bar], and an inversion which suppresses most of the crossing over between the ClB chromosome and the other X chromosome present in the same female). In the F_1 generation, females heterozygous for the ClB chromosome were selected

and outcrossed to untreated wild-type males. Their sons receiving the ClB chromosome die of the lethal contained in it; the sons receiving the other X chromosome survive, provided no lethal mutation has been induced in this chromosome by the treatment. The expected sex ratio is, therefore, 2 females : 1 male. If a lethal mutation is induced in the treated chromosome, the offspring are females only.

If a mutation which is not lethal but which decreases the viability arises in the X chromosome, the resulting sex ratio falls between 2 ♀ : 1 ♂ and 2 ♀ : 0 ♂, depending upon the degree of the deleterious effect produced by the mutation. For technical reasons it was preferable to take into account only the daughters which do *not* carry the X chromosome (ClB); they form about half of all females, and can be recognized by the absence of the marking gene (Bar). The frequencies of such females and males turned out to be 1 ♀ : 0.95 ♂ if no mutation has been induced in the treated chromosome, and 1 ♀ : 0 ♂ if a lethal mutation has been induced. The results of the experiment can be seen in Table 1, showing the sex ratio produced by individual females. The control series shows the ratios obtained in the progeny of males which have not been treated with X rays.

TABLE 1

THE ♀ : ♂ RATIOS OBTAINED BY TIMOFEEFF-RESSOVSKY IN HIS EXPERIMENTS ON MUTATIONS AFFECTING VIABILITY

SEX RATIO	1 : 1.15	1 : 1.05	1 : .95	1 : .85	1 : .75	1 : .65	1 : .55	1 : .45	1 : .35	1 : .25	1 : .15	1 : .05	1 : 0
Control (in %)	2.1	14.1	77.1	5.5	.7	—	—	.5	—	—	—	—	—
Treated (in %)	.7	10.1	44.9	8.8	7.2	5.3	4.2	1.8	1.1	.7	1.4	.9	13.6

In the treated series, 13 percent (56 out of 432) of the cultures produced no males, indicating that mutations having lethal effects appeared. In 3 percent of the cultures, semilethal mutations were observed (sex ratios between 1 : 0.30 and 1 : 0). A large number of cultures gave sex ratios which can be accounted for only on the supposition that mutations which produce slight decreases of the viability have arisen. The exact number of such cultures in the treated series is not easy to determine, since the ratios observed in them

overlap those in the cultures of the control, but they make up no less than 20 percent of the total.

MANIFOLD EFFECTS

Mutant genes are named according to their most prominent characteristics. In *Drosophila*, mutations of the gene "white" turn the eye color from red to white, "vestigial" makes vestigial wings, "stubbloid" causes a shortening of the bristles, and so on. This system of naming is convenient, but the names are not to be taken as complete accounts of the differences between the mutants and the ancestral form, much less as indicative of the total range of the effects of the particular gene on the development. Many mutants, in *Drosophila* as well as in other forms, differ from the ancestral types in complexes of characters. The mutation white changes the eye color, that of the testicular membrane, the shape of the spermatheca, length of life, and general viability. Vestigial reduces wing size, modifies the balancers, makes certain bristles erect instead of horizontal, changes wing muscles, shape of the spermatheca, speed of growth, fecundity, and length of life. Under favorable external conditions vestigial relatively decreases the number of ovarioles in the ovaries while it has the opposite effect under unfavorable conditions. Stubbloid modifies the bristles, wings, legs, antennae, and viability (Dobzhansky 1927, 1930a).

Genes that produce changes in more than one character are said to be pleiotropic or to have manifold effects. The frequency of such genes is not well known. A majority of mutations produce striking changes in a single character, and their manifold effects, if any, involve changes which appear trivial. Thus, the main characteristic of the mutant vestigial in *Drosophila* is a decrease of the wing size. But to conclude that vestigial is a "wing gene" rather than a "bristle gene" would be as naive as to suppose that a change in the hydrogen ion concentration is a "color gene" because it produces a striking change in the color of certain indicators. The mutant as well as the ancestral form possess alleles of the gene producing the mutation. The phenotype of the ancestral form is, then, determined by the gene *A* in cooperation with all other genes composing the genotype, while the phenotype of the mutant is due to the cooperation of the gene *a* with the same residual genotype. Therefore, the differences

between the ancestral form and the mutant are indicative of the effects of the thange $A \rightarrow a$, but not of the sum total of the effects of either A or a.

Interesting data bearing on the problem of total gene effects are obtained through studies on physical losses, or deficiencies, of genes. It is a general experience that in nonpolyploid organisms homozygous deficiencies are inviable. The work of Poulson (1940, 1945) shows that deficiencies for sections of the X chromosome of *Drosophila melanogaster* cause great disturbances in the fundamental processes of embryonic development. Moreover, most deficiencies in *Drosophila* act as cell lethals; that is, the absence of genes is fatal not only to the whole organism but also to a patch of deficient tissue surrounded by tissues in which all genes are present (Demerec 1936, 1939). Exceptions are however known, rarely in *Drosophila* but more frequently in maize (Muller 1935, Stadler 1933, McClintock 1938, 1941, 1944). It is even regarded as probable that in maize a majority of recessive mutants induced by X rays are deficiencies too small to be detected by cytological methods. This suggests either that some genes are less important in the development than others, or that some genes are normally present at more than one locus in the chromosomes.

Some attempts have been made to determine the frequency of manifold effects by examining a random sample of mutant genes for changes in an arbitrarily selected organ. Dobzhansky (1927) studied the shape of the spermatheca in twelve mutants of *Drosophila melanogaster* known to affect such characters as eye and body color and wing shape, but not suspected of differing from each other in the internal anatomy in general or in the spermatheca shape in particular. Nevertheless, ten out of the twelve showed differences in the shape of the spermatheca. It remained uncertain whether the differences in the spermatheca shape are due to modifying genes which lie in the chromosome in the vicinity of the mutant genes responsible for the externally visible changes or to the latter genes themselves (Schwab 1940). Dobzhansky and Holz (1943) obtained several mutations of the genes white and yellow in an inbred strain of *Drosophila melanogaster*, and showed that the mutants differed from the parent strain in the spermatheca shape as well as in the eye and body coloration. Since it is highly improbable that mutations of

genes modifying the spermatheca arose by chance every time when the genes white and yellow mutated, the variation in the spermatheca shape must be ascribed to manifold effects of the loci white and yellow.

Differences between races and species frequently involve traits which appear to have no survival value. These seemingly neutral characters may, however, represent only a part of the total effects of a gene, and physiological traits correlated with the neutral character may be adaptively important. The early theorists on heredity, particularly Weismann, considered the germ plasm to be a mosaic of corpuscles, each representing an anatomically defined body part or function. This preformistic notion has become, perhaps by indirection, attached to the genes as well, and continues to influence the thinking of many geneticists. It is easily refuted if one recalls that genes act in development through production of enzymes. Disappearance or change of an enzyme may alter many traits. A mutation in the rat causes thickened ribs, narrowed lumen of the trachea, emphysema of lungs, hypertrophy of the heart, blocked nostrils, blunt snout, and a sharp lowering of the viability. Grüneberg (1938) believes that the whole syndrome is reducible to a single primary change, namely to an anomaly of the cartilage. Complex syndromes of this sort have been described in mammals and in birds by Dunn (1941), Dunn and Schoenheimer (1947), Landauer (1942, 1945, 1946), Grüneberg (1943), Hadorn (1945), and others. A single primary change on which all other changes would depend is discernible in some of these syndromes but not in others. It is, for example, not at all clear why a single gene change should alter the eye color, shape of the spermatheca, viability, and fecundity in *Drosophila*, as is actually observed. Nor is it easy to see why a single gene should affect the growth habit, branching, shape and size of leaves, and morphology of the flowers, fruits, and seeds of a plant, as is actually observed in *Coffea arabica* (Krug and Carvalho 1945). Nevertheless, Grüneberg (1943) believes in "unity of gene action," and regards all known manifold effects as "spurious pleiotropism". "Genuine pleiotropism" would, according to this view, require a gene to have several primary actions, which is, however, denied. This view is related to the "one gene–one enzyme" theory which has been discussed above (page 13).

POSITION EFFECTS

The classical conception of the germ plasm was that of the sum total of absolutely discrete genes. The genes are independent of each other because they undergo mutational changes and separate from each other by crossing over and by chromosome breakage without affecting the neighboring genes. A chromosome is, then, an aggregate of genes arranged in a constant but fortuitous linear order. This atomistic view had to be modified, because the effects of a gene on the development proved to depend not only on the structure of the gene itself but on its position among the neighboring genes as well. The already voluminous literature on position effects has been reviewed by Dobzhansky (1936b) and by Lewis (1950). The position effect phenomena are obviously important for the general theory of the gene. Only a summary can be given here.

Translocations and inversions in *Drosophila* often produce effects not expected on the basis of the classical gene theory. Since these structural changes alter only the gene order, individuals which carry them must have the same genes as the ancestral type. Alterations of linkage relationships, but not phenotypic effects, are expected in translocation and inversion hetero- and homozygotes. Nevertheless, some translocations and inversions are lethal when homozygous, and some produce visible changes in the morphology of the flies. Lewis (1950) proposes to distinguish position effects of V (variegated) and S (stable) types. The former arise usually when genes which normally lie in the chromosome far from the heterochromatic segments (which in *Drosophila* are concentrated mainly near the centromeres) are transposed to the vicinity of the heterochromatin, or vice versa. The transposed genes may then behave in the somatic, but not in the sex cells, as though they were highly mutable. For example, the mutant gene for white eyes is recessive to the normal allele which gives red eyes. A number of translocations and inversions are, however, known, in which the normal allele is placed in or near the heterochromatic sections of chromosomes. Females which carry the recessive white in a normal chromosome and the normal allele in a rearranged chromosome should have red eyes (because of the dominance). Actually, many of them have "mosaic" eyes, which consist of alternating patches of red, white, or intermediate colored facets.

Another kind of position effect, which Lewis considers related to the V-type, is loss of dominance of genes the position of which with respect to the heterochromatin had been changed. Here belongs the case of Dubinin and Sidorov (1935). These authors observed that the wild-type allele of the gene hairy in *Drosophila melanogaster* loses most of its dominance over the recessive mutant allele when the wild-type allele becomes involved in some translocations. The ostensibly "changed" wild-type allele may be removed, by crossing over, from the translocation chromosome, and replaced by a fresh wild-type allele. Dubinin and Sidorov found that this freshly introduced allele loses its dominance. The changed action of the wild-type allele involved in translocation is, therefore, due to a change in its position in the chromosome, and not to any alteration of its intrinsic properties.

The position effects in the Bar region of the X chromosome of *Drosophila melanogaster*, discovered by Sturtevant (1925) and analyzed further by Bridges (1936), Muller, Prokofieva, and Kossikov (1936), Rapoport (1940) and others, are examples of the S-type. Here a reduplication of the short section of the chromosome has so changed the developmental effects of some of the genes that clear-cut phenotypic effects on the shape of the eyes and on other traits are produced. Lethality of some translocations and inversions in homozygous condition is in all probability also due to the S-type of position effects.

How universal position effects are is an open question. It should be noted that even in *Drosophila* many structural changes seem to be free of such effects. Catcheside (1939, 1947) has observed them in *Oenothera blandina*. They were supposed to be rare or absent in maize, although Roberts (1942) has described one not entirely conclusive case. McClintock (1950) has however published a preliminary account of extensive experiments in which many instances of V-type effects have been observed, apparently associated with shifts in the position of certain heterochromatic sections of the chromosomes.

Regardless of whether position effects will eventually be shown widespread or rare, a chromosome must be considered a system of interdependent genes. Goldschmidt considers that this interdependence "points to a theory of the germ plasm in which the individual

genes as separate units will no longer exist." This view has produced much controversy, but the issue is chiefly one of phraseology.

The existence of genes is inferred from the facts of Mendelian segregation and recombination. A gene is a unit of Mendelian heredity. But segregation and recombination are not sufficient to divide the germ plasm into ultimate units. Deficiencies and duplications may be inherited in a manner simulating single genes. The phenomenon of crossing over furnishes a more sensitive test, since it permits division of the chromosome into finer blocks. But crossing over between some genes is rare or absent. The gene as a unit of mutability permits still finer analysis. Finally chromosome breakage, occurring spontaneously or under the influence of X rays, furnishes clear evidence that discrete blocks of chromosome material are physically separable without loss of the ability to reproduce themselves, although not necessarily without change in function. As Darlington (1939) put it, "the gene is a unit of heredity because it is mechanically separable from other genes in heredity, that is, in cell division." Whether or not this criterion has an unconditional validity is as yet uncertain, and it may well be doubted.

Nevertheless, it is an undeniable fact that, as a rule, all of the above criteria—however imperfect each of them taken separately may be in scattered cases—concur in delimiting the same blocks of chromosomal materials as discrete units, which are described as genes. Genes may be separate molecules or molecular aggregates loosely held together by some relatively inert substance; or they may be links of an enormously long chain molecule; or they may be molecular nuclei connected with their neighbors by chemical bonds. No matter which of these possibilities, if any, will prove to be true, the existence of genes is as well established as that of molecules and atoms in chemistry. It is also virtually certain that genes are bodies of the order of magnitude of large molecules, and hence one must beware of thinking about them and their possible connections in terms of macroscopic mechanical analogies.

INDUCTION OF MUTATIONS BY RADIATION

It is customary to distinguish spontaneous and induced mutations. The former arise in strains not consciously exposed to mutation-producing agents. Since the name "spontaneous" constitutes

an admission of ignorance of the phenomenon to which it is applied, the quest for the causes of mutation has always occupied the attention of geneticists.

A general knowledge of the mutation process permits certain inferences regarding its causes. Mutations arise at all stages of the development cycle: at gametogenesis, in mature gametes, and in somatic tissues. Mutants are on the whole rare; they appear as single individuals among masses of unchanged representatives of a strain. Whenever a mutation takes place in a diploid cell, only one chromosome of a pair is affected. Since a diploid cell has two genes of each kind, the causes of mutation must be so highly localized that only one of the two similar units falls within the field of their action.

For years the attempts to induce mutations remained inconclusive. The announcement by Muller in 1928 that X-ray treatments induce both gene mutations and chromosomal changes constitutes a turning point in the history of the mutation theory. An imposing amount of literature has accumulated since 1928 dealing with the effects of X rays and other radiations on the mutation process. Excellent reviews have been published by Timofeeff-Ressovsky (1937), Muller (1940b, 1941, 1950b), Lea (1947), Catcheside (1948), Fano et al. (1950), and others. It will suffice to give here a condensed summary of only the most important findings and conclusions.

X rays and ultraviolet radiation induce mutations in organisms ranging from plant viruses and bacteria to higher plants, and from protozoans to mammals. Mutations are induced only in chromosomes directly exposed to radiation; no effect is obtained in gametes developing in an irradiated body if the gonads are protected from the rays, nor are chromosomes influenced by irradiated cytoplasm. If no mutations arise in a zygote coming from an irradiated gamete, none appear in subsequent generations. All ionizing radiations are mutagenic, from very soft X rays to hard X rays and gamma rays. There is no doubt that cosmic rays are also mutagenic, although studies on their effects have not progressed very far. The frequency of mutations produced by X rays is proportional to the amount of treatment expressed in r-units, and is independent of the wave length employed, as well as of whether such treatment is given in a single exposure or is fractionated in several exposures. In contrast to this, ultraviolet rays of different wave lengths are unequally mutagenic,

the number of mutations induced being a function of the absorption of the rays in nucleic acids which are constituents of the chromosomes (Stadler and Uber 1942).

In maize, mutations induced by X rays are different from the spontaneous ones, the former being chiefly minute deficiencies due to destruction of genes. Ultraviolet-induced mutations appear to be more like those arising spontaneously (Stadler 1941). In *Drosophila*, X-ray-induced mutations were believed to be similar to the spontaneous mutants, in the sense that the kinds of mutants which are most frequent among the spontaneous ones are also most frequent among the radiation-induced ones. The result of Lefevre (1950) and other investigators indicate however that the effects of X rays on *Drosophila* genes are mostly destructive, just as they are in maize. Because of this, and also because Muller and Timofeeff-Ressovsky have independently demonstrated that the ionizing radiations present in natural habitats cannot be responsible for more than a small fraction of spontaneous mutations, the radiation-induced mutations are of limited direct interest in evolutionary studies. They remain, however, important as a tool for investigation of the gene structure.

The mechanisms of production of structural changes in the chromosomes (translocations, inversions, deficiencies, and duplications) are more complex, and even less well understood than those involved in gene mutation. In *Drosophila*, spontaneous structural changes are rare. Among at least 100,000 larvae of *Drosophila pseudoobscura* the chromosomes of which were examined by the present writer, only two newly arisen structural changes were observed. Giles (1940) and Nichols (1941) found chromosome breakages more frequent in *Tradescantia* and *Allium* than they are in *Drosophila*, and computed that the amount of natural radiation in the environment is approximately 1,800 times too small to account for the observed frequency. Under the influence of X rays, the frequency of recovered structural changes grows in proportion to one-and-one-half power of the dose expressed in r-units, instead of the first power as in the case of gene mutations. Furthermore, the yield of structural changes is greater if the treatment is concentrated than if it is prolonged or fractionated over hours or days.

One of the current interpretations of these relationships is that

two separate processes are involved in the production of structural changes. (1) Chromosomes are broken by the radiation. The frequency of breaks, like that of induced mutations, is proportional to the first power of the dose. (2) The broken ends of the chromosomes retain, for a certain length of time following breakage, the ability to rejoin with other broken ends either in original or in new combinations. If no reunion of broken ends takes place, the chromosomes are usually inviable, and the cells in which breakages have occurred die off (dominant lethals). This explains the relative rarity of terminal deficiencies, i.e., of chromosomes which have lost their free ends. Another condition which must be fulfilled to make the rearranged chromosomes functional is that each chromosome formed through reunion of fragments possess one and only one centromere. The position of the centromere in a chromosome is as fixed as that of any gene, and chromosome fragments without a centromere (acentric) are lost, while those with two centromeres (dicentric) are torn during cell division (see, however, Hughes-Schrader and Ris 1941).

If only a single chromosome breakage takes place in a cell, the resulting fragments may either rejoin in the original position, in which case no rearrangement can be detected, or else the broken ends remain separate, which normally results in death of the cell. Detectable structural changes in chromosomes are formed only in cells in which at least two breaks occur at the same time, for the fragments in such cells have the opportunity to reunite in new positions. The probability of two chromosome breaks appearing in the same cell is, however, the square of the probability of a single break. This explains the rarity of spontaneous origin of new stable rearrangements, as well as the rapid increase of their frequency at higher dosages of X-ray treatments. Since the broken chromosome ends retain the ability to unite with other broken ends for a short time only, concentrated X-ray treatments are more effective than fractionated ones (in *Tradescantia*).

MUTATION AND TEMPERATURE

Only a small fraction of the spontaneous mutability can be attributed to the short-wave radiations present in nature. The ultraviolet

is even less important in most organisms, because of its low penetrating power in living tissues. Mutagenic agents other than radiation must be sought. Muller (1928b) has demonstrated that the frequency of spontaneous mutation in *Drosophila melanogaster* increases with temperature. In the same organism Timofeeff-Ressovsky (1935c) found the following percentages of sex-linked lethals:

TEMPERATURE (°C)	CHROMOSOMES EXAMINED	LETHALS FOUND	PERCENT LETHALS
14°	6871	6	0.087 ± 0.035
22°	3708	7	0.188 ± 0.071
28°	6158	20	0.325 ± 0.072

Notwithstanding the high experimental errors, it seems certain that the mutation rate is doubled or trebled with a 10°C. rise in temperature. Timofeeff-Ressovsky points out, however, that the development of the fly is more rapid at high than at low temperatures: he also finds that mutation is proportional to time, since the frequency of sex-linked lethals in the spermatozoa of old males is higher than that in the sperm of young males. Taking this into consideration, he estimates that the temperature coefficient of the mutation process (i.e., the ratio of increase per 10°C.) is in the neighborhood of 5. However, according to Olenov (1941) and Muller (1946), the situation is complicated by lack of a strict proportionality between mutation and time. More data bearing on this important problem are obviously needed.

The experiments of Muller and Timofeeff-Ressovsky were conducted at temperatures within the normal viability range for *Drosophila melanogaster.* Several investigators have claimed that temperature shocks—that is, brief exposures of larvae to sublethal high temperatures between 36°C. and 40°C.—result in spurts of the mutability far greater than could be expected from the knowledge of normal temperature coefficients. Similar claims have been made for "cold shocks," or brief exposures to low temperatures (see Plough 1941, and Novitski 1949, for further references). Here again more data are needed, since the results of different investigators are not in agreement. At any rate, the early claims of very high mutability following heat and cold shocks have not been substantiated.

CHEMICAL MUTAGENS

Attempts to induce mutations by chemical means were being made even before the discovery of X-ray mutations, and in fact before the rediscovery of Mendel's laws. These early trials have only historical interest, since modern methods of detection and quantitative estimation of mutation were yet unknown. Such techniques were evolved for *Drosophila melanogaster* by Muller (1928b) in connection with his classical experiments on X rays and temperature (see above, the "ClB" method). Using these techniques, Sacharov (1935, 1936), Samjatina and Popova (1934), and Kondakova (1935) obtained suggestive results indicating increases of mutation rates with iodine and potassium iodide solutions, as did Magrzhikovskaja (1938) and Law (1938) with copper sulphate, Lobashov (1934) with ammonia, Naumenko (1936) with potassium permanganate, Kosiupa (1936) with sublimate, Ponomarev (1937-38) with lead salts, and Lobashov (1935) with asphyxia.

It remained however for Auerbach, Robson, and their collaborators (see Auerbach 1949 for bibliography) to discover the first powerful chemical mutagen, namely mustard gas $(Cl \cdot CH_2 \cdot CH_2)_2 S$. Under most favorable conditions, about as high a proportion (up to 25 percent) of the treated X chromosomes of *Drosophila melanogaster* acquire sex-linked lethals as is observed after treatments with the highest doses of X rays which the insect can stand without being completely sterilized. Related compounds, the nitrogen and sulphur mustards, mustard oil, and chloracetone also proved mutagenic, although not to the same degree as mustard gas. Auerbach's results were soon confirmed by several investigators, and extended to such fungi as *Neurospora*, *Penicillium*, *Coprinus*, *Ophiostoma*, and *Aspergillus*, to bacteria, and to barley. Darlington and Koller (1947) and other showed that mustard compounds like X rays, produce not only apparent gene mutations but chromosomal aberrations as well.

A major difficulty in experiments on chemical mutagens is to insure that the chemical in question penetrates into the cells and reaches the chromosomes in which mutations are to be induced. The initial success of Auerbach and Robson may have been due to their use of a gaseous substance. When liquids or solutions are to be used, the treatment is usually administered by addition of the desired sub-

stances to the food, or by immersion of the organism or its parts into aqueous or alcoholic solutions, or by injection into the body cavity. Demerec and his collaborators (1949 and earlier) use very fine mists (aerosols) of solutions of desired substances in water or oil. Hadorn and Niggli (1946) apply the most ingenious method of treating an excised larval gonad of *Drosophila* in vitro with solutions of chemicals, and then implanting the treated gonads into other larvae which are permitted to develop to the adult stage. Microorganisms are most suitable for experiments on chemical mutagenesis, since with them the difficulties of penetration are minimized.

Rapoport (1946), Kaplan (1948), Herskowitz (1950), and Vogt (1950) obtained sharp increases of the mutation frequency in *Drosophila melanogaster* the larvae of which grew on nutrient media with sublethal doses of formalin or urethane. Herskowitz found, in addition, that the mutation rate is increased in treated males but not in treated females. Formalin has no mutagenic effects when applied as a vaginal douche. It is possible that formalin itself is not mutagenic, but that it reacts with some substances in the food to produce a mutagenic derivative. Such indirect mutagenic effects have been demonstrated by Stone et al. (1947) and by Haas et al. (1950), who obtained increased mutation rates in *Staphylococcus aureus* by culturing the bacteria on nutrient media irradiated with ultraviolet rays. Dickey et al. (1949) and Wagner et al. (1950) showed that the effective mutagens are in all probability organic peroxides formed in the medium under the influence of the ultraviolet. Dickey et al. (1949) induced mutations in *Neurospora* with several peroxides. An indirect mutagenic effect may also be involved in the experiments of Hadorn and Niggli (1946) and Hadorn, Rosin, and Bertani (1949). These authors treated ovaries of *Drosophila melanogaster* in vitro with phenol solutions. The results were variable: in some experiments striking increases of mutation rates in the second chromosome were obtained, while other experiments were negative. Similarly erratic results were obtained by Demerec (1949) in *Drosophila* treated with aerosols containing certain carcinogenic substances. Strong (1949 and previous work) has claimed that he obtained increased mutation rates in mice treated with the carcinogene methylcholanthrene.

Using bacteria and *Neurospora*, Demerec et al. (1949), Witkin

(1947), and Kölmark and Westergaard (1949) have explored the mutagenicity of a number of substances. In *Escherichia coli* the frequency of mutation to resistance to bacteriophage invasion (see Chapter IV) has been increased by sodium desoxycholate, pyronin, and acriflavine. The mutability from streptomycin dependence to independence (see Chapter IV) was stimulated by formaldehyde, phenols, urethane, and especially by ferrous and manganous compounds. In *Neurospora crassa* diazomethane has been found effective. Chromosome fragmentation has been induced by mustard compounds (see above), and also by pyrogallol and other phenol compounds (Levan and Tjio 1948, and other publications). Although the work on chemical mutagens is still in its infancy, findings in this field are clearly important for understanding of the mutation process.

THE QUEST FOR DIRECTED MUTATION

X rays, ultraviolet rays, and the chemical mutagens mentioned above seem to be unspecific, in the sense that they increase the frequency of change (or destruction) of apparently all the genes of the organism. There is no way to predict just what genes will be found changed in the offspring of an irradiated *Drosophila* fly, although one can say that each gene has a certain probability of suffering mutation. A better understanding of the mutation process should enable us to alter at will definite genes in definite ways. Thus far, such directed, or specific, mutations proved elusive. Some hopeful avenues of approach are nevertheless being explored.

Sonneborn and his school (see Sonneborn 1950, 1951, and Sonneborn and Beale 1949, for further references) have discovered a most remarkable situation in one of the species lumped under the name of *Paramecium aurelia* (see Chapter IX). When infusorians of certain strains of this species are injected into rabbits, antibodies are formed in the rabbit serum, which immobilize or paralyze other Infusoria of the same strain, but not necessarily of other strains. By means of this immobilization test, infusorial strains can be classified into several "serotypes," denoted A, B, C, D, H, etc. Under standard culture conditions (26°C.-27°C. and enough food to permit one fission per day), the serotype is a hereditary trait: with rare exceptions, it is transmitted to the offspring. Nevertheless, serotype changes can be induced by several environmental agencies. A potent agency is

the antibody which immobilizes the serotype in question. With the exposures employed the immobilized Infusoria recover, but their offspring belong mostly to a different serotype. Thus, antibodies to the serotype D transform about 95 percent of the latter into the serotype B at 32°C., but at 20°C. the serotype H is chiefly obtained. The transformation is reversible, and each stock of Infusoria is potentially capable of producing a certain collection of serotypes. Different stocks differ, however, in the serotype potentialities. Crossing representatives of the serotypes reveals that the serotype differences within a stock are inherited through the cytoplasm, and that their nuclear genes are alike. However, the potentiality of being able to produce a certain variety of serotypes is determined by the genes, and is inherited in a normal Mendelian manner.

The simplest interpretation of these findings is that the cytoplasm of every stock contains discrete bodies of several kinds, plasmagenes, which reproduce themselves, provided that the nuclear genotype is favorable for their perpetuation. The different kinds of plasmagenes are in competition with each other for sources of energy or for materials from which they are built. At any one time, one kind of plasmagene is a majority, and it determines the serotype. But others continue to be present, and under proper conditions may multiply and reach a dominant status. The treatment with antibodies creates such a condition, by interference with the reproduction of the plasmagenes which were dominant before the treatment. The nature of the plasmagenes is not completely clear. Their presence is controlled by the nuclear genes, and they may be produced by the latter, either directly or by imprinting a certain specificity on some common plasmagene precursor.

The transformations of the serotypes suggest directed mutations, since all, or nearly all, individuals of a treated strain transform in a predictable way. On the other hand, this "mutation" does not seem to involve qualitative changes in genes or plasmagenes, but only alterations in the relative frequencies of preexisting kinds in a population of plasmagenes. This may also be the situation in the transformation discovered already some two decades ago in the pneumonia microorganisms, *Diplococcus pneumoniae*, and studies by Griffith, Avery, Dawson, Heidelberger, McCarty, and others (see Avery et

al. 1944, McCarty 1946, and McCarty et al. 1946 for further references).

Several dozen "types" of pneumococci can be distinguished through serological tests. The type differences reside in the "envelope" on the cell surface. The envelope consists chiefly of polysaccharides which are type specific. Each type preserves its identity when it reproduces in infected hosts or on culture media which give optimal growth. If, however, the bacteria are cultivated in the presence of homologous immune sera, or on media otherwise unfavorable for their growth, their virulence is lost, and the shape of the colonies growing on agar plates is changed from the normal "smooth" to a degenerate "rough". The polysaccharide envelope present in the smooth is lost in the rough state, and with it the type specificity also disappears. A reversal from rough to smooth can be accomplished by a passage through a susceptible host, or by other means.

The changes from smooth to rough, and vice versa, are due to the occurrence in all pneumococci of spontaneous mutations to both these conditions with small but finite frequencies. The smooth phase is able to invade susceptible hosts, while the rough one is superior to the smooth on artificial nutrient media. One or the other genotype is selected by the environment in which the strain is placed. Such transformations, involving differential survival of spontaneous mutants are well known in many microorganisms (Chapter IV). More unusual phenomena are enacted if a culture of the rough phase is added to a vaccine consisting of dead cells of the smooth phase. For in this case rough reverts to smooth not of the serological type from which the rough itself had descended, but of the type of the cells of the vaccine. For example, if a small amount of the rough culture derived from a smooth line of Type II is added to a suspension of smooth cells of Type III devitalized by heating, a smooth line of Type III, not of Type II, is produced. By this method it is possible to convert many or all of the known types of the pneumococci into other types. The transformation of the rough into the smooth of the same type from which the rough had been originally derived is, of course, also accomplished by the same method, if a vaccine of that type is used.

The strains "transformed" from one type into another retain their

new properties after cultivation on suitable media or after passage through animal hosts. Hence, they acquire not merely a temporary polysaccharide envelope of a kind different from that which their ancestors have had, but also the ability to synthesize the new polysaccharide indefinitely. Avery et al. (1944) have isolated the "transforming principle" contained in the Type III vaccine, which causes the change from Type II rough to Type III smooth. By means of a series of fractionations, they obtained from the vaccine a highly viscous colorless substance which proved to be a highly polymerized desoxyribonucleic acid with little or no impurities. Desoxyribonucleic acid is, of course, one of the principal constituents of chromosomes. The transforming power of this substance is so great that it is capable of causing transformation in a dilution of 1: 600,000,000.

Whether or not the transformations of pneumococci are comparable to the changes in serotype in *Paramecium* is an open question. It is possible that a pneumococcus cell contains a population of as many kinds of plasmagenes as there are potential types, and that one or the other of them may be stimulated to reproduce by the transforming principle. On the other hand, a qualitative change in some self-reproducing bodies may be involved, specifically directed by the kind of nucleic acids with which these bodies come in contact. That chemically relatively simple substances may act as "transforming principles" has been demonstrated in several cases. Pravosoli et al. (1948) exposed the flagellate *Euglena gracilis* with green chloroplasts to streptomycin solutions, and obtained strains which have permanently lost the chlorophyll, but which are able to grow and reproduce as saprophytes in proper nutrient solutions. Skovsted (1948), and especially Ephrussi and collaborators (Ephrussi et al. 1949, Ephrussi 1951) have induced transformations in yeasts by camphor and by acriflavine respectively. Ephrussi's case has been analyzed in considerable detail; the changes are clearly not due to alteration of nuclear genes but to either quantitative or qualitative changes in plasmagenes.

It remains to mention the attempts of Emerson (1944) to induce mutations in *Neurospora* by exposing this fungus to the culture media which contained immune sera of rabbits which were previously injected with mycelial extracts or culture filtrates of the fungus. Emerson reasons that since antigens are likely to be more or less immediate

products of the gene activity, the molecular surface configurations of genes and antigens may be rather similar (see also Emerson 1945). An antibody formed in response to immunization by an antigen may, then, combine with the gene as well as with the antigen. This may interfere with the reproduction of the gene and cause it to mutate. Emerson claims to have obtained 25 mutants among 695 treated *Neurospora* isolates, and no mutants among 276 untreated ones. Repetition of these experiments is greatly to be desired.

III : Mutation in Populations

PREMISES

As pointed out by Darwin, any attempt to understand the mechanisms of evolution must start with investigation of the sources of hereditary variation. He was able to satisfy himself that hereditary variations are always present, in wild as well as in domesticated species, somewhat less abundantly in the former, more abundantly, on the average, in the latter. But the mode of their origin remained obscure to Darwin, and he was not afraid to confess his ignorance on this point. A solution, though a partial one only, has been arrived at in the present century. Gene mutations and chromosome changes are the sources of variation. Studies of these phenomena have been of necessity confined to the laboratory and to organisms that are satisfactory as laboratory materials. Nevertheless, there can be no reasonable doubt that the same agencies have supplied the materials for the actual historical process of evolution.

There is no contradiction between the foregoing statements and the acknowledgment of our ignorance of the exact nature of mutational changes. In a sense we are in the same position in which Darwin was: the intimate nature of the hereditary variation is unknown. But in another respect we are in a much better position than Darwin, since some of the attributes of the mutation process are no longer a mystery.

The origin of hereditary variations is, however, only a part of the mechanism of evolution. If we possessed a complete knowledge of causes which produce mutations there would still remain much to be learned about evolution. These variations may be compared to building materials, but an unlimited supply of materials does not in itself give assurance that a building is going to be constructed. The origin of variation is a physiological, and in the last analysis physico-chemical, problem. When the hereditary variation is produced and injected into a Mendelian population, it enters, however,

into the field of action of factors which are on a different level from those producing the mutations. These factors—natural and artificial selection, the manner of breeding characteristic for the particular organism, its relation to the secular environment and to other organisms coexisting in the same medium, obey rules *sui generis*, rules of the physiology of populations, not those of the physiology of individuals. The former are determined by the latter only in the same sense in which the structure of a human state may be said to depend upon the physiology of its members.

A misconception caused by the failure to grasp the significance of this distinction is the allegation that genetics denies the importance of environment in evolution. Genetics does assert that the organism is not endowed with providential ability to respond to the requirements of the environment by producing mutations adapted to these requirements. The mutations produced are, however, determined by the structure of the organism itself, which is of course the result of an historical evolutionary process in which the environment has played a part. The historical process itself, the molding of the hereditary variation into racial, specific, generic, and other complexes, is conditioned by the environment through natural selection.

Although population dynamics is an essential part of any evolution theory, it was until recently rather neglected. A number of investigators, among whom Sewall Wright should be mentioned most prominently, have, however, analyzed the evolutionary processes in populations by deducing their regularities mathematically from the known properties of the Mendelian mechanism of inheritance. The importance of this work can hardly be overestimated. It has stated clearly the essential problems of population dynamics, and in so doing has provided a guiding light for experimental approach to these problems.

The fundamental difference between the conception of heredity upon which Darwin had to rely and the one which is at the basis of modern views is the antithesis between the particulate and the blending theories of inheritance (Tschetwerikoff 1926, Fisher 1930). It is known that the hereditary materials consist of self-reproducing particles, genes. The crossing of *Drosophila* flies with white and with normal red eyes gives in the F_2 generation flies with white and red eyes of the same shade as in their ancestors. The difference between

the genes for white and for red eye color is not reduced by hybridization; nó pink or cream-colored eyes, for example, are produced. Even where the heterozygote is intermediate between the parents, no contamination of the genes takes place. Position effects have shown that genes are not quite as discrete and separate from each other as was formerly supposed, but this does not mean that the differences between genes are swamped by hybridization. The notion of blending inheritance, which was held universally in Darwin's time, assumed that the hereditary materials of the parents undergo amalgamation in the hybrid. The difference between the ancestral hereditary materials was supposed to be either lost entirely or at least impaired by passage through the hybrid organism.

The corollaries of the two theories are strikingly different. If two heredities can combine as a dye commingles with water, then the variance present in a Mendelian population must be halved in every generation. Given a population which exhibits a large variability at the start, there must be progressive, rapid, and irretrievable decay of the variability, until homogeneity is reached. The only escape from this conclusion is to suppose that the variability arises *de novo*, at a rate at least equal to the rate of its loss due to crossing. In modern language this would mean that new mutations must occur with a prodigious frequency, far in excess of what is observed.

No such difficulty is encountered if the hereditary materials are particulate, for in this case the variability is maintained despite the interbreeding. Low mutation rates will suffice to furnish the materials for evolution. This deduction is applicable both to genic variation and to that in the chromosome structure. With the obsolescence of the blending inheritance theory, an impediment to the progress of the evolutionary thought was removed. A distinction must obviously be drawn between the assumption of blending of hereditary factors and the assumption that discrete groups of forms, races or species, differing in many genes will lose their discreteness if they interbreed freely. Owing to the free assortment of genes (the second law of Mendel), interbreeding of such groups will result in a single population in which recombinations of the ancestral traits will be present in separate individuals. The amount of variation is not reduced by crossing, but the difference between the formerly discrete groups, as groups, is obliterated (cf. Chapter VII).

THE HARDY-WEINBERG LAW

Let two strains of a sexual and cross-fertilizing organism be introduced in an isolated and previously unoccupied territory. Suppose that the strains are equally well adapted to the environment, that they differ in a single gene, *AA* and *aa*, that they interbreed at random, that they are introduced in the proportions q of *AA* and (1 — q) of *aa*, and that no new introductions or emigrations take place. What will be the genotype of the resulting Mendelian population in the next and all following generations, and what will be the relative frequencies in this population of the genes *A* and *a*? This problem was considered by Karl Pearson and solved independently by Hardy (1908) and Weinberg (1908). The solution is known as the Hardy-Weinberg, or the binomial square, law. This law is the foundation of population genetics and of modern evolution theory. It states that, under the conditions specified above and discussed further in Chapter V, the gene frequencies, q and (1 — q) will remain constant from generation to generation indefinitely, and that the distribution of the genotypes in all generations will be:

$$q^2AA : 2q(1 - q)Aa : (1 - q)^2aa$$

This expression describes the equilibrium condition in a random breeding population. If there is some breeding preference, such as a tendency towards inbreeding or self-fertilization, the relative frequencies of the homozygotes (*AA* and *aa*) and the heterozygotes (*Aa*) will be modified, but the gene frequencies, q and (1 — q), will still remain constant.

The Hardy-Weinberg law is important because it states that the variability once gained by a population is maintained on a constant level, instead of being eroded and finally leveled off by crossing. As mentioned already, this is a corollary to the particulate as contrasted with the blending type of inheritance. The maintenance of the genetic equilibrium is evidently a conservative factor. Evolution is modification of this equilibrium. We shall proceed now to discuss the agents that modify the equilibrium. A significant fact is that each of such agents is counteracted by another opposite in sign, which tends to restore the equilibrium. A living population is constantly under the

stress of opposing forces; evolution results when one group of forces is temporarily gaining the upper hand over the other.

MUTATION AND THE GENETIC EQUILIBRIUM

The value of q, the frequency of a gene or a chromosome structure in a population—can be modified by mutation pressure in the broad sense of the term, that is, by gene mutations and chromosomal changes. If the change from A to the state a takes place at a finite rate, the frequencies q and 1 — q must change accordingly. Let the mutation in the direction $A \rightarrow a$ have a rate u; the change in the frequency of A in the population will be $\triangle q = -uq$, where q is the frequency of A. If the mutation in the direction $A \rightarrow a$ is unopposed by any other factor, the population will eventually reach homozygosis for a. If the frequency of the gene A in a certain generation is q_0, its frequency n generations later q_n, will be:

$$q_n = q_0(1 - u)^n$$

Since the mutation rates, u, of most genes are small, of the orders of 10^{-4} to 10^{-7} (see below), many generations are required to bring about considerable changes in gene frequencies by mutation pressure alone. Nevertheless, since some genes are more highly mutable than others, and since in some organisms the generation length is short, the mutation pressure is not a negligible factor.

Wherever the mutation is reversible, the change in the direction $A \rightarrow a$ is opposed by the change $a \rightarrow A$. With the rate of reverse mutation equal to v, the frequency of A will change as $\triangle q = -uq + v(1 - q)$. An equilibrium will be reached obviously when the change $\triangle q = 0$. The equilibrium value of q determined by the two mutually opposed mutation rates is therefore $q = v/(u + v)$. Taking, for example, the rate of the mutation $A \rightarrow a$ to be equal to one in a million gametes per generation ($u = 0.000{,}001$), and the rate of the mutation $a \rightarrow A$ to be $v = 0.000{,}000{,}5$, the equilibrium value for q will be 0.33, which means that 33 percent of the chromosomes will carry the gene A and 67 percent the gene a. If the mutation rates to and from a given gene are alike ($v = u$), the equilibrium values for both q and 1 — q are evidently 0.5, or equal. Starting from an initially homogenous population, the mutation pressure will tend to in-

crease the hereditary variability until the equilibrium values determined by the opposing mutation rates are reached for every gene. The occurrence of mutation will, accordingly, make the population polymorphic, i.e., composed of two or more genotypes living together in the same habitat. The equilibrium caused by balance of opposing mutation rates will make the polymorphism a constant property of the species or a population. It is possible that the presence in human populations of a variety of blood-group genes, or of genes conditioning such apparently neutral traits as the ability or inability to taste certain rare chemicals, may be caused by a balance of recurring mutations. This will be discussed further in Chapter VII.

It is important to realize that accumulation of mutants in populations will take place even if mutational changes are unfavorable to the organism. This is especially true when the mutational changes are recessive to the ancestral condition. If the heterozygote *Aa* (*a* being a mutant gene decreasing the viability) is as viable as the ancestral homozygote *AA*, the frequency of *a* will increase until the *Aa* individuals become so frequent in the population that their mating is likely to take place, and the homozygotes *aa* are produced. The *aa* condition being unfavorable, the *aa* individuals will be eliminated, and this will impose a check on the further spread of the mutant gene *a* in the population. This reasoning is fully applicable to mutant genes the adaptive value of which is zero (that is, to lethals). It is possible to show that in very large random breeding populations the equilibrium value of a completely recessive lethal is equal to the square root of the mutation rate producing that lethal ($q = \sqrt{u}$). Thus, if a recessive lethal arises once in a million gametes, one tenth of one percent of the chromosomes will eventually carry it. We may now proceed to review the evidence bearing on the magnitude of the mutation pressure, and on the presence of mutant genes in natural populations.

MUTATION RATES

The difficulty of obtaining accurate data on the mutation pressure is apparent. Either one tries to determine the total frequency of mutations for all the genes the organism possesses, or a particular gene is selected and its mutability measured. In the former case, mutations which produce slight changes present an obstacle, for no known ex-

perimental procedure permits the detection of all such mutations, and yet they are suspected to be the most frequent class. If a single gene is selected, the mutation frequency is usually so low that accumulation of accurate data in higher organisms is technically difficult, slight mutations may be overlooked, and there is no assurance that all mutations of the gene in question (because of its manifold effects) produce changes in the same character. Timofeeff-Ressovsky (1937) surmises that in every generation two to three percent of individuals of *Drosophila melanogaster* carry a newly arisen mutation in their genotype, while Muller's (1946) estimate is between three and ten percent.

A considerable amount of data has been collected by various authors on the frequency of lethal and semilethal mutations in the X chromosome of *Drosophila melanogaster*, using the ClB technique (see Chapter II) or its modifications. The advantage of lethals for studies on the mutation pressure is that the detection of lethals is objective and accurate. With mutants that produce changes in visible external traits of the fly, some observers are able to detect slight alterations of the phenotype which are overlooked by other observers. With lethals, such a "personal equation" is unimportant. Some of the data are summarized in Table 2. Most experiments agree in showing that between 0.1 and 0.4 percent of X chromosomes acquire a new lethal in every generation, i.e., that one to four chromosomes per thousand contain a lethal newly arisen by mutation.

The rate of origin of lethal and semilethal mutations in the second chromosome of *Drosophila melanogaster* has been studied with the aid of methods similar in principle to the ClB method (Dubinin 1946, Ives 1945, Wallace 1950). In most samples, between 0.3 and 0.7 percent of the second chromosomes acquire a lethal per generation. However, some strains give considerably higher mutation rates (up to 5.9 $\pm$ 1.2 percent). Comparable data have been obtained by Spassky and the present writer (unpublished) for the second chromosome of *Drosophila willistoni*, which carries mostly the same gene loci as the second of *Drosophila melanogaster*. The figure for the former species is 0.88 $\pm$ 0.12 percent. The rate for the third chromosomes of *Drosophila pseudoobscura* is 0.31 $\pm$ 0.03 percent; this chromosome is a relatively short one, and contains fewer genes than

the second chromosomes of the other species mentioned above (Dobzhansky and Wright, 1941).

TABLE 2

ORIGIN OF SPONTANEOUS LETHAL MUTATIONS IN X CHROMOSOMES OF DIFFERENT STRAINS OF *Drosophila melanogaster* (AFTER DUBININ, 1946, AND OTHER SOURCES)

STRAIN	AUTHORITY	CHROMOSOMES TESTED	PERCENT LETHAL
Sukhum (Caucasus)	Zuitin	2039	1.18
Florida (USA)	Demerec	2108	1.09
Akhalcikh (Caucasus)	Duseeva	1300	0.77
Wooster (USA)	Demerec	1266	0.63
Ticino (Italy)	Buzzati-Traverso	2333	0.56
Vladikavkaz (Caucasus)	Duseeva	1544	0.52
Florida (USA)	Shapiro and Volkova	9228	0.50
Formosa (China)	Demerec	2054	0.39
Nalchik (Caucasus)	Sakharov	5169	0.35
Vladikavkaz (Caucasus)	Zuitin	2348	0.34
Oregon-R (USA)	Demerec and Wallace	130649	0.297
Florida (USA)	Sakharov	81457	0.23
Florida (USA)	Olenov	2397	0.21
London (England)	Timofeeff- Ressovsky	5863	0.19
Buch (Germany)	Timofeeff-Ressovsky	9345	0.17
Florida (USA)	Timofeeff-Ressovsky	8963	0.17
Florida (USA)	Zuitin	8614	0.16
Paris (France)	Timofeeff-Ressovsky	7483	0.16
Steglitz (Germany)	Timofeeff-Ressovsky	8637	0.14
Merv (Turkestan)	Lobashov	1424	0.14
Tashkent (Turkestan)	Timofeeff-Ressovsky	9972	0.13
Samarkand (Turkestan)	Magrzhikovskaya et al.	4416	0.11
Kiev (Russia)	Timofeeff-Ressovsky	12481	0.11
Florida (USA)	Berg	1041	0.096
Madrid (Spain)	Timofeeff-Ressovsky	5476	0.091
Florida (USA)	Zuitin	4601	0.087
Oregon (USA)	Demerec et al.	51156	0.035

The mutation rates of different genes have been studied by several authors, especially in microorganisms in which very large numbers of individuals can be raised relatively easily. Some of the available data are summarized in Table 3. In general, the genes in higher animals and plants mutate more frequently, per generation, than those in microorganisms. But it must be kept in mind that in bacteria the length of a generation is measured in minutes, while in *Drosophila* it takes days, in maize months, and in higher animals and in trees years or decades. Muller (1928) has pointed out that if the mutabil-

ity per unit time were the same in man as it is in *Drosophila*, human chromosomes would be riddled with lethals and other deleterious genes within a few generations. Nevertheless, some genes are distinctly more mutable than others in the same species, as can be seen especially clearly among the genes studied by Stadler (1942) in maize (Table 3). Similarly, the mutant relatively resistant to the killing action of the ultraviolet and X radiations in *Escherichia coli*, arises much more frequently (Witkin 1947) than do mutants in the same species which confer on these bacteria the resistance to attacks by bacteriophages (see Chapter IV).

Studies on rates of lethal mutation of separate genes in *Drosophila* would be prohibitively laborious, but the aggregate mutation rates per chromosome can be determined relatively easily (see above). It is, however, possible to estimate the minimum numbers of gene loci in the chromosomes which are capable of giving lethal mutants. Thus, Dobzhansky and Wright (1941) calculated that the third chromosome of *Drosophila pseudoobscura* contains at least 289 such genes, while Ives (1945) and Wallace (1950) derived estimates of 400 to 495 lethal-producing genes in the second chromosome of *Drosophila melanogaster*. Dividing, then, the lethal mutation rates per chromosome per generation (see above) by the estimated number of genes, we obtain estimates of the order of 10^{-5} per gene per generation (Table 3). It is an interesting coincidence that estimates of the same order of magnitude have been arrived at for some human genes which give rise to certain hereditary diseases (data of several investigators reviewed by Haldane, 1949).

Unfortunately, no data at all exist on rates of mutations which give rise to minor gene changes responsible for the continuous (polygenic) variability. Such minor mutations are probably most important in evolution. Some experiments on *Drosophila* suggest that these mutations may be rather frequent (see Dobzhansky and Spassky 1947), while others indicate their relative rarity (Mather and Harrison 1949). Information bearing on this problem would be most valuable for understanding evolutionary processes.

GENETIC CONTROL OF THE MUTABILITY

It is frequently stated, particularly in popular scientific writings, that mutations are haphazard, chance, accidental, random, etc.,

TABLE 3

SPONTANEOUS MUTATION RATES PER GENERATION FOR CERTAIN GENES IN VARIOUS ORGANISMS

SPECIES	GENE	RATE	AUTHORITY
Bacteriophage	Host range	2.5×10^{-9}	Hershey 1946
Bacteriophage	Lysis inhibition, direct	10^{-3}	Hershey 1946
Bacteriophage	Lysis inhibition, reversal	10^{-8}	Hershey 1946
Escherichia coli	Phage resistance	2×10^{-8}	Luria and Delbruck 1943
Escherichia coli	Phage resistance	10^{-7} to 10^{-8}	Demerec and Fano 1945
Escherichia coli	Phage resistance	2×10^{-7} to 3×10^{-9}	Luria 1946
Escherichia coli	Radiation resistance	10^{-5}	Witkin 1947
Escherichia coli	Histidinless, reversal	5×10^{-8}	Ryan and Schneider 1949
Staphylococcus aureus	Penicillin resistance	ca. 10^{-7}	Luria 1946
Staphylococcus aureus	Sulfathiazole resistance	ca. 10^{-9}	Luria 1946
Phytomonas stewarti	Virulence	5×10^{-5}	Lincoln 1940
Zea mays (corn)	R (color factor)	4.9×10^{-4}	Stadler 1942
Zea mays (corn)	I (color inhibitor)	1.1×10^{-4}	Stadler 1942
Zea mays (corn)	Pr (purple color)	1.1×10^{-5}	Stadler 1942
Zea mays (corn)	Su (sugary)	2×10^{-6}	Stadler 1942
Zea mays (corn)	Y (yellow seeds)	2×10^{-6}	Stadler 1942
Zea mays (corn)	Sh (shrunken seeds)	1×10^{-6}	Stadler 1942
Zea mays (corn)	Wx (waxy)	$<1 \times 10^{-6}$	Stadler 1942
Oenothera organensis	Self-sterility	1.9×10^{-6}	Lewis 1948
Drosophila melanogaster	Average lethal gene in the second chromosome	2.6×10^{-5}	Ives 1945
Drosophila melanogaster	Average lethal gene in the second chromosome	10^{-5}	Wallace 1950
Drosophila willistoni	Average lethal gene in the second chromosome	2.2×10^{-5}	Spassky and Dobzhansky (unpublished)
Drosophila pseudoobscura	Average lethal gene in the third chromosome	10^{-5}	Dobzhansky and Wright 1941
Homo sapiens	Chondrodistrophy	4×10^{-5}	Haldane 1949
Homo sapiens	Haemophilia	3×10^{-5}	Haldane 1949
Homo sapiens	Retinoblastoma	1.4×10^{-5}	Haldane 1949
Homo sapiens	Aniridia	$>1.2 \times 10^{-5}$	Haldane 1949
Homo sapiens	Epiloia	$4\text{–}8 \times 10^{-6}$	Haldane 1949
Homo sapiens	Pelger anomaly	8×10^{-5}(?)	Haldane 1949
Homo sapiens	Thalassemia	4×10^{-4}(?)	Haldane 1949

changes of the genes. Such characterizations are misleading when given without qualification. For the only respect in which mutations are haphazard is that they arise regardless of the needs of the organism at a given time, and hence are far more likely to be deleterious than useful. But the kinds of mutations that a gene is capable of producing as well as the frequencies with which it produces them are far from indeterminate. They are controlled by the structure of the gene itself as well as by the genetic constitution of the organism.

Studies on the mutation rates have disclosed that these rates are higher in some strains than in other strains of the same species (see Table 2). Such differences in the mutability have been studied in *Drosophila* by several authors (Muller 1928b, Dubovskij 1935, Demerec 1937, Valadares 1937, Shapiro and Volkova 1938, Tiniakov 1939, Timofeeff-Ressovsky 1940c, Buzzati-Traverso 1942a, Neel 1942, Shapiro and Ignatiev 1945, Lamy 1947, Ives 1950, and others). All these authors found strains characterized by exceptionally high mutation rates, the high mutability being a genetically conditioned property of the strain. Demerec was able to locate a mutability enhancer in the second chromosome, and Neel found another enhancer in the third chromosome. It is evident that genetic variants which enhance or depress the mutability are fairly common in natural populations of *Drosophila*, and probably of other organisms as well. Most of these mutability modifiers are nonspecific, in the sense that they influence the general mutability, rather than that of specific genes.

In a series of brief communications, Berg (1941–1942) has attempted to correlate the mutation rates observed in populations of *Drosophila melanogaster* with the ecological situations in which these populations are found. She believes that the mutability of dense and flourishing populations is in general higher than that of small populations which live in rigorous environments. On the other hand, intense inter-group competition tends to increase mutation rates. According to Berg, mutation rates are easily and rapidly modified in the process of evolution, making the species genetically more variable and plastic, or more constant and uniform, depending upon the demands of the environment. Confirmation and development of these findings are greatly to be desired; Dubinin (1946), Dubinin and Khvostova

(1948), and Spencer (1947b) are inclined to question their general validity.

Mampell (1943, 1945, 1946) discovered a dominant gene located apparently in the second chromosome of *Drosophila persimilis*, which increased the mutability about 34 times in heterozygous, and 70 times in homozygous condition. Another "mutator" is a recessive gene, also in the second chromosome. A singular property of this latter gene is that it is effective only in individuals which carry a Y chromosome (males and XXY females), as though that chromosome is necessary to produce a "mutator substance". Even more startling is the claim that flies which do not carry the mutator may become infected with high mutability when raised in the same culture bottles with mutable flies. Sturtevant believes that a high mutability observed by him (1939) in hybrids between *Drosophila persimilis* and *Drosophila pseudoobscura* may have been due to the presence of Mampell's mutator, rather than to the hybridity, as originally supposed. A similar phenomenon may be involved in the outbursts of mutability observed in *Drosophila melanogaster* by Goldschmidt (1945, 1947).

Many, and perhaps all, genes may be changed in various ways, and produce series of multiple alleles. The frequencies of different kinds of mutations depend upon the structure of the gene itself and upon the genotype as a whole. Timofeeff-Ressovsky (1937 and earlier work) found that the gene *W* (for the normal red eye color) in *Drosophila melanogaster* changes to *w* (for white eye color) more frequently than to intermediate states, such as w^e (eosin color) or w^a (apricot). The "normal," *W*, alleles of this gene may, however, be slightly different in different strains. In an experiment of Timofeeff-Ressovsky, a strain of American, and another of Russian origin, were given identical X-ray treatments. In the former, 55 mutations at the white locus were observed among 59,200 chromosomes; and in the latter, 40 mutations among 75,000 chromosomes. The "Russian allele" changed mostly to white and the "American" one to white and to intermediates (eosin) with about equal frequency. Through special experiments Timofeeff-Ressovsky proved that the difference in the behavior of the Russian and the American strains was due to different mutability of the white gene itself, and not to modifying

genes at other loci. Similar modifiers of the mutability of the *R* locus (pigmentation) in maize have been described by Stadler (1948, 1949).

Rhoades (1938, 1941) has described an unusually clear instance of genotypic control of mutability in maize. The gene A_1 produces, in cooperation with certain other genes, the purple anthocyanin pigmentation; the allele a_1 causes absence of anthocyanin. Under normal conditions all these alleles mutate very infrequently. The gene "dotted" lies in a chromosome different from that in which A_1 is located; it has two alleles, *Dt* and *dt*. By itself, the dotted gene has no visible effects; but the gene a_1 becomes highly unstable in the presence of *Dt*, and changes to A_1 both in the somatic and in the germinal tissues. As a result, the a_1Dt plants have dots or streaks of anthocyanin pigmentation. The number of these dots or streaks is proportional to the frequency of mutation, while their size indicates the developmental stage at which the mutations take place. The frequency of mutation is proportional to the number of the a_1 genes. Seeds may be obtained having one, two, or three a_1 genes in the aleurone tissue; the numbers of colored dots formed on such seeds approach the ratio 1 : 2 : 3. Similarly, seeds may be obtained with one, two, or three doses of *Dt;* the number of dots on these seeds shows an exponential relation to that of the *Dt* genes. The effect of the dotted gene on the mutability, is highly specific: the mutability of the a_1 gene is increased many fold, while that of the other alleles at the A_1 locus, or of the genes at other loci, is unaffected. The direction of the mutations is also determined: in the presence of *Dt* the allele a_1 mutates to A_1 about a thousand times more frequently than it does to still another allele, namely $a^p{}_1$. Furthermore, the mutability of a_1 in combinations with *Dt* is modified by the gene, or genes, designated *M*.

The influence of *Dt* thus transforms a normally stable gene A_1 into a highly mutable one. Such mutable genes are known in maize, in *Drosophila*, and other organisms, including some bacteria (Demerec 1941, Bunting 1946). Although mutable genes as such are probably of no importance in evolution, they are valuable for studies on the genetic control of the mutation process. Demerec was the first to show that the mutability of a gene may be controlled by other genes. Mutant alleles of the gene miniature in *Drosophila virilis*

modify the size and texture of the wings. Some of these alleles are about as stable as the ancestral gene; others are very unstable and revert to the wild type or change into each other with considerable frequencies. Some are mutable only in somatic cells, producing mosaic patches of normal and mutant tissues; others undergo changes mainly in the sex cells. Some mutate early and others late in the development. In addition to the properties inherent in the miniature locus itself, the mutability of the locus is influenced by at least four other genes located in different chromosomes; the mutability modifiers by themselves produce no visible effects.

Sitko (1938) and Heptner (1938) examined the possible relations between the mutation rates of genes and the position of the latter in the chromosomes. The mutability of several genes in normal X chromosomes of *Drosophila melanogaster* was compared with that of the same genes lying in X chromosomes which had been broken by translocations and inversions. Statistically significant increases of the mutability in the broken chromosomes were found. Sitko concludes that the mutability is enhanced in genes which lie in the proximity of breakage points. Sitko's data are not entirely convincing, but if the relation alleged by him were confirmed, it would follow that the evolutionary courses of races and species differing in gene arrangement are likely to diverge owing to the modification of the rates, and possibly of the direction, of mutation in certain genes. Kaufmann (1940) found no change in the breakability of chromosomes that had suffered a gene rearrangement, but this does not necessarily contradict Sitko's findings.

MUTANTS IN WILD POPULATIONS

Mutants that arise in laboratory cultures of *Drosophila* are classic material for studies on the mutation process. Nevertheless, *Drosophila* flies found in nature are, if anything, less variable than insect species often are. Since many biologists were unaware of the fact that visible external differences between some good species of *Drosophila* are very small, a misapprehension became current that laboratory mutants have no counterparts in nature. This is not the case. Mutants with gross bodily changes, like those described and pictured in genetics texts, are not expected to be frequent in nature. They are usually poorly viable, and are rapidly eliminated by natural selection.

Nevertheless, mutants do occur as rare aberrant individuals in natural populations, and have been recorded even by some pioneer students of *Drosophila.*

The available information has been ably summarized by Spencer (1947b). Spencer himself found a population of *Drosophila hydei* at Wooster, Ohio, in which 6.5 percent of the males were vermilion eyed. This sex-linked recessive mutant continued to occur in this population for at least six years. Some populations of this species contain up to several percent of individuals showing the mutant bobbed. A remarkable variety of alleles at the bobbed locus has been discovered. Their frequencies varied from locality to locality. Dubinin, et al. (1937) examined almost 130,000 wild *D. melanogaster* from several localities in southern Russia, and found among them about 2,800 "aberrant" individuals. A part of the latter contained noninheritable abnormalities, but others were mutants, for the most part identical with well-known laboratory types (among them, extra bristles, ebony, sepia, and yellow). The relative frequencies of different mutants vary from locality to locality and from year to year; most of the mutants are recessives, although a few semidominants are recorded; mutants that produce slight changes in the appearance and viability of the flies are more common than more drastic and deleterious variants. At one collecting station—a deep pit with decomposing fruit—many individuals were found homozygous for the gene divergent which makes its carriers flightless. Buzzati-Traverso and Cavalli (1945) found in an Italian population of *Drosophila melanogaster* some individuals homozygous for the well-known mutant gene ebony, which turns the body color from the normal grayish-brown to black. Ebony heterozygotes were also found in this population.

Aberrant individuals found among masses of "normal" representatives of their species have often been recorded (see, for example, Baluzac, 1948, for an elaborate review of such findings among beetles). Old-line naturalists classified such individuals as aberrations, phases, monstrosities, etc., and ascribed their origin to developmental accidents. That developmental accidents produce teratological specimens (morphoses, see Chapter II) is certain, but in a number of cases it has been established that aberrations of this sort are in reality mutants, mostly recessive to the normal condition. They represent rare instances when recessive genes long carried in the

population in heterozygous state, emerge as homozygotes because of the occasional mating of two carriers. Dunn (1921), Storer and Gregory (1934), and others have studied aberrant individuals in wild species of rodents (albinism, pink eyes, yellow, black, or white-spotted specimens among the agouti-colored normals). The aberrations found in nature resemble well-known breeds of domestic species (rabbits, mice, and guinea pigs), in which these characteristics are inherited as Mendelian recessives.

POTENTIAL GENETIC VARIABILITY IN DROSOPHILA POPULATIONS

No matter how carefully one examines the phenotypes of wild representatives of a species, the information thereby gained about the genetic variability in natural populations will be incomplete. Since many mutants are recessive to the "normal" condition, an individual may be heterozygous for one or more mutants and yet preserve the "normal" phenotype. Chetverikov (Tschetwerikoff 1926, 1927) was the first to point out that a genetic analysis of natural populations is necessary to reveal the concealed, or potential, variability. Several techniques are used for such analysis (see Spencer 1947b). Taking, for example, *Drosophila* females which have already been fertilized in nature, one may discover in their immediate offspring any sex-linked mutant genes and autosomal dominants which these females or their mates may have carried. Inbreeding F_1 individuals will permit the detection in F_2 and F_3 generations of the recessive autosomal mutants. Wherever practical, more refined methods are used. In principle, these methods consist of crossing individuals collected in nature to laboratory strains with known mutant genes which serve as "chromosome markers". This is the start of a series of crosses so designed as to produce in the end individuals homozygous for the chromosome to be tested. If the "wild" chromosome in question contains any recessive genetic variant, such as a lethal, a semilethal, or a gene producing visible external characters or physiological modifications, its effects will be detectable in the homozygotes.

The pioneer experimental work designed to test the validity of the above reasoning was carried out by Chetverikov (Tschetwerikoff 1926, 1927), Timofeeff-Ressovsky (1927), and Dubinin et al. (1934, 1936), using populations of *Drosophila melanogaster* as ma-

terial. Populations of this species proved to carry a hitherto quite unsuspected profusion of recessive mutants concealed in heterozygous condition. This was the case also in every other species of *Drosophila* so far examined (*D. pseudoobscura*, *D. willistoni*, *D. subobscura*, *D. repleta*, *D. prosaltans*, *D. immigrans*, *D. hydei*, and also *D. robusta*, *D. persimilis*, *D. phalerata*, *D. transversa*, *D. vibrissina*, and *D. buskii*). Reviews of this work have been published by Dobzhansky (1939), Dubinin (1946), and Spencer (1947b). The situation found by Pavan et al. (1951) in Brazilian populations of *D. willistoni* may be considered as an example.

Drosophila willistoni has three pairs of chromosomes: an X, a second, and a third chromosome. By means of appropriate crosses, 2,004 second and 1,166 third chromosomes derived from flies caught in nature were tested for their effects in homozygotes. About 29 percent of the second and 20 percent of the third chromosomes contained one or more recessive lethal genes, since the flies which carried these chromosomes in duplicate (homozygotes) proved completely inviable (Table 4). Further, 13 percent of the second and 12 percent

TABLE 4

PERCENTAGE FREQUENCIES OF SECOND AND THIRD CHROMOSOMES IN BRAZILIAN POPULATIONS OF *Drosophila willistoni* WHICH PRODUCE VARIOUS TYPES OF GENETIC EFFECTS IN HOMOZYGOUS INDIVIDUALS (AFTER PAVAN ET AL., 1951)

EFFECT	SECOND CHROMOSOME	THIRD CHROMOSOME
Lethal	28.6	19.7
Semilethal	12.6	12.4
Subvital	57.5	49.1
Supervital	1.2	0.8
Sterile	31.0	27.7
Retarded Development	31.8	35.7
Accelerated Development	13.7	2.8
Visible Mutants	15.9	16.1

of the third chromosomes carried recessive semilethals, since, under the conditions of the experiment, they killed more than half of the homozygotes. The proportions of the homozygotes which survived and which died can be judged by observing the departures from the

expected Mendelian ratios in cultures, in which the homozygotes are produced together with heterozygotes marked by convenient visible mutants. About 57 percent of the second and 49 percent of the third chromosomes which were free of lethals or semilethals were "subvital" in homozygotes. A subvital is a deleterious gene or gene complex which causes, in a certain environment, the death of less than half of the homozygotes. To put it in a different way, a recessive subvital chromosome permits more than half of the homozygotes to survive to the adult stage. In man and in higher animals, semilethals and subvitals are referred to as hereditary diseases or hereditary constitutional weaknesses (the mutational origin of subvitals has been discussed in Chapter II, see Table 1). Only about one percent of the chromosomes were "supervital," i.e., made the homozygotes more vigorous than normal flies (see Chapter IV for further discussion of this class). Deleterious variants are, in any case, vastly more common than useful ones.

Apart from their effects on the vitality of their carriers, the chromosomes of *Drosophila willistoni* were tested for their effects on fertility, speed of the development, and the external appearance of the homozygotes (Table 4). Among the chromosomes which were free of lethals and semilethals, about 31 percent of the second and 28 percent of the third chromosomes made their carriers sterile, when homozygous, either as males or as females, and rarely as both sexes. From the standpoint of adaptation, sterile individuals are at least as useless to the species as inviable ones (except, of course, in social insects and other social forms). The high incidence in natural populations of recessive sterility mutants is, thus, an example of accumulation of deleterious variants. At least 32 percent of the second and 36 percent of the third chromosomes contained recessive genes which made the homozygotes develop more slowly than normal flies do. Some chromosomes, on the contrary, accelerated the development. Finally, about 15 percent of the chromosomes contained recessive genes which influence externally visible traits of the flies, such as the eye color, and the shape of the wings or of the bristles.

To appreciate the magnitude of the store of concealed recessive mutants in *Drosophila willistoni*, one must recall that each fly has two second and two third chromosomes. Taking into consideration the proportions of these chromosomes carrying concealed mutants, it

is certain that only very few flies in natural populations are free of at least one recessive abnormality in their chromosomes. The data of Dobzhansky et al. (1942) indicate a similar situation in natural populations of *Drosophila pseudoobscura.*

Comparison of the stores of potential variability in different species and populations may lead to interesting discoveries. The available data are suggestive, but too incomplete to be interpretable at present. Dubinin and his collaborators have analyzed for recessive lethals an impressive number of second chromosomes of *Drosophila melanogaster* from different parts of Russia (Dubinin et al. 1934, and 1936, Dubinin 1946, Dubinin and Khvostova 1948). In most samples from 8 to 20 percent of the chromosomes carried lethals or semilethals, although one sample had no lethals at all, and a few samples contained 30 and even 39 percent of lethal-bearing second chromosomes. Ives (1945) obtained figures ranging from 34 to 67 percent for American populations from Maine, Massachusetts, Ohio, and Florida.

The origin of so wide a variation in the concentration of concealed lethals is unexplained. Dubinin (1946) and Postnikova (1948) believe that lethals are relatively rare in populations during spring, and grow in frequency during summer and fall. Since populations of *Drosophila melanogaster* are large in late summer and fall, but are drastically reduced during winter, there may be close inbreeding, and consequently elimination of lethals through homozygosis, in winter and in spring. The summer rise of lethals is, then, due to accumulation of newly arisen mutants. It is, however, doubtful if the seasonal variation could account for more than a fraction of the observed amplitude in the frequencies of lethals in different population samples. Dubinin himself (Dubinin and Khvostova 1948) surmises that the greater frequency of lethals in the population of Moscow than in that of Astrakhan is due to higher mutation rates in the former than in the latter. In *Drosophila pseudoobscura,* 16.5 ± 1.4 percent of the third chromosomes from the Death Valley region of California carry recessive lethals or semilethals, compared to 13.9 ± 1.0 percent from Mount San Jacinto in California and 30.0 ± 4.2 percent from Mexico and Guatemala. The mutation rates producing lethals proved, nevertheless, to be the same in Californian (0.297 ± 0.04 percent per generation) and in Mexican and Guatemalan (0.325 ± 0.065 percent) populations (Dobzhansky and Wright 1941, Wright et al. 1942). The

data on the stores of the concealed variability in *Drosophila subobscura* in England and in Italy (Gordon 1936, Buzzati-Traverso 1942b), in *D. prosaltans* (Cavalcanti 1950), and other species (Spencer 1947b) are as yet too incomplete to make comparisons profitable. The concealed variability is probably controlled by the breeding structure of the species or population (see Chapter V).

POTENTIAL GENETIC VARIABILITY IN ORGANISMS OTHER THAN DROSOPHILA

Exact quantitative studies on the concealed variability are practicable only in those few organisms which are genetically sufficiently well known to enable one to follow the course of chosen chromosomes in inheritance, by means of suitable marker genes. One may nevertheless suspect that the enormous stores of potential variability found in *Drosophila* should be paralleled in other organisms. Indeed, accumulation of recessive genetic variants is a necessary consequence of the mutation process in sexually reproducing and cross-fertilizing diploid or polyploid populations. This inference is confirmed by the frequent appearance of recessive aberrations in the offspring of consanguineous matings in normally outcrossed species. In man, the high incidence of consanguinity among parents of victims of rare recessive hereditary diseases is well known. In fact, the occurrence of consanguinity in pedigrees is often looked for as indirect evidence of recessivity of rare traits where the exact course of inheritance is uncertain.

Lethal and semilethal homozygotes are also frequent in inbred lines of the normally outbred domesticated animals (a review in Lerner 1944). Emergence of deleterious recessives following inbreeding of wild species has been described by Sumner (1932) in the mouse *Peromyscus* and by Spooner (1932) and Sexton and Clark (1936) in the crustacean *Gammarus chevreuxi*. H. Timofeeff-Ressovsky (1935) obtained a mutation in the beetle *Epilachna chrysomelina*, which resembled a type of this species previously recorded in some localities. Similar data exist for cross-fertilizing plants. Jenkins (1924) examined 3,750 lines of commercial maize and found 18.1 percent of them to be heterozygous for chlorophyll defects in seedlings and 6.1 percent for chlorophyll defects in mature plants; Hayes and Brewbaker (1924) obtained similar results. According to Man-

gelsdorf (1926), approximately 3 percent of maize plants are heterozygous for lethal or semilethal genes producing, when homozygous, defective seedlings. Chlorophyll defects, dwarf plants, and other variants appear in inbred progenies of the grasses *Festuca pratensis*, *Dactylis glomerata*, and *Phleum pratense* (Nilsson 1934), *Alopecurus myosuroides* (Johnsson 1944), and of the white mustard *Synapis alba* (Saltykovsky and Fedorov 1936). Johnsson records also numerous chromosomal disturbances in the inbred progenies. Such disturbances have also been described by Müntzing (1946) and Müntzing and Akdik (1948) in inbred lines of rye.

No recessive mutants have been found by Gershenson (1946) in several dozen inbred progenies of the wasp *Mormoniella*, in which, as in other representatives of the order Hymenoptera, the males are haploid. Deleterious recessive mutant genes would be expected to be rapidly eliminated by natural selection in haploid males, where they are not sheltered by their normal dominant alleles. It is for this reason that no accumulation of deleterious recessives takes place in the X chromosomes of *Drosophila* populations. Since the order Hymenoptera is supposed to be one of the rapidly evolving groups of insects, Gershenson concludes that concealed potential variability is not important in evolution. A contrary argument is advanced by White (1945) and by Kerr (1950). In Hymenoptera, some mutant genes which are deleterious in homozygous females do not affect adversely the haploid males. Loss of vigor following inbreeding has been observed in at least some Hymenoptera, such as the honey bee. Haploidy of one sex is, thus, compatible with accumulation of a store of potential variability. On the other hand, the concealed store of variability will be small in populations which reproduce mainly by self-fertilization (for example, in wheats). In such populations the raw materials of evolution will be supplied by mutation and by occasional hybridization with other populations or other species (see Chapter X).

POLYGENES

Studies on potential variability reveal the existence of great stores of mutant genes concealed in *Drosophila* populations. These stores contain numerous genes with sharp discontinuous effects, such as lethals, sterility genes, and genes which cause striking alterations in the external morphology of the flies. It must, however, be empha-

sized that, together with these "major" mutants, there is found an enormous mass of genetic variants which give rise to individually less striking but numerous changes in many traits. Here belong the subvitals and the supervitals, the relatively minor changes in the development rates of the flies, minor variations in the fly morphology, etc. This continuous, or polygenic, variability is probably the most important in evolution.

The technical difficulties met with in the analysis of the continuous variability are so great that in the past some authorities believed this variability to be nongenic and non-Mendelian. The classical studies of Nilsson-Ehle on the genetics of cereals first established the principle of multiple factors, termed polygenes by Mather (1943). An inherited difference between individuals or strains may be due to "the joint action of many genes, each having an effect small in relation to the total nonheritable fluctuation of the character in question." Some authors have attempted to draw a sharp distinction between major genes and polygenes, but such distinctions are gratuitous. Polygenes are carried in chromosomes, and consequently are inherited exactly as other genes. But the smallness of the individual effects of polygenes makes it difficult or impossible to follow them in inheritance one by one. As pointed out by Mather (1943, 1949) and Darlington and Mather (1949), polygenic inheritance must be studied with the aid of specialized statistical techniques, rather than by counting representatives of sharply distinct genotypic and phenotypic classes found in segregating progenies of hybrids between parents which differ in major genes.

One of the important properties of polygenic inheritance is that it favors storage of potential variability. Suppose, for example, that strains of a species differ in four pairs of genes which produce cumulative effects on some continuously varying trait, such as body size. If the genotypes of the strains are AAbbCCdd and aaBBccDD, and if the phenotypic effects of the alleles denoted by capital letters are alike, the representatives of these strains will be alike in average body size. When, however, such strains are crossed, an array of genotypes arises in the F_2 generation. Among these genotypes, there will be AABBCCDD, aaBBCCDD, aabbccdd, aabbccDD, etc., which may differ greatly in body size from both parental strains and from the carriers of other gene combinations among the hybrids. In such a way

natural populations may carry genes potentially capable of producing numerous and diverse new genotypes, if recombined in segregating hybrid progenies. Dobzhansky (1946) and Mather and Harrison (1949) found the storage of potential variability to be most efficient in linked polygene complexes carried in certain chromosomes.

Three different second chromosomes isolated from a wild population of *Drosophila pseudoobscura* were used by Dobzhansky (1946). At the temperature of 25°C., the chromosome denoted A was lethal in homozygous flies, while the chromosome denoted B was normal or slightly subvital, and chromosome C gave normally viable homozygotes. At a lower temperature, 16°C., chromosome A gave subvital homozygotes, while B homozygotes were normal, and C supervital. Except for the extraordinary differences in the viability of A homozygotes at different temperatures, these chromosomes were in no way remarkable. The experiments consisted in obtaining females heterozygous for the chromosome combinations A/B, A/C, and B/C, outcrossing them to males which carried certain marking mutant genes, and testing the viability effects of the chromosomes obtained in the progenies. Some of the eggs deposited by the A/B, A/C, and B/C females carried chromosomes which were identical with the ancestral A, B, and C (noncrossovers), while other eggs carried crossover chromosomes compounded of sections of the ancestral ones.

A remarkable variety of chromosomes were obtained in the hybrid progenies. All degrees of the viability have been observed in the homozygotes: from supervital, to normal, subvital, semilethal, and completely lethal. The properties of many chromosomes were similar to or intermediate between the parental ones. But other chromosomes arose in the hybrids which had quite new properties. Thus, several chromosomes in the progeny of A/B are lethal not only at 25°C. but also at 16°C., although neither A nor B is lethal at the latter temperature. The A/C progeny contained several chromosomes semilethal in homozygotes at 16°C., which, again, is not the property of either parental chromosome. Finally, the B/C progeny contained at least three chromosomes which were semilethal to homozygotes at 25°C., although B is normal and C even supervital at that temperature. Examination of other properties of the chromosomes (their effects on the speed of the development of the homozygotes, etc.) disclosed an

impressive amount of genetic variability released by crossing over between only three initial chromosomes taken from a natural population. This explains the fact which has puzzled many geneticists and breeders: it is often possible by careful selection to obtain genotypes with properties very different from those of the strains or populations which served as the initial material for selection (see Chapter IV).

CONCLUSIONS

The studies on the genetic variability in natural populations have revealed a situation which appears highly paradoxical at first sight. The mutation process constantly and unremittingly generates new hereditary variants—gene mutations and chromosomal changes. These variants accumulate in populations of sexually reproducing and cross-fertilizing organisms, and form a great store of potential variability, mostly concealed as a mass of recessive mutants carried in heterozygous condition. According to the succinct metaphor of Chetverikov, a sexual species is "like a sponge" which absorbs and stores the genetic variability. And yet, a majority of mutations, both those arising in laboratories and those stored in natural populations, produce deteriorations of the viability, hereditary diseases, and monstrosities. Such changes, it would seem, can hardly serve as evolutionary building blocks.

The situation seems even more difficult to understand because the mutation rates are subject to a genotypic control: genetic factors reducing and enhancing the mutability occur apparently not infrequently. Sturtevant (1937, 1939), Shapiro (1938), Shapiro and Ignatiev (1945) and others have pointed out that, since a majority of mutants are injurious, the adaptive value of strains with high mutability will tend to be lower than that of strains in which the mutability is reduced. Natural selection will, therefore, favor the genotypes in which the mutability is kept at a minimum. Looked at from another angle, accumulation of germinal changes in the population genotypes is, in the long run, a necessity if the species is to preserve its evolutionary plasticity. The process of adaptation may be looked at as a series of conflicts between the organism and its environment. The environment is in a state of flux, and its changes, whether slow or rapid, make the genotypes of the bygone generations no longer fit

for survival. The ensuing contradictions can be resolved either through extinction of the species, or through reorganization of its genotype.

An ideal situation would be if the organism were to respond to the challenge of the changing environment by producing only beneficial mutations where and when needed. But nature has not been kind enough to endow its creations with such a providential ability. Mutations are changes that occur regardless of whether they are or may be potentially useful. Haldane (1937), Shapiro (1938), and the writer (in the first edition of this book) have pointed out that the preservation of a living species demands a store of concealed genetical variability. This store will contain variants which under no conditions will be useful, other variants which might be useful under a set of circumstances which may never be realized, and still other variants which are neutral or harmful at the time when they arise but which will prove useful later on.

Mutations which are unfavorable in a given environment may be valuable in a changed environment (see Chapter IV). Since natural selection operates not with separate genes or separate mutations, but with gene patterns or genotypes, a mutation that decreases the viability when present together with certain genes may increase the viability when placed on a different genic background. If the environment were absolutely constant, one could conceive of formation of ideal genotypes each of which would be perfectly adapted to a certain niche in this environment. In such a static world, evolution might accomplish its task and come to a standstill; doing away with the mutation process would be the ultimate improvement. The world of reality is, however, not static. A species perfectly adapted at present may be destroyed by a change in the environment if no hereditary variability is available in the hour of need. Depending upon the speed and character of environmental changes, and also upon the reproductive biology of the species, greater or lesser mutability will be favored. The store of potential variability, and the rate at which the potential variability becomes actualized will be controlled by natural selection (Mather 1943, Berg 1941 and 1942, and others).

The process of evolution is opportunistic: natural selection favors those variants useful at a given time, regardless of their eventual value. Possessing no foresight, selection always tends to suppress

mutability. But opportunism leads in the long run to retribution: species or races which become "well adapted" to the point of abolishing mutability do not respond to the challenge of a shifting environment. Evolution viewed in historical perspective tends to perpetuate types which are, in a sense, not too well adapted. This long range process is a kind of selection *sub specie aeternitatis.*

IV : Selection

HISTORICAL

ADUMBRATED in classical antiquity, the principle of natural selection was raised to the status of a scientific theory by Darwin. If a population is a mixture of genetically distinct types, some of them are likely to produce more surviving progeny than others. Certain genes, gene complexes, and chromosome structures will, then, become more, and others less frequent, in succeeding generations. The gene frequencies, q and $(1 - q)$, will accordingly become altered.

Perhaps the most frequently voiced objection against the theory of natural selection is that it takes for granted the existence of the hereditary variations with which selection works. Those who advance this objection commit an act of supererogation: the origin of variation is a problem entirely separate from that of the action of selection. In the beginning of the present century Johannsen showed that selection is effective in genetically mixed populations but inoperative in genetically uniform ones. Johannsen's work was preceded by De Vries's discovery of the origin of hereditary variations through mutation. Following this discovery, some writers contended that De Vries and Johannsen had disproved Darwin's theory of evolution by natural selection and had supplanted it by a theory of evolution by mutation. The polemics that ensued both in popular and in scientific literature seem in retrospect a sort of modern confusion of tongues. The theory of mutation relates to a different level of the evolutionary process than that on which selection operates, and therefore the mutation and selection theories are not alternatives. On the other hand, the discovery of the origin of hereditary variation through mutation accounts for the presence in natural populations of the material upon which selection acts. The greatest difficulty in Darwin's theory of evolution, of the existence of which Darwin himself was well aware, is hereby removed.

The theory of natural selection is primarily an attempt to account for adaptation of organisms to their environment. Whether it explains not only adaptation but evolution as well is another matter. According to Fisher (1936), "evolution is progressive adaptation and consists of nothing else. The production of differences recognizable by systematists is a secondary by-product, produced incidentally in the process of becoming better adapted." And further: "For rational systems of evolution, that is for theories which make at least the most familiar facts intelligible to the reason, we must turn to those that make progressive adaptation the driving force of the process." A contrast to this is provided by the statement of Robson and Richards (1936): "We do not believe that natural selection can be disregarded as a possible factor in evolution. Nevertheless, there is so little positive evidence in its favor . . . that we have no right to assign to it the main causative role in evolution." The development of population genetics in the last two decades has considerably strengthened the theory of natural selection. It is fair to say that, among the two opinions just cited, the first is believed by a majority of modern evolutionists to be much nearer the truth than the second. Nevertheless, Goldschmidt (1940), Vandel (1949), and some others have steadfastly maintained their opposition to this view.

THE CONCEPT OF ADAPTIVE VALUE

It is well known that Darwin's conception of natural selection was derived from the idea of Malthus, that even the slowest breeding organisms tend to produce more offspring that can survive without eventually outrunning the food supply. Death and destruction of a part of the progeny undoubtedly take place in all organisms. It was the differential mortality of the carriers of different genotypes composing a population that was supposed to make selection effective. Unfortunately, this process was also described by metaphors which were more picturesque than accurate, such as "struggle for life" and "the survival of the fittest". Natural selection became associated in too many minds with emotional slogans like "eat or be eaten," and this led to misuse of Darwinism by propagandists and bigots.

In reality, the essence of selection is that the carriers of different genotypes in a population contribute differentially to the gene pool of the succeeding generations. The contributions of some genotypes

are relatively greater on the average than the contributions of others in the same environment. The relative capacity of carriers of a given genotype to transmit their genes to the gene pool of the following generations constitutes the adaptive value, or the Darwinian fitness, of that genotype. The adaptive value is, then, a statistical concept which epitomizes the reproductive efficiency of a genotype in a certain environment. Now, the adaptive value is obviously influenced by the ability of a type to survive. The adaptive value of a homozygote for a lethal gene is evidently zero. But the individual's somatic vigor, its viability, is only one of the variables which determine the adaptive value.The duration of the reproductive period, the number of eggs produced (fecundity), the intensity of the sexual drive in animals, the efficiency of the mechanisms which conduce to successful pollination in plants, and many other variables are likewise important.

Natural selection need not necessarily involve competition or struggle, in the sense of direct combat between individuals. In fact, a genotype favored by differential survival at certain stages of the life cycle may have a lower net Darwinian fitness, if its superior viability is overbalanced by, for example, a lower fertility. This has actually been observed in an experiment involving interracial hybrids in *Drosophila pseudoobscura* (Dobzhansky 1950c). Wallace (1948) has compared the homozygotes and heterozygotes for certain inversions in the same species with respect to several physiological properties important in the determination of adaptive values. Some genotypes were superior to others in some but inferior in other properties. Indirect evidence of a similar situation has been obtained by da Cunha (1949) for genetically determined color types in *Drosophila polymorpha.*

In social organisms the survival and vigor of an individual is adaptively important only if it contributes to the perpetuation of the colony or the group. This is strikingly apparent in insect societies, in which a majority of individuals are completely sterile. Competition between members of a colony is entirely eliminated and supplanted by cooperation and mutual help. Allee et al. (1949), Simpson (1949), and others pointed out the adaptive importance of cooperation also in organisms which do not form highly organized societies. A solitary individual wholly independent of others is largely a fiction. In reality,

most or even all living beings exist in more or less integrated communities, and the ability to maintain these associations entails some cooperation, or at least "protocooperation". By far the most widespread and important form of association among sexual organisms are Mendelian populations (Dobzhansky 1950d, see also Chapters III, VII, and IX). We shall see in Chapter VI that Mendelian populations, rather than individuals, are the units of natural selection and adaptation.

Recognition of the adaptive importance of cooperation and mutual help in no way contradicts the theory of natural selection, as it was construed to do by Kropotkin and others (see Montagu 1950). Cooperation, competition, struggle, and various combinations of these forms of relationships between organisms may, under various circumstances and at different times, augment or reduce the adaptive values of carriers of certain genotypes. Whether cooperation or disoperation prevails at a given time in a given environment depends upon the adaptive exigencies of the situation.

SELECTION COEFFICIENTS

A fallacy met with in many discussions of natural selection is the assumption of all-or-none utility or deadliness of traits in the "struggle for existence". In reality, the adaptive value is a continuously varying quantity. If the carriers of one genotype produce, on the average, 1,000 offspring when the carriers of another genotype produce 999,the difference in the adaptive values will in time bring about a change in the genetic composition of the population. The action of selection is a statistical problem. The pioneer work in mathematical analysis of this problem was carried out by Haldane, Fisher, Wright, and their followers. A simplified but accurate presentation of the main results of this analysis may be found in Li (1948) and in Lerner (1950).

Suppose that a dominant gene *A* has the frequency q, and its recessive allele *a* the frequency $(1 - q)$, in the gene pool of a sexual random breeding population. According to the binomial square rule (Chapter III), the population will consist of three genotypes with frequencies $q^2AA + 2q(1 - q)Aa + (1 - q)^2aa = 1$. Let the adaptive values (W) of the dominants, *AA* and *Aa*, be equal to unity, and that of the recessive to $(1 - s)$. In other words, for every unit of offspring

produced by the dominants, the recessive produce $(1 - s)$ offspring on the average: The value s is called the selection coefficient. The frequencies of the three genotypes before and after selection will be:

Genotypes	*AA*	*Aa*	*aa*	Total Population
Adaptive values (W)	1	1	$(1 - s)$	$\overline{W}$
Initial frequency	q^2	$2q(1 - q)$	$(1 - q)^2$	1
Frequency after selection	q^2	$2q(1 - q)$	$(1 - s)(1 - q)^2$	$1 - s(1 - q)^2$

The frequency, q_1, of the gene *A* in the next generation will be:

$$q_1 = [q^2 + q(1 - q)/[1 - s(1 - q)^2] = q/[1 - s(1 - q)^2]$$

The increment, $\triangle q$, of the frequency of the gene *A* in one generation will be:

$$\triangle q = sq(1 - q)^2/[1 - s(1 - q)^2]$$

Let, for example, the genes *A* and *a* be equally frequent in the original population, so that $q = (1 - q) = 0.5$. Let the adaptive value of the dominants (*AA* and *Aa*) be unity, and suppose that the recessives (*aa*) have the adaptive values of 0 (a recessive lethal), or of 0.4 (a semilethal), or 0.9, or 0.99 (subvitals), or 1.5 (supervital). The frequencies, q_1, of the gene *A* in the next generation, and the increments of the gene frequency, will be then:

Adaptive value (W)	0	0.4	0.9	0.99	1.5
Selection coefficient (s)	1.0	0.6	0.1	0.01	−0.5
Frequency after one generation of selection (q_1)	0.67	0.58	0.5128	0.5012	0.444
Increment of gene frequency ($\triangle q$)	+0.17	+0.08	+0.0128	+0.0012	−0.056

For small selection coefficients (s), an approximate formula for the number of generations (n) necessary to change the frequency of a deleterious recessive gene from q_o to q_n is as follows:

$$ns = \frac{q_o - q_n}{q_o q_n} + \log_e \left(\frac{q_o}{1 - q_o} \cdot \frac{1 - q_n}{q_n} \right)$$

For the special case of complete selection, s = 1.0, against a recessive (i.e., selection against a recessive lethal, or, in artificial selection, against an undesirable trait), the above formula is simplified to:

$$q_n = q_o/(1 + nq_o)$$

The efficiency of selection of a given intensity depends upon the gene frequency in the initial population. Suppose that a recessive gene for some undesirable trait has to start with a frequency of 0.5, and that the homozygous recessives are sterilized or otherwise eliminated from the population in every generation (s = 1). The frequency of this gene will, then, change as follows:

GENERATION	FREQUENCY	GENERATION	FREQUENCY
1	0.500	20	0.048
2	0.333	30	0.032
3	0.250	40	0.024
4	0.200	50	0.020
5	0.167	100	0.010
9	0.100	200	0.005
10	0.091	1000	0.001

The progress of selection is rapid at first, while the gene is frequent enough for an appreciable number of recessive homozygotes to be produced in the population, but it becomes slow as the gene frequency declines. For other forms of selection, such as selection for or against genes with no dominance, sex-linked genes, etc., see Li 1948, Lerner and Dempster 1948, and Lerner 1950.

INTERACTION OF SELECTION AND MUTATION

The above calculations are based on the somewhat unrealistic assumption that mutation does not occur. With mutation, the process of selection may be either enhanced or slowed down. If mutation to an allele favored by selection takes place more frequently than away from that allele, the speed of the process is greatly accentuated in its initial stages. After an initial increase in frequency, the relative importance of the mutation declines, and the further increase has to proceed by selection alone (unless, of course, the mutation rate is very high). Thus, with an allele *A* mutating to *a* at a rate 1 : 1,000,000, the change of the gene frequency from q = 0.000,001 to q =

0.000,002 is accomplished in a single generation, while a similar change without mutation requires 321,444 generations for a recessive type with a selective advantage of 0.001.

If the mutation is away from the allele favored by selection, the gene frequency will never reach zero or unity, and a genetic equilibrium will be established instead. The population will consist of several genotypes which will occur in certain proportions. In other words, the population will be more or less polymorphic. The proportions of the genotypes in the population and of the genes in the gene pool will remain fixed as long as the mutation rates and the selection coefficient stay constant.

Suppose that the gene A mutates to a at a rate u per generation, but that the recessive homozygote, aa, has an adaptive value $(1 - s)$, which is lower than that of the dominants. The rate of change of the frequency of the recessive allele will be approximately $\triangle (1 - q) = uq - sq (1 - q)^2$. The attainment of an equilibrium means that no further change takes place, that is $\triangle (1 - q) = 0$. Solving the equation, we find the equilibrium gene frequency, which is $(1 - q) = \sqrt{u/s}$. If the mutation occurs from a favorable recessive to an unfavorable dominant, a to A, at a rate u per generation, an equilibrium is likewise established, but at the level $q = u/s$. Taking the mutation rate, u, to be 10^{-5}, and the selection coefficient $s = 10^{-3}$, the equilibrium values will be 0.01 for the dominant and 0.10 for the recessive mutant genes, respectively. It is evident that unfavorable recessive mutants will be allowed to accumulate in populations to a much greater extent than the equally disadvantageous dominants. This is, of course, exactly what the analysis of the genetic variability in natural populations has shown to be the case (Chapter III).

ENVIRONMENTAL MODIFICATION OF THE ADAPTIVE VALUES

The rarity or even absence of mutations which increase the adaptive value of a normal species genotype in environments in which the species usually lives is not surprising. The reaction norms of the genotypes which occur frequently in natural populations are molded in the evolutionary history controlled by natural selection. As pointed out in Chapter II, these reaction norms are so adjusted that environmental agencies which the species commonly meets evoke adaptively valuable modifications. On the other hand, rare and unusual environ-

mental influences result in adaptively haphazard morphoses. Mutations create genotypes which have not gone through a process of adjustment in the evolutionary history. In fact, a majority of mutations which we can observe in our experiments have taken place in the history of the species. Most mutations which improve the "normal" genotypes have had opportunities to become established. Those which have failed to do so are probably unfit in normal environments. Evolution is, however, possible because some mutants and their combinations happen to produce adaptively valuable phenotypes in environments which the species encounters in space or in time. The evidence on which this statement is based must now be considered.

Banta and Wood (1927, 1939) observed a mutation in the water flea *Daphnia longispina*, which normally has the temperature optimum at 20°C. The mutant had an optimum between 25°C. and 30°C. and did not survive at 20°C. This case is very suggestive when compared to that of the little fish *Crenichtys* which inhabits isolated springs in Nevada, some of which have warmer water than others. Sumner and Sargent (1940) have shown experimentally that *Crenichtys* from warm springs may survive in cold ones, but not vice versa. Classification of mutations as favorable or harmful is meaningless if the nature of the environment is not stated.

Timofeeff-Ressovsky (1934a and b) demonstrated that the adaptive values of some of the mutants in *Drosophila* depend upon both the external and the genetic environment (Table 5). Thus, the mutant "eversae" in *Drosophila funebris* is at 15°–16°C. and at 28°–30°C. inferior, and at 24°–25°C. superior to the wild type in viability. The viability of venae abnormes and miniature is only slightly inferior to wild type at 15°–16°C., and much inferior at 28°–30°C. On the contrary, the viability of bobbed is low at 15°–16°C. and approaches normal at 28°–30°C. Overpopulation of the cultures decreases the relative viability in the mutations eversae, venae abnormes, and miniature, but has an opposite effect on bobbed. Combinations of venae abnormes and lozenge, each of which decreases the viability, produce a summation of the deleterious effects; combination of miniature and bobbed gives a compound which is more viable than either mutation by itself. Analogous results have been reported by Altschuler (1930), Csik (1935), and Lüers (1935) for *Drosophila melanogaster*. Kalmus (1941, 1945) found that in three

species of *Drosophila*, the mutant yellow body color is less resistant, while mutants which increase the body pigmentation (black and ebony) are more resistant than the wild type to desiccation. The ebony mutant seems to be less viable than wild type at high tempera-

TABLE 5

VIABILITY OF SOME MUTATIONS AND THEIR COMBINATIONS IN *Drosophila funebris*, EXPRESSED IN PERCENTAGE OF THE VIABILITY OF WILD TYPE (AFTER TIMOFEEFF-RESSOVSKY)

MUTATION	TEMPERATURE (C.)			COMBINATION	TEMPERATURE (C.)
	15°–16°	*24°–25°*	*28°–30°*		*24°–25°*
eversae	98.3	104.0	98.5	eversae singed	103.1
singed		79.0		eversae abnormes	83.7
abnormes	96.2	88.9	80.7	eversae bobbed	85.5
miniature	91.3	69.0	63.7	singed abnormes	76.6
bobbed	75.3	85.1	93.7	singed miniature	67.1
lozenge		73.8		abnormes miniature	82.7
				abnormes lozenge	59.3
				abnormes bobbed	78.7
				miniature bobbed	96.6
				lozenge bobbed	69.2

tures, but not at low ones. Kühn (1932) has found in the moth *Ephestia kühniella* mutant genes that modify the color of the eyes, wing scales, or wing pattern, and that simultaneously reduce the viability of their carriers. A combination of two of these mutants proved, however, to be equal in viability to the wild type.

Dobzhansky and Spassky (1944) have studied the viability in different environments of homozygotes for some second chromosomes derived from natural populations of *Drosophila pseudoobscura* of California (cf. Chaper III). As shown in Table 6, some of the chromosomes have, within the limits of experimental errors, the same effects on the viability at the three temperatures used (Nos. 4, 8, 9). Other chromosomes (Nos. 2, 5, 7, 10, 12) make the homozygotes most viable at 16½ °C., less so at 21°C., and least at 25½°C.; still others do relatively better at the intermediate temperature (Nos. 1, 3, 6, 14), or at the two lower (No. 15), or at the two higher temperatures (No. 13).

Some of the chromosomes shown in Table 6 were, by means of a series of appropriate crosses, transferred into flies of different geographic origin: from Colorado, Mexico, Guatemala, and the state of Washington. Flies were thus obtained which carried the desired second chromosomes of California origin but which had other chromosomes from geographically different strains. The viability of such flies was found to be sometimes significantly lower, but sometimes higher, than that of the flies with pure California genetic background. The conclusion follows that the effects of a chromosome on the viability of its carriers is determined not only by its own gene contents but by the genes carried in other chromosomes as well.

TABLE 6

VIABILITY AT DIFFERENT TEMPERATURES OF HOMOZYGOTES FOR SOME WILD SECOND CHROMOSOMES OF *Drosophila pseudoobscura*, EXPRESSED IN PERCENTAGES OF THE NORMAL VIABILITY (AFTER DOBZHANSKY AND SPASSKY)

CHROMOSOME NUMBER	TEMPERATURE (C.)		
	16½°	21°	25½°
1	0	39	3
2	78	38	7
3	97	104	93
4	108	107	97
5	95	82	68
6	95	103	81
7	89	43	0
8	97	106	98
9	99	98	99
10	83	55	27
11	69	41	30
12	81	64	61
13	90	103	104
14	95	111	90
15	109	109	92

As shown in Chapter III, the homozygotes for some of the chromosomes found in natural populations are "supervital," i.e., display, under the conditions of the experiment, a viability superior to the average for normal flies. It is noteworthy that not one of the "super-

vital" chromosomes tested at the three temperatures proved uniformly superior in all environments. In point of fact, the genotype superior at one temperature usually proved of inferior viability at other temperatures. Gustafsson (1941, 1946a, 1947a, 1950) has, nevertheless, found several agriculturally useful mutants in cereals, and Stubbe and Pirschle (1941) and Brücher (1943) obtained some superior mutants in the snapdragon, *Antirrhinum majus*. These findings are most interesting, but by no means unexpected. The organisms concerned are cultivated plants, which live in environments assuredly different from those in which their wild forbears lived. Their genotypes underwent a short, though rapid, evolution under domestication. The possibilities of improvement by mutation, particularly in traits desired by man, which would not necessarily be useful to plants in natural habitat, are by no means exhausted. Induced mutations may well supply genetic materials valuable to breeders if not to the plants themselves.

A mutational change in the structure of the mouth parts of *Drosophila* which prevents the access of food into the alimentary canal (the mutant proboscipedia) is a monstrosity, and one can scarcely imagine an environment in which such a mutation would be favorable; yet whole families in different orders of insects have mouth parts unfit for feeding. Reduction or disappearance of the eyes is a deterioration, but many insects have no eyes. The mutation "rotated abdomen" has the male genitalia not in the plane of the body symmetry, so that males cannot copulate and are sterile. Nevertheless, twisted genitalia are one of the distinguishing characteristics of some families of flies (Syrphidae and others). An asymmetry of the bill is decidedly deleterious when it appears as an inheritable abnormality in the fowl and in other birds; this does not prevent its being a "normal" character in the crossbill (*Loxia*) (Landauer 1938). A mutation which prevents flowering would spell disaster to most species of higher plants, and yet plants are known that produce flowers only seldom or not at all (for example, *Elodea canadensis* in Europe).

MUTATION AND SELECTION IN MICROORGANISMS

Rapid advances have been made during the last decade in the genetics of bacteria, viruses, and other microorganisms. The fast

reproduction and the small size permit experimentation with numbers of individuals and of generations far greater than could be obtained in higher forms. This makes microorganisms especially suitable for studies on mutation and selection, although the absence or rarity of sexual reproduction in many species is a drawback. Occurrence of changes in bacterial strains has been known for about half a century, but their interpretation had a Lamarckian flavor, as implied by the words "dissociation," "adaptation," "training," etc., used in this connection. It took the brilliant analysis by Luria and Delbrück (1943) and by Demerec and Fano (1945) to open this field for genetic study. Reviews of the field have been published by Luria (1947), Braun (1947), Lederberg (1949), and others. Only some examples of the phenomena observed can be given here.

Cultures of the colon bacteria, *Escherichia coli*, are attacked by bacteriophages, which reproduce in, and cause the breakdown, or lysis, of the bacterial cells. If bacteriophage particles are added to a culture of bacteria, the latter are destroyed within minutes or hours, whereupon the medium contains great numbers of bacteriophage particles capable of infecting other bacterial cells. However, a few cells occasionally survive and form colonies of bacteria that are henceforward resistant to the bacteriophage strain in the presence of which they appeared. Luria and Delbrück showed that the resistance arises by mutation, at the rate of about 2×10^{-8} cell generations, regardless of the presence or absence of the bacteriophage in the environment. The bacteriophage does not, then, produce resistant bacteria; its role is only that of a selective agent which destroys all non-mutant cells. In the presence of bacteriophages the adaptive value of normal bacteria is zero, and only the mutants can survive and reproduce.

Several bacteriophage strains are, however, known, that differ in physiological properties and sometimes also in morphology as seen under the electron microscope. A mutant bacterial strain which is resistant to one bacteriophage may or may not be resistant to others: the resistance is specific. Demerec and Fano (1945) found in a strain of *Escherichia coli* at least eight different kinds of mutants, each resistant to one or more of the seven bacteriophage strains used by these authors. If the bacteria are exposed to the proper bacteriophage, each kind of mutant can easily be obtained. By exposing bacteria to

a succession of bacteriophages, it is possible to build up strains resistant to several or to all phage strains. The rates of mutation to resistance to a given phage strain are independent of what other mutations have occurred previously. This strongly suggests that bacteria, like higher organisms, possess discrete self-reproducing entities, genes, which can undergo changes independently of each other. Coupled with the discovery of a nuclear apparatus in bacteria (Robinow 1941, Delaporte 1950), and with the evidence that sexual fusion and recombination occur in at least some strains (Lederberg 1947), these findings suggest that the genetic mechanisms in bacteria are not radically different from those in other living beings. Luria and Dulbecco (1949) have observed a kind of recombination of genetic traits even in bacteriophages. In another paper Luria (1945) proved that mutations arise in bacteriophages as well as in bacteria. If a large inoculum of phage particles is introduced in a bacterial culture which is resistant to that particular phage, a new phage may be obtained which is able to attack the bacteria resistant to the parental phage strain. The bacteria may, however, become resistant to the new phage by further mutation, and this resistance may be overcome by still another mutation in the bacteriophage.

Since bacteriophage resistance arises by mutation regardless of exposure of the bacteria to the phage, and since resistant bacteria are protected against destruction by phages, it might seem that all bacteria should eventually become resistant. This does not happen because resistant bacteria probably have lower adaptive values than susceptible ones in the absence of phages. Indeed, Anderson (1946) showed that a resistant strain requires for growth the presence in the medium of a certain substance which is not required by susceptible bacteria. Selection keeps down the frequency of resistant mutants in bacterial strains when bacteriophages are absent, but the survival of the species is wholly dependent upon these mutants in the presence of bacteriophages.

The interplay of mutation and selection has been demonstrated with diagrammatic clearness in several instances. If a culture of *Escherichia coli* is treated with enough ultraviolet or X rays to kill most of the bacteria, the survivors give rise to strains which are relatively resistant to these rays. Witkin (1947) has shown that the

resistance arises by mutation regardless of whether the bacteria are irradiated, although the irradiation may increase the frequency of this mutation, just as it increases the frequencies of other mutations unrelated to resistance. The radiation-resistant mutants are not only relatively protected from the injurious effects of ultraviolet rays, but also have shortened lag periods, which enable the mutants to outgrow the parental type. Yet, in cultures which contain mixtures of resistant and normal cells which have ceased to divide because of exhaustion of the food medium, the resistant type is rapidly eliminated.

Demerec (1950) exposed cultures of *Escherichia coli* to streptomycin, which, in proper concentrations, kills all the bacteria except streptomycin-resistant mutants. Some of these mutants are, however, not only genetically resistant to streptomycin, but also streptomycin-dependent, i.e., unable to grow without the presence in the nutrient medium of this substance, which was fatal to their ancestors. However, reverse mutations, which remove the streptomycin dependence occur; by placing a large inoculum of streptomycin-dependent bacteria on streptomycin-free medium, independent strains of the bacteria can be selected. Emerson (1947) similarly obtained strains of the fungus *Neurospora*, which are not only resistant to, but also dependent for growth on the presence in the medium of a certain concentration of sulfonamides, which are poisonous to the normal fungus. Ryan (1946) found a mutant of *Neurospora* which requires leucine in the medium for growth, while normal strains of this fungus grow well without leucine. On media lacking leucine the normal form is the only one able to grow, but on media including leucine the mutant is superior to the parental type. Similar, but more complex, relationships were discovered by Ryan and Schneider (1949a and b, and other papers) in *Escherichia coli*, which grows independently of the presence of histidine in the medium, and its mutant which requires histidine. Demerec (1945) and Luria (1946) showed that penicillin-resistant strains of *Staphylococcus aureus* arise by mutations which survive in the presence of enough penicillin in the medium to kill most individuals of the parental strain. Resistance to very high doses of the drug can be built by summation of several mutational steps. This accounts for the gradual adaptation of bac-

terial strains to unusual environments, which was known in bacteriology for a rather long time but was misinterpreted in a Lamarckian fashion.

LABORATORY EXPERIMENTS ON NATURAL SELECTION IN DROSOPHILA

Natural selection in the laboratory may seem a contradiction in terms. This is, of course, a matter of definition. Artificial selection involves control by man of the reproduction of the organism through choice of individuals which are to be preserved and bred. Placing an organism in an environment in which certain biotypes have an advantage over others does not constitute choice by man of the producers of succeeding generations. Natural selection operates in domestic as well as in wild forms.

L'Héritier and Teissier (1934, 1937) have constructed "population cages," in which containers of culture medium can be introduced or withdrawn without permitting the flies to escape. A mixture with known proportions of flies of desired kinds is introduced into the cage; samples of the developing population can be taken when wished. In a mixture of wild type *Drosophila melanogaster* and its mutant Bar, the frequency of the mutant drops rapidly; the same is true for the mutant vestigial; the mutant ebony is reduced in frequency at first, but after some time the population is stabilized at a level of about ninety percent wild to ten percent ebony. If, however, a mixed population of wild type (winged) and vestigial (short wings, incapable of flight) is kept in a place open to wind, it is the vestigial, rather than the wild type, which increases in frequency (L'Héritier, Neefs, and Teissier 1937). Nikoro and Gussev (1938) and Reed and Reed (1948b, 1950) have devised other types of artificial populations of *Drosophila.* In competition between the wild type and the white-eyed mutant, the latter is eventually eliminated. Reed and Reed find, however, that the lower adaptive value of the mutant is not due to a deficient viability but to an inefficiency of white males in mating. Both red and white-eyed females discriminate against white males, so that for every 100 matings of red males only 75 white succeed (Merrell 1949).

Dobzhansky and Spassky (1947) used seven strains of *Drosophila pseudoobscura* homozygous for certain chromosomes from natural populations, which were known to diminish the viability of the

homozygotes (see Chapter III). In some cases the homozygotes had also reduced development rates, or reduced fertility, or structural abnormalities. Each strain was subdivided into four lines, two of which were bred for 50 consecutive generations in homozygous condition in deliberately overpopulated cultures. Two other lines of each strain were genetically "balanced," in such a way that the chromosomes were transmitted for 50 generations in heterozygous condition; the balanced cultures were not overpopulated. A strong selection pressure must have existed in the crowded cultures, which favored mutations or gene combinations which improved the adaptive values of the flies under the experimental conditions. On the contrary, in the balanced cultures deleterious mutations could accumulate freely, so long as they were recessive and were located in the chromosomes which were transmitted always in heterozygous conditions. The outcomes were strikingly different in the overpopulated homozygous and in the uncrowded balanced lines. Eleven out of the fourteen of the former exhibited significant, and in some instances quite striking, improvements of the viability. In some of the lines the viability, which at the start of the experiment amounted to less than half of normal, reached a normal value; in some lines the development rates of the flies became faster, or the fertility improved, or the structural abnormalities decreased in extent or disappeared. In contrast to this, eight of the fourteen balanced chromosomes became lethal when homozygous, five were not changed significantly, and one improved slightly.

Here, then, we have adaptive genetic changes, obtained in an experiment in response to selection. Such changes do not in any way contradict the argument presented above, to the effect that useful mutations are unlikely to be discovered in normal strains under normal conditions. For the initial materials in the experiment consisted of seven subvital or even semilethal genotypes which are individually rare in nature; and the mutations have caused merely a partial restoration of the normal fitness in the homozygous strains. On the contrary, more than half of the balanced chromosomes acquired recessive lethals. This is a consequence of the fact that harmful mutations are much more frequent than useful ones, and that the balanced chromosomes were sheltered from the control by natural selection for fifty generations.

EXPERIMENTS ON SELECTION IN ORGANISMS OTHER THAN DROSOPHILA

Experiments on competition of different strains of the dandelion (*Taraxacum officinale*) have been made by Sukatschew (1928). This plant reproduces usually by apogamy (parthenogenesis), so that the offspring of an individual are, in general, genotypically like their parent. The dandelions growing in a locality usually do not form a Mendelian population, but simply a collection of non-interbreeding strains. Three plants were collected on the same meadow near Leningrad, and the strains, denoted as A, B, and C, respectively, were established from them; the strains proved to be morphologically recognizable. Seedlings were planted on experimental plots in two densities, namely, at a distance of three and of eighteen centimeters from each other, respectively. On some plots, representatives of a single strain, and on others of all three strains, were planted. After a lapse of two years the number of surviving individuals was counted. The percentage of individuals that had died on plots bearing a pure stand of a single strain was found as follows:

DENSITY	STRAIN A	STRAIN B	STRAIN C
Low	22.9	31.1	10.3
High	73.2	51.2	75.9

Strain C is most viable at a low and B at a high density. But in mixed stands, where the three strains grow side by side and compete with each other, the percentages of the individuals that die prove to be different, namely:

DENSITY	STRAIN A	STRAIN B	STRAIN C
Low	16.5	22.1	5.5
High	72.4	77.6	42.8

Strain C is distinctly superior to A and B at both densities employed. Besides the survival of individual plants, the numbers of flowers per plant was recorded. At the low density in pure stands, the number of flowers was highest in strain B and lowest in C, but in mixed stands C was highest and A lowest. At the high density in pure stands, strain C had least and A and B most flowers, but in mixed stands the relation was reversed. It is clear that the flower production

in a strain is not always correlated with its viability, and the adaptive value of a strain is a function of the environment in which it is placed.

In a second series of experiments, Sukatschew compared the viability of strains of different geographical origin grown under the climatic conditions of Leningrad. The two local strains, B and C, were used, and also a strain X from the extreme north (Archangel), Y from the northeast (Vologda), and Z from the south (Askania-Nova, north of Crimea). In pure stands the strains gave the following percentages of mortality:

DENSITY	B	C	X	Y	Z
Low	31.1	10.3	39.6	22.9	73.0
High	51.2	75.9	63.0	71.6	82.0

The southern strain (Z) is a failure in the new environment, but the Vologda strain did at least as well as one of the local ones (B) at the low, and the Archangel strain at the high, density. For technical reasons it was not convenient to grow all the five strains in mixed cultures, but two experiments were carried on, each with four strains in a mixture. The results are shown in Table 7.

TABLE 7

PERCENTAGE OF DEAD INDIVIDUALS IN MIXED CULTURES OF DIFFERENT STRAINS OF *Taraxacum officinale*
(AFTER SUKATSCHEW)

DENSITY	FIRST EXPERIMENT				SECOND EXPERIMENT			
	B	C	X	Y	B	X	Y	Z
Low	66.3	37.5	66.6	50.0	4.2	12.5	8.3	41.6
High	99.5	96.3	56.0	49.2	89.0	29.3	72.8	99.0

The results obtained may seem paradoxical: the Archangel and the Vologda strains (X and Y) show in dense stands definitely greater survival values than the local strains, B and C. At the lower density, however, the local strains at least hold their own in competition with foreign ones.

Experiments very similar to those of Sukatschew were performed by Harlan and Martini (1938, see also Stebbins 1950) on eleven

varieties of barley planted at ten stations located in various parts of the United States. Different varieties proved to be victorious in competition in different environments.

HISTORICAL CHANGES IN THE COMPOSITION OF ANIMAL POPULATIONS

Darwin conceded that evolution is so slow that no changes are noticed within a human lifetime in wild species. The changes brought about by artificial selection are a model of evolution rather than evolution as such. Since Darwin's time, instances of historical changes have been recorded. Major evolutionary steps are still beyond reach of direct observation, but we need not make such a concession regarding microevolutionary processes. Instances now to be reviewed unmistakably owe their origin to natural selection.

Fumigation with hydrocyanic gas is a most efficient method of controlling scale insects (Coccidae), attacking citrus trees in California. A concentration of the gas sufficient to kill nearly 100 percent of scales had been worked out and applied at regular intervals. In 1914 it was noticed that in orchards near Corona the standard fumigation was insufficient to destroy the red scale (*Aonidiella aurantii*), although in previous years no difficulty had been encountered. This condition has persisted at Corona since 1914 and has spread to several other citrus-producing areas; in other localities the standard fumigation continues to give satisfactory results (Fig. 2).

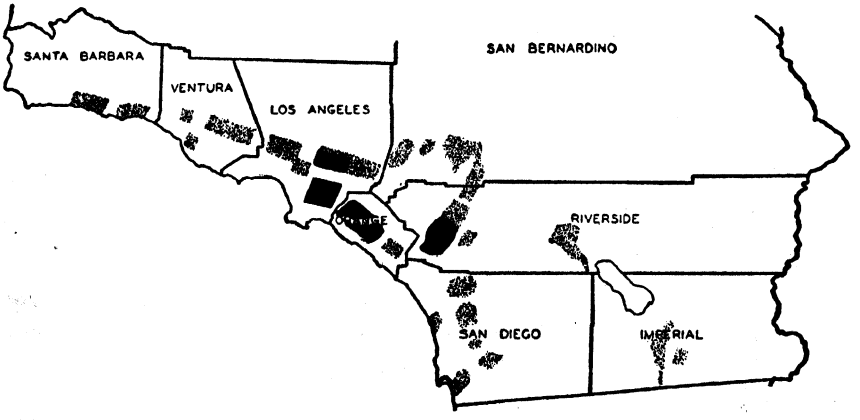


Fig. 2. The distribution of the resistant (black) and of the nonresistant (stippled) races of the red scale (*Aonidiella aurantii*) in southern California. (After Quayle.)

Experiments of Quayle (1938), Dickson (1940), and others, showed the presence of genetically distinct strains of red scale, one nonresistant and the other relatively resistant to hydrocyanic gas. According to Dickson, exposure for 40 minutes at 24°C. to the concentration of 0.188 mg. of HCN per liter of air permits the survival of only 4 percent of individuals of the nonresistant, and of 45 percent of the resistant, strain. A similar exposure to 0.351 mg. of HCN per liter of air leaves 0.75 percent survivors in the nonresistant and 22 percent in the resistant strain. Dickson has crossed the two strains. The F_1 is intermediate in resistance, and in F_2 a segregation takes place which shows that the two strains differ in a single incompletely dominant gene. The question whether the gene for resistance in the Corona population arose by mutation or was introduced from elsewhere is largely academic. The former possibility is on the whole more probable; populations of the red scale in badly infested orchards are so large that even if the mutation rate producing the gene for resistance is very low, mutant individuals should be present in the citrus-growing area at any time. However that may be, the emergence of the resistant red scale is probably due to differential survival of resistant and nonresistant genotypes in fumigated orchards. According to Hardman and Craig (1941), the physiological basis of the resistance is an ability of the insect to keep its spiracles closed for at least 30 minutes under unfavorable conditions, while the nonresistant strain has its spiracles closed only for one minute. This has not, however, been confirmed by other investigators.

Cyanide-resistant strains have appeared also in the citricola scale, *Coccus pseudomagnoliarum*, near Riverside, California, in 1925, and in the black scale, *Saissetia oleae*, near Charter Oak, California, in 1913. By 1915, the resistant black scale spread over a solidly planted citrus belt for a distance of about 40 miles. Attempts to control it by fumigation were abandoned (Quayle 1938). In recent years, origin of strains of the housefly, *Musca domestica*, relatively resistant to DDT and certain other insecticides has been observed in diverse parts of the world, among them Italy, northern Sweden, and several parts of the United States (see Babers 1949, and King and Gahan 1949 for references). In all cases failures of DDT sprays which were known to control fly populations are observed, whereupon this failure becomes chronic in a given locality. Some authors

were able to observe the development of resistance in laboratory colonies of the fly exposed to sublethal doses of DDT insecticides for 14 to 17 generations, the survivors of the treatment serving as progenitors of the following generations of the strain. Furthermore, it has been claimed that the resistance is lost in about the same number of generations if the resistant strain is bred without further exposure to the insecticide. If this is confirmed, the most probable interpretation would be that the population is a mixture of relatively resistant and nonresistant genotypes, and that the latter have higher adaptive values in the absence of DDT. In any case, the parallelism between the development of resistance to insecticides in insects, and of that to bacteriophages or to antibiotics in bacteria, is striking. Smith recognized as early as 1941, that economic entomologists are confronted with a situation when methods of control once considered satisfactory may no longer suffice, because the pests to be controlled undergo changes themselves.

It has been known for a long time that artificial selection for desirable qualities in domestic animals and plants must be steadily kept up if "deterioration" of the breeds is to be prevented. Such "deterioration" is especially rapid if domesticated forms escape from cultivation and revert to wild (feral) existence (see Hutchinson and Manning, 1945, for a discussion of "deterioration" in cotton). The simplest, although hypothetical, explanation of these phenomena is that some traits of domesticated species which are valuable to man are more or less deleterious to the organisms themselves, and that natural selection tends to suppress or eliminate such traits. A striking case of this sort is the Porto Santo rabbit, which was quoted by Darwin as the only known instance of species formation in historical times. Some domestic rabbits were liberated on the island of Porto Santo, in the Atlantic Ocean, in the fifteenth century, and their progeny now differs from any domestic breeds in many structural traits, as well as in being difficult to tame. Nachtsheim (1941) has recently reinvestigated the situation, and found that, although the Porto Santo rabbit unquestionably belongs to the same species as the domestic one, the differences are largely genotypic. The English sparrow introduced in the United States from Europe has changed detectably in its new home; the average size of the birds has increased, and they became differentiated into incipient local races

(Calhoun 1947). A significant change has taken place also in the bird *Serinus canaria* in Germany to which this species has spread since the year 1800 (Rensch 1941). An unmistakable trend towards a rounder (brachycephalic) skull shape is noticeable in historic times in human populations of Europe, and in fact of the entire world (Weidenreich 1941, 1945, 1946). The adaptive significance of this trend is, however, purely conjectural.

HISTORICAL CHANGES IN PLANT POPULATIONS

Very extensive and carefully collected data are available in the phytopathological literature on changes in the stem rusts of wheat, *Puccinia graminis tritici*, and other species attacking crop plants. Some species of rust fungi are differentiated into "biological races" adapted to different hosts, on which they live as parasites. A variety of *Puccinia graminis* (var. *tritici*), attacks wheat, another attacks rye, oats, *Poa*, and other grasses. The wheat rust is in turn subdivided into numerous "races," as they are called by phytopathologists, of which at least 189 are known. These "races" are identified by testing their ability to infect, and by studying the form of the lesions produced on, a collection of wheat varieties; each wheat variety is immune to some but susceptible to other "races" of the

TABLE 8

PERCENTAGE FREQUENCIES OF "PHYSIOLOGIC RACES" OF THE RUST *Puccinia graminis tritici* IN THE UNITED STATES IN DIFFERENT YEARS (AFTER STAKMAN ET AL.)

	RACES								
YEAR	*11*	*17*	*19*	*21*	*34*	*36*	*38*	*49*	*56*
1930	4.0	0.3	0.6	6.7	0.6	36	30	20	0.2
1931	22	0.6	1.3	4.0	2.1	28	15	25	1.0
1932	4.9	1.4	4.9	1.6	0.9	9.6	46	27	2.1
1933	1.7	1.4	1.4	4.5	7.1	3.7	33	37	3.7
1934	0.6	0.6	0.3	7.4	22	21	2.8	1.3	33
1935	19	1.5	1.3	1.8	18	6.1	4.6	1.4	44
1936	12	4.4	1.2	0.8	4.2	3.0	22	1.2	47
1937	8.4	6.1	3.1	0.6	1.1	6.0	8.7	7.4	56
1938	2.0	3.0	6.4	1.0	0.8	1.2	16	0.9	66
1939	3.2	10	3.3	0.4	0.6	0.8	24	0.6	56
1940	4.2	34	2.2	0	0.5	1.8	10	1.2	44
1941	1.3	51	3.8	0	0	2.5	6.0	2.4	32
1942	0.3	27	6.2	0	0.2	2.3	27.3	3.9	31
1943	0.1	23	1.9	0	0.1	0.4	24.4	0.3	49
1944	0	21	6.6	0	0	0.2	26.1	0.2	43

rust (Stakman 1947). A census of the frequencies of the different "races" has been taken in the United States and other countries for about two decades (Stakman et al. 1943). The rust population has altered during this period (Table 8).

The "races" Nos. 36 and 49 were prevalent until 1933, but later became much less common. No. 56 was rare until 1934 but became the most widespread after that; No. 34 was common between 1933 and 1935, etc. These quite spectacular changes have been caused largely by planting of new wheat varieties, and, presumably, also by climatic fluctuations. Wheat breeders select and introduce in agricultural practice new varieties, which are more or less resistant to rust "races" which are prevalent at the time and in the geographic regions where the breeding is practiced. Thus, rust "race" No. 56 was first found in the United States in 1928, soon after the wheat variety *Ceres* susceptible to it was planted on a large scale. The rapid increase of No. 56 caused a drastic reduction first of the yield, and then of the plantings, of the *Ceres* variety. What is involved, then, is a competition between artificial selection directed by man at the wheat plant, and natural selection in the rust fungus.

It is by no means accidental that evolutionary changes observed during historic time involve mostly the organisms directly or indirectly associated with man. Human activities have caused environmental alterations on a quasi-geological scale and of unprecedented rapidity; as a consequence, many organisms had either to undergo adaptive changes or to die out. A change in some English populations of the primrose, *Primula vulgaris*, described by Crosby (1949) seems however unrelated to man. Three types of flowers exist in this plant: those with a long style and anthers deep in the corolla tube (termed "pin"), with a short style and anthers at the opening of the corolla (called "thrum"), and those with the stigma and anthers at the same level (termed "homostyle"). This polymorphism is due to three alleles of a gene: S for thrum, s for pin, and s′ for the homostyle condition. Populations which consist of pin and thrum plants reproduce mostly by crosses between these two types of plants, since the matings pin × pin and thrum × thrum are rarely successful. Homostyles usually reproduce by self-pollination, but their pollen can also fertilize thrum plants. Thus, the homostyles send a part of their pollen to thrum plants but do not receive thrum pollen in return.

This gives to the homostyles, and to the gene allele s′, a selective advantage in populations containing the three types of plants. Indeed, population counts in two localities where homostyles occur suggest that their frequencies are increasing with time.

CORRELATED RESPONSES TO SELECTION

The differences observed between races and species of primitive as well as of complex organisms very often involve characters the adaptive value of which is highly problematic. This apparent adaptive neutrality of genetic differences forged in the process of evolution seems to be perhaps the greatest obstacle encountered by the theory which regards evolution as essentially a process of adaptation to the environment through natural selection. Darwin was fully aware of this difficulty. It would, indeed, verge on the ridiculous to believe that every particular of the organic structure must necessarily be useful as such. However, it was pointed out in the discussion of manifold effects of genes (Chapter II), that a seemingly neutral trait may represent only a part of the total field of action of a gene. The evolutionary fate of a gene is determined by its effect on the overall adaptive value of the genotypic "gestalt". Perfection of certain organs may confer so great an advantage on a species by making it an undisputed possessor of an ecological niche that other organs may undergo rudimentation. According to Murphy (1939), species of man-o'-war (*Fregata*) are among the most common and successful types of marine birds in the tropical zone. Yet, these unsurpassed fliers are awkward out of the air because of their nearly rudimentary legs. "The birds sometimes lose their balance and, before they can launch into flight, slither helplessly down the branches . . . to a lingering death made certain by their inability to clamber out of the tangles to some jumping-off place." They are even more helpless in water; they can neither swim nor rise into the air from water surface or from flat ground, and their plumage easily becomes waterlogged.

A spectacular illustration of usefulness of an apparently neutral trait is provided by the work of Jones et al. (1946) and Walker (1951) on the resistance of varieties of onions to the smudge, *Colletotrichum circinans*. Two alleles of a gene, *I* and *i*, determine the coloration as well as the resistance to the fungus: the homozygous,

II, bulbs are white and highly susceptible to the infection, the heterozygotes, *Ii*, are cream-colored and slightly susceptible, and the homozygotes, *ii*, are deeply colored and highly resistant. The scales of colored bulbs contain protocatechuic acid and catechol. These substances can be shown to be toxic to ungerminated spores and to mycelia of the fungus.

The existence of correlations between different body parts and functions has been known since pre-Darwinian times (Cuvier). A living body is not a sum of independent parts but an integrated whole. This is in no sense contradicted by recognition of the corpuscular nature of heredity. A mosaic of genes engenders an integrated development. Because of manifold effects of genes, a change in an organ often brings alterations in developmentally related organs. Thus, relatively slight increases in body size result, because of heterogonic growth, in great increases of antler sizes in deer (Huxley 1932). Or else, establishment of a genetic change in one organ may require readjustments elsewhere in the body through selection of mutations of other genes, to restore a balanced genotype. The adaptive significance of some traits may, then, be quite obscure if the correlational systems are unknown. Rensch (1947, 1948, 1949) and his school have undertaken comparative morphological and histological studies to clarify this old problems of correlations. Both in vertebrates and in invertebrates, they find that changes in general body size are accompanied by diverse alterations in cell size and cell numbers in various organs, by differences in eye structure, in relative sizes of some endocrine glands, in brain size relative to that of the head capsule (in insects), in spatial arrangement of muscles in the thorax, in behavior and learning ability, etc.

Paleontological data on the phylogeny of many groups of organisms reveal more or less persistent trends of changes of various kinds. This has led to theories of orthogenesis, according to which evolution is impelled by some autonomous directive force, rather than by selection of genotypes useful in certain environments (see, for example, Vandel 1949). Simpson (1944, 1949), Rensch (1947), Newell (1949), and others have shown that such persistent trends may be accounted for by "orthoselection" for some adaptively useful traits, such as progressively increasing body

size may, however, bring in its wake numerous correlated changes in traits which have no adaptive significance by themselves.

A quite different mechanism of correlation of traits in selection has been studied by Wigan and Mather (1942) and Mather and Harrison (1949). Artificial selection for high and low numbers of bristles on abdominal sternites was made in a strain of *Drosophila melanogaster* for 112 generations. Apart from changes in bristle numbers, the selection brought about unexpected effects on fertility: several of the lines selected for low bristle numbers became sterile. Some of the selected lines acquired also another trait which was not manifest in the original strain: up to 35 percent of the females had 0, 1, 3, 4, or 5 spermathecae, instead of the normal number, which is 2. Other traits altered were body pigmentation, eye form, and mating behavior. The most probable interpretation of changes in these several traits, although only bristle numbers were selected, is as follows. These traits are determined by complexes of genes with small individual effects (polygenes). The polygenes are scattered at random in the chromosomes, and it often happens that polygenes which, for example, lower the bristle number lie in the same chromosomes with polygenes which influence fertility, or spermatheca number, or mating behavior. A selection for a low bristle number brings, therefore, unexpected correlated changes in these other traits, which are not physiologically correlated with bristles. Since natural selection augments the adaptive value of the genotype as a whole, neutral, and even slightly deleterious, traits may be promoted by selection if they happen to be connected with useful ones.

PROTECTIVE AND WARNING COLORATIONS AND RESEMBLANCES

Becoming inconspicuous in normal surroundings, or acquiring a resemblance to some object which is dangerous or distasteful to natural enemies, are among the possible ways in which an organism may become adapted to its environment. By the first method, the organism escapes the notice of its predators, or, in the case of the predator itself, is able to approach the prey without being prematurely noticed by the latter. The second method leads the organism, contrariwise, to become as conspicuous as possible to advertise its presence and to warn its potential enemies of its obnoxiousness. A special kind of

warning coloration and form is *mimicry*, whereby a harmless creature resembles some other which is in fact obnoxious (Batesian mimicry). The different forms protected by being dangerous or unpalatable and by having warning colorations may become even more thoroughly protected if they resemble each other, so that their enemies need learn a single sign of distastefulness instead of many (Müllerian mimicry).

Theories of protective resemblance and of mimicry were developed and widely used by the early Darwinists as illustrations of the action of natural selection and of evolution in general. The greatest effervescence of these theories was in the late nineteenth and early twentieth centuries. Undoubtedly much uncritical speculation has been indulged in by some writers, bringing disrepute to the whole theory. The dangers of assuming that a given coloration is protective or mimetic are admittedly great. What to a human eye may seem to be a similarity between an organism and some inanimate object or some other organism need not be such to the eyes of a predator against whom the protection is supposed to operate. Some of the alleged protections and warnings have been shown to be armchair protection and museum mimicry. Nevertheless, the theory has survived both criticism and the damage done by its overenthusiastic supporters (see Cott 1940 for an excellent review).

The theory of protective coloration is no longer based on mere belief that this or that animal is not easily visible in its natural surroundings. Initiated by the at first unappreciated work of Thayer in the second decade of this century, the techniques of camouflage by countershading, by dazzling or disruptive patterning, and concealment of the shadow have grown to be a full-fledged branch of technology having important applications, among other things, in military affairs (Cott 1940). There can no longer be a reasonable doubt that many animals are camouflaged in their natural surroundings. It is of course, a different problem whether the camouflage has developed under the influence of natural selection, because of the protection from enemies which these properties confer on their carriers. Here one can proceed only by inference, with experiments pointing the way. Such experimental data as are available support the natural selection theory. Thus, Sumner (1935 and other works) showed that fishes whose color contrasts with their surroundings are caught by

predators more easily than those with harmonizing colors. He used the little fish *Gambusia partuelis*, which, owing to the expansion and contraction of its pigment-bearing cells, becomes darker or lighter when placed in tanks with respectively dark or light bottoms. Galapagos penguins, fish-eating birds, caught 70 percent of fishes which were contrastingly colored and only 34 percent of those which were adaptively colored. In another experiment, with the sunfish *Apomotis cyanellus* as the predator, 53 percent of the nonadapted and 25 percent of the adapted *Gambusia* were destroyed. Analogous experiments have been published by Dice (1947), who studied the selection by owls of different local races of the mice *Peromyscus maniculatus* which contrast in color with the experimental background. Protectively colored mice were eaten less frequently than the contrastingly colored ones. For other experimental evidence, see Cott (1940).

McAtee (1932) examined the stomach contents of about 80,000 birds, and recorded the insects found therein. The insects which were regarded as being protectively or warningly colored are eaten by birds, allegedly in numbers proportional to the abundance of the different insects in the environment of the respective birds. It is, however, evident that our information on the relative abundance of different insects in natural habitats is, to put it conservatively, inexact. To conclude, as McAtee has done, that the whole theory of protection is a myth, is to succumb to the old fallacy that only absolute immunity from attacks by predators can make natural selection effective.

ORIGIN OF DOMINANCE AND THE STABILIZING SELECTION

Studies on the origin of Mendelian dominance may shed light on some basic mechanisms of evolution. The most pertinent facts concerning dominance may be briefly summarized as follows. Among the numerous mutants known in *Drosophila melanogaster* and related species, a majority are nearly or completely recessive to the normal, or wild-type, condition (Bridges and Brehme 1944). A similar situation obtains in the snapdragon, *Antirrhinum majus* (Stubbe 1941), and in most other organisms in which mutants have been observed (in poultry a considerable proportion of the mutant genes are, however, dominant, see Fisher 1935). In *Drosophila*, none of the relatively rare mutants classified as dominants suppress the action of

their normal alleles completely; these mutants are more correctly described as neither dominant nor recessive. When, however, a gene produces several mutant alleles, no dominance is usually exhibited in heterozygotes which carry two such mutants. Dominance is the rule only where gene alleles commonly found in natural populations are involved.

The pioneering work of Harland (1932a and b, 1933, 1935, 1936, Harland and Atteck 1941), ably developed by Hutchinson (1934, 1946), Hutchinson and Gadkari (1937), Silow (1939a, b), Stephens (1944, 1945), and others on species of cotton, *Gossypium*, has established the important fact that the existence, as well as the extent, of dominance and recessiveness are determined by the structure of the genotype as a whole. In some cotton species mutant genes are known which exhibit fairly complete dominance and recessiveness in F_1 hybrids within a species, and which give clear-cut segregations in 3 dominants: 1 recessive in F_2 hybrids. The same mutant types which, when tested within a species, give clear-cut Mendelian segregation ratios, display a blending type of inheritance in the species hybrids. Thus, both in *Gossypium barbadense* and in *G. hirsutum* there exist variants with and without purple spots on the petals. Within either species the presence of this spot is a simple dominant compared to its absence. In the *G. barbadense* × *G. hirsutum* hybrids, the F_1 has a small spot, and in F_2 there occur plants with very large spots, without spots, and with intermediate spots of all sizes. By proper backcrossing of the hybrids to the parental species it is, however, possible to extract strains having either predominantly *G. barbadense* or predominantly *G. hirsutum* germ plasms. In such strains the presence or absence of the petal spot is again inherited in a simple manner. An analysis of this situation has led to the following conclusions. The presence of the petal spot in either species is caused by the gene S^B and its absence by its allele S^b; moreover, in *G. barbadense* there exist a complex of modifying genes the combined effects of which is to give a large spot in the presence of S^B. In *G. hirsutum* there is a modifier complex which makes the petal spot small. In the interspecific hybrid both the gene S^B and the modifying genes undergo segregation, hence the inheritance of the petal spot is blending instead of simple.

Inheritance similar to that of the petal spot is observed for many other characters studied in *Gossypium barbadense* × *G. hirsutum* as well as in other hybrids. In fact, clear-cut Mendelian segregations prove to be an exception in interspecific crosses. Not only are complexes of modifying genes involved, but also the "major" genes are frequently represented by different alleles in different species. The interactions of such major and minor gene complexes result, then, in development of characters "normal" for a given species. But even when the species are similar with respect to some characters, the similarity may prove illusory, since the genetic bases of these characters, as shown by the segregations in the interspecific hybrids, may be different. Harland concludes that species of *Gossypium* differ in hundreds or in thousands of genes combined to form coordinated systems, and that "the modifiers really constitute the species". Even when the end products of two or more evolutionary lines appear rather similar, the similarity may be attained by different means.

Variations in dominance may, thus, arise from two causes. First, a species may carry several wild-type alleles, some of them more and others less completely dominant over recessive mutant alleles at the same locus. Secondly, the dominance of the normal over mutant alleles may be bolstered by a system of modifying genes at other loci. Apart from cotton, dominance modifiers and the presence of several dominant alleles of varying potency have been established in several organisms. Helfer (1939) found considerable variations in the degree of dominance of the gene Scute in crosses with wild strain of *Drosophila pseudoobscura* from different geographic regions, and showed that these variations were caused by modifying genes located mostly in chromosomes other than that which carries Scute itself. Spencer (1944) discovered a remarkable multiplicity of wild-type alleles of the gene bobbed in natural populations of *Drosophila hydei*. Dunn and Landauer (1934, 1936), Dunn (1937a), Mather and North (1940), and others studied dominance modifiers in poultry and mice. These authors showed that some dominance modifiers affect the expression of genes only in heterozygotes, while others affect heterozygotes as well as homozygotes. Most important, dominance modifiers frequently have various effects of their own, aside from their influence on the expression of other genes. This amounts to saying that

dominance modifiers are not a class of genes subsidiary to others, but merely genes with manifold effects which influence, among other things, the expression of certain mutants at other loci.

Fisher (1928, 1930, 1931, 1932, 1935) proposed a theory of the origin of dominance through selection of modifying genes which tend to make mutant heterozygotes resemble the wild type. We know that a great majority of mutations that arise in any species are deleterious to their carriers. It is also known that deleterious mutants are present in natural populations mostly as heterozygotes, homozygotes being relatively rare (Chapter III). It follows that natural selection deals mainly with mutant heterozygotes. Fisher argued, then, that any genes which suppress the effects of mutants in heterozygotes, in other words which make the mutants recessive, will be selectively advantageous, and will tend to become established in the species genotype. Haldane (1930, 1939), Muller (1932), and Plunkett (1932) pointed out that dominance may also arise through selection at each locus of potent alleles able to suppress the deleterious effects of most mutants which arise at that locus.

Wright (1929, 1934), Muller (1932, 1950a), and Schmalhausen (1949) have pointed out that the origin of dominance, either through modifiers or through selection of strong wild-type alleles, must be considered not something apart from the formation of generally adapted genotypes, but a necessary corollary of the fact that the development is an integrated system of physiological reactions. As stated in Chapter II, the end result of development is, in environments which the species frequently encounters, what we describe as the normal, or wild-type, condition. The reaction norms of the wild genotypes are such that the usual range of environmental variations evokes adaptive modifications, and insures the development of vitally necessary organs and traits. The development is buffered against environmental shocks. The formation in evolution of genotypes with safely buffered reaction norms is due, according to Schmalhausen, to a form of natural selection which he calls stabilizing selection, in contrast to the dynamic selection which acts to produce genotypes adapted to new environments or to new ecological opportunities. The genes guide development through production of enzymes; each gene must yield its normal quota of these gene products. It may well be that threshold reactions are frequently involved, and doubling or

even multiplication of the effectiveness of a gene results in no appreciable modification of the normal course of the development, but a halving of the activity leads to retardation or arrest of the whole chain of reactions. Under such conditions, wild-type alleles which possess a "factor of safety," that is which have an activity well above the necessary minimum, will be of advantage to the organism. A mutation that curtails the activity of such a gene will, then, be recessive to the normal allele. Stabilizing selection favors alleles dominant over mutants which limit the efficiency of the respective genes.

V : Adaptive Polymorphism

TYPES AND POPULATIONS

PLATONIC PHILOSOPHY considers the elusively multiform, always changing natural phenomena to be mere shadows of the immutable ideas, of the eternally fixed essences of things. This philosophy has appealed to many scientists. Individual organisms and living populations are often supposed to represent imperfect incarnations of ideas, patterns, or types of their respective races, species, genera, etc. In 1896, the great anthropologist and pathologist Virchow defined human races as "acquired deviations from the original type" (see Count 1950). Acceptance of the biological evolution theory did not completely overcome the notion that the annoying variability of individuals is somehow a false front which conceals slowly changing racial or species types. The fiction of types is indeed helpful for the purpose of classification and of cataloguing of organisms (Chapter IX). It is also a great, though highly misleading, simplification for a physiologist or a medical man to believe that different individuals, or different patients, should react alike to similar treatments. The fictitiousness of the types has been shown by the Hardy-Weinberg's demonstration of the genetic equilibrium (Chapter III). The spatio-temporal entities in sexually reproducing and cross-fertilizing organisms are individuals and Mendelian populations. Every individual carries a constellation of genes, which is not likely to be found in other individuals. A population has a gene pool, from which the genes of individuals spring and to which they usually return. Gene frequencies and variances, rather than averages, characterize Mendelian populations. Superficially considered, natural populations of most species seem to consist of normal, or wild-type, individuals, among which are scattered aberrant specimens, which owe their origin to mutation. A closer study shows that the wild-type is also a fiction. "Normal" individuals are actually a heterogeneous collection of genotypes, the common property of which is that they possess a tolerable adapted-

ness to the prevailing environments. When the heterogeneity happens to be striking to the eye, or easily detectable by some method, it is referred to as polymorphism. Polymorphism is a loose descriptive term; all Mendelian populations are more or less polymorphic.

GAUSE'S PRINCIPLE

Gause (1934) has stated a simple principle, the significance of which has been pointed out by Lack (1947), Mayr (1947), Crombie (1947), Pittendrigh (1950), and others. Two or more forms with identical ecological requirements cannot coexist indefinitely in the same environment, because one of them will in all likelihood be more efficient than the others, and will eventually outbreed and supplant its competitors. Indeed, absolute equality of adaptive values of two biological forms is, like absolute equality of any two continuously varying characteristics, highly improbable. Now, if the adaptive value of one form is unity, and of the other $1 - s$, then, no matter how small is s, the less well adapted form will be, given enough time, eliminated.

Theoretically, an absolutely uniform and absolutely constant environment could be inhabited by only a single species. So stated, Gause's principle becomes unrealistic, because the very presence of inhabitants in an originally uniform environment makes the latter heterogeneous. The inhabitants may, for example, serve as food for a predator or a parasite, and thus the environment may support at least two ecologically complementary organisms (see Allee et al. 1949). But Gause's principle remains useful, because it emphasizes an important and often overlooked fact. Different living beings with ecological requirements of the same kind (i.e., different herbivores, different predators, etc.) can be sympatric only provided that the environment in a territory which they inhabit is heterogeneous. The heterogeneity may be spatial or it may be temporal. Two species, A and B, can be sympatric if A is more efficient than B in utilization of some food, while B is superior to A in exploitation of another food source in the same territory. Or, A may be better adapted than B in summer, while B is superior to A during the winter season. In reality, environments are always heterogeneous, although some are much more so than others. The heterogeneity permits the development of sympatric diversity of organisms.

Looked at from another angle, polymorphism within a species, or any other kind of diversity of sympatric forms, increase the efficiency of the exploitation of the resources of the environment by the living matter. A single genotype, no matter how versatile, could hardly function with maximal efficiency in all environments. Hence, natural selection has preserved a variety of genotypes, more or less specialized to render the organism efficient in a certain range of the existing environments. As pointed out almost a century ago by Herbert Spencer, division of labor is at least as important on the biological as it is on the sociological level.

CHROMOSOMAL POLYMORPHISM IN DROSOPHILA

Although polymorphism is nearly universal in sexual species, it happens that the most thorough, although by no means complete, understanding of this phenomenon has been secured for a rather covert trait, namely for inverted sections in chromosomes of *Drosophila* flies (cf. Chapter II). The first inversions were detected in *Drosophila melanogaster* through the suppression of crossing over in inversion heterozygotes (Sturtevant 1926, 1931). A less laborious and more exact method of study of inversions is observation of the giant chromosomes in the salivary gland cells of fly larvae (Heitz and Bauer 1933, Painter 1934). These chromosomes appear as cross-striped cylinders or ribbons. The stainable discs which form the striations may or may not correspond each to a single gene, but they form a constant pattern which reflects the gene arrangement in the chromosomes.

Suppose an inversion heterozygote has two chromosomes ABCDEF and AEDCBF. These chromosomes pair by forming a loop, shown schematically in Fig. 3 in the upper right corner. Suppose further that the original, ancestral gene arrangement in a chromosome is ABCDEFGHI. An inversion of the section from B to E gives rise to an arrangement AEDCBFGHI (Fig. 3). A second inversion may take place in this chromosome. The location of the second inversion may be outside the limits of the first: AEDCBFGHI → AEDCBFHGI. Such inversions may be described as independent. An individual heterozygous for ABCDEFGHI and AEDCBFHGI will have a double loop shown second from the top in Fig. 3. The second inversion may occur inside the first, forming included inversions:

ABCDEFGHI → AEDCBFGHI → AECDBFGHI (second from the bottom in Fig. 3). Finally, the second inversion may have one end inside and the other end outside the limits of the first. Such inversions are termed overlapping: ABCDEFGHI → AEDCBFGHI → AEHGFBCDI (the lower right corner in Fig. 3).

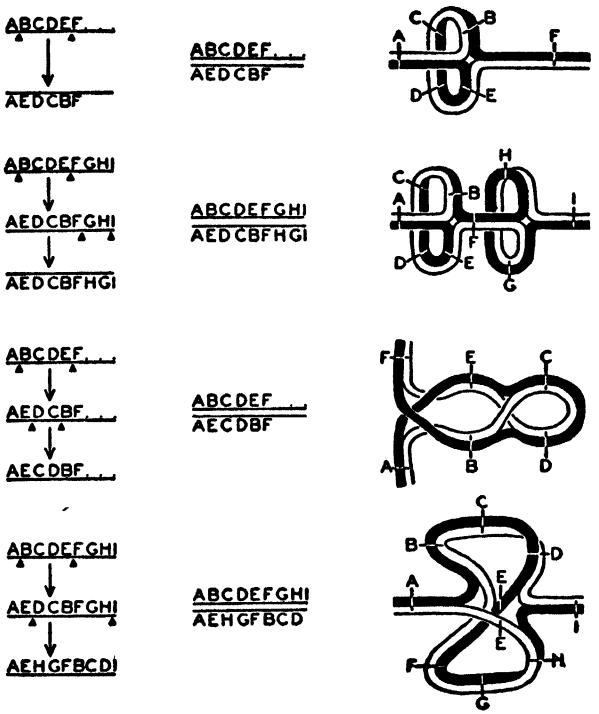


FIG. 3. Chromosome pairing in the salivary gland cells of individuals heterozygous for inversions. Upper row, a single inversion; second from the top, two independent inversions; third from the top, two included inversions; lower row, overlapping inversions.

Overlapping inversions have interesting properties. Suppose we observe in different strains the arrangements ABCDEFGHI, AEDCBFGHI, and AEHGFBCDI. The first can arise from the second or give rise to the second through a single inversion. The same is true for the second and the third. But the third can arise from the first, or vice versa, only through the second arrangement as the probable intermediate step in the line of descent. If we find in natural popula-

tions of some species only the first and the third arrangements, it is probable that the second remains to be discovered, or at least that it existed in the past. If all three are actually observed, the probability of the first and the third being related through the second becomes almost a certainty. To recapitulate, the phylogenetic relationship of the three gene arrangements indicated above is $1 \rightarrow 2 \rightarrow 3$, or $3 \rightarrow 2 \rightarrow 1$, or $1 \rightarrow 2 \rightarrow 3$, but not $1 \rightleftarrows 3$. With independent and included inversions, no determination of the sequence of origin is possible; they are phylogenetically ambiguous. The existence of previously unknown gene arrangements in *Drosophila pseudoobscura* and *D. azteca* was predicted with the aid of the theory of overlapping inversions, and most of these predictions were subsequently verified by discovery of the requisite inversions in nature (Dobzhansky and Sturtevant 1938, Dobzhansky 1941).

Dobzhansky and Sturtevant (1938) and Dobzhansky and Epling (1944) have found that most natural populations of the two closely related species, *Drosophila pseudoobscura* and *D. persimilis*, are mixtures of individuals with different gene arrangements in their chromosomes. The gene arrangement is especially variable in one of the five chromosome pairs which these species have, namely in the third chromosome. Sixteen different gene arrangements are known in the third chromosome of the former and eleven in the latter species. Only one of the gene arrangements, called the Standard, is common to both species (Fig. 4). All these arrangements must have arisen from each other through inversions of some sections of the chromosome, and nearly all of them proved to be related to each other as overlapping inversions. This fact made it possible to construct the phylogenetic chart of the gene arrangements in the third chromosome shown in Fig. 4. Each arrangement is designated by the name of the geographical locality in which it was first encountered. Any two arrangements connected in Fig. 4 by an arrow give a single inversion loop in the heterozygotes. Some of the arrangements (Santa Cruz, Tree Line) had been postulated theoretically as the necessary "missing links" between the other arrangements, and subsequently found when more strains were examined. One of the arrangements (see Fig. 4) remains hypothetical as far as the species *D. pseudoobscura* and *D. persimilis* are concerned, but an arrangement possessing the essential properties

of this hypothetical one has been met with in a related species, *D. miranda.*

None of the gene arrangements shown in Fig. 4 occur over the entire distribution areas of their species; and in no natural population is the complete collection of the arrangements found. The geographic

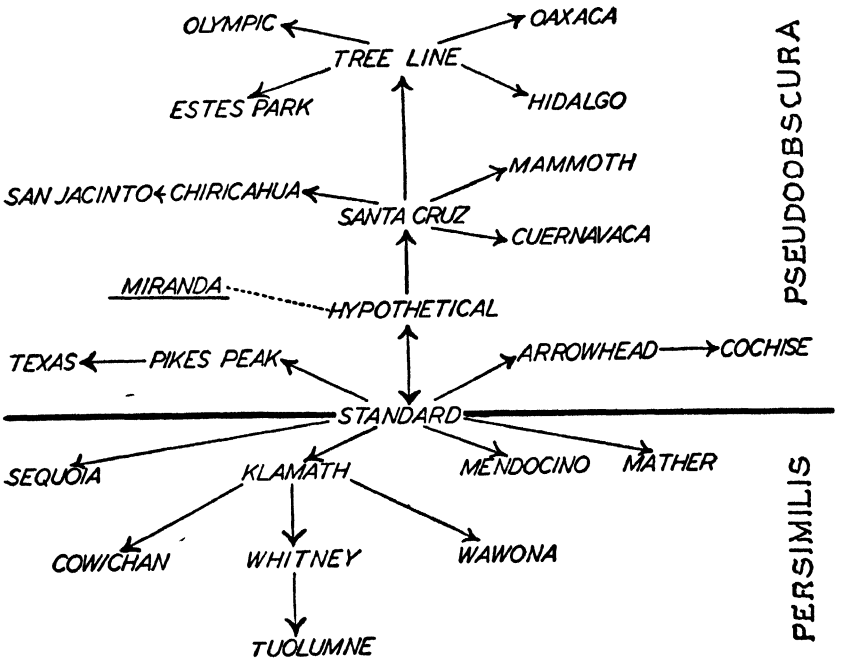


FIG. 4. A phylogenetic chart of the gene arrangements encountered in the third chromosome of *Drosophila pseudoobscura* and *Drosophila persimilis.*

distribution of the gene arrangements will be discussed in Chapter VI. It is sufficient to state here that in some localities up to eight arrangements occur together, and that both inversion homozygotes (flies having two chromosomes with the same gene arrangements) and inversion heterozygotes (flies with two chromosomes of a pair having different gene arrangements) are encountered in nature. The chromosomal inversions thus give rise to a remarkable polymorphism in fly populations.

Chromosomal polymorphism due to inversions is known in natural populations of about 30 species of *Drosophila.* The principal works

in this field are those of Sturtevant (1931), Dubinin et al. (1937), and Ives (1947) on *D. melanogaster*, Kikkawa (1938) on *D. ananassae*, da Cunha et al. (1950) and Dobzhansky et al. (1950) on *D. willistoni* and its relatives, Pavan (1946b) on *D. nebulosa*, Dobzhansky and Sokolov (1939) on *D. azteca*, Miller (1939) on *D. algonquin*, Novitski (1946) on *D. athabasca*, Cavalcanti (1948) on *D. prosaltans*, Dubinin and Tiniakov (1946) on *D. funebris*, King (1947a) on *D. guarani* and its relatives, Carson and Stalker (1947, 1949) and Levitan (1951) on *D. robusta*, and Patterson et al. (1940) and Warters (1944) on species related to *D. virilis* and *D. repleta*. Among the species examined in any detail, only *D. virilis* and *D. hydei* have so far failed to reveal chromosomal polymorphism (Warters 1944).

BEHAVIOR OF INVERSIONS IN EXPERIMENTAL POPULATIONS OF DROSOPHILA

Since representatives of a species of *Drosophila* appear to be alike in visible traits regardless of the gene arrangements in their chromosomes, it seemed at first that the chromosomal polymorphism had no adaptive significance. It is now known that the contrary is the case. The clearest evidence is obtained from experimental populations, which can be maintained for many fly generations in population cages of a type similar to that devised by l'Héritier and Teissier (see Chapter IV). Such populations are started with desired proportions of flies with different gene arrangements. From time to time, samples of larvae in the population are taken, and the incidence of the chromosomal types among them determined by cytological examination.

Figure 5 presents an example of results obtained in an experimental population of *Drosophila pseudoobscura*, which at the start of the experiment contained about 11 percent of Standard (ST) and 89 percent of Chiricahua (CH) chromosomes derived from a natural population of a locality in California. It can be seen that, within approximately 4 months, the frequency of ST chromosomes in the population about quadrupled, then rose more slowly to about 70 percent, after which no further changes occurred. It is clear, that the carriers of ST chromosomes had some adaptive advantages under the conditions of the experiment over the carriers of CH chromosomes, and that the rapid increase of the incidence of the former was

caused by natural selection. But if so, why has selection failed to eliminate CH chromosomes altogether, and to make the population uniformly ST ? As explained below, the establishment of the equilibrium, at which both ST and CH chromosomes are present in the gene pool with definite frequencies, is due to the chromosomal polymorphism being balanced, because the heterozygotes (individuals

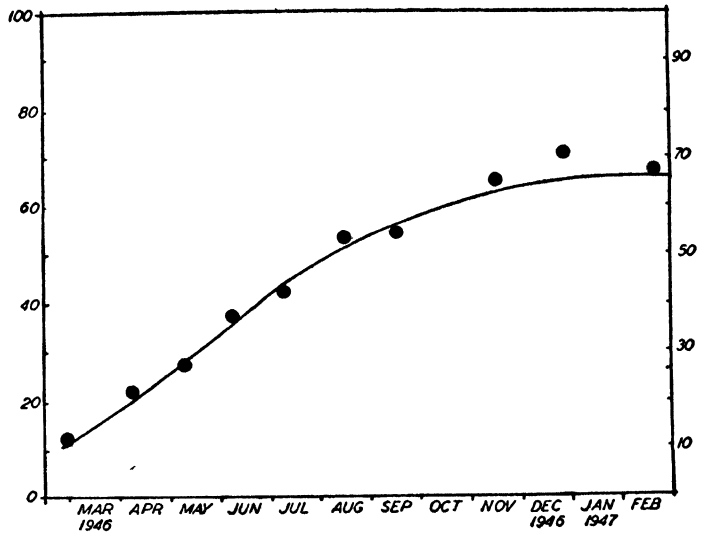


FIG. 5. The frequency of chromosomes with the Standard gene arrangement in an experimental population of *Drosophila pseudoobscura*. At the start of the experiment, this population contained about 11 percent of chromosomes with the Standard, and about 89 percent with the Chiricahua gene arrangement.

having one ST and one CH third chromosome) are superior in adaptive value to both chromosomal homozygotes (ST/ST and CH/CH).

In *Drosophila pseudoobscura*, the establishment of stable equilibria in experimental populations is the rule whenever the competing chromosomal forms are derived from flies collected in the same geographical locality (Dobzhansky 1947a and b, 1949, Wallace 1948). A similar situation has been discovered by Spiess (1950) in *D. persimilis* and by Levitan (1951) in *D. robusta*. It is probable that the chromosomal polymorphism in other species is also balanced. A further interesting fact is an extraordinary sensitivity of the adaptive values of the chromosomal forms to environmental conditions. The experiment

reported in Fig. 5 was carried out at a temperature of 25°C. Populations which contain ST and CH chromosomes show, however, no changes in the relative proportions of the two types if kept at 16°C. In *D. persimilis*, Spiess has, on the contrary, observed changes at 16°C. but in some cases not at 25°C. This means that the chromosomal types are greatly different in adaptive value at one temperature but are nearly or completely equal at another temperature, differing from the first by only 9°C. Da Cunha (unpublished) found that nutritional variables (feeding the flies on different strains of yeasts) also modify these adaptive values. *Drosophila* populations are mixtures of genotypes which differ greatly in environmental optima.

THEORY OF BALANCED POLYMORPHISM

The theory of balanced polymorphism has been developed by Haldane, Fisher, Ford, Wright, and others. Its essentials can be gleaned from the following example. Suppose that in a population of *Drosophila pseudoobscura* a fraction, q, of the gametes carry the Standard, and (1 — q) the Chiricahua gene arrangement in the third chromosomes. Suppose, further, that the flies mate at random with respect to the gene arrangement in their chromosomes, that the adaptive value of the inversion heterozygotes, ST/CH, is unity, and that the homozygotes, ST/ST and CH/CH, have adaptive values $1 - s_1$ and $1 - s_2$ respectively. The frequencies of the chromosomal types before and after selection will, according to the binomial square rule (Chapter III) be as follows:

GENOTYPE	ST/ST	ST/CH	CH/CH	TOTAL POPULATION
Adaptive value (W)	$1 - s_1$	1	$1 - s_2$	$\overline{W}$
Initial frequency	q^2	$2q(1 - q)$	$(1 - q)^2$	1
Frequency after the selection	$q^2(1 - s_1)$	$2q(1 - q)$	$(1 - q)^2(1 - s_2)$	$1 - s_1q^2 - s_2(1 - q)^2$

The rate of change, $\triangle q$, of the frequency of standard chromosomes in the population in one generation will be:

$$\triangle q = \frac{q(1 - q)\,[s_2(1 - q) - s_1 q]}{1 - s_1q_2 - s_2(1 - q)^2}$$

Making $\triangle q = 0$, and solving the equation for q, we obtain: $q = s_2/(s_1 + s_2)$. This means that natural selection will not eliminate

either ST or CH chromosomes from the population, but will establish an equilibrium at which the population will be polymorphic and will contain the two kinds of chromosomes in the gene pool, with frequencies dependent upon the selection coefficients, s_1 and s_2. From the speed of the changes in the frequencies of ST and CH chromosomes observed in the population which is represented in Fig. 5, the adaptive values of the chromosomal types can be calculated. If that of the heterozygotes, ST/CH, is 1, that of the ST/ST homozygotes turns out to be approximately 0.7 ($s_1 = 0.3$), and that of the CH/CH about 0.4 ($s_2 = 0.6$). The frequency of ST chromosomes at equilibrium should, then, be $q = 0.6/(0.6 + 0.3) = 0.67$, which is approximately what has been found in the experiment (Fig. 5). As stated above, these selection coefficients are very strongly influenced by temperature and other environmental variations (Wright and Dobzhansky 1946).

The validity of the application of the natural selection theory to the chromosomal polymorphism in *Drosophila* can be tested by other methods as well. If the differences in the adaptive values of the chromosomal forms lead to a differential mortality between the egg and the adult stage, then the proportions of those types should be different among the eggs and among adult flies. (To be sure, differential mortality need not necessarily be present, since differences in adaptive values may as well be expressed in different fecundity, or longevity, or different sexual activity of the carriers of the chromosomal types.) With experimental populations, the test can be arranged as follows. Samples of eggs deposited by the flies in the population cages are taken, and the larvae from these eggs are raised under optimal conditions, to enable all of them to survive. Examination of the chromosomes in such larvae reveals the chromosomal types to be present in proportions demanded by the binomial square rule, q^2ST/ST : $2q(1 - q)$ ST/CH : $(1 - q)^2$CH/CH. This shows that flies mate at random with respect to the chromosomal type. Now, samples of the adult flies developed in the population cages, under stringent competition of larvae for a limited food supply, are taken, and the chromosomal constitution of these flies is determined. Among the adult flies, the heterozygotes are more, and the homozygotes are less, common than they should be according to the binomial square rule. The differential mortality of the chromosomal types is thus demon-

strated (Dobzhansky 1947b). Wallace (1948) and Heuts (1948) have found some physiological differences between the carriers of certain chromosomal types in *Drosophila pseudoobscura* which may be responsible, in part, for the observed differences in the adaptive values of these types. More information of this kind is, however, needed to correlate the genetical and the physiological pictures.

Dobzhansky and Levene (1948) have adduced evidence of selection pressure on the balanced chromosomal polymorphism also in natural populations of *D. pseudoobscura.* Females, which had mated with males in their natural habitats, were collected, and allowed to produce offspring in the laboratory, under optimal conditions. In these offspring, the inversion homozygotes and heterozygotes were present with frequencies conforming to the binomial square rule. A small but significant excess of heterozygotes, and a corresponding deficiency of homozygotes, were however found among the adult flies (males) captured outdoors. Thus, in natural, like in the experimental, populations the mating is at random with respect to the chromosome structure; but a differential mortality favoring the heterozygotes relative to the homozygotes takes place during the development of the flies.

BIOLOGICAL FUNCTIONS OF THE CHROMOSOMAL POLYMORPHISM IN DROSOPHILA

The experiments just described throw light on certain very remarkable phenomena observed in natural populations of *Drosophila pseudoobscura* and other species. If samples of populations are taken repeatedly in the same localities, the relative frequencies of chromosomal types can be shown to undergo cyclic seasonal changes. A summary of observations in a locality on Mount San Jacinto, in California, conducted from 1939 to 1946 is presented in Fig. 6. The three commonest gene arrangements in this population are Standard (ST), Arrowhead (AR), and Chiricahua (CH). The frequency of ST decreases, and that of CH increases, from March to June; the opposite change takes place during the hot season, from June to August.

Now, since the gene arrangement in a chromosome is a hereditary trait, we are dealing here with genetic changes in the constitution of a population. These are evolutionary changes by definition. Further-

more, these changes are brought about by natural selection. With balanced polymorphism, the equilibrium point depends upon the relative adaptive values of the homozygotes, $(1 - s_1)$ and $(1 - s_2)$. During the hot season, selection evidently favors ST homozygotes relatively more than it does in spring, when CH homozygotes have a relatively higher adaptive value. In fact, the speed of the changes observed in nature during the hot season can be accounted for if the

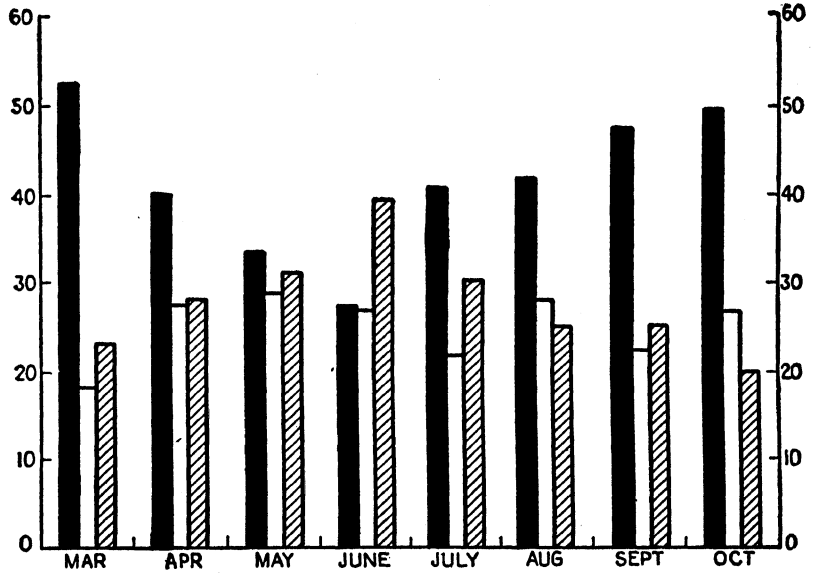


FIG. 6. Seasonal changes in the relative frequencies of the third chromosomes with the Standard (black), Arrowhead (white), and Chiricahua (cross-hatched columns) gene arrangements in a natural population of *Drosophila pseudoobscura*. The ordinates indicate percentages.

chromosomal types have adaptive values which they are observed to have in experimental laboratory populations at 25°C. (see above). At a lower temperature, 16°C., no changes occur in experimental populations, and none seem to occur in nature from September to March. The system operates in such a way that the average adaptive value of the population as a whole remains high in different seasonal environments.

Dubinin and Tiniakov (1945, 1946b and c) observed cyclic seasonal changes in the incidence of chromosomal types in *Drosophila*

funebris. They have also shown that in this species some chromosomal types survive more often than others when known mixtures of flies are exposed to low temperatures in artificial "hibernation" tests. In another experiment they released 100,000 flies homozygous for a certain inversion in a locality near Moscow, and observed a gradual decline of the frequency of this inversion towards the equilibrium value which it has naturally in the population of this locality. Another seasonal genetic change involves the fecundity of the female flies: the average fecundity is higher in females which survive the winter hibernation than it is in flies collected in the natural habitats in late summer and fall. It appears that the genotypes which give high fecundity are advantageous for survival during hibernation, but relatively disadvantageous during the summer season. Small seasonal changes in the incidence of chromosomal inversions have also been found by Carson and Stalker (1949) in *D. robusta*. The same authors (Stalker and Carson 1949) observed seasonal genetic variations in the frequencies of certain morphological traits of the flies. More startling is the finding of Gershenson (1945) that small but statistically significant changes in relative frequencies of the gray and black phases occur in the Russian population of the hamster (*Cricetus cricetus*). In this mammal, an individual may live more than one year, but it gives several broods of young at different seasons. The color phases differ, as far as known, in a single gene. Gershenson believes that one of the color phases survives relatively better during the hot, and the other phase during the cool season.

Adaptation to seasonal changes in the environment is assuredly not the only biological function of the chromosomal polymorphism in *Drosophila*. Table 9 shows differences in the incidence of ST, AR, and CH chromosomes in populations of *D. pseudoobscura* at different elevations in the Sierra Nevada mountains of California. It can be seen that ST chromosomes are more frequent at low than at high elevations; conversely, AR chromosomes increase in frequency as one ascends to higher elevations; CH chromosomes are relatively more constant in frequency. Here, then, the chromosomal polymorphism serves the function of adaptation to altitudinal variations in the environment. But seasonal changes are observed in these populations as well: the incidence of ST increases, and that of AR chromosomes decreases, as the summer progresses, while the opposite

changes presumably occur during winter. In other words, during the warm season the populations of localities at higher elevations come to resemble in composition those of localities at lower elevations earlier in the season (Dobzhansky 1948). Changes in the frequencies of chromosomal types with elevation have also been found by Stalker and Carson (1948) in *D. robusta* in the Great Smoky Mountains of Tennessee. Dubinin and Tiniakov (1946a) found that in *D. funebris* the incidence of certain chromosomal types is much greater in urban than in rural populations. This species lives as a scavenger in human households, and is therefore common in cities; but it also occurs in undisturbed natural habitats, in the vicinity of Moscow, Russia. Some chromosomal types have considerably higher equilibrium frequencies in man-made environments than in natural ones.

TABLE 9

INCIDENCE OF THIRD CHROMOSOMES WITH DIFFERENT GENE ARRANGEMENTS IN POPULATIONS OF *Drosophila pseudoobscura* WHICH LIVE AT DIFFERENT ELEVATIONS IN THE SIERRA NEVADA OF CALIFORNIA

ELEVATION OF THE LOCALITY (FEET)	GENE ARRANGEMENT (%)			
	Standard	*Arrowhead*	*Chiricahua*	*Others*
850	46	25	16	13
3,000	41	35	14	10
4,600	32	37	19	12
6,200	26	44	16	14
8,000	14	45	27	14
8,600	11	55	22	12
10,000	10	50	20	20

BALANCED POLYMORPHISM AND HETEROSIS

It has been shown above that hybrid vigor or heterosis, in other words adaptive superiority of heterozygotes over homozygotes, is the essential condition for the establishment of balanced polymorphism in a Mendelian population. If a mutant produces a heterotic heterozygote, natural selection will retain this mutant in the population, regardless of how poorly adapted, or even lethal, may be the mutant homozygote. The fitness of the homozygotes influences only

the equilibrium frequencies, but not the preservation, of heterotic mutants. The origin of such mutants has been observed by Gustafsson (1946a) and Gustafsson et al. (1950) in barley. The chromosomal polymorphism in *Drosophila pseudoobscura* and other species is, however, due to heterotic effects produced not by single gene mutations but by heterozygosis for inverted sections of chromosomes. Now, an inverted section may modify the physiological characteristics of its carriers either through position effects (cf. Chapter II), or through possession of mutant genes different from those in chromosomes with the alternative gene arrangement, or through a combination of these causes.

Experimental data which shed some light on this problem have been obtained in *D. pseudoobscura.* In this species, any two gene arrangements found in the population of any one locality give, as a rule, a heterotic heterozygote. Some of the gene arrangements occur, however, in rather extensive geographical areas (see Chapter VI). Experiments have been arranged in artificial populations, in which chromosomes with one gene arrangement from a locality in California were made to compete with chromosomes with a different gene arrangement from localities several hundred miles away from the first, either in California or in Mexico. When the chromosomes are derived from geographically remote populations, the inversion heterozygotes show heterosis only in a minority of cases; in others the adaptive values of the heterozygotes are intermediate between those of the homozygotes; and in one case the heterozygote proved only as viable as the least viable homozygote. The adaptive value of a heterozygote is, accordingly, not always determined by the gene arrangements in the chromosomes which it carries. It must be determined at least in part by the genes in these chromosomes (Dobzhansky 1950c).

The most probable interpretation of these facts is as follows. The chromosomes with different gene arrangements carry different complexes of genes (arising ultimately through mutation). The gene complexes in the chromosomes found in the population of any one locality have been, through long continued natural selection, mutually adjusted, or "coadapted," so that the inversion heterozygotes possess high adaptive values. But the genes in chromosomes with the same or with different gene arrangements vary also from locality to locality. The gene complexes in different localities are not coadapted

by natural selection, since heterozygotes for such foreign gene complexes are seldom or never formed in nature. Heterosis is, therefore, an outcome of a historic process of adaptation to the environment. This adaptation is, however, increasing the fitness of the Mendelian population as a whole, and it is attained despite the production of relatively ill-adapted inversion homozygotes. Indeed, the adaptive value ($\overline{W}$) of the whole population under balanced polymorphism can be shown to reach the highest level when the equilibrium proportions of the competing variants, $q = s_2/(s_1 + s_2)$, are established (see above).

Balanced polymorphism has certain advantages as a method of adaptation over a polymorphism unconnected with heterosis. Imagine a population like *Drosophila pseudoobscura* in the California localities discussed above, in which carriers of ST chromosomes, whether heterozygous or homozygous, would be favored during the hot part of the year, while the carriers of AR chromosomes would be superior during the cool season. Now, an exceptionally hot or prolonged summer could, conceivably, result in elimination of all AR chromosomes. A population in which this would happen, would be placed at a disadvantage during the winter season, because in winter the carriers of AR are superior. No such "adaptive accident" can take place if the polymorphism is balanced. Here natural selection does not eliminate either ST or AR chromosomes, but conduces the population towards the equilibrium point which is adaptively most favorable in a given environment (Dobzhansky 1949, 1950c).

CHROMOSOMAL POLYMORPHISM IN ORGANISMS OTHER THAN DROSOPHILA

It is not difficult to see why balanced polymorphism is so often, at least in *Drosophila*, connected with inverted sections in the chromosomes. The principal genetic effect of inversions is suppression of recombination of genes located in the chromosomes involved in inversion heterozygosis. If the high fitness, the heterosis, of the inversion heterozygotes is due to interaction of gene complexes carried in the chromosomes, then the preservation of these gene complexes as units (Darlington and Mather's "supergenes," 1949) is advantageous. Crossing over and gene recombination would break up these gene complexes. Inversions acquire selective advantages if they arise in

chromosomes which carry adaptively valuable gene complexes (Dobzhansky 1950c).

The detection of chromosomal polymorphism is technically simplest in the representatives of the order Diptera (flies) which have giant chromosomes in the salivary glands. Inversion heterozygotes have been found in the natural populations of some, but not of all, species of midges (Chironomidae) studied by Bauer (1936, 1945), Hsu and Liu (1948), and other investigators. Carson (1944) and Rohm (1947) found inversions in some species of *Sciara*, Wolf (1941) in *Dicranomyia*, and Mainx (1949) in *Liriomyza*. Inversions are rare in natural populations, but occur in hybrids between species of mosquitoes (Frizzi 1950).

In organisms which do not have giant chromosomes, resort may be had to examination of the meiotic divisions. In inversion heterozygotes, the chromosomes undergo pairing by formation of loops represented schematically in Fig. 7. If a chiasma becomes established within the inversion loop, the result of meiosis is as represented diagrammatically in Fig. 7. Two normal non-crossover chromatids, one dicentric chromatid, and an acentric chromosome fragment are formed. At the anaphase of the first meiotic division the dicentric chromatid becomes a "chromatid bridge" connecting the two poles of the spindle, as shown in Fig. 7. The chromatid bridge may be seen under the microscope; it is, however, evident that only those inversions which permit formation of chiasmata and crossing over within the inverted regions may be detected with the aid of this method. This is not always the case, and short inversions, which suppress the chiasma formation inside the inversion loops, produce no cytologically visible effects at the meiotic divisions. Negative evidence, absence of chromatid bridges and acentric fragments, does not exclude the possibility that inversions may be present.

Among species in which inversions are detected through observation of chromatid bridges and acentric fragments at meiosis, the Tyrolean populations of the plant *Paris quadrifolia* are most remarkable (Geitler 1938). Every individual studied proved heterozygous for one or more inversions, and it appears that inversions exist in every chromosome of the complement. Stebbins (1938) and Walters (1942) found inversion heterozygotes in every species of *Paeonia* studied by them. The list of plant species in which some inversions

have been recorded is a long one; rye (Lamm 1936), *Elymus* (Stebbins and Walters 1949), *Fritillaria* (Frankel 1937), *Tradescantia* (Swanson 1940), *Rumex* (A. Löve 1944), *Melandrium* (D. Löve 1944), *Polygonatum* (Suomalainen 1947), oats (Howard 1948), and *Clematis* (Meurman and Therman 1939) may serve as examples. Inversion heterozygotes in animal populations seem to be less common than in plants, if flies are excepted. Koller (1936) recorded them in

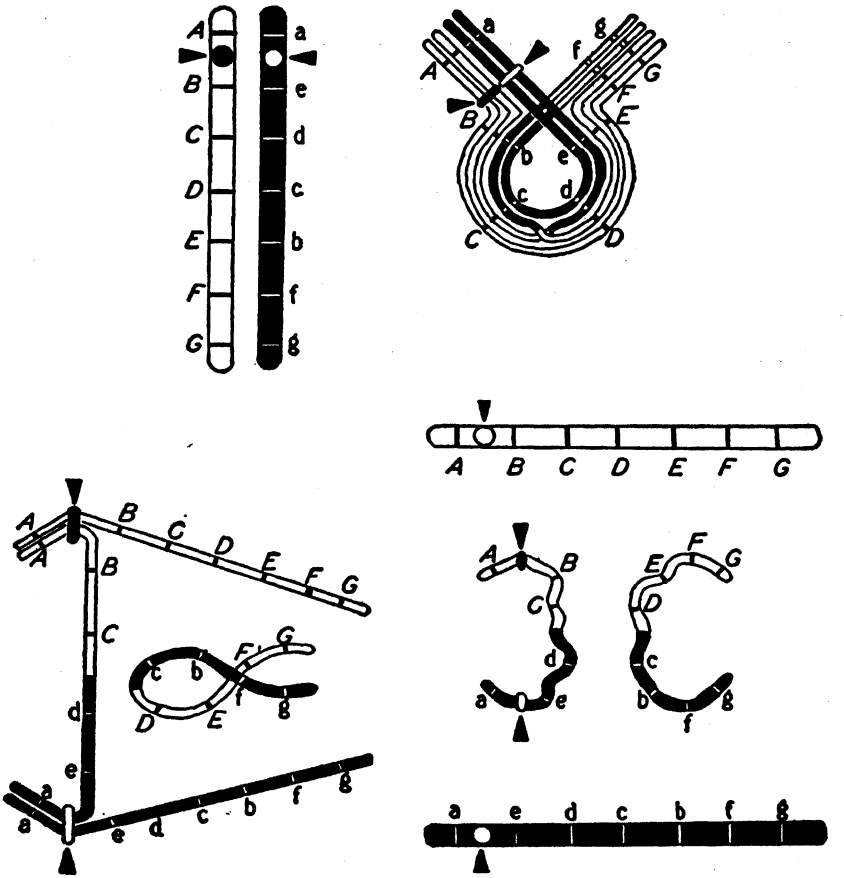


FIG. 7. Crossing over in an inversion heterozygote. Upper left, two chromosomes which differ in a paracentric inversion; upper right, chromosome pairing at the diplotene stage of meiosis; lower left, the "chromatid bridge" and the acentric fragment formed at the first meiotic division; lower right, the two viable and the two inviable chromosomes formed through crossing over. The black triangles indicate the centromeres.

the squirrel *Sciurus carolinensis*, and found a perhaps doubtful case in man (Koller 1937). Darlington (1936) and Coleman (1947) described isolated instances among grasshoppers, but White's (1949) far more extensive studies on many species show that in this cytologically unusually favorable group of insects inversions are decidedly rare in natural populations.

Here it must be emphasized that inversion heterozygosis is merely one of the genetic mechanisms which can serve the biological function of suppression of recombination between coadapted gene complexes. Any other agency that decreases the frequency of chiasmata in a section of a chromosome may perform the same service. Instances of localization of chiasmata in a part of a chromosome are indeed known (Darlington 1937). In many species of grasshoppers, individuals are found showing so-called unequal or heteromorphic bivalents (White 1945, 1949, see these papers for further references). Unequal bivalents consist of two chromosomes which have centromeres in different positions, or have one chromosome longer than its mate. Shifts in the position of the centromere within a chromosome may be caused by pericentric inversions (Chapter II), but White argues that in the grasshoppers transpositions of the centromeres, with perhaps a short adjacent block of chromosomal materials, are involved. However that may be, it is reasonable to believe that effective crossing over is reduced in the unequal bivalents. Further data that would permit comparison of the chromosomal polymorphism in flies and in grasshoppers must be awaited with great interest.

Heterozygosis for translocations likewise reduces the frequency of crossing over between the chromosomes involved, especially in the vicinity of the breakage points. At the same time, chromosome disjunction in translocation heterozygotes is often such that the number of functional gametes produced is reduced by one half or even more. In other words, translocation heterozygotes are often semisterile (see Chapter VIII). Since sterility may lower disastrously the adaptive values of genotypes which otherwise possess excellent adaptive properties, the occurrence of translocations in natural populations is possible only under exceptional circumstances (Wright 1941a). A translocation may, conceivably, produce position effects favorable enough to counterbalance the semisterility, or it may, through suppression of crossing over, tie together a highly adaptive gene system.

More important is the fact that the disjunction of chromosomes at meiosis in translocation heterozygotes may be modified by gene mutations in such a way that the sterility is reduced or even eliminated. Genes which regulate the meiotic disjunction of chromosomes have, indeed, been observed by Rhoades in maize (unpublished data). Finally, in plant species in which self-pollination is the predominant method of reproduction, translocations become fairly easily established in homozygous condition. In plants the semisterility of translocation heterozygotes is expressed in abortion of a part of the pollen grains and ovules; in animals it leads to abortion of a part of the fertilized eggs. It is probably for these reasons that translocation heterozygotes occur more often in some plant than in animal populations.

Extensive data on the occurrence of translocations in the Jimson weed (*Datura stramonium*) of different geographic origin have been reported by Blakeslee and his collaborators (Bergner et al. 1933, and Blakeslee et al. 1937 for further references). This plant possesses twelve pairs of chromosomes, which normally form twelve bivalents at meiosis. In crosses between certain strains, one or more circles of four or six chromosomes appear, the remainder of the chromosomes forming bivalents as usual. The circle formation at meiosis is due to translocations involving two or more chromosomes. The chromosomes of two strains are shown in Fig. 8 a and b respectively. The chromosome structure observed in one of these strains might arise from that in the other by means of a translocation; for instance, the chromosomes 1.2 and 3.4 (Fig. 8a) might exchange sections, giving rise to the chromosomes 1.3 and 2.4 (Fig. 8b). Since like parts of chromosomes come together and pair at meiosis, a cross-shaped configuration (Fig. 8d) will be formed in the hybrid between the two strains. At the metaphase of the first meiotic division, the cross-shaped figure will be transformed into a twisted circle shown in Fig. 8e. A translocation in which three different chromosomes have exchanged sections gives a circle of six chromosomes (Fig. 8j); two translocations between two different pairs of chromosomes produce two circles of four chromosomes each, etc.

Datura stramonium is a weed which at present is nearly cosmopolitan in distribution, because of its involuntary transport by man with agricultural products. In organisms so deeply influenced by man

clearly defined geographical races are seldom found. Even more interesting, therefore, is the fact that populations of *D. stramonium* from different geographical regions proved to be unlike in their chromosomal constitution. Plants having chromosomes apparently identical with those of the standard line have been grown from seed collected in the United States, in the West Indies, Brazil, France, Portugal, Italy, Japan, Portuguese West Africa, and Australia. The

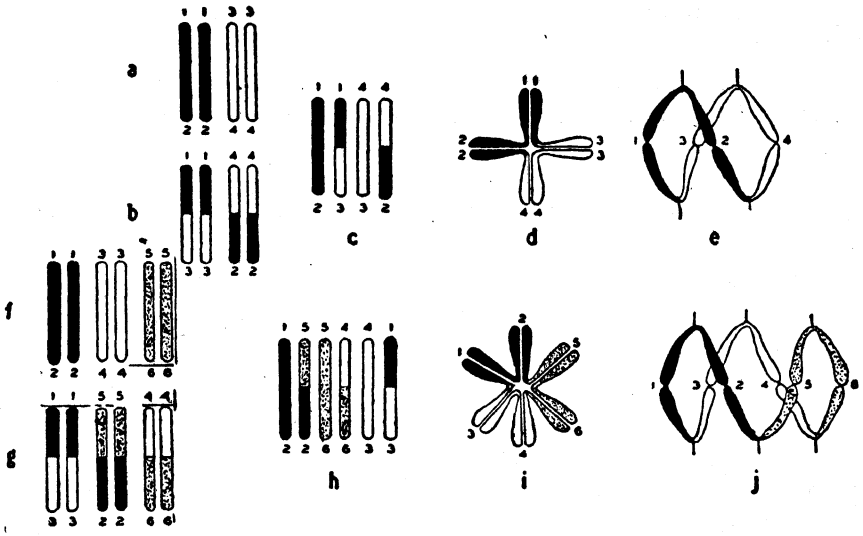


FIG. 8. Translocation between two (b-e) and between three (g-j) chromosomes. Normal chromosomes (a) and (f); (b) and (g) translocation homozygotes; (c) and (h) translocation heterozygotes; (d) and (i) chromosome arrangement at pairing stages; (e) and (j) arrangement of chromosomes at the metaphase of the meiotic division.

populations from Brazil and from the United States, except along the Atlantic seaboard, seem to have only standard chromosomes. The "translocation 2" has a wider distribution; it is very common in Central and South America (except in Brazil and Argentina), on the Atlantic seaboard in the United States, in Europe, in Asia (except Japan), and in Africa (except the eastern Portuguese colonies). The "translocation 3" is restricted to Peru, Chile, and Central America, but has been found once in Spain. The translocations 4 and 7 occur in the eastern United States, the West Indies, the Mediterranean countries of Europe, South Africa, and Australia.

The extraordinary behavior of many representatives of the plant genus *Oenothera* was for many years one of the outstanding puzzles in genetics. It is now known to be caused by many strains of *Oenothera* being balanced translocation heterozygotes, with the corresponding homozygotes eliminated by certain special mechanisms (see Cleland 1940, 1944, and Stebbins 1950 for reviews and references). The whole situation may be characterized as a genetical tour de force, which makes maintenance of heterosis compatible with prevalence of self-pollination in the plants concerned. A similar situation exists in a few other plants, such as *Rhoeo discolor.* In *Godetia whitneyi* and its relatives, many populations contain numerous translocation heterozygotes, suggesting that in these forms an *Oenothera*-like situation may be in the process of development (Håkansson 1942, Stebbins 1950). Translocation heterozygotes are known also in many other plants (see Darlington 1937), Müntzing 1939, Stebbins 1950, and Darlington and La Cour 1950 for references).

Probably for the reasons discussed above, translocation heterozygotes are decidedly rare in animals. In *Drosophila,* a single instance of the occurrence of a translocation in a population of *D. ananassae* is known (Dobzhansky and Dreyfus 1943). In grasshoppers, several instances have been recorded by White (1940, 1945) and other workers, the clearest being in *Metrioptera brachyptera.* A single heterozygote was found in a certain locality in England in 1934; in 1937 several more translocation individuals were encountered in the same locality. The translocation has evidently persisted in the population for at least three years. Suomalainen (1946) found a translocation heterozygote in the cockroach *Phyllodromia germanica.*

GENIC POLYMORPHISM

Up to now, our attention has been confined to consideration of instances of polymorphism in which chromosomal changes and blocks of genes, rather than single genes, were the units. In a great majority of polymorphic species known to systematists, the variable morphological traits are all that has been studied. In the relatively few cases in which the heredity of such traits has also been examined it is not possible to decide whether the genes which condition the polymorphism are or are not connected with chromosome aberrations. There

is, of course, no reason why single gene mutations could not cause heterosis and polymorphism, and in point of fact the work of Stubbe and Pirschle (1941), Gustafsson (1946a), and Gustafsson et al. (1950) already referred to above suggests that they sometimes do. Thus, the instances of polymorphism now to be discussed may or may not be due to single genes.

Timofeeff-Ressovsky (1940b) has described cyclic seasonal changes in the ladybird beetle *Adalia bipunctata*. This species produces at least two generations per year and hibernates as an adult insect. Several color phases, due to a series of multiple alleles, coexist in all European and American populations; these phases may be classified into light and darkly pigmented groups. In the vicinity of Berlin the relative frequencies of the dark individuals increase, and those of the light ones diminish, from spring to autumn. Among the hibernating beetles, the mortality is heavy. Timofeeff-Ressovsky has been able to show that the proportion of survival is greater among the light than among the dark phase. It appears, then, that the dark form is superior to the light one during the breeding season, but the opposite is the case in winter.

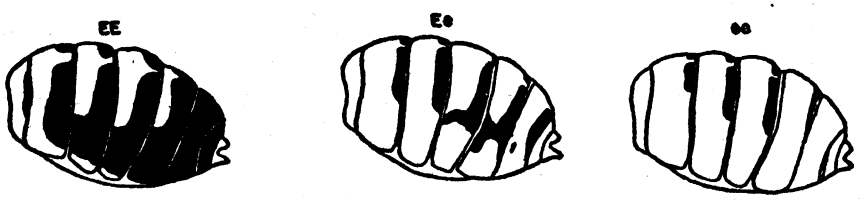


FIG. 9. The color patterns of the abdomen of *Drosophila polymorpha*. The heterozygote is shown in the middle, and the two homozygotes are on the right and on the left. (After da Cunha.)

Drosophila polymorpha, a species native in tropical America, shows three types of coloration of the abdomen represented in Fig. 9. Da Cunha (1949) found that these types are inherited as if caused by two alleles of a single gene, *E* and *e*, the dark and the light types being the homozygotes, *EE* and *ee*, and the intermediate type the heterozygote, *Ee*. Among 8,070 flies of this species found in the state of Paraná, Brazil, 3,969 were dark, 3,174 intermediate, and 927 light. This corresponds to frequencies of 0.69 of *E* and 0.31 of *e* in the gene pool. Polymorphism is observed in populations of this

species from all parts of Brazil, although the frequencies of the gene *E* vary from 0.61 to 0.82 in different samples. An experimental demonstration of heterosis in *Ee* heterozygotes has been secured as follows. When dark and light flies are intercrossed in the laboratory, the offspring in the F_2 generation should segregate in the ratio 1*EE*: 2*Ee*: 1*ee*. In reality, the heterozygotes are more, and the homozygotes are less frequent than expected, as shown in the following table:

	DARK	INTERMEDIATE	LIGHT
Observed	1,605	3,767	1,310
Expected	1,670.5	3,341	1,670.5
Deviation	−65.5	+426	−359.5

If the viability of the heterozygote is taken to be 1, that of the dark homozygote turns out, on the basis of these data, to be 0.85, and that of light homozygotes 0.695. Da Cunha observed the competition of the three genotypes in an apparatus which resembled in principle the population cages mentioned in the present and in the preceding chapters. Natural selection in such experimental populations rapidly leads to establishment of equilibrium, at which the populations consist of 40–45 percent dark, 35–45 percent intermediate, and about 15 percent light flies. Taking the adaptive value of the heterozygote, *Ee*, to be 1, the observed speed of the selection process indicates the adaptive value 0.56 for the dark, *EE*, and 0.23 for the light, *ee*, homozygotes. These adaptive values differ from the viability quotients computed on the basis of the deviations from normal segregation ratios. This difference is not unexpected, since the competition in experimental populations is far more stringent than in ordinary culture bottles. The really unexpected result obtained by da Cunha is that in natural populations the heterozygotes, *Ee*, are actually less frequent among the adult flies than expected on the basis of the binomial square rule. The cause of this is not clear. It is possible that in the natural environments the heterozygotes are less viable than the homozygotes, but that the deficient viability is offset by some advantage in the adult stage, such as a greater fecundity. As shown in Chapter IV, the adaptive value of a genotype is not necessarily proportional to the viability of its carriers.

The color polymorphism in wild populations of the grasshopper

Paratettix texanus is due, according to Fisher's (1939) analysis of the hybridization experiments of Nabours, to the presence of a variety of dominant mutant alleles which are adaptively favorable when heterozygous but deleterious when homozygous. Alleles of this sort cause the polymorphism also in the bird *Poephila* (Southern 1945) and the moth *Ephestia* (Caspari 1950).

POLYMORPHISM AND MIMICRY

Balanced polymorphism, based on adaptive superiorities of heterozygotes, is not the only possible kind of adaptive polymorphism. A species will be polymorphic if it contains a variety of genotypes each of which is superior in adaptive value to the others in some habitats which occur regularly in the territory occupied by this species. Mutation pressure producing a variety of gene alleles which are close to adaptive neutrality may also make a species polymorphic (this nonadaptive polymorphism will be discussed in Chapter VI).

The appearance and spread of melanic variants of several species of moths in the vicinity of large industrial cities is one of the spectacular instances of the origin of polymorphism in natural populations (see Hasebroek 1934, Ford 1937, 1945, and Huxley 1942 for reviews and references). Variants more darkly pigmented than the norm appear in a population, and in the course of several decades become more frequent than the original form, finally supplanting the latter. In a number of instances the melanic forms have been shown experimentally to differ from the paler relatives in a single dominant gene. The first appearance of the melanic forms is always recorded in the vicinity of large industrial cities, and the spread of the dark variants goes hand in hand with the industrialization of the country. Thus, the black form of *Biston betularia* was observed near Manchester in 1850, and in the twentieth century it has superseded the normal form. In Germany the development of "industrial melanism" was observed somewhat later, beginning with the Rhine district and the environs of Hamburg. Still later, analogous phenomena appeared in France and elsewhere. Ford has discovered that, in at least some species, the melanic forms are superior to the light-colored ancestors in viability. According to Ford's ingenious hypothesis, the spread of melanic mutants was precluded before the advent

of industrial developments owing to the destruction of such mutants by predators, since dark individuals are not protectively colored. This disability is removed in industrial regions by the general darkening of the landscape. The superior viability of the melanics is able, then, to assert itself, and their rapid increase in frequency is the result.

Ford (1937, 1940a, 1940b, 1945) has reviewed and analyzed the data on several species of butterflies in which the polymorphism is restricted to one sex, usually the female, the other sex being uniform.

Systematists and collectors described and gave some two dozen varietal, and even specific, names to the color forms of the highly variable moth *Zygaena ephialtes*. Bovey (1941) showed that all these forms can be satisfactorily accounted for as due to recombinations of just three pairs of alleles. The gene *P* makes the hind wings of the moth red or yellow with a black margin, while the allele *p* makes them black except for some colored spots. The heterozygote, *Pp*, is intermediate in color. The dominant gene *R* makes the spots in the wings red, while the recessive makes them yellow. The dominant *B* makes the colored spots on the hind wings double, while the recessive *b* causes them to be single. Populations of different countries are characterized by different incidence of the dominant and recessive alleles of these genes.

ADAPTIVE POLYMORPHISM AND ECOLOGICAL OPPORTUNITY

It should now be evident that adaptive polymorphism is a widespread phenomenon in the living world. As pointed out at the beginning of the present chapter, adaptively polymorphic populations should, in general, be more efficient in the exploitation of ecological opportunities of an environment than genetically uniform ones. It can be further surmised that, other things being equal, populations which occupy many habitats in a given territory should be genetically more diversified than populations restricted or specialized for occupation of only few habitats.

This hypothesis has been submitted to a test by da Cunha et al. (1950) and Dobzhansky et al. (1950). Four very closely related species, *D. willistoni*, *D. paulistorum*, *D. equinoxialis*, and *D. tropicalis* occur in the American tropics. The first two of these species occur in the entire tropical zone, are among the commonest repre-

sentatives of the genus in most of their distribution areas, and live on a great variety of food substances. At least 40 and 34 inversions respectively have been recorded in the chromosomes of natural populations of these species. *D. tropicalis* and *D. equinoxialis* are restricted to the basin of the Amazon or a part of it. They are fairly rare in most localities, and appear to be ecologically specialized species. Only four inversions have been found in each of these species.

Even more suggestive are the data on frequencies of inversion heterozygotes in the populations of species related to *Drosophila willistoni*. A wild individual of *D. tropicalis* is heterozygous, on the average, for 0.14 ± 0.06 inversions, and *D. equinoxialis* for 0.11 ± 0.05 inversions. In *D. paulistorum* the numbers of heterozygous inversions per individual vary from 0.55 ± 0.20 to 1.77 ± 0.31 in different localities, while in *D. willistoni* the averages range from 0.81 ± 0.03 to 9.36 ± 0.26 inversions per individual in different parts of the distribution area. The most highly polymorphic populations of *D. willistoni* occur in the central part of the species area, and the polymorphism becomes more limited towards the margins of the area. Ecologically favorable areas with diversified food sources (tropical jungles) are inhabited by more highly polymorphic populations than are rigorous environments (deserts). Polymorphism is higher where the species is more abundant and widespread than its competitors, and less where the competitors exceed in abundance the species in question.

Vavilov (1926) advanced the generalization that the genetic variability in populations is greatest in the territory in which the species arose and from which it subsequently spread elsewhere. This "center of origin" hypothesis may at present be re-stated as follows. The evolutionary process which generates adaptive polymorphism, and thereby enables the species to conquer and control more and more habitats, requires time. Therefore, the longer a territory is occupied by a species the greater will tend to be the adaptive polymorphism and the variability in populations. Conversely, at the margins of its distribution area, unless the species is stopped by an insuperable geographic barrier, it is likely to have a toehold in only few ecological niches. A limited adaptive variability is likely to characterize marginal populations.

VI : Race Formation

GENETICS AND GEOGRAPHY

MENDELIAN POPULATIONS are seldom, if ever, genetically uniform. A Mendelian population is a system of individuals united by mating and parentage bonds. Individuals which compose a Mendelian population are often genetically diverse. Some of the genotypes are adaptively incompetent. They are transient products of the mutation process, interdicted by natural selection. Other genotypes, or groups of genotypes, possess optimal fitness in certain environments. If these environments recur regularly in the territory occupied by the population, the adaptively coherent genotypes become normal and lasting genetic components of the population and the species.

Some genotypes occur together, sympatrically, while others are allopatric and live in different territories. It is important to distinguish between sympatric and allopatric diversity. Every form of life possesses more or less efficient means of distribution. An individual may move actively from place to place, or it may be transported passively. Sex cells, spores, or seeds are scattered over a certain area. A certain average distance intervenes between the points in space at which the individual and its offspring are born. Organisms which occur within that distance are sympatric, those which occur at greater distances are allopatric. Both sympatric and allopatric organisms encounter a variety of environments. Adaptation to these environments in sympatric forms gives rise to the intrapopulational polymorphism dealt with in the foregoing chapter. Since environments vary also in different parts of the globe, allopatric populations respond to environmental differences by genotypic differentiation. Genetically distinct allopatric populations of a species are termed geographic races, subspecies, local varieties, or simply races. There exist fundamental similarities as well as critical differences between polymorphism and geographic races. Both are compounded

of the same genetic units, gene alleles and chromosomal variants, which are observed to arise by mutation in experimental animals and plants. Both arise mainly through the action of natural selection (the problem of non-adaptive diversity will be discussed below). The carriers of sympatric genotypes are, however, members of the same polymorphic Mendelian population. They interbreed, and their origin and dissolution are due to gene segregation and recombination within the same gene pool. The gene exchange between allopatric populations is always more or less limited, and it may be absent altogether. Allopatric diversity has one more dimension than the sympatric one. Transitions between sympatric polymorphism and allopatric races nevertheless occur.

CHROMOSOMAL RACES IN DROSOPHILA PSEUDOOBSCURA

It has been stated repeatedly in the preceding chapter that, when populations of a species are polymorphic, allopatric populations are often unlike in genetic composition. The incidence of gene arrangements in the third chromosomes in populations of *Drosophila pseudoobscura* which occur at different elevation in the Sierra Nevada of California has been reported in Table 9. The same gene arrangements occur at all elevations, but not with equal frequencies. The Arrowhead chromosomes form a fairly regular ascending gradient, or cline, upward, while Standard chromosomes increase in a gradient towards the foot of the mountain range. Such gradients can be observed on a much grander scale if, instead of a single mountain range, one considers the whole distribution area of the species, which extends from British Columbia to Guatemala, and from the Pacific Ocean to the western Great Plains (Dobzhansky and Epling 1944).

As shown in Fig. 4, sixteen different gene arrangements occur in the species. Each chromosomal type occurs in populations of only a certain area. Some (for example, San Jacinto and Hidalgo) have been encountered in populations of only a single locality. Others occur over hundreds of thousands of square miles. Every population can be characterized in terms of relative frequencies of the different chromosomal types in its gene pool (Fig. 10). Thus, the populations which inhabit the Pacific Coast, from British Columbia to Lower California, have some 50 to 60 percent of Standard (ST) chromosomes in their gene pools, 10–30 percent Arrowhead (AR), 10–20

percent Chiricahua (CH), 1–30 percent Santa Cruz (SC), and from 0 to 6 percent of Pikes Peak (PP), Tree line (TL), and Olympic (OL) chromosomes. From 100 to 200 miles eastward from the coast, along the Sierra Nevada–Cascade mountain chain, ST chromosomes fall in frequency to 25–50 percent, AR increase to 30–50 percent, CH fall to 5–30 percent; other chromosomal types remain rare. Further eastward, in the states of Nevada, Utah, Arizona, and western New Mexico and Colorado, AR increases very rapidly in frequency, until from 85 to 95 percent of the chromosomes in the gene pool carry this gene arrangement, other types being rare or absent. In eastern Colorado, New Mexico, and Texas, PP chromosomes become very common, 50 to 75 percent, AR 5 to 25 percent, TL 5 to 15 percent, while ST becomes very rare and SC absent. Southward, in northern Mexico, CH increases in frequency, until in some populations it amounts to more than 90 percent of the gene pool. Further southward, in central Mexico and Guatemala, one of the most frequent gene arrangements is Cuernavaca (CU) which is altogether absent in the United States, and apparently also in northern Mexico. The SC, PL, OL, and certain other gene arrangements which are rare or absent in the United States are frequent in Mexico; conversely, ST and AR are predominant in the United States but are absent in central Mexico and Guatemala (Dobzhansky and Epling 1944).

The fundamental fact which emerges from these data is that allopatric populations of *Drosophila pseudoobscura* differ in relative frequencies of the same genetic variants in which sympatric individuals may also differ. If we are presented with a fly which has AR third chromosomes, it can be safely surmised that this fly, or its ancestors, came from somewhere in the United States or Canada, and not from central Mexico. A fly with CU chromosomes stems from Mexico or Guatemala, and not from the United States. In order to determine the geographic origin more precisely, an individual fly is not sufficient, and a population sample is needed. Suppose that we have a sample of 10 chromosomes, taken at random from a population, and find that 6 chromosomes are ST, 2 are AR, and 2 are CH in gene arrangement. Consulting Fig. 10, it can be seen that such a sample is unlikely to occur anywhere except on the Pacific Coast. With samples of 100, 500, or more chromosomes, the geographic origin of the population can be determined more and more precisely.

Races may be defined as Mendelian populations of a species which differ in the frequencies of one or more genetic variants, gene alleles, or chromosomal structures. Race differences of diverse orders of magnitude are observed. The populations of the elevational belts in the Sierra Nevada of California are racially distinct (Table 9), although they live only a few miles apart and contain qualitatively

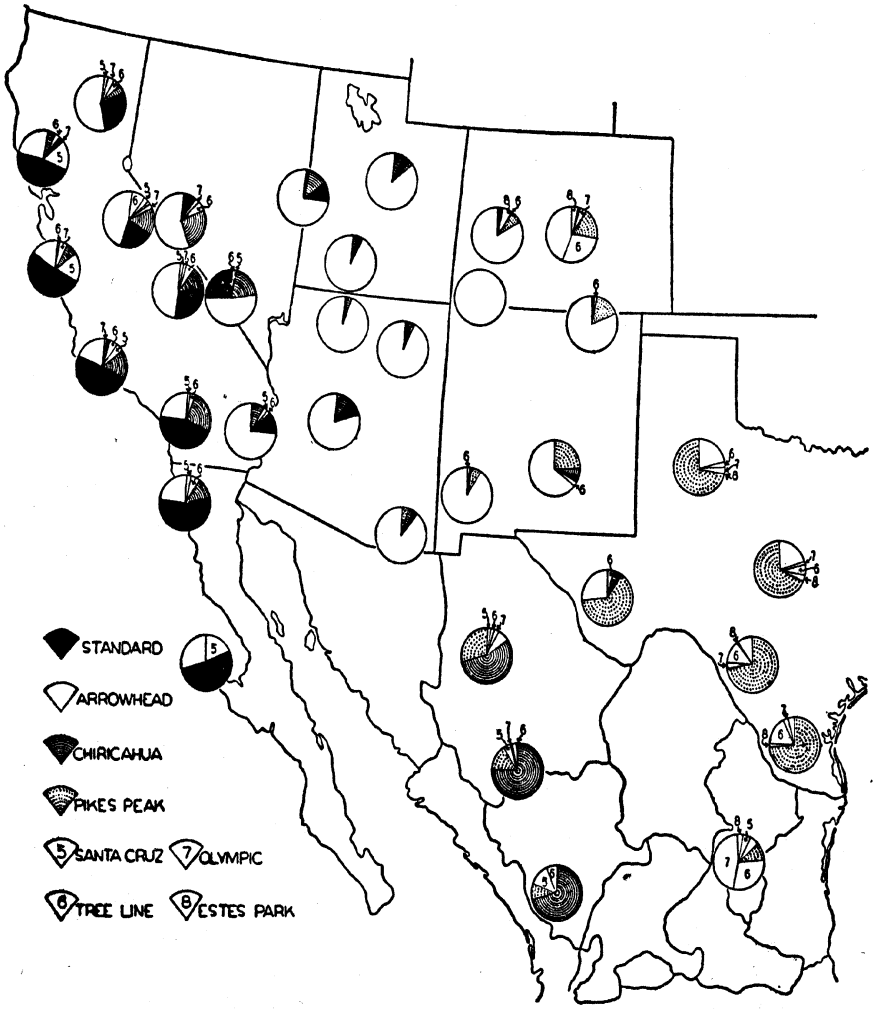


FIG. 10. Relative frequencies of various gene arrangements in the third chromosomes of different populations of *Drosophila pseudoobscura* in the western United States and in northern Mexico.

the same genetic variants. Populations of the Sierra Nevada and of central Mexico are also racially distinct. But these populations are separated by a distance in excess of 2,000 miles, and each of them contains some genetic variants which are wholly absent in the other. They are, however, connected by a chain of populations intermediate in composition. In other words, the frequencies of the chromosomal types in populations form geographic gradients. The populations at the geographic extremes are very different, but neighboring populations differ little. In some regions the gradients are fairly uniform—the frequencies of, for example, the AR gene arrangement change by so many percent for each 100 miles of horizontal distance. But in other regions the gradients are irregularly steeper. For example, the populations of *Drosophila pseudoobscura* which live along the entire pacific Coast of the United States, at distances of hundreds of miles, are rather similar in composition. But the populations on the western and the eastern slopes of the Sierra Nevada, a distance less than 100 miles, differ rather sharply. The Sierra Nevada mountain range forms a racial boundary between populations on either side of it.

RACE DIFFERENCES AND RACE LIMITS

Two logically and methodologically separate problems should be distinguished in racial studies. First, one may wish to decide whether certain populations of a species are racially distinct. This can be answered objectively and conclusively, by a statistical comparison of the incidence of genetic variants in the gene pools of the populations in question. For example, the populations of *Drosophila pseudoobscura* at different elevations of the Sierra Nevada are distinct. Second, one may ask into how many races a species is divided. This is a matter of convention and convenience. The genetic differences between most distinct populations of a species, such as those of *D. pseudoobscura* in Mexico and in Nevada and Utah, may for some purposes seem so important that one may wish to recognize them by technical racial names. But a systematist who does not study chromosomes may regard the differences as trivial, and naming such races may appear needless overburdening of the nomenclature. Furthermore, the extreme populations are connected by intermediates. This exacerbates the difficulties from the standpoint of a systematist. We

find, however, that the geographic gradients are steeper in some regions and more gradual in others. The unevenness of the gradients mitigates the difficulties, and validates the delimitation of the races.

The question of how many races exist in the human species has provoked endless disagreement. Different anthropologists have recognized from two to more than 100 races. In the light of genetics the contradiction can be seen to be spurious. The number of races which are recognized depends chiefly on whether grosser or finer subdivision is preferred, and on how sharp are the breaks in gene or character gradients that are regarded sufficient to draw race boundaries. Among recent authors, Boyd (1950) recognizes 5 living races, while Coon, Garn, and Birdsell (1950) find 30 races. However, the latter authors group their 30 races in 6 "putative stocks," 5 of which coincide with Boyd's races. And yet, setting up races is not an arbitrary procedure. The basic requirement, which was repeatedly infringed upon in classical anthropology, is that races are Mendelian populations. People with O and with A blood groups are not distinct races, because they do not form different populations, although different populations often differ in the incidence of these blood groups. Similarly, people with long and with short heads, or slender and fat people, are not races. Calling them races leads to the absurd situations when brothers and sisters would differ in race from each other and from their parents. On the other hand, Coon, Garn, and Birdsell rightly recognize the North-American Colored, South-African Colored, Ladino, and Neo-Hawaiian races. These are genetically distinct populations, although they arose in historic time by interbreeding of other races, and have not yet reached genetic equilibria.

RACIAL VARIATION DUE TO SINGLE GENES

Gershenson (1945) has assembled data on almost two million pelts of the hamster, *Cricetus cricetus*, obtained in southwest Russia between 1934 and 1939. As mentioned in Chapter V, this species is polymorphic; a dominant black and a recessive gray (agouti) phase occur in many populations. Fig. 11 shows that in southwest Russia there are four nuclei of populations in which up to 27 percent of individuals are black. These nuclei lie in the forest-steppe vegetational zone, in which, according to Gershenson, the black gene is favored by natural selection. To the north and to the south, in the

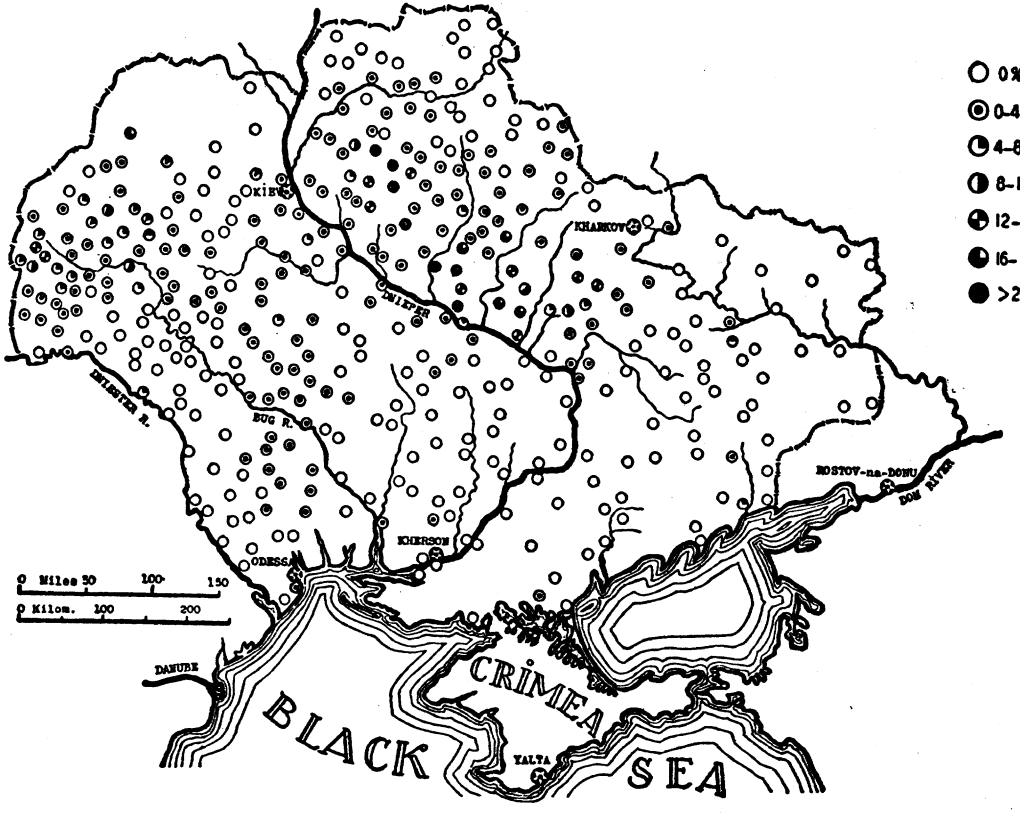


FIG. 11. Percentage frequencies of black individuals in the populations of the hamster (*Cricetus cricetus*) in southern Russia. (After Gershenson.)

boreal forests and in the open steppe, few or no blacks occur. Gershenson has, however, observed that some expansion of the populations including black individuals has taken place during the period of observation.

The Asiatic beetle, *Harmonia axyridis*, is highly variable in the color pattern (Fig. 12). According to Hosino (1940), Tan (1946), and Komai et al. (1950), these color patterns are determined by a series of multiple alleles of a single gene. The geographic distribution of the patterns has been studied by Dobzhansky (1933), by Komai et al., and by other authors. A short summary of the data is shown in Table 10. West-central Siberia (Altai, Yeniseisk Province) is occupied by a race which is nearly uniform for the *axyridis* pattern (Fig. 12e). Farther eastward, the populations become polymorphic, with the yellow phases (Fig. 12a, b, c) rapidly increasing in frequency. The *axyridis* pattern is rare in eastern Siberia and in China, but it occurs in 1 to 14 percent of individuals in Japan. The *spectabilis* and *conspicua* patterns (Fig. 12f and g) are found in the Far East only. The *Harmonia axyridis* situation differs from that in the hamster in that the geographic differentiation of populations is much sharper: one can distinguish at least a western race, which

TABLE 10

FREQUENCIES OF COLOR PATTERNS (IN PERCENTS) IN *Harmonia axyridis* FROM DIFFERENT REGIONS

REGION	SUCCINEA, FRIGIDA, 19-SIGNATA	AULICA	AXYRIDIS	SPECTABILIS	CONSPICUA	UNCLASSIFIED	NUMBER EXAMINED
Altai Mountains	0.05	—	99.95	—	—	—	4,013
Yeniseisk Province	0.9	—	99.1	—	—	—	116
Irkutsk Province	15.1	—	84.9	—	—	—	73
West Transbaikalia	50.8	—	49.2	—	—	—	61
Amur Province	100.0	—	—	—	—	—	41
Khabarovsk	74.5	0.3	0.2	13.4	10.7	—	597
Vladivostok	85.6	0.8	0.8	6.0	6.8	0.1	765
Korea	81.3	—	—	6.2	12.5	—	64
Manchuria	79.7	0.5	—	11.2	8.6	—	232
North China (Peiping)	83.0	0.4	—	8.8	7.3	0.5	9,676
West China (Szechwan)	42.6	2.9	0.01	28.8	25.1	0.8	1,074
East China (Soochow)	66.6	0.6	—	16.5	16.1	0.2	6,231
Japan	27.2	—	11.0	14.3	47.4	—	154

is almost exclusively *axyridis* in pattern, and an eastern polymorphic race.

For further data on the distribution of gene and character frequencies in human populations, see Boyd (1950). Lundman (1948) has published convenient maps of the distribution of the blood group genes in the populations of the world, and Goldstein (1948) has published data on the frequencies of shovel-shaped incisors in certain populations. For data on other organisms, see the general treatments of Goldschmidt (1940), Mayr (1942), Huxley (1942), Bauer and Timofeeff-Ressovsky (1943), and Stebbins (1950). Crampton (1916, 1932) and Welch (1938) have published extensive data on variations in snails, some of which are summarized in map form in Lundman (1947). Interesting figures on the incidence of cellular antigens in three populations of the mouse, *Peromyscus maniculatus*, can be found in Moody (1948), and color phases of *Colias* butterflies in Hovanitz (1950).

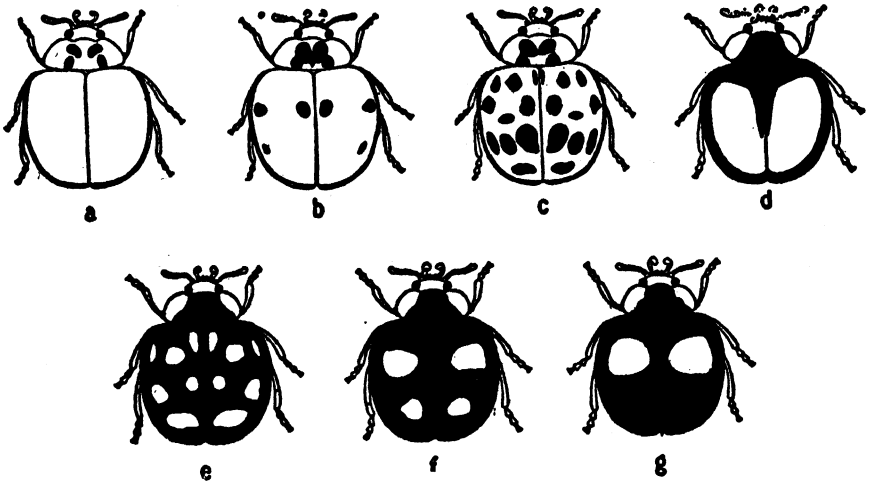


FIG. 12. color patterns in *Harmonia axyridis*. (a) var. *succinea;* (b) var. *frigida;* (c) var. *19-signata;* (d) var. *aulica;* (e) var. *axyridis;* (f) var. *spectabilis;* (g) var. *conspicua*.

POLYGENIC RACIAL VARIABILITY

Up to now, we have chosen to consider instances of racial variability due to chromosomal variations, or to different incidence in popu-

lations of genes which produce discrete and easily perceptible effects. Perusal of any modern taxonomic monograph (for example, Miller, 1941, on a genus of birds, Stebbins, 1949, on a genus of salamanders, or Woodson, 1947, on a species of *Asclepias* plans) discloses that continuous geographic variability is a far more common phenomenon. The racial variability of most human traits is also continuous. For example, all degrees of pigmentation of human skin, from nearly albinotic to deep black, occur in individuals and in populations. The same is true for height, head shape, and other body proportions.

Because of the technical difficulties encountered in studies on the inheritance of characters determined by polygenes (cf. Chapter III), the continuous racial variability has for a long time proved refractory to genetic analysis. In fact, some early geneticists believed that continuous variability obeys laws altogether different from those of Mendelian genetics. The classical work in this field, which has established the Mendelian interpretation of race differences, is that of Sumner (1930, 1932) on races of deer mice (*Peromyscus*), and of Tedin (1925) and Philiptchenko (1934) on plants. The geographic races of *Peromyscus* differ in such characters as size of the body; length of the tail, feet, and ears; the extent of the colored portion of the pelage; coloration of the pelage; proportionate numbers of different types of hairs, and so on. The result of interracial crosses is usually that the F_1 generation is intermediate between the parents, and about as variable as the parental races themselves. In the F_2 generation the mean values of the characters are likewise intermediate, and mostly similar to those of the F_1 generation. The variability is, however, greater, so that the extreme variants fall within the range of the normal variation of the ancestral races. Backcrosses to the ancestral races cause shifts of the mean values in the direction of the parents.

The increase of the variability in the F_2 is evidence of Mendelian segregation. Taking a theoretical example of two races differing in five genes (AABBCCDDEE and aabbccddee), the F_1 will consist of a single genotype AaBbCcDdEe), or at most of a few genotypes (if the ancestral races are not homogeneous). But in F_2 the number of genotypes is much greater; for a character determined by five genes this number equals 3^5, or 243. Moreover, only a small fraction of the offspring will be identical in genotype with either of the

parents; for the case of five genes this fraction is 4^{-5}, or 1 : 1,023. Evidently, the difficulty encountered in the analysis of a character determined by polygenes will vary depending upon the number of genes involved, the equal or unequal effectiveness of these genes in modifying the character, and the absolute size of the effect. The extremes of two races may differ, in a number of genes, AABBCCDDEE ... and aabbccddee ... The intermediate populations may be AAbbccddee, AABBccddee, AABBCCddee, AABBCCDDee, or mixtures of these genotypes. The characteristics of the intermediate races will then be determined by the average number of the polygenes of different kinds present in the population in a given locality.

EXPERIMENTS ON ADAPTEDNESS OF RACES IN PLANTS

The adaptive nature of race differences is more often presumed than proven. This is true, for example, for differences between human races. The skin color is almost a symbol of race distinction. From the geographic distribution of dark- and light-skinned races, it is inferred that dark pigmentations may be adaptive in countries with intense sunshine, because they confer protection against sunburn. Another conjecture is that scantily pigmented skin enables its possessors to secure an adequate supply of vitamin D with little exposure to sunlight. The evidence on which these views are based is, however, far from conclusive. The situation is, fortunately, much clearer with some plant races. The experiments of Turesson (1922, 1925, 1930) in Sweden, of Clausen, Keck, and Hiesey (1940, 1947, 1948, Clausen 1949) in the United States, and of Gregor (1938, 1939, 1946) and Turrill (1940, 1946) in England (a critical discussion in Stebbins 1950) have yielded most valuable and abundant data on the relationships between races of several species of plants and their environments.

It is well known that the plant phenotype can be greatly modified by the environment, and classical botanists were inclined to regard the differences exhibited by a species in different habitats as nongenetic. Turesson showed that if representatives of a species from different habitats are grown together in an experimental garden, they and their offspring preserve distinctive characteristics. These characteristics are hereditary. The method of reciprocal transplants, mas-

terfully applied by Clausen, Keck, and Hiesey, is even more instructive. Representatives of the population of the habitat A are transplanted in the habitat B, and those from B are planted in A. Comparison of the native and transplanted strains permits us to discriminate between the changes induced by the environment and those intrinsic to the strains themselves.

Californian races of *Potentilla glandulosa* may serve as examples. One of the races occurs at low elevations in the Coast Ranges of California. This habitat has a rainless summer and an equable climate permitting the plants to grow throughout the year. Two other races occupy respectively the dry slopes and the meadows in the foothills of the Sierra Nevada Mountains. Here the climate is continental with much snow in winter and some rain in spring; the summer is hot. The subalpine and alpine races occur in the highest reaches of the Sierra Nevada, where the growing season is short, winters are cold, and precipitation is relatively abundant. The coastal and the foothill races, when transplanted in each other's environments, do not thrive as well as they do in their native habitats. Nevertheless, the coastal race becomes dormant during the winter in the foothills, and the foothill races remain active during the winter on the coast. The coastal and foothill slope races seldom survive for a year when transplanted in the alpine zone; the foothill meadow race does better than the others in the alpine environment. None of these races produce ripe seeds in the alpine zone, although they may flower before the advent of the killing frosts. The alpine races are dwarfish in their own environment. They remain so when planted on the coast, are dormant from mid-November to mid-February, prove to be very susceptible to diseases, and are injured by the dry summers. Yet, they grow rather tall in the foothills, where they appear to be in general more vigorous than in their own environment.

Clausen, Keck, and Hiesey (1947) and Clausen (1949) have intercrossed some of the races of *Potentilla glandulosa*. The F_1 hybrids are both vigorous and fertile. In F_2, a very complex Mendelian segregation is observed; the authors state that no two plants were alike among 1,000 F_2 individuals from one such cross, and among 578 individuals from another, which were grown from 7 to 9 years in experimental gardens (the plants are perennial herbs). The minimum numbers of genes in which these races differ are estimated to be

between 60 and 100. Such polygenic causation of race differences is, as pointed out above, the usual condition. Most significant is the experiment in which each of the 578 F_2 hybrids from a cross between the foothill and the subalpine races (see above) were cut into three parts, and the parts replanted in three environments—on the coast, at mid-altitude, and in the subalpine zones of the Sierra Nevada. In such a way, the norms of reaction and the fitness of the 578 genotypes arising through recombination of the genes which distinguish the races were partially tested in the three environments.

The responses of these genotypes in the three environments are stated to be "more diverse than in all the wild forms of *Potentilla glandulosa* from many diverse native environments of the western United States that were tested at the transplant stations." Some of the genotypes were "super-alpine," because they thrive by far the best at the alpine station, while the alpine parent race grows most vigorously at the mid-altitude station. Others seemed most vigorous on the Coast, although no coastal race was among their ancestors. Some grew best at mid-altitudes, but others were weakest there. Some gene recombinations gave plants which were weak in all three environments, while others seemed vigorous everywhere. This last observation should not, however, be interpreted to mean that adaptive types superior to those found in natural populations were created. The available data tell us nothing about the ability of any recombination genotype to survive in competition with the native vegetation of any one of the stations. Nevertheless, it is remarkable and significant for understanding of the process of race formation, that a great variety of adaptive types can arise by recombination of genes carried in only two races.

Turesson (1922, 1925) quite correctly interpreted the origin of adaptive races in plants as constituting a "genotypic response" of a species to the environments which prevail in different habitats. Such races Turesson called ecotypes. The ecological and experimental concept of ecotype was contrasted with the then prevalent morphological concept of race or subspecies. The validity of this distinction has progressively diminished during the last quarter of a century, as the realization has become more general that most races are ecotypes in Turesson's sense. The term "ecotype" has become largely superfluous (Mayr 1942, Stebbins 1950, and others). It may

retain its usefulness only in cases in which a certain constellation of genes and of hereditary traits recurs in populations of a species in a definite type of habitat whenever the latter is encountered in the distribution area of the species. Thus, the sea-cliff ecotype and the sand-dune ecotype of *Hieracium umbellatum* recur wherever the proper habitats are available; on the southern coast of Sweden these habitats alternate, and so do the ecotypes (Turesson 1922). The same may be observed on a grander scale in alpine ecotypes. Populations of *Solidago virgaurea* from the alpine zone of Scandinavia and of the Altai Mountains have convergent characteristics (low growth and earliness), which distinguish them from populations of the same species which reside in the adjacent foothills and lowlands. In the European Alps a subalpine ecotype of *Solidago virgaurea* is present. In other plants alpine ecotypes had been formed, however, only in Scandinavia, or only in the Alps, whereupon the respective species occupies the alpine habitats in one of these regions but is barred in the other (Turesson 1925, 1930). The ability of some species to evolve convergent ecotypes in remote but ecologically similar regions is as interesting as the failure of other species to do so. Convergent ecotypes are formed by selection of analogous genotypic constituents: similar challenges evoke similar responses. But a challenge does not in itself insure the occurrence of the response, since a species may not have the proper genetic variants available when they are needed, even though that species is potentially able to produce such variants.

EXPERIMENTAL STUDIES ON ADAPTEDNESS OF ANIMAL RACES

Timofeeff-Ressovsky (1933, 1935a) compared the survival values of strains of *Drosophila funebris* of different geographic origin. Since geographic races of this fly are morphologically indistinguishable, strains of *D. funebris* were compared with a standard strain of *D. melanogaster*. Equal numbers (150) of eggs of *D. melanogaster* and of a known strain of *D. funebris* were placed in a culture bottle with a definite amount of food, which was deliberately made insufficient for an optimal development of 300 larvae. Due to the crowding and the competition for food, the numbers of the adult flies which hatched were below 300. By counting the numbers of the flies of the two species which did hatch, it was possible to gauge the viability of each strain of *D. funebris* relative to that of the standard *D. mel-*

anogaster. Table 11 shows that the viability of *D. funebris* is in general lower than that of *D. melanogaster*, the difference being more pronounced at higher temperatures than at the lower one. This may be correlated with the fact that *D. melanogaster* is a species native to the Tropics while *D. funebris* occurs in the Temperate Zone. A

TABLE 11

THE RELATIVE VIABILITY OF THE STRAINS OF *Drosophila funebris* OF DIFFERENT GEOGRAPHICAL ORIGIN
(FROM TIMOFEEFF-RESSOVSKY)

STRAINS OF D. FUNEBRIS	VIABILITY IN % OF THAT OF DROSOPHILA MELANOGASTER			VIABILITY IN % OF THAT OF THE BERLIN STRAIN OF D. FUNEBRIS		
	15°	*22°*	*29°*	*15°*	*22°*	*29°*
Berlin	81	42	18	100	100	100
Sweden	88	40	21	108.6	95.2	116.6
Norway	80	41	21	98.7	97.6	116.6
Denmark	79	44	22	97.5	104.7	112.2
Scotland	84	43	20	103.7	102.4	111.1
England	78	42	21	96.3	100.0	116.6
France	80	44	25	98.7	104.7	138.8
Portugal	71	45	28	87.6	107.1	155.5
Spain	69	48	30	85.2	114.3	166.6
Italy	78	43	25	96.3	102.4	138.8
Gallipoli	75	44	26	92.6	104.7	144.4
Tripoli	64	47	31	79.0	111.9	172.2
Egypt	68	46	30	83.9	109.5	166.6
Leningrad	90	43	22	111.1	102.4	122.2
Kiev	91	44	28	112.3	104.7	155.5
Moscow	101	43	28	124.7	102.4	155.5
Saratov	92	42	30	113.6	110.0	166.6
Perm	98	41	26	121.0	97.6	144.4
Tomsk	96	42	28	118.5	100.0	155.5
Crimea	87	42	28	107.4	100.0	155.5
Caucasus I	89	43	31	109.9	102.4	172.2
Caucasus II	86	45	32	106.2	107.1	177.7
Turkestan	90	44	34	111.1	104.7	188.8
Semirechje	92	46	36	113.6	109.5	200.0

comparison of the geographic strains of *D. funebris* with each other is facilitated if their viabilities are expressed in percentages of that of some one arbitrarily chosen strain. The right half of Table 11 presents the data recalculated taking the viability of the Berlin strain of *D. funebris* to equal 100. It can be seen that at 15° C. the viability of the strains from the Mediterranean region is lower, and that of

the strains from Russia higher, than that of strains from western, central, and northern Europe. At 29°C. the strains from Russia and the Mediterranean countries are more viable than the western European ones. Western and northern Europe has a relatively mild climate throughout the year; the climate of Russia and Siberia is more rigorous, with cold winters and hot summers; the Mediterranean region enjoys a mild winter but has a hot summer. The sensitivity of western European strains both to heat and to cold, the adaptability of the Mediterranean ones to heat but not to cold, and the hardiness of strains from Russia and Middle Asia in both extremes appear to be correlated with the exigencies of the climates in their habitats.

Comparative studies on adaptively significant physiological traits in different species of North American frogs, and in geographic races of the leopard frog, *Rana pipiens*, have been made by Moore (1942, 1949a, 1949b). The frog species of predominantly northern distribution have lower minimum and maximum limiting temperatures for normal embryonic development than species of more southerly distribution. Thus, *Rana sylvatica*, which lives in Canada and in northern United States, has the temperature tolerance of 2.5°–24°C., while *R. catesbeiana* of the eastern half of the United States and northern Mexico has the limits 15°–32°C. The strains of *R. pipiens* from Canada and northeastern United States have the tolerance of 5°–

TABLE 12

GEOGRAPHIC VARIATION IN EMBRYONIC TEMPERATURE TOLERANCE (IN °C.), DIAMETER OF UNCLEAVED FERTILIZED EGGS (IN MM), AND IN HOURS REQUIRED BY THE EMBRYOS TO REACH A CERTAIN STAGE OF THE DEVELOPMENT IN THE FROG *Rana pipiens*
(AFTER MOORE)

LOCALITY AND LATITUDE	TEMPERATURE TOLERANCE	DEVELOPMENT IN HOURS		EGG DIAMETER
		At 12°C.	*At 28°C.*	
Quebec, 46°N	?–28			1.80±0.05
Vermont, 45°N	5–28	325	50	1.77±0.03
Wisconsin, 44°N	?–28			1.76±0.04
New Jersey, 40°N	5–28			1.77±0.04
Louisiana, 30°N	5–32	348	41	1.60±0.02
Ocala, Florida, 29°N	9–33	354	42	1.43±0.02
Englewood, Fla., 27°N	11–35	364	38	1.32±0.02
Texas, 32°N	10–32	429	47	1.61±0.04
Axtla, Mexico, 22°N	12–33	396	42	2.00±0.03

28°C. (Table 12). It should, however, be noted that in Canada this species breeds in May or June, in northern New York around April 11, and near New York city around April 1. These differences in breeding dates provide a "northern environment" for the developing eggs. Further south, the tolerance limits move to a higher temperature range; the breeding season in North Carolina is February-March, while in Georgia and Florida the frogs may breed in any month of the year.

Northern frog species develop more rapidly than southern ones at low temperatures, but at high temperatures the difference is diminished or even inverted. The same is true of the geographic races of *Rana pipiens* (Table 12). Northern species tend to have larger eggs than southern ones, and the same is true for the geographic strains of *R. pipiens*, except that the Mexican strain has the largest eggs of all. Northern species deposit their eggs in a submerged globular egg mass, while southern ones deposit them in smaller groups or in a single layer on the water surface. The northern method probably protects the eggs against sudden freezing of the water, while the southern one facilitates the oxygen diffusion to the developing embryos. As far as known, the North-American frog species other than *R. pipiens* do not show clear racial physiological differentiation of the type encountered in the latter species. Moore reasonably surmises that this fact explains the geographic area of *R. pipiens* being much the greatest and including a wide variety of climatic conditions. Somewhat similar situations have been described earlier by Goldschmidt (1932, 1933, 1934) for the populations of the gypsy moth (*Lymantria dispar*) in different parts of Japan and of northern Eurasia.

Situations reminiscent of Turesson's plant ecotypes which recur wherever certain ecological conditions are encountered in the geographic area of a species (see above) have been described in animals by Dice and Blossom (1937), Dice (1939a and b), and Blair (1947a and b). The pelage color of the rock pocket mouse *Perognathus intermedius* is correlated with that of the soil in its habitats. The preferred habitat of this mouse is the so-called rock-hill association, which occurs in many parts of Arizona in the form of islands surrounded by sandy deserts or other types of terrain. The soil color in the rock-hill association varied from light decomposed granite to a

dark lava. In the eighteen colonies examined the light mice lived on light and dark mice on dark soil. In the cactus mouse (*Peromyscus eremicus*), dark races have been recorded from three localities in California, Arizona, and Sonora, where the soil color is dark. But in certain other localities in Arizona where outcroppings of dark lava are present only some dark individuals occur in the mice populations. Dice (1939a) advances the very reasonable conjecture that in these localities darkly colored ecotypes are in the process of development. Dice and Blair are inclined to believe that the parallelism between the pelage and soil colors in mice is due to a selection by predators which favors protective colorations.

REGULARITIES IN GEOGRAPHIC VARIATION

In the absence of experimental data, the adaptive significance of some racial traits can be inferred from indirect but still convincing evidence. Thus, structural and physiological peculiarities of desert, alpine, prairie, tundra, tropical rain forest, and other types of vegetation have been known since pre-Darwinian times. Reduction of the evaporating leaf surface, transformation of leaves into spines, development of pubescence or waxy covering on the epidermis, presence of chlorophyll in the surface layers of the bark, fleshiness of the leaves, twigs, and stems are well-known examples of the adaptations in desert plants. Astonishing resemblances between certain American cacti and African euphorbias are among the best illustrations of evolutionary convergence.

Rensch (1929, 1936, 1938, 1939, 1943, 1947) has been the pioneer of critical studies on rules of geographical racial variation among animals (see also Mayr, 1942). Gloger's rule has been known since the nineteenth century. It states that in mammals and birds, races which inhabit warm and humid regions have more melanin pigmentation than races of the same species in cooler and drier regions; arid regions are characterized by accumulation of yellow and reddish-brown phaeomelanin pigmentation. Among insects, the pigmentation increases in humid and cool and decreases in dry and hot climates, the humidity being apparently more effective than temperature (Zimmermann 1931 in wasps, Dobzhansky 1933c in ladybird beetles). For the ladybirds, eastern Asia (eastern Siberia, Japan) is the center of heavily pigmented races; to the southwest and southeast of this re-

gion, lighter and lighter races are encountered, until centers of very pale races are reached in California in the Western, and in Turkestan in the Eastern Hemisphere.

In mammals and birds, races which live in cooler climates are larger in body size than races of the same species in warmer climates (Bergmann's rule). Petersen (1947) finds, however, that in Scandinavian butterflies the wing length decreases northwards. In warm-blooded animals, races which inhabit cooler regions have relatively shorter tails, legs, ears, and beaks than those from warmer ones (Allen's rule). Petersen (1949) finds this rule to apply to some, although not to all European butterfly races. According to Rensch (1943), Mediterranean races of species of *Carabus* beetles tend to be smaller, more elongate, and have relatively longer antennae and legs than those from central and northern Europe. In birds, races with relatively narrower and more acuminate wings tend to occur in colder, and those with broader wings in warmer, climates (Rensch's rule). In mammals, shorter but coarser hair and a decrease in the amount of down is observed in warm countries. In birds, the inhabitants of colder countries deposit more eggs per clutch than those of warm countries. Fish of cooler waters tend to have a larger number of vertebrae than those living in warmer waters; increase of salinity has the same effect as decrease in temperature; the forms which inhabit swiftly flowing waters tend to be larger and to have more streamlined body shapes than inhabitants of sluggish or stagnant waters; cyprinidin fishes isolated in desert springs tend to lose their pelvic fins (Hubbs 1940). The size of the shells in local races or species of mollusks is greatest in climates that show a certain optimum relation between temperature and the amount of precipitation (Rensch 1939).

The adaptive significance of some of the rules is evident, of other rules more or less conjectural. Thus, the function of the longer pelage and the greater amounts of wool in mammals of cold lands is sufficiently obvious. Bergmann's rule (large body size in cool and small size in warm climates) is most likely concerned with the temperature regulation of the animal. Larger body size means a relatively smaller body surface, and consequently a more limited loss of heat. A similar explanation would appear to apply to Allen's rule as well. The protruding body parts, the extremities, tails, and ears, are subject to a

rapid loss of heat. The increase of the body surface in just these regions is therefore unfavorable in cold, and desirable in warm climates. Gloger's rule for the vertebrates resembles the sun tanning reaction of the human skin, and may have an analogous significance (Rensch 1936).

Strange as it may seem, the correlations between racial traits and the environment revealed by the rules were in the past used by some authors as arguments against the natural selection theory. This confusion was due to the prevalence among biologists of the belief in inheritance of acquired characteristics. Racial differentiation was considered a result of direct modification by the environment, perpetuated by a gradual change of the germ plasm in the direction of the phenotypic change. This interpretation seemed borne out by experiments which showed that changes analogous to those observed in a particular geographical race may also be brought about in other races of the same species by exposure to certain environmental agents. Thus, in the classical experiments of Standfuss, exposure to heat treatment produced, from the pupae of the central European races, butterflies which resembled the varieties from Syria or southern Itlay. On the other hand, treatment of the central European races with cold resulted in a resemblance to races from northern Scandinavia. Exposure of a mammal to cold or heat may produce, respectively, increase or decrease of the hair length, a change analogous to that distinguishing the geographic races from the high and the low latitudes. Bergmann's, Allen's, and Gloger's rules (see above) have their counterparts among the changes that can be induced in animals by application of appropriate environmental stimuli, namely, changes in temperature and humidity or combinations thereof. The same is true for plants, where the phenotypic changes wrought by treatments with external agents may simulate the characteristics of races and species existing in nature.

The parallelism between the rules of genotypic racial variability and those of phenotypic modification has, however, a more subtle and significant meaning than was supposed by Lamarckists. As pointed out in Chapter II, the adaptedness, the harmony between the organism and its environment, means possession of a genotype with a favorable norm of reaction. A norm of reaction is favorable if the frequently recurring environmental stimuli evoke phenotypic

modifications which enable the organism to stay alive and to have progeny. Genotypes that condition the most adaptive modifications are retained and multiplied in the process of natural selection. It is, therefore, no accident that mammals which inhabit cold lands react to exposure to low temperatures by development of warm fur. The amount of phenotypic plasticity is, however, also set by the genotype. As pointed out by several authors, notably by Gause (1947) and Schmalhausen (1949), there is a trend in evolution towards fixation of long established and adaptively important traits. A perhaps unnecessary term, "organic selection," was coined to describe this very real and important trend. In a group of animals which has evolved in cold climates the genes for the warm fur may become fixed, and the capacity to have a less warm pelage on exposure to heat may be lost. The opposite may occur in tropical forms.

THE PROBLEM OF ADAPTIVELY NEUTRAL TRAITS

It has been stated in Chapter V that no two genotypes are likely to be exactly equal in adaptive value. Taken literally, this means that any genetic change must be either useful or harmful to its possessors, and that no adaptively neutral traits can exist. This is indeed the view esposued by Fisher (1930), Ford (1940a, 1945), Fisher and Ford (1947), and their schools. Such a view leads, however, to difficulties when applied to many concrete situations. Most human populations are polymorphic with respect to genes which produce variations in such traits as blood groups, ability or inability to taste phenyl-thio-carbamide, and presence or absence of hair on the middle segment of the fingers. The M-N blood groups, conditioned by the two alleles of a gene, M^M and M^N, may serve as an example. The frequency of the allele M^M in most human populations varies from 0.50 to 0.65; a few populations (chiefly American Indians) have higher frequencies, up to 0.92, and Australian aborigines have low ones, down to 0.16. The situation with genes for tasting phenyl-thiocarbamide is rather comparable to that with M-N blood groups (Boyd 1950). Fisher et al. (1939) found however that alleles for tasting and not tasting this substance exist not only in the human species but among the anthropoids as well. The great apes are polymorphic also for the A-B-O blood groups. The polymorphism in these traits has, accordingly, not arisen recently in human populations. It

is a very ancient condition, inherited possibly from the common ancestors of man and the apes. Fisher et al. infer that the polymorphisms in the blood groups, tasting phenyl-thio-carbamide, etc., must be balanced by heterozygotes possessing higher adaptive values than the homozygotes.

There is, however, absolutely no evidence that heterozygosis or homozygosis for most of the blood-group genes, or for tasting phenyl-thio-carbamide, bring any advantages or disadvantages whatsoever to their possessors. It must be conceded that the absence of such evidence does not prove the converse proposition, that these traits are neutral. But to assume that the polymorphism is always adaptive and governed by selection means to take for granted what has thus far proved impossible to demonstrate. There is no compelling necessity to adopt such a course, because alternative possibilities certainly exist. It is not unreasonable to suppose that mutations to and from various alleles of blood-group genes, or of genes for tasting certain substances, may be taking place in human populations, and that such mutation pressure obtained also in the past, in our human and prehuman ancestors. The finding of analogous polymorphisms in man and in the apes does indicate that these polymorphisms are ancient. We may be dealing with equilibria of alleles of certain genes maintained by opposing mutation rates (Chapter III). There is, of course, the fact that the frequencies of these alleles vary in different human populations. Such differences need not necessarily be cause by natural selection. They may, as far as one is able to judge at present, be explained also by random fluctuations in gene frequencies in effectively small populations. Such random variations of gene frequencies are referred to as the genetic drift, or the Sewall Wright effect. It must be emphasized at the outset that the genetic drift hypothesis does not exclude the participation of natural selection in the diversification of populations. The frequencies in populations of many genes may often be controlled by interaction of genetic drift and natural selection. This is especially true for genes so close to adaptive neutrality that they are subject to only small or intermittent selective pressures.

The idea of genetic drift was adumbrated by Brooks (1899) and by Hagedorn and Hagedorn (1921). Its development was started largely independently by Fisher (1928, 1930), Dubinin (1931),

Dubinin and Romashov (1932), and especially by Wright (1921, 1931a and b, 1932). Modern and concise formulations and discussions can be found in Wright 1948 and 1949, Li 1948, and Lerner 1950.

The complete constancy of the gene frequencies in the absence of mutation and selection, demonstrated by Hardy and Weinberg (Chapter III), may obtain only in ideal infinitely large Mendelian populations. In reality, no population is infinite, and many are small. Suppose that two alleles of a gene, A and a, are equally frequent in a finite population. Their frequencies in a certain generation are $q = (1 - q) = 0.5$. In the next and the following generations, the frequencies will fluctuate up and down from 0.5. Wright shows that these fluctuations may lead to important results. So long as the values of q remain between 0 and 1, the fluctuations are reversible, but as soon as the latter values are reached an irreversible change has taken place: one of the two alleles is lost and the other has reached a state of fixation, that is, the population is now homozygous for it. The deviations from the constancy of gene frequencies are inversely correlated with the absolute number of breeding individuals in the populations, with its "population number" denoted by the symbol N. Wright (1931, pp. 110–111) defines the population number as follows: "The conception is that of two random samples of gametes, N sperms and N eggs, drawn from the total gametes produced by the generation in question. ... Obviously N applies only to the breeding population and not to the total number of individuals of all ages. If the population fluctuates greatly, the effective N is much closer to the minimum number than to the maximum number. If there is a great difference between the number of mature males and females, it is closer to the smaller number than to the larger."

The greater the effective population size, the more nearly constant will be the gene frequencies in the absence of mutation and selection. In small populations the gene frequencies are variable. The relation between the effective population size and the variance of gene frequencies in one generation, σ_q^2, is given by Wright's simple formula $\sigma_q^2 = q\ (1 - q)/2N$. This variance will grow in proportion to the

number of generations, and thus may become important with time even if the increment per generation is small.

SCATTERING OF THE VARIABILITY

Imagine a Mendelian population which remains numerically stationary from generation to generation. In a stationary population a pair of parents produce on the average two offspring which survive to the adult stage. A mutation of the gene *A* to a gene *a* gives a single heterozygous individual, *Aa*. The mutant must mate with a normal individual, $Aa \times AA$. The offspring of this mating is expected to consist of equal numbers of normal, *AA*, and mutant carrier individuals, *Aa*. But, owing to chance, the numbers of surviving offspring may be none, 1, 2, 3, 4, or more individuals, forming a so-called Poisson Series. If the entire progeny fails to survive, the mutant is lost; if one individual survives, the probability of loss of the mutant is 0.5; with two individuals surviving the probability of loss is 0.25, and with r survivors it is 2^{-r}. The aggregate probability that a single mutant will be lost in a stationary population is 0.3679 in every generation, 0.3679 that it will be represented in the next generation also by a single individual, 0.1839 that it will be represented by two individuals, 0.0613 by three, 0.0153 by four, 0.0031 by five individuals, etc. If the mutant is not lost in the first generation, it is exposed to the risk of extinction in the next and in the following generations. To be sure, some mutants will, owing to change, be represented by two, three, or more individuals. But since the loss of a gene is irreversible, the conclusion follows that most mutants never become established in the populations, and are lost to the species. Furthermore, as shown by Fisher (1930), this is true not only for neutral and harmful but even for advantageous mutants (see Table 13).

The scattering of the hereditary variability may be visualized in another way. Imagine a population in which every gene is represented only one, that is to say, every individual carries two different alleles neither of which is present in any other individual. If the population is numerically stationary from generation to generation, 36.79 percent of the variety of alleles will be lost in the next generation, some will be represented once, others twice, thrice, and more times. The loss of some and the increase in frequency of other alleles will go on in subsequent generations as well. If no mutation occurs, the popula-

tion will ultimately become homozygous for a single allele. Dubinin and Romashov (1932) and Moody (1947) have devised models to illustrate this process of drift of alleles in finite populations.

According to Wright in a population of N breeding individuals, $\frac{1}{2}$N genes either reach fixation or are lost in every generation. Suppose that in a population many genes are represented each by two alleles which are equivalent with respect to selection, and that the

TABLE 13

PROBABILITY OF EXTINCTION AND OF SURVIVAL OF A MUTATION APPEARING IN A SINGLE INDIVIDUAL
(AFTER FISHER)

GENERATION	PROBABILITY OF EXTINCTION		PROBABILITY OF SURVIVAL	
	No Advantage	*1% Advantage*	*No Advantage*	*1% Advantage*
1	0.3679	0.3642	0.6321	0.6358
3	0.6259	0.6197	0.3741	0.3803
7	0.7905	0.7825	0.2095	0.2175
15	0.8873	0.8783	0.1127	0.1217
31	0.9411	0.9313	0.0589	0.0687
63	0.9698	0.9591	0.0302	0.0409
127	0.9847	0.9729	0.0153	0.0271
Limit	1.0000	0.9803	0.0000	0.0197

initial frequency of each allele is 50 percent (q = 0.5). With no mutations taking place, the frequencies of the different alleles will in the following generations fluctuate up and down from 50 percent, some becoming more and other less frequent owing to chance. Sooner or later a condition will obtain when gene frequencies from 0 percent to 100 percent will become equally numerous, and $\frac{1}{4}$N of the genes will reach fixation and $\frac{1}{4}$N will be lost in every generation. Wright's formula describing this process is

$$L_T = L^{-T/2N}$$

where L_0 and L_T are the numbers of the unfixed genes in the initial and in the T generation of breeding respectively, N is the population number, and e the base of natural logarithms.

The interrelations of selection and the genetic drift have been examined by Wright (1931a, 1940a and b, 1948 and others). His mathematical arguments are too abstruse to be presented here, but

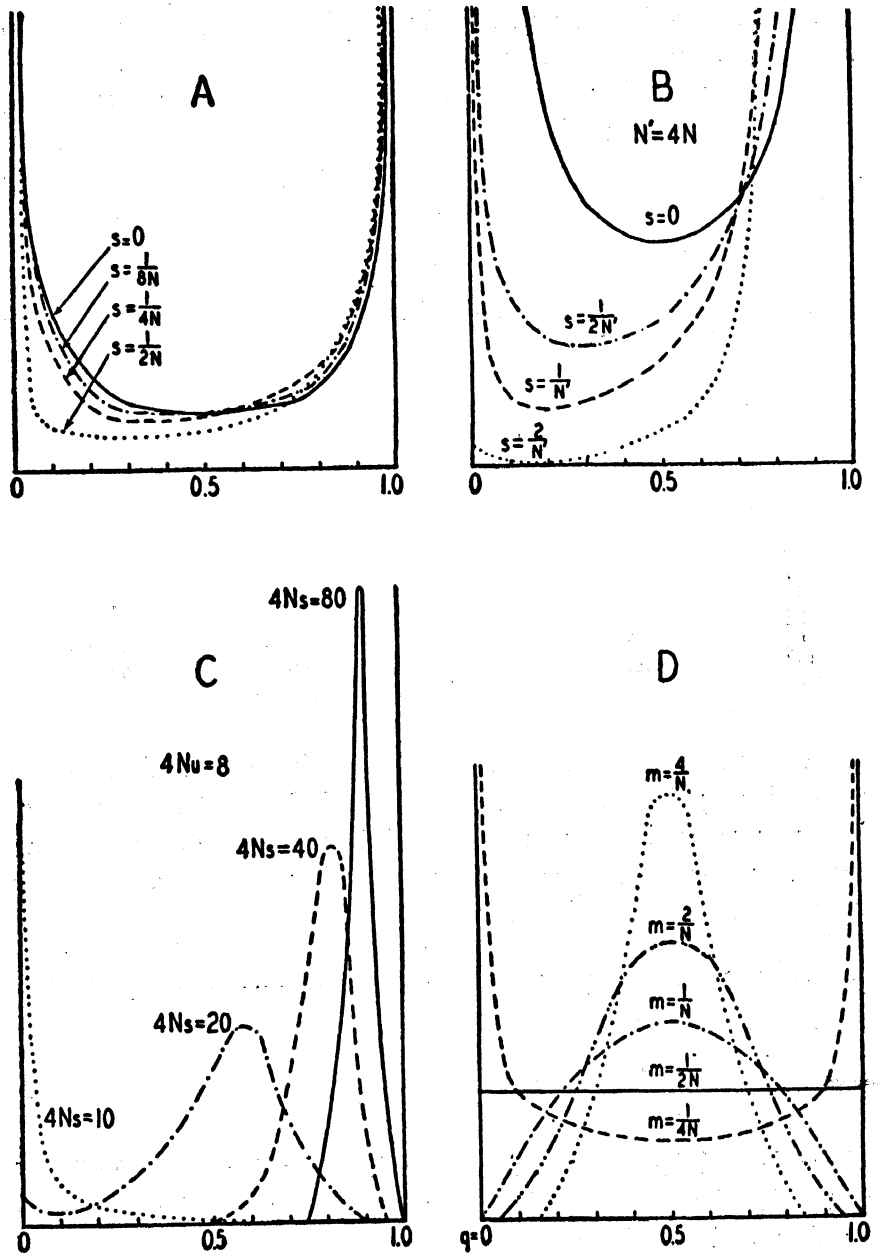


FIG. 13. Distribution of gene frequencies in populations of different size under different selection, mutation, and migration pressures. Further explanation in text. (From Wright.)

his conclusions are simple enough. The smaller the effective population size, the greater are random variations in gene frequencies, and the less effective become weak selection pressures. In small populations, alleles favored by selection may be lost and the less favored ones may reach fixation. In very large populations, even very small selective advantages and disadvantages will eventually be effective; but a more rigorous selection must be applied to overcome the genetic drift in small populations.

The relations between population size and selection intensity are illustrated in the diagrams in Fig. 13. In these diagrams the abscissae indicate the gene frequencies from 0 (loss) to 1 (fixation). The ordinates may be interpreted in any one of the three following ways. First, we may consider the fate of the different variable genes in a single population, for natural populations may vary with respect to many genes. Some of these genes may reach fixation, others may be lost, and still others may remain unfixed, that is to say, they are represented by two or more alleles with different frequencies ($0 < q < 1$). The ordinates in the diagrams indicate, then, the frequencies of the different gene frequencies in a population. Second, one may follow the fate of the same gene in different populations, for example, in the subgroups of the same species, that is to say, in the colonies into which the species is broken up. The ordinates in Fig. 13 refer then to the frequencies of the subgroups in which a given gene frequency is reached. Third, the ordinates may be interpreted to show how often, in the long run, any one gene comes to possess a given frequency.

In small populations (Fig. 13A) the gene frequency curves are U-shaped. This means that in such populations a majority of the variable genes are either fixed or lost most of the time; in a majority of the colonies into which a species may be subdivided any given gene is either totally absent, or else present to the exclusion of all but one of its possible alleles. The curves show that the effectiveness of weak selection is low in small populations. With small selection coefficients, of the order $s = 1/8N$ to $s = 1/2N$, the shape of the curves is little modified. Genes are lost or fixed at random, with little reference to the selection pressure. Fig. 13B represents the action of a selection of the same absolute intensity as in Fig. 13A, but in a population that is four times larger ($N' = 4N$). Here a selection

of the order $s = 2/N'$ is rather effective; the curve is no longer U-shaped but has a definite maximum at the right, indicating that the gene alleles favored by selection mostly reach fixation and supplant the less favored ones. The equation describing this family of curves is, according to Wright (1931a), $y = Ce^{4Nsq}\, q^{-1}\, (1 - q)^{-1}$, where e is the base of natural logarithms, q the gene frequency, s the selection coefficient, and $\mathcal{N}$ the population number.

The interaction of the mutation pressure with selection and the population size factor presents naturally an even more complex problem. Under certain conditions, namely, if the selection pressure is of the same order of magnitude as the mutation rate, and both are very small, the random variations of the gene frequencies in small populations become important. The curve of the gene frequencies is U-shaped, indicating that gene alleles are likely to reach fixation or loss largely irrespective of the mutation and selection pressures. Mutation and selection rates that may be regarded as small are such as make the products 4Nu and 4Ns smaller than unity. The greater the mutation and selection pressures, the greater is their effectiveness. An example borrowed from Wright (1931a) is reproduced in Fig. 13C. It refers to a population of an intermediate size with a moderate mutation rate ($4Nu = 8$) opposed by a selection of varying intensity. With selection of the order $4Ns = 10$, the mutation pressure gets the upper hand. The allele favored by selection is mostly lost. A doubling of the selection intensity ($4Ns = 20$) changes the situation very appreciably. The gene frequencies fluctuate over a great range of values. In a species segregated into numerous isolated subgroups this means a great differentiation of the species population into local races, some of which will possess characteristics favored by selection and others the relatively unfavorable ones. With a selection becoming more stringent ($4Ns = 40$ and $4Ns = 80$), the amplitude of variation is gradually restricted, the gene frequencies being kept within rather narrow limits centered upon the equilibrium values. The equation describing the curves is $y = Ce^{4Nsq}\, q^{-1}\, (1 - q)^{4Nu} - 1$, where u is the mutation pressure.

The biologically highly significant corollary of the above analysis is that a species, broken up into isolated colonies, may differentiate as a result of the restriction of the population size in these colonies. Even if the environment is homogeneous for all the colonies, and

selection and mutation rates are the same and the initial composition of the populations identical, a sufficient lapse of time will bring about a differentiation. It must be stressed that the differentiation need not, theoretically, be of an adaptive kind. The latter point, however, must be much qualified by the consideration that in practice the separate colonies are exposed to a variety of environments. Although in the abstract the differentiation may be pictured as taking place under the influence of the restriction of the population size alone, or under the influence of the selection alone, in nature the process is going on because of both these factors, one or the other gaining the upper hand, probably only temporarily. The genetic equilibrium in a living species population seems to be a delicately balanced system which can be modified by a number of agents.

THE BIOLOGICAL MEANING OF THE VALUE N

The genetically effective population size, N, is not identical with the total number of individuals of a species or a race. The simplest situation is that of a colony isolated from the rest of the species by secular barriers, within which the population is panmictic, remains stationary in numbers from generation to generation, and in which each pair of parents produces the same number of surviving offspring. For such a colony, N is equal to the number of individuals of the generation now living which will be the actual progenitors of the following generation, or to the number of the actual parents of the now living generation. In reality, the surviving progeny of some parents is large, that of others is small, and that of still others is destroyed entirely. If N_0 is the number of parents, and K that of their gametes giving rise to the surviving offspring ($K = 2$ on the average), the effective population $N = \frac{4N_0 - 2}{2 + \sigma_k^2}$ (Wright 1939, 1940b). Populations of most species vary, often within an enormous range, from generation to generation. Such variations are either connected with seasonal cycles (as in insects which produce several generations per year), with climate, or with fluctuations in the abundance of parasites, enemies, or prey. Wright has shown that the effective N is much closer to the number of individuals attained at the maximum contraction, than to that attained at maximum expansion, of the population. For example, a population may increase tenfold

in each of the six succeeding generations, and then return to its initial size, its minimum being N_0 and maximum $N_0 \times 10^6$. The effective size is then $N = 6.3N_0$ (Wright 1940b).

Segregation of a species into colonies completely isolated from each other and yet perfectly panmictic within themselves is not a common situation. Usually there is some migration, that is, exchange of individuals between the colonies. Migration increases the genetically effective population size. On the other hand, the population of a colony is often not panmictic, because individuals born at a given point may have a greater chance to mate with their neighbors than with residents of remote parts of the same territory. As the territory occupied by the population increases, the genetic situation resembles more and more that of a species continuously and uniformly distributed over the whole species area. This extreme situation, which is the opposite of that in a species broken up into completely isolated colonies, has been analyzed mathematically by Wright (1940b, 1943a and b, 1949, Dobzhansky and Wright 1943). If a population is distributed uniformly over a two-dimensional territory, the parents of an individual are drawn from a certain average area. It may be assumed that this average area is a circle with a diameter D, and a population of N breeding individuals. The grandparents would have come, however, from a larger territory with a greater population, which Wright shows to be $\sqrt{2}$ D and 2N respectively. For n generations the territory becomes $\sqrt{n}$ D and the population nN. The amount of local differentiation of the populations due to genetic drift in a continuously inhabited territory is much less than is expected in isolated colonies. With less than 100 breeding individuals within a circle of diameter D ($N < 100$) considerable differentiation will occur, provided that mutation and selection do not overpower the genetic drift. With N greater than 1,000 there will be little differentiation, and with N greater than 10,000 substantially no differentiation.

ECOLOGICAL VARIABLES AND POPULATION SIZE

It is not possible at present to reach definitive conclusions regarding the role played by genetic drift in evolutionary processes. If genetically effective population sizes in many species are small, at least at some periods of their evolutionary histories, the genetic drift

would have to be recognized as an important factor. If, on the other hand, the population sizes are usually so large that they may be regarded for practical purposes as infinite, the genetic drift will remain only an interesting theoretical possibility. Some polemics, more acrimonious than enlightening, have arisen in biological literature concerning this problem. The only conclusion to be drawn from these polemics is that the available observational and experimental evidence is altogether insufficient, and that more work in this field is urgently necessary.

The total numbers of individuals of many species are very large. The human species, numbering at present close to 2,200 millions, is probably equaled by some higher animals and plants (e.g., trees) and is certainly exceeded by many microorganisms. Only a few total population estimates are, however, available. Dice (1939c) concluded that in the late summer of 1939 the 4,986 square miles of territory in the Black Hills of South Dakota were inhabited by between one million and five million mice of the species *Peromyscus maniculatus osgoodi.* The distribution area of this mouse is much wider than the territory studied. According to Blair (1946), between 9,270 and 17,655 individuals composed the subspecies *Peromyscus polionotus leucocephalus* on the Santa Rosa Island, off Florida. In 1939 the population of the bird *Sula bassana* was about 167,000 of which 109,000 resided in twenty-two colonies in the British Isles (Fisher and Vevers 1939). The adult population of the butterfly *Polyommatus icarus* on the small isle of Tean was about 450 to 500 (Dowdeswell et al. 1940). The distribution areas of some species are very small and the total numbers of existing individuals are correspondingly limited. Thus, *Oenothera organensis* occurs only in some canyons of the Organ Range, New Mexico, and its total population is in the neighborhood of 500 (Emerson 1939). For more data on population sizes, see Allee et al. 1949, and Elton 1930, 1942.

All the individuals of a species very rarely constitute a panmictic breeding unit. Isolation by distance, formation of isolated or partially isolated colonies, and combinations of these factors, may reduce genetically effective population sizes even in very common species down to values which make the genetic drift an important agent in evolution (Elton 1930, 1949). Wright (1939) has shown this to be the case even in *Oenothera organensis.* The 500 individuals of this species

appear to be broken up into about 50 colonies with an average size of 10 individuals. In about 98 percent of cases, the pollination of the plants is by members of the same colony, and in 2 percent from other colonies. Erickson's (1945) analysis has revealed within the subspecies *Clematis fremontii riehlii* an hierarchy of colonial subdivisions, down to elementary "aggregates" numbering from several dozen to several hundred individuals. The colonies are more or less isolated from each other, and often show morphological differences that may perhaps be ascribed to the genetic drift. Such colonies are formed most easily in species restricted to certain soils or to other environmental conditions which occur spotwise in the general distribution area. However, Baldi et al. (1945) found them also in the pelagic crustacean *Mixodiaptomus laciniatus* in Lake Maggiore in Italy.

A fundamental consideration to be kept in mind in studies both of colony formation and of isolation by distance is that organisms provided with excellent means of locomotion may nevertheless be restricted to small territories. Birds provide especially striking illustrations of such restriction. Gross (1940) has studied the behavior of herring gulls (*Larus argentatus*) nesting on Kent Island, off Nova Scotia. A total of 23,434 individuals were banded on the islands, and the recovery of the banded specimens has shown that they tend to return to Kent Island for breeding. Although seasonal migrations take them as far as the Gulf of Mexico and beyond, not only the adults but also the young born on Kent Island come back to their breeding places. Much work has been done on another aspect of bird biology, namely their territoriality. Many migratory as well as resident species, forms which, out of the breeding season, are gregarious or single, exhibit a curious behavior pattern when the breeding season approaches. Namely, individuals subdivide the available territory among themselves, and forcibly eject intruders of the same species and sex. Nice (1937, 1943), and Erickson (1938) have published excellent accounts of the situation in the song sparrow (*Melospiza melodia*) and the wren tit (*Chamaea fasciata*), respectively. In these birds the effective populations are small and the territory of a breeding unit is definitely restricted, sometimes to within a few hundred square meters. (See Mayr, 1942, for further discussion and references.)

A considerable literature has accumulated concerning territoriality also in mammals, some of which exhibit the territorial behavior in a very striking fashion (Blair 1940a and b, 1948, Burt 1940, Eisentraut 1934, Howard 1949, and others). Elton (1930) has elaborated a very plausible scheme to show how the territorial behavior, combined with repeated expansions and contractions of the populations owing to famines and epidemics, might result in genetic drift and genetic differentiation of local populations. Restriction to a territory to which the animals actively seek to return if forcibly removed by the experimenter, is known also in toads and in some reptilians (Bogert 1947). Despite the large-scale migrations which occur regularly in many fish species, individuals return for breeding often not only to the river system but actually to the identical tributary stream in which they were originally hatched. Instances of this amazing phenomenon are especially known popularly in various species of migratory salmon.

Among the invertebrates, the phenomena of territoriality and homing are known in social insects and in some solitary ones (tsetse flies). More frequently, the movements depend upon the distribution in the environment of food and shelters, and are more or less at random if the environment is homogeneous. The rates of movement vary greatly from species to species. Timofeeff-Ressovsky (1939a and b), Dobzhansky and Wright (1943, 1947), and Burla et al. (1950) released a known number of *Drosophila* flies, marked with innocuous mutant genes or with a spot of paint on the thorax, in natural habitats. At desired intervals of time after the release, traps which attract *Drosophila* flies are exposed at regular distances from the point of the release, and the numbers of marked and of wild flies which come to the traps are recorded. The dispersion rates of the flies are measured in terms of the variance (in square meters or other appropriate measure) of their distribution around the point of the release. The dispersion is much more rapid in *Drosophila pseudoobscura* than in *D. willistoni* and *D. melanogaster*, and in each of these species more rapid at higher than at lower temperatures. One year after the release of mutant flies of *D. pseudoobscura* in a locality in the Sierra Nevada of California, about half of the progeny of the released flies were found within a circle with a radius of about 0.86 of a kilometer from the point of the release. About 95 percent of the

progeny were found within a circle with a radius of 1.76 kilometers, and about 99 per cent within a circle of 2.2 kilometers.

The rates of dispersion in mosquitoes are vastly greater than even in the rapidly moving *Drosophila* species (Bates 1949). *Anopheles culicifacies* reaches roughly the same degree of dispersion one day after the release as *D. pseudoobscura* does after one year. A review of the data available for other organisms has been published by Wolfenbarger (1946). One certain conclusion which can be drawn from these data is that the mobility is very different in different organisms. This is likely to be reflected in a corresponding diversity of genetically effective population sizes.

MICROGEOGRAPHIC RACES

Variations in gene frequencies in colonies with limited effective population sizes would produce genetic differences between these colonies. Such variations are also expected between local populations of a species in a continuously inhabited territory, provided that the effective population density within the ambit of activity of an individual is on the average small (see above). Such genetically different local populations are sometimes referred to as microgeographic races. Needless to say, there is no sharp distinction between the microgeographic and the major geographic races.

Epling and Dobzhansky (1942) and Wright (1943b) have studied the populations of *Linanthus parryae*, a small annual desert plant. It occurs in two phases, with white and with blue flowers respectively. In the southern Mojave Desert, in California, the species occurs in a piedmont area about 70 miles long and five to fifteen miles broad. The proportions of white and blue plants were determined in 1,261 samples of 100 plants each in different parts of the distribution area. Most samples consisted exclusively of whites, but in three "variable areas" (Fig. 14) the proportions of blues varied from 0 to 100 percent. Uniformly blue and uniformly white microgeographic populations were more frequent than mixed ones, so that the distribution curve of the frequencies of the two phases in these micropopulations resembled Wright's U-shaped curves expected in small populations (Fig. 13). Populations which occurred in territories 750 feet or less apart exhibited a strong correlation in the frequencies of the two color phases; populations at distances up to one mile still showed

some correlation, but at greater distances the frequencies were independent. Efforts to detect some relationship between the frequencies of blue and white plants in the micropopulations, and any topographic, soil, vegetational, or other characteristics of their environment, were quite unsuccessful. The variation seems entirely haphazard. Nevertheless, Wright's analysis indicates that the concentra-

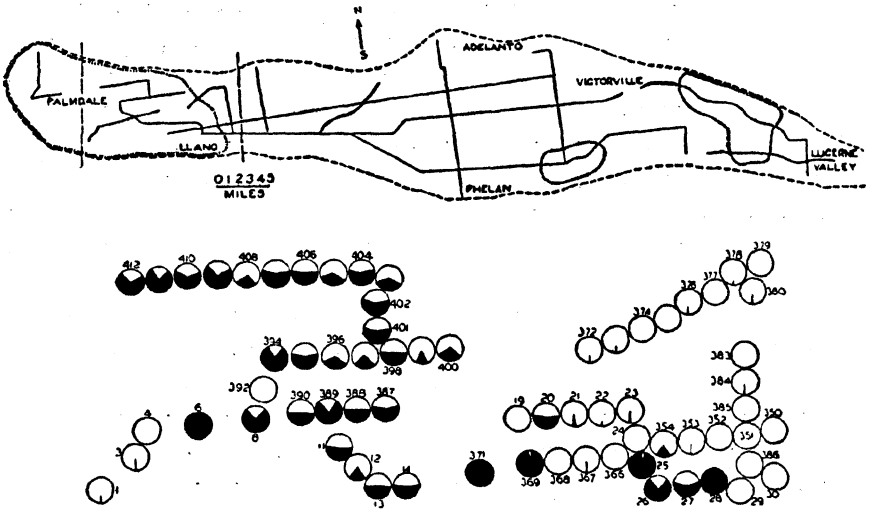


FIG. 14. Above map showing the distribution of *Linanthus parryae* in Southern California (broken line), the location of the three areas in which blue-flowered plants are found (dotted lines), and the routes taken for sampling the population (continuous lines). Below, an enlarged diagram of a part of the western end of the area shown in the map above (that bounded on the map by two vertical broken lines), showing the relative frequency of white- and blue-flowered plants at each collection station in that area. Numbers are those arbitrarily assigned to the stations. Black sectors, blue flowers; white sectors, white flowers. (From Stebbins.)

tion of the blues in the three "variable areas" must be caused by some unknown selective factor. As to the microgeographic variation within these areas, the most reasonable hypothesis is that it is caused by genetic drift. The species seems to be cross-pollinated by insects; the distance to which pollen is transported is, unfortunately unknown. Wright's calculations indicate the genetically effective population size, N, in *Linanthus* to be between 14 and 27 individuals in the area from which the parents of an average individual are drawn.

Species of land snails, owing to their low mobility, are particularly

apt to be subdivided into colonies the members of which seldom pass over the barriers separating one colony from the others. From the centre of most of the volcanic islands in the South Seas arises a mountain cone, with slopes crevassed by radiating valleys separated by narrow ridges. The snail species which inhabit the valleys, such as *Achatinella* on Hawaii (Gulick 1905) and *Partula* on Tahiti and Moorea (Crampton 1916, 1932), show an extreme diversity of local races. The racial characteristics vary from valley to valley with no consistent relation either to geographical sequence or to the obvious peculiarities of the environment. Populations of adjacent valleys may differ more widely in some characters than populations of remote valleys. Different species inhabiting the same territory may vary in different directions. Thus, the shells of *Partula taeniata* in the northwestern part of the island of Moorea are smaller and stouter, and those of *Partula suturalis* are longer and more slender than in other parts of the island, and yet the two species are found on the same food plants. Welch (1938) found that populations of *Achatinella mustellina* on the island of Oahu form significantly different colonies within the same valley, and in fact within a few meters of each other.

Diver (1939, 1940) has described an analogous situation in several snail species in England. An average colony of *Cepaea hortensis* is estimated to consist of 79 individuals, although colonies may contain from ten to more than 2,000 individuals. The variation may be extremely localized. Thus, in a population continuously occupying a 45-yard strip, all subsamples for 15 yards yielded some brown-colored shells, while in the next 20 yards no browns were found. Cain and Sheppard (1950) find, however, that at least some of these microgeographic variations are correlated with certain features of the local environment. Thus, unbanded reddish snails are common in populations of beechwoods, while banded ones predominate in the hedgerows. Cain and Sheppard rightly argue that such correlations indicate that the variations observed by them fall in the class of adaptive polymorphism, possibly balanced polymorphism (see Chapter V). The local differentiation in the traits which they observed to be correlated with the environment is, then, due to natural selection and not to genetic drift. It should, however, be noted that not all variable characteristics in the snail show such correlations, and, hence, the participation of the genetic drift in the microgeographic

differentiation is by no means excluded in the species which Cain and Sheppard have studied. The differentiation of human populations with respect to the skin color is almost certainly caused by selection, but it does not follow from this fact that the racial differentiation of, for example, the blood-group frequencies is also conditioned by selection. Indeed, Birdsell (1951) has published detailed data on variation of blood-group frequencies in some tribes of Australian aborigines which are strongly indicative of genetic drift in these populations.

In animals with good means of locomotion and in plants with effective mechanisms for the distribution of seeds the situation is the same in principle as in the snails, although the absolute distances which separate the colonies are of a different order. Kramer and Mertens (1938), and Kramer (1946) have examined the variations in the lizards of an archipelago in the Adriatic Sea. The differences between the island and mainland populations are positively correlated with the length of time elapsed since the separation of the island from the mainland, as measured by the depth of the intervening channels. More important still, the divergence has progressed further on small islands on which the populations are numerically limited than on large islands of equal geological age. An analogous situation has been described by Marshall (1940) for mammals of the islands in the Great Salt Lake, in Utah. Recognizable subspecies have evolved on well isolated islands, the duration of the isolation being surmised to be around 20,000 years. Mayr (1940) has formulated similar rules for nonmarine birds of the islands in the Pacific Ocean. According to Dice (1939c), mice populations of even geologically young islands are apt to be racially different from those of the adjacent mainland; moreover, the individual variability of the mainland populations is greater than that of the insular ones. This is exactly what would be expected if the formation of insular races were due to restriction of population sizes. Participation of selection in the formation of these races, or microraces, is however by no means excluded.

CONCEALED GENETIC VARIABILITY AND THE GENETIC DRIFT

As shown in Chapter III, natural populations of *Drosophila* and of other cross-fertilizing organisms carry a wealth of concealed re-

cessive mutant genes. This variability is controlled by several factors, such as mutation and selection rates, inbreeding, and the effective population size. Analysis of this variability might yield an insight into the working of these factors, and permit at least a rough estimation of their magnitude. Recessive autosomal lethals are most favorable materials for such studies. The genotype contains many genes capable of producing lethals by mutation. In infinitely large panmictic populations, the equilibrium values for recessive autosomal lethals equal the square roots of the mutation rates giving rise to the lethals. In populations of small effective size the gene frequencies vary within a range that is inversely correlated with the population size (N). In a small colony some of the lethals will be altogether absent, others may be as common as their mutation rates would permit them to be in large populations, and still others may be even more common. Wright (1937) showed that in a species segregated into colonies with small breeding populations, each lethal will at any given time be present in a certain proportion of the colonies, but absent in others. To put it in a different way, each colony will at any time contain only some of the lethals which may exist in the species. Moreover, the average equilibrium frequencies of all lethals in a species as a whole will be smaller if the species is subdivided into small colonies than if it represents a very large undivided population. For a lethal which arises by mutation once in 100,000 gametes the relationships will be, according to Wright, as follows:

POPULATION SIZE, N	EQUILIBRIUM FREQUENCY, q	PERCENT OF THE COLONIES FREE OF THE LETHAL
1,000,000 or more	0.0032	0
100,000	0.0030	0
10,000	0.0020	15
1,000	0.0008	87
100	0.00026	99
10	0.00008	99.9
Self-fertilization	0.00002	99.996

If a species of *Drosophila* is a single breeding population, or if it is subdivided into very large breeding units, there should be no differentiation with respect either to kind or to frequencies of lethals present in various component populations. The frequencies of all lethals should equal the square roots of their respective mutation

rates. The nearest known approach to this situation seems to exist in the tropical species, *D. willistoni*. Pavan et al. (1951) examined the incidence of lethals, semilethals, sterility genes, and other concealed mutants in populations of this species from remote and bioclimatically diverse regions of Brazil. Although some statistically significant variations were encountered, no striking and systematic differences between the populations were brought to light. *D. willistoni* is very common and widespread throughout Brazil. Its breeding populations are probably large.

The situation is quite different in *D. melanogaster* and *D. pseudoobscura* (cf. Chapter III). Dubinin et al. (1936, 1943, 1946, and other works) found wide variations in the incidence of lethals in Russian populations of *D. melanogaster*. Ives (1945) discovered in the American populations frequencies quite appreciably greater than in any Russian ones. Although the mutation rates also varied in different populations, there is little evidence that the magnitudes of the mutation rates are correlated with the sizes of the stores of concealed mutants in the same populations. In countries with cold winters, *D. melanogaster* does not hibernate outdoors, and its populations are reduced to scattered foci in fruit stores and human dwellings. This creates favorable conditions for the genetic drift, which probably accounts for at least a part of the observed fluctuations in the frequencies of lethals. In *D. pseudoobscura*, the proportions of the third chromosomes carrying recessive lethals are about twice as high in populations of Mexico and Guatemala as they are in California. On the other hand, the mutation rates in Mexico and in California populations are similar (Chapter III). The most likely hypothesis to explain these relationships is as follows. The climates of Mexico and Guatemala permit *D. pseudoobscura* to breed more or less continuously throughout the year, while in California the populations are periodically reduced owing to summer heat and aridity, or to severe winters, or to both. Periodic contractions and expansions of the populations result in reduction of their genetically effective sizes (see above).

A most suggestive case of microgeographic differentiation with respect to the concealed mutational variability has been described by Spencer (1946, 1947a) in *Drosophila immigrans*. Samples of the population of this species collected in a locality in western Pennsylvania

contained very high frequencies of heterozygotes for the recessive mutant "stubble bristles," and of certain other mutants, which were found rarely or not at all in other populations of the same species. Such high concentrations of mutant genes in heterozygous condition can be produced by genetic drift in populations of small breeding size.

Dobzhansky and Wright (1941, 1943), and Wright et al. (1942) demonstrated that populations of *Drosophila pseudoobscura* from different localities carry different sets of autosomal recessive lethals. Population samples were taken repeatedly at about monthly intervals during the breeding season, at nine stations on Mount San Jacinto, California. Each "station" was a territory of at most a hundred yards square, in which traps were exposed always in the same positions. The nine stations were in three groups or "localities" .The distances between the localities are from ten to fifteen miles, while the distances between the stations within a locality vary from a quarter of a mile to two miles. The flies are found throughout the territory, which has no insuperable barriers to migration from station to station or from locality to locality. As expected, some lethal-carrying third chromosomes were detected in every sample. The strains containing these lethals were then intercrossed, to determine which of the lethals were allelic (and, consequently, were due to mutation of the same gene loci) and which were not allelic (mutants at different loci). The chances of allelism, expressed in percentages of the intercrosses which involved allelic lethals, were found to be as follows:

Within a locality:	
Collected simultaneously	2.07 ± 0.29
Collected 1 to 11 months apart	1.30 ± 0.20
Total	1.64 ± 0.17
Different localities	0.41 ± 0.08

It is clear that lethals found in populations which live within territories less than two miles apart are alleles much more frequently than those found ten to fifteen miles apart. As a matter of fact, no significant difference in the chances of allelism was observed among lethals collected in different localities on San Jacinto and those collected on San Jacinto and in the Death Valley region (a distance of two hundred miles or more).

Allelic lethals found within a station or a locality often have a common origin, i.e., they are descended from a single mutation; the occurrence of alleles among lethals from remote populations is almost always due to independent origin of similar mutations. The knowledge of the chances of allelism enables one to calculate the probable number of loci in the third chromosome of *Drosophila pseudoobscura* which produce lethals by mutation. Dobzhansky and Wright (1941) found this number to be about 289. It must be noted that this estimate involves the assumptions that the lethals are completely recessive, and that the mutation rates at all the loci are equal. If these assumptions are incorrect (as they almost certainly are), the figure 289 is an underestimate; it happens, however, that for the purposes for which this figure is used an underestimate is preferable to an overestimate. Through experiments in the laboratory it has been found (cf. Chapter III) that the gross mutation rate producing lethals and semilethals in the third chromosome of *D. pseudoobscura* (that is, the sum of the mutation rates at all loci) is 0.307 ± 0.036 percent, or about 3 new lethals per 1,000 gametes per generation. With 289 loci producing the lethals, the mutation rate per locus is $u = 0.000,0106$ (that is, $0.003,07 \div 289$). In an infinitely large population the equilibrium frequency of each lethal is $q = \sqrt{u} = 0.003,209$. Yet only about 15 percent of the chromosomes in the California populations carry lethals. The concentration per locus is $q = 0.15 \div 289 = 0.000,519$.

Taken at its face value, the discrepancy between the observed and the computed equilibrium frequencies indicates very low effective sizes of the populations studied. These calculations are, however, based on the assumption that the lethals are completely recessive, and hence that the viability of the heterozygous carriers is not lowered. A reduction of the viability of the heterozygotes so small as to be undetectable in the experiments so far carried out in *D. pseudoobscura* would, nevertheless, suffice to account for the discrepancies between the observed and the calculated frequencies of the lethals. Furthermore, a discrepancy of this kind could arise because of very local inbreeding, such as mating of the members of the same brood soon after the emergence from the pupae, in natural populations. These so far undefined variables do not explain, however, the basic finding reported above, namely that the lethals found within a

population of a small territory are alleles more frequently than those from distant localities. This finding strongly indicates that the genetically effective size of the populations sampled was limited. Wright (in Dobzhansky and Wright 1943) has computed from these data on the frequencies of allelism of the lethals, that the parents of an individual of *D. pseudoobscura* in the localities studied are drawn from a population of some 500 to 1,000 individuals.

To recapitulate: restriction of the genetically effective size of natural populations is in all probability an important agent of differentiation of species into local groups possessing different genotypes. It must be admitted that even approximate estimates of the magnitude of population numbers are available for only very few species. And yet much evidence secured by different biological disciplines, attests the existence of phenomena which can most plausibly be accounted for by genetic drift.

GENETIC CONCEPTION OF RACE

In classical morphology and anthropology, races were described in terms of the statistical averages for characters in which they differ from each other. Once such a system of averages is arrived at, it begins to serve as a racial standard with which individuals and groups of individuals can be compared. This simple method of racial studies is unquestionably convenient for some practical purposes. The difficulty is, however, that from the point of view of genetics such an attempt to determine to which race a given individual belongs is sometimes an unmitigated fallacy. The fact which is very often overlooked in making such attempts is that racial differences are more commonly due to variations in the relative frequencies of genes in different parts of the species population than to an absolute lack of certain genes in some groups and their complete homozygosis in others. Examples quoted above show that gene frequencies in different races of a species may vary from 0 percent to 100 percent, these being no more than limiting values. Individuals carrying or not carrying a certain gene may sometimes be found in many distinct races of a species (Boyd 1950).

The fundamental units of racial variability are populations and genes, not complexes of characters which connote in the popular mind a racial distinction. Much confusion of thought could be avoided if

all biologists would realize this fact. How important it is may be illustrated by the following analogy. Many studies on hybridization were made before Mendel, but they did not lead to the discovery of Mendel's laws. In retrospect, we see clearly where the mistake of Mendel's predecessors lay: they treated as units the complexes of characteristics of individuals, races, and species and attempted to find rules governing the inheritance of such complexes. Mendel was the first to understand that it was the inheritance of separate traits, not of complexes of traits, which had to be studied. Some of the students of racial variability consistently repeat the mistakes of Mendel's predecessors.

An endless and notoriously inconclusive discussion of the "race problem" has been going on for many years in the biological, anthropological, and sociological literature. Stripped of unnecessary verbiage, the question is this: is a "race" a concrete entity existing in nature, or is it merely an abstraction with a very limited usefulness? To a geneticist it seems clear enough that all the lucubrations on the "race problem" fail to take into account that a race is not a static entity but a process. Race formation begins when the frequency of a certain gene or genes becomes slightly different in one part of a population from what it is in other parts. If the differentiation is allowed to proceed unimpeded, most or all of the individuals of one race may come to possess certain genes which those of the other race do not. Finally, mechanisms preventing the interbreeding of races may develop, splitting what used to be a single collective genotype into two or more separate ones. When such mechanisms have developed and the prevention of interbreeding is more or less complete, we are dealing with separate species. A race becomes more and more of a "concrete entity" as this process goes on; what is essential about races is not their state of being but that of becoming. But when the separation of races is complete, we are dealing with races no longer, for what have emerged are separate species.

Racial variability must be described in terms of the frequencies of individual genes in different geographical regions or in groups of individuals occupying definite habitats. Such a description is more adequate than the usual method of finding the abstract average phenotypes of "races" because it subsumes not only an account of the present status of a population, but to a certain extent also that of its

potentialities in the future (e.g,. presence of certain genes in heterozygous state which, if increased in frequency, may change the phenotype of the race). The geography of the genes, not of the average phenotypes, must be studied. To date, only a few attempts to apply this method in practice have been made. The most successful one among them is that concerning the blood groups in man (Boyd, 1950). The scarcity of similar data for other organisms is due less to any difficulty in obtaining such data than to a lack of appreciation of their importance.

VII : Isolating Mechanisms

PREMISES

THE IMPORTANCE of isolation has been recognized for a long time. Lamarck and Darwin pointed out that interbreeding of genetically distinct populations results in swamping of the differences. Among Darwin's immediate followers the role of isolation was stressed by M. Wagner and by Romanes. The latter originated the maxim, "without isolation or the prevention of interbreeding, organic evolution is in no case possible." These early ideas about the role of isolation confused two different problems. First, the differences between individuals and populations may be due to a single gene or a single chromosome change. Such differences cannot be swamped by crossing, since, in the offspring of a hybrid, segregation takes place and the ancestral traits reappear unmodified. No isolation is needed to preserve the variation due to changes in single genes, and if one consents to dignify the origin of single gene differences by applying to it the name evolution, the latter is independent of isolation. The second class of differences is genetically more complex. Races and species usually differ from each other in many genes and chromosomal alterations. Interbreeding of races and species results in a breakdown of these systems, although the gene differences as such are preserved. Hence, the maintenance of species and races as distinct populations is contingent on their isolation. Race and species formation without isolation is impossible.

The process of mutation engenders a great variety of genes and chromosomal structures. The process of sexual reproduction generates a diversity of gene combinations which is vastly greater than the number of gene elements. With n genes each represented by only two alleles, 3^n combinations are possible, 2^n of which would be homozygous. The biological significance of the sexual process, of the interbreeding of carriers of distinct genotypes, lies in the proliferation of a multitude of gene combinations. Some of these combinations are

the harmonious genotypic systems adapted to the different ecological niches in the environment. But the interbreeding could be just as efficient in breaking down the harmonious gene combinations as it was in forming them. Unlimited interbreeding of distinct species would result in submergence of the existing genetic systems in a mass of recombinations. Among the recombinations some may be as harmonious, or in fact better, than the existing gene patterns, and thus by hybridization the species may "discover" new evolutionary possibilities. But the chance of discovery is pitted against the fact that a majority, and probably a vast majority, of the new genic patterns are discordant, unfit for any available environment, and represent a total loss to the species.

If life is to endure, the gene combinations whose adaptive value has been vouchsafed by natural selection must be protected from disintegration. Without isolation the ravages of natural selection would be too great. But too early and too rigid isolation of the favorable gene combinations formed in the process of race differentiation would mean too much specialization of the organism to environmental conditions that may be only temporary. The end result may be extinction. Favorable conditions for progressive evolution are created when a certain balance is struck: isolation is necessary but it must not come too soon.

GEOGRAPHIC AND REPRODUCTIVE ISOLATION

The interbreeding of, and the gene exchange between, Mendelian populations is limited or prevented by many different means in different cases. Even in closely related forms, the isolation of species is accomplished by often quite dissimilar means. Furthermore, the interbreeding of a given pair of species is, as a rule, prevented not by a single mechanism but by several cooperating ones. Considered physiologically, the agents which hinder or prevent the interbreeding of species have scarcely a common denominator. And yet, they have the same genetic effects: curtailment or stoppage of the gene exchange between populations. The term "isolating mechanisms" has been proposed as a generic name for all such agents (Dobzhansky 1937).

Direct gene exchange between allopatric populations is precluded

simply by the fact that they are allopatric. This is geographic isolation. Geographically isolated populations may exchange genes only indirectly, through a chain of geographically intermediate populations, or through occasional migrants which overcome the distance barriers. Sympatric sexual populations can be maintained distinct only if the gene exchange between them is limited or prevented by their intrinsic, genetically conditioned, properties. Such genetically conditioned isolating mechanisms result in reproductive isolation (Mayr 1942). Allopatric populations may or may not show reproductive isolation if brought together artificially or as a result of expansion of their distribution areas. A synopsis of the principal isolating mechanisms follows:

I. *Geographic or Spatial Isolation.* The populations occur in different territories, either within a continuously inhabited area, or separated by distributional gaps.

II. *Reproductive Isolation.* The gene exchange between species is restricted or suppressed owing to genotypically conditioned differences between their populations.

- A. *Ecological Isolation.* Representatives of the populations occur in different habitats in the same general region.
- B. *Seasonal or Temporal Isolation.* Mating or flowering periods occur at different seasons.
- C. *Sexual, Psychological or Ethological Isolation.* Weakness or lack of mutual attraction between males and females of different species.
- D. *Mechanical Isolation.* Physical non-correspondence of the genitalia or floral parts.
- E. *Gametic or Gametophytic Isolation.* Spermatozoa, or pollen tubes, of one species are not attracted to the eggs or ovules, or are poorly viable in the sexual ducts of another species.
- F. *Hybrid Inviability.* The hybrid zygotes are inviable, or adaptively inferior to those of the parental species.
- G. *Hybrid Sterility.* Failure of the hybrids to produce a normal complement of functional sex cells.
- H. *Hybrid Breakdown.* Inviability, or adaptive inferiority, of all, or a part, of the F_2 or backcross hybrids.

Classifications and examples of isolating mechanisms have been given by Mayr (1942, 1948), Muller (1942), Patterson (1942), Huxley (1942), Allee et al. (1949), Stebbins (1950), and others. The validity of the distinction between geographic and reproductive isolation has been questioned by some authors. Geographic isolation is on a different plane from all the reproductive isolating mechanisms, because the former is independent of any genetic differences between populations, while the latter are necessarily genetic. Genetically identical populations may be geographically isolated (on islands, for example). It is true that populations which inhabit different territories usually become genetically different. Genetic differences arise either owing to natural selection brought about by environmental differences, or owing to genetic drift. It is also true that in concrete situations geographic isolation is often intimately allied with some forms of reproductive isolation (e.g., ecological or temporal isolation). It should, however, be kept in mind that genetic differences do not automatically produce reproductive isolation. The fact that allopatric populations are often genetically distinct does not in itself guarantee that they would show even the slightest reproductive isolation if brought together. In a sense, reproductive isolation is caused by a special class of genetic differences (see below the discussion of the origin of reproductive isolation). Geographic isolation is ultimately caused by spatial parameters, reproductive isolation by biological factors.

ECOLOGICAL AND SEASONAL ISOLATIONS

Two ecologically and physiologically distinct populations of the stickleback fish, *Gasterosteus*, occur in Belgium (Heuts 1947). One of them lives the year round in fresh waters, mainly in small creeks. The other lives in the sea in winter, but migrates to river estuaries in spring and in summer, where it breeds. The two populations differ in the averages of certain morphological traits, but the variations overlap broadly. The fresh-water form has an osmoregulatory capacity which maintains the chlorine content of its blood at a fairly constant level in waters of low salinity. The migratory form looses chlorine ions in waters of low salt concentrations, below one quarter of that of sea water. This leads to death in a few days. The morphologi-

cal intergrades found in natural habitats are not physiologically intermediate: they belong to either one or the other physiological type. Hybrids between the two forms can be obtained by artificial insemination of the eggs, but they appear rarely in natural habitats. Even if they were produced in nature, they would not find suitable environments to live in, since waters of a proper salinity are scarce. According to Ricker (1940, 1950), migratory and nonmigratory populations of salmon occur in certain lakes in British Columbia. They differ also in the season of spawning, as well as in environments which are preferred for this purpose.

Arctostaphylos mariposa and *A. patula* are large bushes or small trees, which differ strikingly in several easily visible traits. In the Sierra Nevada of California, the former species occurs at lower elevation, up to about 4,800 feet, and the latter at higher ones, from about 4,600 feet upwards. In the narrow altitudinal belt where both species live, *A. mariposa* occupies the drier and more exposed, and *A. patula* the more sheltered, situations. Even in that belt at least 90 percent of the trees clearly belong either to one or to the other species, and in some localities the altitudinal replacement of the species occurs without any hybrids being produced. But in many localities a certain number of hybrids can be identified. In contrast to the conditions described below in toads, almost all the *Arctostaphylos* hybrids are presumably the F_1 generation; only a small number of the trees are, from their morphological traits, judged to be backcross individuals. The F_1 hybrids are, however, not sterile and produce fruit about as abundantly as the parental species. The mechanisms, in addition to the ecological isolation, which prevent these species from losing their identities in the zone of the altitudinal overlap are unknown (Epling 1947a). A rather similar situation has been described by Valentine (1948) in the primrose species *Primula vulgaris* and *P. elatior*. In England these species are kept apart by preference for different soils and moisture relationships. Hybrids between them are sporadically found. The gene exchange between the sage species, *Salvia mellifera* and *S. apiana* is prevented by a combination of causes, among which ecological and seasonal isolation are important (Epling 1947b).

A much more complex situation has been discovered by Blair

(1941, 1942) in the toads *Bufo americanus, B. fowleri, B. woodhousii,* and *B. terrestris* which inhabit eastern and central United States. These species are crossable in the laboratory, and the hybrids are, as far as one can tell, fully viable and fertile. The distribution areas of *B. americanus* and *B. fowleri* are rather similar, but they overlap those of the other two species only to a slight extent. Where two or three species occur together, hybrid individuals are encountered. The question of what permits the maintenance of the species as discrete entities is especially acute for the geographically coincident *B. americanus* and *B. fowleri.* In the vicinity of Bloomington, Indiana, three populations of toads are found: one breeds early in the season, and is apparently pure *B. americanus;* the second breeds late, and is pure *B. fowleri;* while the third, whose breeding period overlaps the first two, includes individuals which resemble the two pure species as well as the hybrids. Mating pairs consisting of intermediates, and of intermediates and the pure species, have been observed in nature. There are some differences between the species in ecological preferences. At the junction of their distribution ranges in Oklahoma, *B. fowleri* breeds mainly in streams and *B. woodhousii* mainly in prairie ponds. Where the habitats preferred by these species are geographically separate, the distribution areas do not overlap. A difference between *B. americanus* and *B. fowleri* in ecological preferences is also indicated, from which Blair infers that the intercrossing of these species may be of recent origin, brought about by man's activities, such as the destruction of forests and damming of streams.

SEXUAL ISOLATION

An obvious prerequisite for a sexual union is that the sexes meet and perform the series of acts that precede and enable fertilization to occur. In some forms this is relatively short and simple. In the oyster the chemical substances that are released in water, together with the eggs and spermatozoa, stimulate other individuals to eject further masses of sex cells (Galtsoff 1930). In other animals the procedure is more complex. Leiner (1934) gives the following account of the behavior patterns in the two species of fish, *Gasterosteus aculeatus* and *G. pungitius,* which build special nests in which the eggs are deposited:

G. pungitius	*G. aculeatus*
The nest is built hanging on water plants.	The nest is built on the bottom, in a furrow dug by the fish.
The nest is composed of soft materials.	Hard materials are used in the construction of the nest.
The nest has an entrance and an exit.	The nest has a single entrance.
No preference for light or dark building materials.	On a light bottom, dark building materials are preferred.
The nest is not changed after the eggs are deposited.	After egg deposition the nest is somewhat altered.
The male swims toward the nest in zigzags, attracting the female to follow him.	The male makes some zigzags in front of the female, and then swims straight to the nest followed by her.
The process of leading the female to the nest and the mating play coincide.	A special mating play is enacted.
The female enters the nest with little prodding by the male.	The male forces the female into the nest.

Regardless of whether the behavior patterns preliminary to mating are simple or complex, any incongruity in this respect may engender sexual isolation. The physiological basis of sexual isolation may, however, be as unlike as the mating reactions themselves (Huxley 1938). Nevertheless, in higher animals where the mating reactions involve complex systems of unconditioned and conditioned reflexes, large deviations from the normal behavior can be induced in experiments (see review by Serebrovsky 1935). Stallions can be trained to mount a stuffed effigy of a mare and even that of a cow, and the same is true of bulls, boars, and male sheep. Mule turkeys were induced to attempt copulation with fowls. These results show that sexual isolation can be surmounted experimentally. In general, hybrids that never occur in nature can sometimes be obtained in experiments.

The involved courtship antics practiced by spiders not only differ in different species, but the whole behavior pattern is set in motion by different stimuli (Kaston 1936). In some families, males recognize their females by sight, in others the male must both see and touch the female, and in still others visual stimuli play no part and the sense of touch is paramount. Kaston proved that the stimulus of touch comes from a substance present on the cuticle of females—males court parts of a female body, such as autotomized legs. This substance is ether soluble, so that a female leg washed in ether does not stimulate the male, while a glass plate on which an ether extract was allowed to evaporate does elicit the courtship response. Crushed in-

ternal organs fail to elicit such a response. The courtship behavior is often quite different in species of mollusks (see Gerhardt 1938, 1939, for references). Similar data with reference to species of mosquitoes have been reviewed by Bates (1949).

A number of investigators have studied the sexual isolation between various species of *Drosophila* (see Mayr 1950, Merrell 1949, Patterson et al. 1947, Patterson 1947a and b, Spieth 1949 for further references). The "multiple choice method" is most frequently used in these studies. Equal numbers of females of two species are placed together with males of one of the species in suitable containers; after a desired time interval the females are dissected, and their sperm receptacles are examined for presence or absence of sperm. A typical result of such experiments is, if remote species are involved, that only females of the same species to which the males belong are inseminated, and there is no insemination of the females of the other species. With closely related species, some females of both species may be inseminated, but the proportion of inseminated conspecific females is higher than that of females of the foreign species. Thus, in an experiment with *Drosophila pseudoobscura* and *D. persimilis* the following results were obtained:

	D. pseudoobscura ♀ ♀		*D. persimilis* ♀ ♀	
	Inseminated	*Virgin*	*Inseminated*	*Virgin*
D. pseudoobscura ♂ ♂	87%	13%	3%	97%
D. persimilis ♂ ♂	25%	75%	68%	32%

It is evident that *D. pseudoobscura* males inseminated many more *D. pseudoobscura* than *D. persimilis* females, while with *D. persimilis* males the results were reversed. If females of a species are confined with males of a foreign species ("no choice experiments"), still much fewer females are inseminated than with conspecific females and males under similar conditions. Levene and Dobzhansky (1945) found no evidence that, with *D. pseudoobscura* and *D. persimilis*, the presence of conspecific females diminishes the probability of insemination of foreign females. The results are consistent with the interpretation that encounters between conspecific females and males have more probability of resulting in copulation than encounters between individuals of foreign species, and that these prob-

abilities are, within certain limits, independent of what other females and males may be present in the environment. This conclusion need not, however, apply to other species.

Spieth (1949) observed directly, under the microscope, the behavior of males and females of different species related to *D. willistoni*. He found that every species has its own courtship and mating techniques; both males and females perform certain actions in certain ways, to which the opposite sex responds by definite reactions, which stimulate either the continuation or interruption of the process. Males usually approach females of foreign species, but they are rebuffed either at once or after they have "postured". According to Mayr (1946b, 1950), males of *D. pseudoobscura* and *D. persimilis* court females of either species at random, but they are rejected by foreign females more often than by conspecific ones. In other words, the "choice" is, in this case, exercised by females, not by males. Females with amputated antennae, or etherized females (Streisinger 1948), are inseminated by normal males indiscriminately. Bateman (1948) argues very cogently that "undiscriminating eagerness in males and discriminating passivity in females" should be induced by natural selection in all bisexual species, except where strict monogamy combined with a sex ratio of unity eliminates the intrasexual selection. Indeed, an excess of male sex cells contrasts, in most organisms, with a relatively limited production of female ones. The female fertility is limited by the egg production and by the capacity to feed and rear the young. The male fertility is largely a question of the number of inseminations of different females. The "eagerness" and "passivity" of males and females are, thus, consequences of the fact that females produce much fewer gametes than males do.

Races and strains of the same species show, as a rule, no sexual isolation, but it is important that exceptions to this rule are known (Baker 1947, Dobzhansky 1944b, Patterson and Wheeler 1947). Thus, strains of *Drosophila sturtevanti* from Mexico, Guatemala, and from different parts of Brazil show weak but consistent sexual isolation from each other in "multiple choice" experiments. These strains are visibly identical in appearance. More frequent is the occurrence within a species of so-called "one-sided sexual preference". Males of *D. pallidipennis pallidipennis* from Brazil inseminate more of their own females than of those of the Mexican sub-

species, *D. pallidipennis centralis;* but males of the latter inseminate females of the two subspecies indiscriminately. The hybrids of these subspecies are fertile as females but sterile as males (Patterson and Dobzhansky 1945). Geographic strains of *D. prosaltans* form a graded series in their sexual behavior. The distribution area of this species extends from Mexico to southern Brazil. When males of more northern origin are kept together with a mixture of northern and southern females, more of the former than of the latter are inseminated. But southern males also inseminate more northern than southern females (Dobzhansky and Streisinger 1944). Similar situations occur with certain mutants. The yellow body color mutants in at least three species of *Drosophila* are cases in point. When a mixture of normal and yellow females is exposed to yellow males, more yellow than normal females are inseminated. But normal males inseminate the two kinds of females equally often. Bateman (1948), Merrell (1949), and Mayr (1950) interpret these facts to mean that normal females are averse to mating with yellow males, but normal males do not discriminate between normal and yellow females. The situation in *D. prosaltans* indicates that the more northern races are sexually more excitable than the southern ones. Spieth (1949) has shown that differences in the thresholds of sexual excitability exist between species related to *D. willistoni.* The intraspecific differences in sexual reactions are the genetic materials from which the interspecific sexual isolation may be built.

The experiments of Haskins and Haskins (1949, 1950) have revealed in poeciliid fishes a situation quite significantly and characteristically different from that found in *Drosophila.* The fishes *Lebistes reticulatus, Micropoecilia parae,* and *Poecilia vivipara* are sympatric in the West Indies. When kept in mixed populations, males of each species mate with conspecific females much more often than with foreign ones. Males which have been kept only with conspecific females show very poor species discrimination when placed with females of other species; however, within a very few days they learn to distinguish the species of the available females and matings with alien species become rare. The discrimination is exercised mainly or exclusively by the males, and is based chiefly on visual stimuli. In *Lebistes reticulatus* males may be conditioned to mate with females of a certain color type in preference to those of other

color types found in this extremely polymorphic species. The conditioning may, however, be altered by retraining the males with females of other genotypes. This very plastic selective mechanism seems, nevertheless, to be quite effective in the maintenance of isolation in the native habitats of these fishes.

MECHANICAL ISOLATION

The complex structure of the genitalia in many animals, especially among insects, has attracted the attention of morphologists and systematists, because closely related species can often be accurately classified by their genitalia. On this fact much theoretical superstructure has been built. The "lock-and-key" theory was propounded by Leon Durfour in the pre-Darwinian days and later elaborated especially by K. Jordan (1905). According to Durfour, the female and the male genitalia are so exactly fitted to each other that even slight deviations in the structure of either make copulation impossible. The genitalia of each species are "a lock that can be opened by one key only." Different species are isolated from each other by the noncorrespondence of their genitalia.

The experimental evidence in favor of mechanical isolation is scanty. Standfuss (1896) described crosses between species of moths where copulation leads to injuries to the female organs that result in death. Federley (1932) has stated that *Chaerocampa elpenor* males may copulate with females of *Metopsilus porcellus* (moths of the family Sphingidae), but are sometimes unable to withdraw the penis, making egg deposition impossible. The reciprocal cross succeeds easily.

There is no doubt that mechanical isolation is effective as a bar to crossing in some organisms. The "lock-and-key" theory in its original form cannot, nevertheless, be sustained. Copulation between insect species with fairly different genitalia occurs sporadically, both in nature and in experiments, with no evidence of injury to either participant. It is immaterial as far as mechanical isolation is concerned that such matings usually do not result in production of hybrid offspring. Variations in body size within insect species do not seem to hinder copulation. In *Drosophila* giant and dwarf mutants, and large- and small-bodied flies produced from well fed and from starved larvae, cross easily and produce offspring. Kerkis

(1931) showed by means of a statistical study that the genitalia of the bug *Eurygaster integriceps* are no less variable than the external morphological traits in the same species. Sengün (1945) amputated parts of male genitalia in the silkworm moth and found that some of the mutilated males produced offspring. The usefulness of insect genitalia for distinguishing species does not necessarily mean that they are important in mechanical isolation. The reason of their usefulness is that the complexity of genitalic structures is often so great that the species differences are more likely to be manifested in these structures than in the relatively simple external ones.

Differences in the floral structures in related plant species may prevent the formation of hybrids. This is especially true in families with elaborate and distinctive floral morphology (orchids, Asclepiadaceae, Leguminosae, and some others). The relevant evidence has been reviewed by Grant (1949) and by Stebbins (1950). Mather (1947) and Grant (1949) showed that isolation of plant species may be caused by the habit of some fertilizing insect species of becoming temporarily conditioned for visiting flowers of the same color and structure.

FERTILIZATION IN SPECIES CROSSES

Copulation in animals with internal fertilization, or release of the sexual products in forms with external fertilization, or placing of the pollen on the stigma of the flower in plants are followed by chains of reactions that bring about the actual union of the gametes, or fertilization proper. These reactions may be out of balance in different species, with a consequent hindrance or prevention of the formation of hybrid zygotes.

Lillie (1921) has crossed two species of sea urchins, *Strongylocentrotus purpuratus* and *S. franciscanus*. *S. purpuratus* occurs between the tidemarks and slightly below the low-water mark, while *S. franciscanus* rarely lives above the low-water mark. There exists consequently a partial ecological isolation between the two. Eggs of each species were placed in sea water containing spermatozoa of the same or of the other species in different concentrations. The concentrations of the *S. franciscanus* sperm that give from 73.3 to 100 percent of fertilization of the eggs of the same species produce from 0 percent to 1.5 percent of fertilization in *S. purpuratus* eggs.

With a sperm concentration of *S. franciscanus* that is forty times greater than necessary to produce a 100 percent fertilization of *S. franciscanus* eggs, only 25 percent of *S. purpuratus* eggs are fertilized. A similar, though less pronounced, disability of *S. purpuratus* sperm to fertilize the eggs of *S. franciscanus* was also detected.

The environment which spermatozoa encounter in the reproductive organs of females of foreign species may be unsuitable for them. Patterson et al. (1942, 1947) observed cross-inseminations between the related species *Drosophila virilis*, *D. americana*, *D. montana*, and *D. lacicola*. The mobility of the sperm in the sperm receptacles of females of foreign species is lost rather rapidly, while in conspecific females the mobility is retained for a long time. Similar situations are observed in species of the *mulleri* group of the genus *Drosophila* (Patterson 1947a), and in *D. affinis* females mated to *D. athabasca* males (Miller 1950). It should, perhaps, be noted that no trace of this particular isolating mechanism is observable between certain other *Drosophila* species. Thus, the sperm of *D. pseudoobscura*, *D. persimilis*, and *D. miranda* is equally viable in females of any of these three species. Nevertheless, the numbers of offspring which result from such intraspecific inseminations in *D. pseudoobscura* and *D. persimilis* are greater than from interspecific ones. This is most probably due to intraspecific copulations resulting in delivery of larger numbers of spermatozoa than are transferred in interspecific matings (Dobzhansky 1947c).

Some species of *Drosophila* show the so-called insemination reaction following copulation (Patterson 1946, 1947a). A rapid secretion of a fluid into the cavity of the vagina takes place immediately after the copulation, causing a great swelling of the organ. This swelling persists for some hours after intraspecific copulations, whereupon the vagina returns to its normal condition. Insemination by a male of a foreign species gives a more violent reaction. The vagina remains swollen for days, and sometimes the secretion inside the vagina solidifies and obstructs the passage of eggs, making the female sterile. Again, this condition occurs by no means in all *Drosophila* species: some species and species groups show no insemination reaction either after normal or after interspecific copulations.

Mangelsdorf and Jones (1926) and others found in crosses between sugary and nonsugary maize (*Zea mays*) deviations from normal segregation ratios, the numbers of sugary kernels being below the expectation. Sugary differs from nonsugary in a single gene. If a mixture of sugary and nonsugary pollen is applied to the silks of a nonsugary plant, a competition between the pollen grains ensues. The rate of growth of sugary pollen tubes is less than that of the normal pollen tubes. The growth rates of the two kinds of pollen tubes on sugary silks, however, are alike. Demerec (1929) has described an even more extreme case of incompatibility between popcorn and other varieties of maize. If popcorn is used as a female parent in crosses where nonpop pollen is applied, almost no seeds are formed. Crosses in which pop is used as a male succeed without difficulty. If a popcorn plant is double pollinated (i.e., if a mixture of pop and nonpop pollen is applied), many selfed and very few hybrid seeds are obtained.

An extensive series of experiments with crosses between different species of *Datura* has been described by Buchholz et al. (1935). The speed of the pollen tube growth in the style of the same species is frequently greater than in the style of a foreign species. Species of *Datura* differ in the length of the style, and there is a correlation between the speed of the pollen tube growth and the style length. The crosses in which the species with a short style is used as the female parent and that with a long style as the male parent are more likely to succeed than the reciprocal crosses. Moreover, the pollen tubes may burst in the style of a foreign species before they reach the ovary, the frequency of the bursting pollen tubes being characteristic for each cross. The crossability of different species is, therefore, a function of several variables: the speed of pollen tube growth, length of the style, frequency of bursting pollen tubes, and the viability of the embryos (see below).

HYBRID INVIABILITY

Union of gametes of different species does not necessarily result in production of hybrid progeny. The life of a hybrid zygote may be cut short at any stage. In animals with external fertilization, spermatozoa may enter eggs of representatives of different classes and phyla (echinoderms × mollusks, echinoderms × annelids), but the

sperm nucleus, or its chromosomes, may be eliminated from the cleavage spindle. Eggs of species of fish can be inseminated by sperm of different species, genera, or even families. All sorts of disturbances may, however, occur in the zygotes, from chromosome elimination during cleavage, arrest of gastrulation or of organ formation, to death of the embryos in advanced stages (a review in Hertwig 1936). Sheep × goat hybrids appear to be normal as early embryos, but die much before birth (Warwick and Berry 1949).

In some instances the weakness of the hybrid is due to physiological disturbances which can be overcome in experiments. The classical example are Laibach's (1925) hybrids between species of flax. In the cross *Linum perenne* ♀ × *L. austriacum* ♂, hybrid seeds fail to germinate if left to their own devices. If, however, the embryos are freed from the seed coat (the seed coat being a maternal tissue), germination does take place, and the seedlings give rise to luxuriant hybrid plants that are fertile and produce normal seeds of the F_2 generation. Still greater is the suppression of the seed development in the cross *L. austriacum* ♀ × *L. perenne* ♂, and yet if the diminutive embryos are extracted from the seeds and placed in a nutrient solution they continue to grow. After some days they may be transferred to moist paper, and allowed to germinate. The seedlings are then planted in soil. Blakeslee (1945) and his collaborators obtained by similar methods viable hybrids between species of *Datura*. For further examples see Stebbins (1950).

Moore (1946, 1949b) has studied the isolating mechanisms in a group of North American species of frogs (*Rana*). The situation for the six species examined in most detail is summarized in Table 14. The distribution areas of all these species overlap, making them sympatric in a greater or lesser part of their ranges. Because of preferences for different habitats during the breeding season, the species are to some extent, but never completely, isolated ecologically. Some species pairs show complete seasonal isolation. Following artificial insemination of the eggs, from none to 100 percent of the hybrid embryos develop normally to the adult stage, the remainder dying at various earlier stages. Moore's estimates of the efficacy of the isolating mechanisms taken separately are shown in Table 14. Taken in conjunction, they seem to give complete or nearly complete isolation in all cases.

Even more remarkable is the occurrence of inviability in hybrids between geographic races of one of the species—*Rana pipiens* (Moore 1949b). As stated in Chapter VI, these races differ in their adaptedness to different climatic conditions (cf. Table 12). The out-

TABLE 14

ESTIMATION OF THE MAGNITUDE OF GEOGRAPHIC ISOLATION (G), ECOLOGICAL ISOLATION (E), SEASONAL ISOLATION (S), AND DEVELOPMENTAL INCOMPATIBILITY (HYBRID INVIABILITY, D) IN NORTH AMERICAN SPECIES OF FROGS

Complete isolation = 100, absence of isolation = 0.

(AFTER MOORE 1949)

Females \ Males	Rana sylvatica	Rana pipiens	Rana palustris	Rana clamitans	Rana catesbeiana	Rana septentrionalis
Rana sylvatica		G 29 E 70 S 60 D 100	G 61 E 40 S 100 D 100	G 59 E 30 S 100 D 100	G 68 E 70 S 100 D 100	G 80 E 60 S 100 D ?
Rana pipiens	G 59 E 70 S 60 D 100		G 74 E 70 S 40 D 0	G 67 E 70 S 100 D 100	G 62 E 85 S 100 D 100	G 88 E 80 S 100 D 100
Rana palustris	G 13 E 40 S 95 D 100	G 0 E 70 S 40 D 0		G 3 E 60 S 95 D 100	G 23 E 70 S 100 D 100	G 72 E 50 S 100 D ?
Rana clamitans	G 28 E 30 S 100 D 100	G 0 E 70 S 100 D 100	G 24 E 60 S 95 D 100		G 18 E 30 S 50 D 100	G 22 E 20 S 0 D 100
Rana catesbeiana	G 51 E 70 S 100 D 100	G 0 E 85 S 100 D 100	G 47 E 70 S 100 D 100	G 29 E 30 S 50 D 100		G 93 E 30 S 50 D ?
Rana septentrionalis	G 0 E 60 S 100 D ?	G 0 E 80 S 100 D 100	G 37 E 50 S 100 D 100	G 36 E 20 S 0 D 100	G 79 E 30 S 50 D 95	

comes of race crosses appear to be correlated with the adaptive differentiation of the species. Thus, the eggs of the Vermont race give normal development when fertilized with Wisconsin sperm. Fertilization by New Jersey or Oklahoma races results in normal or slightly

retarded development rates and a slight enlargement of the head of the embryo. With Louisiana sperm the retardation is slight and the head enlargement is moderate. With Florida or Texas sperm, a marked retardation and a strong enlargement of the head are observed. With eggs of southern and the sperm of northern races, the embryos have markedly reduced heads and retarded developments. In either case, the hybrids between geographically extreme members of the series are inviable. Zimmermann (1936) and Strasburger (1936) obtained somewhat similar results in geographic races of the ladybird beetle *Epilachna chrysomelina* from southern Europe, western Asia, and Africa. The crosses between most of the races gave hybrids without difficulty, but the cross between the South African and the European forms resulted in disturbances of the embryonic development and death of the eggs. Pictet (1936) states that the viability of the hybrids between the moths *Lasiocampa quercus* from different localities is inversely proportional to the distance between the localities.

The appearance of unisexual progenies is a fairly common phenomenon in interspecific hybrids; individuals of one sex die, while the viability of the other sex is affected little or not at all. Haldane (1922) has formulated a rule that, with some exceptions, holds rather well: "when in the F_1 offspring of two different animal races one sex is absent, rare, or sterile, that sex is the heterozygous sex." In mammals, Amphibia, and most insects, male hybrids are defective more frequently than females. In birds, butterflies, and moths, female hybrids tend to be less viable than males.

A possible mechanism that may underlie Haldane's rule was suggested by Dobzhansky (1937b). *Drosophila pseudoobscura* and *D. miranda* differ in the gene arrangement, and some genes that lie in one of these species in the X chromosome lie in the other in the autosomes, and vice versa. The cross *D. miranda* ♀ × *D. pseudoobscura* ♂ produces viable female and abnormal male hybrids; the reciprocal cross gives rise to viable females, but the males die off. Suppose that *D. pseudoobscura* has in its X chromosome a certain group of genes A that lie in the autosomes of *D. miranda*, and that a group of genes B which in *D. miranda* lie in the X chromosome are located in the autosomes of *D. pseudoobscura;* with respect to these genes, the constitution of the females of both species and of the female

hybrids is alike, namely AABB. Males of *D. pseudoobscura* and the male hybrids from the cross *D. miranda* ♀ × *D. pseudoobscura* ♂ are ABB; *D. miranda* males and the male offspring from the cross *D. pseudoobscura* ♀ × *D. miranda* ♂ are AAB. The genotypes of the pure species are so adjusted that the constitution ABB in *D. pseudoobscura* and AAB in *D. miranda* permits the development of "normal" males. The constitution AABB is normal for females of either parent and for hybrid females as well. The constitution ABB is however incompatible with the genotype of *D. miranda*, and AAB with that of *D. pseudoobscura*. The hybrid males suffer from a disturbance of the genic balance, and consequently have an impaired viability. Muller (1940) has expressed the above suggestion in more specific language by pointing out that the recessive and semidominant sex-linked genes which had become established in either parental species will be as strongly expressed in the heterozygous sex in the hybrid as in the maternal species itself, while the corresponding genes in the autosomes of the hybrid will be suppressed by their dominant alleles.

HYBRID BREAKDOWN

We have seen that F_1 hybrids between species, and occasionally between races, may be poorly viable or lethal. This is evidence that combining in one genotype two gene complements each of which is harmonious by itself often results in an adaptively incompetent genetic system. This bears out the premise stated at the beginning of this chapter, that gene combinations of proven adaptive value may be endangered by hybridization. When the F_1 hybrids are viable and vigorous, the union of the gene complements of the parental forms is shown to be concordant. But this concordance does not guarantee that all the recombinations to which the two gene complements may give rise in F_2 and in further generations will likewise be satisfactory. The opposite is proven by the appearance of degenerate hybrid segregates in many species crosses which give robust F_1 progenies.

The closely related species *Drosophila pseudoobscura* and *D. persimilis* can be crossed in laboratory experiments, although no hybrids are known in natural populations. The F_1 hybrids appear to be fully as vigorous as the parental species, although the hybrid males

are sterile (see Chapter VIII). F_1 hybrid females produce numerous eggs, and are fertile when backcrossed to either parental species. The general viability of the backcross progenies is, however, low in comparison with the parental species and with F_1 hybrids. Since a majority of individuals in these progenies have various mixtures of the chromosomes of the two species, their decreased vitality may be due, in part, to formation of unfavorable recombinations of the parental genes. The actual situation is, however, even more complex, as shown by the following data.

Drosophila pseudoobscura females homozygous for the sex-linked recessive genes beaded (*bd*), yellow (*y*), short (*s*), the dominant Bare (*Ba*, second chromosome), and the recessive purple (*pr*, third chromosome) were crossed to *D. persimilis* males homozygous for the recessive orange (*or*, third chromosome) and heterozygous for the dominant Curly (*Cy*, fourth chromosome). The following results were obtained in the F_1 generation:

Ba	432	845	*bd y s Ba*	401	786
Ba Cy	413		*bd y s Ba Cy*	385	

Males are somewhat less numerous than females, which is undoubtedly the result of a slight decrease of the viability of the former due to the sex-linked recessives *bd*, *y*, and *s*. The *Ba Cy* hybrid females were backcrossed to *D. pseudoobscura* males homozygous for purple (*pr*) and orange (*or*). It may be noted that the females used have every chromosome, except the small fifth, marked with at least one mutant gene. Therefore in the backcross progeny the genetic constitution of every male may be ascertained from its appearance. Disregarding the crossing over in the X and in the third chromosomes, sixteen classes of males must appear in equal numbers, carrying the combinations of the chromosomes of the parental species represented diagrammatically in Figs. 16 and 17. Only eight classes of females are distinguishable (since, in this experiment, the sex-linked recessive genes do not manifest themselves in the female progeny). The results actually obtained are summarized in Table 15; the column marked "class number" refers to the diagrams in Fig. 16.

Table 15 shows that males are fewer than females, and that representatives of the different classes are far from equally numerous.

Since the yield of adult backcross individuals per mother is very small, some, perhaps a majority, of the backcross individuals evidently die. An important, and at first sight paradoxical, feature is that class I of the males, which consists of individuals having only *Drosophila pseudoobscura* chromosomes, is almost obliterated. If

TABLE 15

(*Explanation in Text*)

CLASS NUMBER	MALES		FEMALES	
	Phenotype	Observed	Phenotype	Observed
1	*bd y s Ba pr*	2	*Ba pr*	41
2	*bd y s Ba pr Cy*	—	*Ba pr Cy*	32
3	*bd y s Ba or*	4	*Ba or*	92
4	*bd y s pr*	7	*pr*	190
5	*bd y s Ba or Cy*	1	*Ba or Cy*	89
6	*bd y s pr Cy*	7	*pr Cy*	372
7	*bd y s or*	14	*or*	140
8	*bd y s or Cy*	13	*or Cy*	336
9	*or Cy*	147		
10	*or*	143		
11	*pr Cy*	62		
12	*Ba or Cy*	17		
13	*pr*	58		
14	*Ba or*	21		
15	*Ba pr Cy*	14		
16	*Ba pr*	6		
Crossovers		121	Crossovers	311
Total		637	Total	1603

the decrease in viability were due only to mixing the chromosomes of the two species, class I would be expected to be the most viable one.

Closer examination of Table 15 shows that the number of individuals of a given class recovered in this backcross is inversely proportional to the number of mutant genes this class carries. All the classes carrying *bd*, *y*, and *s* are much decreased in frequency. The gene *Ba* also depresses the viability greatly, *pr* follows next, while *or* and *Cy* are relatively innocuous. And yet, the same mutant genes produce no disastrous effects on the viability in pure species and in F_1 hybrids. The results indicate that the eggs deposited by F_1 hybrid

females give rise to individuals afflicted with a general constitutional weakness. Mutant genes that do not impair greatly the viability of the pure races or of F_1 hybrids act as semilethals in individuals developing from the eggs deposited by hybrid females. To test the above assumption, experiments were so arranged that the class of backcross progeny which is identical in constitution with *D. pseudoobscura* (corresponding to class 1 in Table 15) was free from mutant genes, and the class having hybrid autosomes (corresponding to 9 in Table 15) carried several mutants. The result was the opposite of that observed in the first experiment: class 9 was depressed in frequency more than class 1.

Harland (1936), Hutchinson et al. (1947), Stephens (1946, 1950), and others found that the tetraploid species of cotton, *Gossypium hirsutum*, *G. barbadense*, and *G. tomentosum* intercross freely and give fertile and vigorous F_1 hybrids. In the F_2 generation unbalanced types of low viability make their appearance. For example, among 110 F_2 seeds from the cross *G. hirsutum* var. *punctatum* × *G. tomentosum*, there were found:

7 seeds with small embryos that failed to germinate
36 with apparently normal embryos that failed to germinate
9 seedlings that failed to expand the cotyledons
22 seedlings that died within three weeks
16 unthrifty seedlings at three weeks old
20 strong seedlings at three weeks old.

Similar contrasts between the vigor of F_1 hybrid plants and the weakness of the F_2 progenies have been described in *Zauschneria cana* × *Z. septentrionalis* (Clausen et al. 1940) and other crosses.

GENETIC ANALYSIS OF ISOLATING MECHANISMS

If species evolve from races, any type of difference observed between species must be detectable, in at least a rudimentary form, within species as well. This principle is evidently applicable to reproductive isolating mechanisms which constitute species characters par excellence. It can, indeed, be demonstrated in at least some instances that genetic raw materials from which isolating mechanisms can be constructed are available in species populations. The classic

example is that of the cross *Crepis capillaris* × *C. tectorum*, which may give F_1 hybrids all of which die in the cotyledon stage, or F_1 progenies in which only half of the seedlings die, or finally hybrids all of which are viable. Hollingshead (1930) has shown that certain strains of *C. tectorum* carry a dominant gene which in the pure species produces no visible effects; if, however, a hybrid between *tectorum* and *capillaris* carries this gene, it does not develop beyond the cotyledon stage. The crosses in which the *tectorum* parent is homozygous for the gene in question produce accordingly no viable seedlings, while 50 percent, or 100 percent, of such seedlings occur in cultures in which the gene is heterozygous or absent respectively. The same gene is lethal for the seedlings of the hybrids *C. tectorum* × *C. leontodontoides* and *C. tectorum* × *C. bursifolia*, but not in the crosses *C. tectorum* × *C. setosa* and *C. tectorum* × *C. taraxacifolia*. It is obvious that the isolation between *C. tectorum* and certain of its congeners would become complete if *C. tectorum* were homozygous for the gene which is lethal in the hybrids. The data of Hollingshead indicate that some populations of *C. tectorum* do and others do not carry this gene. According to Kostoff (1936), the hybrids *Nicotiana rustica* var. *humilis* × *N. glauca* die as embryos, while in the cross *N. rustica texana* × *N. glauca* viable hybrids are obtained.

When certain strains of the cotton *Gossypium barbadense* are crossed to definite strains of *G. hirsutum*, the F_1 hybrids are weak, have a bushy growth habit, shortened internodes, and have the stem, petiole, and leaf midribs covered with a layer of cork. Hybrids between other strains of the same species give vigorous hybrids without the "Corky" syndrome. Stephens (1948) has shown that the strains which produce Corky hybrids carry complementary alleles, or complementary genes, ck^x (in *G. hirsutum*) and ck^y (in *G. barbadense*). The Corky syndrome is due to simultaneous presence in the genotype of a plant of these complementary genes. This case differs from that of Hollingshead in *Crepis*, because in the cotton both parental species may or may not carry the genes which incapacitate the hybrids. Much more important is the finding of Stephens that the geographic distributions of the ck^x and ck^y alleles show a highly suggestive relationship. The species areas of *G. barbadense* and *G. hirsutum* are different, but they overlap in the West Indies and on the northern fringe of South America. The genes which give rise to the Corky

syndrome occur almost exclusively in strains of the two species native in the zone of the overlap. The Corky hybrids are poorly viable and rarely give F_2 generation in nature. When an F_2 generation is obtained from non-Corky F_1 hybrids, the F_2 hybrids are deficient in vigor (see above). Thus, the Corky condition eliminates the F_1 hybrids, and prevents the production of a degenerate F_2.

Patterson and Crow (1940), Crow (1942), Patterson and Wheeler (1947), and Baker (1947) have secured excellent data on the genetics of isolating mechanisms in certain species of *Drosophila*, particularly in *D. mulleri* and *D. aldrichi*. The cross *D. mulleri* ♀ × *D. aldrichi* ♂ produces sterile hybrids of both sexes; the reciprocal cross gives no offspring. If, however, males from certain strains of *D. aldrichi* are crossed to *D. mulleri* females the offspring consists of about 10 percent female and 90 percent male hybrids. By means of an analysis of crosses between strains of *D. aldrichi* giving different results when hybridized to *D. mulleri*, Crow has shown that in populations of the former species there occurs a sex-linked gene which produces no visible effects in pure *D. aldrichi*, but which acts as a dominant semilethal in the *D. mulleri* × *D. aldrichi* female hybrids.

Tan (1946) has analyzed the genetic mechanisms underlying the sexual isolation between *D. pseudoobscura* and *D. persimilis* (cf. the description of this isolating mechanism above, in the present Chapter). Strains of the two species with chromosomes marked by mutant genes were intercrossed. The F_1 hybrid females were backcrossed to males of the parental forms. In the backcross progenies, several classes of individuals with various combinations of the chromosomes of the two species make their appearance (Figs. 16 and 17). The mutant markers were so chosen that the classes were distinguishable by inspection. The females of some of these classes were then tested for sexual preference by the usual "multiple choice" method (see above). The results showed clearly that the preference of females of either species for conspecific males is conditioned by a polygene complex, the constituent genes of which are scattered in apparently all chromosomes. Tan infers that the genetic elements from which the isolating complex is built may be found in populations of both pure species.

Kosswig (1929a, 1937), and especially Gordon (1937, 1948, and other publications) found that mutants which are neutral or even

useful within a species may have their effects exaggerated to pathological proportions in species hybrids. Natural populations of the platyfish, *Platypoecilus maculatus* are often polymorphic. The dominant gene *Sp* produces an irregularly spotted pattern consisting of macromelanophores. The dominant *N* gives a broad black band of pigment cells on the flanks of the fish. The dominant *Sr* multiplies the macromelanophores to form a series of horizontal lines. The dominant *Sd* gives dark spots in the dorsal fin. Finally, the dominant *Sb* causes a darkening of the ventral parts. If, however, strains of *Platypoecilus maculatus* carrying any of the above genes are crossed to the related swordtail, *Xiphophorus helleri*, the effects of the genes in the F_1 hybrids are greatly hypertrophied. The gene *Sp* initiates the development of cutaneous melanomas; *N* gives melanotic tumors anywhere along the black band on the side of the body; *Sd* causes melanotic tumors on the dorsal fin; *Sb* gives melanomas along the mid-ventral line. The effects of *Sr* are exaggerated in F_1 hybrids but no tumors appear; if, however, the F_1 is backcrossed to the swordtail, some individuals in the backcross progeny develop tumors along the flanks. It is evident that the swordtail carries genes, or gene complexes, which interact with certain platyfish genes in a manner which makes the latter deleterious in the hybrids.

THE MULTIPLE GENE HYPOTHESIS OF THE ORIGIN OF REPRODUCTIVE ISOLATING MECHANISMS

Reproductive isolation has always two aspects: the interbreeding of the species A with the species B is made difficult or impossible, while individuals of A as well as of B are fully able to breed *inter se*. The reproductive biology of any species is organized to insure the procreation of a sufficient number of offspring. And yet the same reproductive biology militates against the gene exchange with other species. It is important to visualize how this state of affairs develops. Mutations that alter the sexual behavior, or the breeding time, or the structure of the genitalia may occur in any species, but such mutations do not produce workable reproductive isolating mechanisms. Genetic changes which engender reproductive isolation must not only prevent crossbreeding between the mutant and the original type, but must simultaneously insure a normal reproduction of the mutants. Where isolation involves an inviability or a sterility of the hybrids,

these effects must be confined to heterozygotes and leave the homozygotes unaffected.

In sexual and cross-fertilizing species, a great difficulty is encountered in the establishment of any reproductive isolating mechanism in a single mutational step. Since mutants appear in populations at first as heterozygotes, inviable and sterile heterozygotes are eliminated, regardless of how well adapted might be the corresponding homozygotes. This consideration is fatal to Goldschmidt's (1940) theory of evolution by "systemic" mutations. These mutations are supposed to induce isolation of the newly emerged species from its ancestor. Even if the inviability or sterility of heterozygotes be supposed to be incomplete, these heterozygotes will be discriminated against by natural selection. Forms of isolation other than hybrid inviability and sterility fare scarcely better if they arise in a single step. Suppose that a mutant and the ancestral form reach sexual maturity at different seasons, or that the germ cells of a mutant are incompatible with those of the original type. Since the mutation rates for most genes are known to be low, the number of the mutants produced in any one generation would be so small that they could hardly find mates among masses of unchanged relatives.

The initial disadvantage of isolation-producing mutants is mitigated in organisms with facultative self-fertilization, parthenogenesis, or asexual generation. The mutants (unless they are inviable or sterile in heterozygotes) may become multiplied and form a small colony in which cross-fertilization may then be resumed. It is significant that many polyploids, which are at least partly isolated from their diploid ancestors by the doubling of the chromosomal complement, are capable of reproduction by methods other than obligatory cross-fertilization.

It is probable that the formation of isolating mechanisms entails not single mutational steps but the building up of systems of complementary genes. Assume that a population has the genetic constitution *aabb*, where *a* and *b* are single genes or groups of genes, and that this population is broken up into two allopatric, geographically isolated parts. In one part, *a* mutates to *A* and a local race *AAbb* is formed. In the other part, *b* mutates to *B*, giving rise to a race *aaBB*. Since individuals of the constitutions *aabb*, *Aabb*, and *AAbb* interbreed freely, there is no difficulty in establishing in the population

the gene *A*. The same is true for the gene or genes *B*, since *aabb*, *aabB*, and *aaBB* interbreed freely. But the cross *AAbb* × *aaBB* is difficult or impossible, because the interaction of *A* and *B* produces one of the reproductive isolating mechanisms. If the carriers of the genotypes *AAbb* and *aaBB* surmount the extrinsic barriers separating them, they are now able to become sympatric, since interbreeding is no longer possible.

To summarize: reproductive isolation between pairs of sexually reproducing and cross-fertilizing species is produced usually by complementary gene complexes carried by the species concerned; the minimum number of genes that can form a workable isolating mechanism is two. Hybrid inviability and hybrid sterility are caused by complementary genes or genetic conditions which act as dominants, and hence manifest themselves in heterozygotes. A hypothesis which must now be examined is that the development of reproductive isolation between Mendelian populations occurs when these populations are territorially separated. In other words, the reproductive isolation observed between species that are at present partly or wholly sympatric had developed, or at least originated, while their ancestors were allopatric.

ALLOPATRIC AND SYMPATRIC SPECIES FORMATION

Since Darwin, and especially since Wagner, the theory that species develop from geographic races, or subspecies, has been held by most systematists and biogeographers. Geographic isolation of allopatric populations is, according to this theory, a usual, or even a necessary, antecedent of species formation. In the early part of our century, this theory was advanced especially by K. Jordan (1905), D. S. Jordan (1905), Semenov-Tian-Shansky (1910), and later by Rensch (1929). The views of these authors were more or less strongly tinged with Lamarckism: allopatric populations become genetically different, and diverge more and more in the course of time, because they are changed by the different environments which prevail in the countries which these populations inhabit. Unsatisfactory as this formulation sounds today, it is only fair to note that while genetics was only groping for its fundamental concepts, the view that organisms are changed by the environment represented no more than a restatement of the observed facts in ambiguous terms.

The modern version of the theory of allopatric speciation has been arrived at chiefly by Rensch (1933), Mayr (1940, 1942, 1947, 1948, 1949), Simpson (1945), Lack (1947), as well as in the previous editions of this book. The essential points of this view are two. First, the differentiation of races in sexual and cross-fertilizing organisms is due to modification of gene frequencies in allopatric populations by natural selection and by the genetic drift. The environment is, in the final analysis, the directing agent, but it acts through interaction of the genetic mechanisms just named. Second, allopatric populations attain the status of species by becoming reproductively isolated. Species may or may not become partly or wholly sympatric after the reproductive isolation has appeared. A number of authors (Huxley 1942, Thorpe 1945, Allee et al. 1949, and others) believe, however, that in at least some cases vestiges of reproductive isolation may arise without antecedent geographic isolation and may cause a split-up of a Mendelian population into two or more derived ones. Sympatric races so initiated may then diverge and strengthen their reproductive isolation, owing to different selective forces which prevail in adjacent habitats in the same general territory.

A careful analysis of this theory of "sympatric speciation" has been made by Mayr (1947). In large part, the differences between the allopatric and the sympatric theories of species formation are due to semantic difficulties. Allopatric populations need not be isolated by large distances or by formidable geographic barriers. Particularly in organisms with weak distribution means, or in those which breed in limited and fixed territories (like many birds), the inhabitants of adjacent biotopes may be geographically disjunct, and hence allopatric. Parasites which are host specific may be allopatric, even though their hosts may be sympatric (Clay 1949). And there is no doubt that in organisms which are at least facultatively self-fertilizing, parthenogenetic, or asexual, sympatric speciation is possible under certain conditions. The real problem is how much gene exchange between the diverging populations is possible without arresting and reversing the divergence. It will be agreed that if two populations become panmictic, interbreeding at random, they are fused into a single population. Hybridization, gene exchange, between populations tends to make their gene pools progressively more similar. But populations may continue to diverge despite gene exchange, because

of the differentiating forces: selection and the genetic drift. Genetic convergence or divergence will be decided by the balance of the opposing forces. How much geographic isolation is needed to permit race formation and divergence depends upon the intensity of the differentiating selection. In theory, sympatric speciation is possible if one is willing to make sufficiently drastic assumptions regarding the selection intensity, migration rates, etc.

That allopatric speciation does occur is not denied apparently by anyone. The evidence for this is overwhelming. Geographic subspecies in all stages of divergence, up to and including the stage when it is an arbitrary matter whether they are to be called subspecies or species, occur profusely in nature (see Rensch 1929, Mayr 1942, and Stebbins 1950 for examples). Evidence of sympatric speciation is rare, and all of it is contested by some authors, on apparently valid grounds (see especially Mayr, 1947, for references). Perhaps the most impressive arguments for sympatric speciation have been made by authors who studied the so-called "species flocks" in ancient lakes and no oceanic islands. Thus, Galapagos Islands have 14 species of an endemic subfamily, Geospizinae, Darwin's finches. Lake Baikal has some 300 species of gammarid shrimps, more than the rest of the world. Superficially considered, it seems most probable that these species flocks have developed where they are now, sympatrically. Yet, Lack (1947), and Brooks (1950) showed very convincingly that the speciation in these cases was allopatric. The "explosive speciation" of the Darwin's finches took place because the ancestral finch, which came to Galapagos from the mainland of South America, found a much greater variety of unoccupied habitats than it had in its original home. The species have become differentiated on the different islands of the archipelago. Some of the reproductively isolated species were then able to become sympatric, subdividing among themselves the available habitats. Similarly, the shrimp species diverged while geographically isolated in different parts of the lake, and at different depths.

REPRODUCTIVE ISOLATION AND NATURAL SELECTION

Certainly not every race of a species is itself an incipient species. Race formation is a reversible process; race divergence may be replaced by race convergence, as has occurred in man. Races become

species only if they develop reproductive isolation. This brings us face to face with the problem: what causes bring about the development of reproductive isolating mechanisms? Mayr (1948) has stated what is probably the prevailing opinion among systematists in these words: "If the [geographic] isolation is sufficiently complete and lasts sufficiently long, it will permit the evolution of isolating mechanisms, which will inhibit the interbreeding of the two daughter species after the elimination of the extrinsic isolating factors." Yet, not all genetic differences produce even partial isolation, and there is no reason to believe that isolation results automatically when a certain number of genetic differences have accumulated.

Muller (1939, 1940a, 1942, 1950a) supposes that reproductive isolation arises through phylogenetic change in gene functions. Muller's premise is that, since a functional genotype is an integrated system of genes, evolutionary changes are not mere additions or subtractions of unrelated gene elements. The initial advantage of most mutations that arise and become established in a species is slight; some mutations may, to begin with, even be neutral. But as the accumulation of gene differences goes on, genes which at one time might have been easily dispensed with become essential constituents of the genotype (Harland 1936, Schmalhausen 1949). In the course of evolution, the functions of a gene in the development may undergo such changes that a gene may subtend developmental processes other than those with which it was previously concerned. If the gene functions in two or more races or species diverge, the gene systems may become no longer compatible in hybrids. In Muller's opinion, all kinds of isolating mechanisms may arise in the manner just indicated: "Which kind of character becomes affected earliest, and to what degree ... will depend in part upon its general complexity (which is correlated with the number of genes affecting it), in part on the nicety or instability of the equilibria of processes necessary for its proper functioning, and in part on the accidental circumstances that determined just which incompatible mutations happened to become established first."

This very ingenious scheme is best adapted to explain the inviability of the hybrids of remote forms, and the breakdown observed in the F_2 and in backcrosses of other hybrids. Whether it is sufficient to account for the development of all isolating mechanisms is doubt-

ful. Isolating mechanisms encountered in nature appear to be *ad hoc* contrivances which prevent the exchange of genes between nascent species, rather than incongruities originating in accidental changes in the gene functions. Dobzhansky (1940) has proposed a hypothesis based on the suggestion of Fisher (1930) that physiological isolating mechanisms may be a product of natural selection. This hypothesis, which is complementary to Muller's, starts from the same premise, namely that the genotype of a species is an integrated system adapted to the ecological niche in which the species lives. Gene recombination in the offspring of species hybrids may lead to formation of discordant gene patterns. This decreases the reproductive potentials of both interbreeding species.

Assume that incipient species, A and B, are in contact in a certain territory. Mutations arise in either or in both species which make their carriers less likely to mate with the other species. The non-mutant individuals of A which cross to B will produce a progeny which is adaptively inferior to the pure species. Since the mutants breed only or mostly within the species, their progeny will be adaptively superior to that of the non-mutants. Consequently, natural selection will favor the spread and establishment of the mutant condition. Sturtevant (1938) has pointed out one of the possible causes which may initiate such a process. Suppose that the gene arrangement in a chromosome ABCDEFGH is modified in one race to AFEDCBGH and in another race to ABGFEDCH. Heterozygotes carrying the ancestral and either of the modified arrangements will produce few or no inviable offspring. In a hybrid carrying the two modified arrangements, crossing over in the section CDEF will give chromosomes AFEDCH and ABGFEDCBGH. Such chromosomes may be inviable. Prevention of the interbreeding of the carriers of AFEDCBGH and ABGFEDCH will have a selective advantage.

Once reproductive isolation is initiated, natural selection will tend to strengthen it and eventually to make the isolation complete. If, for example, the hybrids between species are partly sterile, it is advantageous for these species to modify their breeding seasons in such a way that no such hybrids be produced. The reproductive potential of individuals whose offspring are partly sterile is, evidently, lower than that of individuals which do not produce such offspring. Addition of sexual isolation will be advantageous if it makes the isolation

secure. Isolating mechanisms between species are interdependent, and natural selection tends to strengthen the whole complex of these mechanisms until the possibility of gene exchange between these species is severely limited or stopped.

A striking experimental verification of the above hypothesis has been provided by Koopman (1950). At low temperatures (16°C.), the sexual isolation between *Drosophila pseudoobscura* and *D. persimilis* is much weaker than it is at higher ones (Mayr and Dobzhansky 1945). In a series of generations, Koopman placed in population cages equal numbers of females and males of the two species. The species were made homozygous for two different recessive mutants, so that the proportions in the progeny of both species and of hybrids could be determined by inspection of the flies. Since the hybrid flies were destroyed in every generation, the flies which mated with representatives of their own species were leaving more surviving offspring than the flies which mated with individuals of the foreign species. Promiscuity was, consequently, made selectively disadvantageous, and mating within the species adaptively advantageous. In Koopman's three experiments carried out at 16°C., the first generation produced respectively 36, 22, and 49 percent of hybrids. The second generation gave 24, 6, and 18 percent hybrids respectively. From the fifth generation on, the proportions of the hybrids were, with some exceptions, below 5 percent. In other words, the natural selection resulted in formation in population cages of strains which show high sexual isolation at low as well as at high temperatures. The rapidity with which this genetic intensification of the isolating mechanism was brought about by selection is indeed remarkable. It may be noted that the selection is in this case properly called natural, rather than artificial, because the hybrids between *D. pseudoobscura* and *D. persimilis* are effectively sterile under the competitive conditions that obtain in the population cages.

The hypothesis that reproductive isolation is built by natural selection can also be tested by indirect evidence. If the hypothesis is correct, the isolating mechanisms between related species should, in general, be strongest in those parts of their distribution areas where the danger of hybridization between the species is greatest. This is exactly what has been observed by Stephens (1948) in the cottons *Gossypium hirsutum* and *G. barbadense*. As stated above, the

"Corky" genetic complex occurs most frequently in those regions where the species are sympatric. In the opinion of Stephens, "Corky" is effective as an isolating mechanism in natural populations. Dobzhansky and Koller (1939) found that sexual isolation between *Drosophila miranda* and *D. pseudoobscura* is stronger or weaker depending upon the geographic origin of the strains used. The strains of *D. pseudoobscura* from regions in which, or close to which, *D. miranda* also occurs, show, in general, greater sexual isolation than do strains from distant regions. King (1947b) studied the sexual isolation between the closely related species, *D. guarani* and *D. guaru*, which occur sympatrically in Brazil, and *D. subbadia* from Mexico, where the other species apparently do not live. The sexual isolation between the Brazilian species is nearly absolute, and the rare inseminations give no hybrids. The sexual isolation is relatively weak between either of the two Brazilian and the Mexican species. The cross *D. guaru* × *D. subbadia* produces viable hybrids; hybrid females are fertile and can be backcrossed to either parent, as well as to *D. guarani*, to which neither parent can be crossed. Triple hybrids were obtained. The reproductive isolation is obviously stronger between sympatric than between allopatric species.

The principal weakness of the view that reproductive isolation develops in response to the challenge of hybridization leading to formation of poorly adapted genotypes lies in its corollary. It is difficult to explain how reproductively isolated species can develop in noncontiguous territories, such as oceanic islands, where opportunities for hybridization are absent (Dobzhansky 1940). How serious this difficulty really is, we have no way of determining at present, since no experimental data on reproductive isolation in allopatric island species are available. Systematists are, however, familiar with species that are sympatric at our time level, although these species had developed presumably on separate islands (Mayr 1940, 1942). In such cases reproductive isolation might have arisen because these species have repeatedly invaded each other's territories; these attempts have led to the formation of isolating mechanisms, whereupon the invaders were able to establish themselves as an independent sympatric population.

It is important to remember that the formation of reproductive isolation is a process which requires time. The first vestige of the isola-

tion develops probably always in allopatric populations. Inviability of F_1 hybrids, and low average adaptedness of the F_2 and of backcross products are probably by-products of the genetic differentiation of allopatric populations. Here the mechanism suggested by Muller is probably most important. The hybrid inviability and breakdown provide, then, the stimulus for natural selection to build up other reproductive isolating mechanisms. Reproductive isolation diminishes the frequency of the appearance of hybrids, prevents the reproductive wastage, permits the populations of the incipient species gradually to invade each other's territories, and finally to become partly and wholly sympatric. It is during the latter stages of this process that the selection pressure bolstering the reproductive isolation becomes strongest, helping to complete the process of speciation (cf. Mayr 1947, Stebbins 1950, Lack 1947, Pittendrigh 1950).

An important, and so far very little studied, aspect of the process of speciation is the development of genetic differences between diverging species which are by themselves adaptively neutral, but which acquire selective value because they serve as "recognition marks". Sexual isolation in animals may very well be bolstered by making the species traits easily recognizable to conspecific individuals as well as to individuals of distinct but sympatric species. When, as in the fish species studied by Haskins and Haskins (1949, 1950), the recognition is chiefly visual, distinctive colorations and shapes may be favored by natural selection. In other forms distinctive smells or distinctive behaviors may be favored. In plants conspicuous differences between insect-pollinated species may assist in diminishing the wastage of outgoing pollen and the delivery of foreign pollen grains. To what extent such selection processes may explain the apparently neutral species differences is at present problematic.

VIII : Hybrid Sterility

HISTORICAL

THE PROBLEM of hybrid sterility goes back to Aristotle, who discussed at length the sterility of the mule. Some authors regarded hybrid inviability and sterility as criteria of species distinction, and proposed to define species as groups of individuals which fail to produce viable and fertile offspring when crossed (for example, Standfuss 1896). Such definitions are invalid. Species may be maintained distinct by any, or a combination of several, reproductive isolating mechanisms. Viable and fertile hybrids can be obtained in experiments between some undoubtedly distinct species, which are completely reproductively isolated in nature. Hybrid inviability and sterility are not even biologically the most efficient isolating mechanisms, since they entail a wastage of gametes of both species, as well as of hybrid zygotes. Reproductive isolating mechanisms which preclude the formation of hybrid zygotes are probably more important in the maintenance of natural species (the mechanisms marked A to E, page 181). Hybrid sterility is, however, the most extensively studied, and probably the best understood of isolating mechanisms.

Some authors supposed that hybrid sterility is a sign of a general weakness of the hybrid organism, and that the reproductive system is the place of least resistance where such weakness first manifests itself. This is not the case. Many hybrids with reduced viability are fertile (e.g., the flax hybrids described by Laibach, see Chapter VII). Constitutional weaknesses in pure species (in poorly viable mutants, for example) are by no means always accompanied by sterility. The male hybrids between *Drosophila pseudoobscura* and *D. persimilis* have very abnormal spermatogenesis and are sterile. Dobzhansky and Beadle (1936) transplanted testes of hybrid larvae into larvae of the pure species, and vice versa. If a transplanted testis of a pure species becomes attached to the sexual ducts of a hybrid, the latter becomes fertile, the functional sperm coming, of course, from the

implanted testis. Hybrid testes do not develop functional spermatozoa in the bodies of pure species, and the gonads of the host are not affected by the presence of a hybrid testis. Ephrussi and Beadle (1935) obtained fertile eggs from the ovaries of *D. simulans* implanted in *D. melanogaster*, although the hybrids between these species are completely sterile.

A fundamental discovery concerning hybrid sterility was made by Federley (1913). He discovered that the chromosomes usually fail to form bivalents at meiosis in the sterile or semi-sterile hybrids between the moth species *Pygaera anachoreta*, *P. curtula*, and *P. pigra*. Various abnormalities (fused spindles, failures of cell division) are observed in the spermatocytes; the spermatids usually degenerate. Federley's observations have been confirmed by many investigators in sterile hybrids of both plants and animals. The essential fact is that a failure of pairing between chromosomes of different species is observed at meiosis in most (although not in all) sterile hybrids. In detail, the situation varies greatly. Some chromosomes may pair and form bivalents, others remain univalent. The proportion of bivalents and univalents varies not only in different hybrids but also in individuals and cells of the same hybrid. The bivalents disjoin normally, that is, at each division half of the bivalent passes to each pole of the spindle. The univalents split either at the first or at the second meiotic division; at the division at which no splitting takes place the univalents are distributed at random to the poles of the spindle, so that the daughter cells may come to have unequal numbers of chromosomes. The cell division mechanism itself may break down, and all sorts of degenerative phenomena appear in the cells. Few or no functional gametes are produced (see the excellent reviews by White 1945, for animals, and Stebbins 1950, for plants).

The fact that the meiotic chromosome pairing is frequently the starting point of abnormalities in the gametogenesis in sterile hybrids leads to the supposition that a cause and effect relationship exists between these phenomena. As a general theory this supposition is vitiated, however, by the occurrence of sterile hybrids in which chromosome pairing at meiosis is normal. Such hybrids have been described in *Digitalis* by Haase-Bessell (1921), in *Epilobium* by Håkansson (1934), in *Lolium perenne* × *Festuca pratensis* by Peto (1933), and in *Saxifraga* by Drygalski (1935). (For further examples, see Steb-

bins 1950). In *Chorthippus bicolor* × *Ch. biguttulus* chromosomes pair normally but the disjunction is highly abnormal (Klingstedt 1939). The F_1 hybrid males from the crosses of *Drosophila pseudoobscura* and *D. persimilis* are always sterile, although the amount of chromosome pairing is highly variable (Dobzhansky 1934). Within each species, strains are encountered that produce hybrids in which no bivalents are formed at meiosis, and other strains that produce hybrids with bivalents only and no univalents. The meiotic divisions are, however, abnormal in either case: the first division spindle elongates enormously, bends into a ring, the cell body fails to divide, the second meiotic division is absent, and the giant binucleate spermatids which are formed degenerate.

In other hybrids the cells of the gonads degenerate before the advent of the meiotic stages. In the hybrids between *Drosophila melanogaster* and *D. simulans*, the gonads are rudimentary, and, as shown by Kerkis (1933), spermatogenesis and oogenesis do not advance beyond spermatogonia and oogonia. Apparently similar conditions are encountered in some of the hybrids between species of birds, and of mammals (horse × zebra, yak × domestic cow). The malformations of flowers and anthers observed in some plant hybrids may belong to the same category.

GENIC AND CHROMOSOMAL STERILITY

The great diversity of the phenomena of hybrid sterility shows that many sterility mechanisms occur in nature. Federley (1928) and Renner (1929) distinguished gametic and zygotic sterility; the former consists in production of degenerate gametes, and the latter of inviable zygotes. Müntzing (1930) prefers the terms "haplontic" and "diplontic" sterility; the former is due to the lethality of the haplophase and the latter to disturbances in the diploid part of the life cycle. These terms may be convenient for descriptive purposes, but such classifications hardly penetrate below the surface of the phenomena. More basic is the distinction between genic and chromosomal sterility (Dobzhansky 1933b).

Meiosis, like any other physiological process, is controlled by the genotype of the organism. The normal course of meiosis involves a succession of events which are so delicately balanced that a failure of any one of them, or simply a change in timing, causes derangement

of the whole process. Gene mutations can attack this process at any stage. Chromosome pairing may fail despite the presence of pairs of chromosomes with similar genes arranged in identical linear series. The resulting sterility will be due to the genetic constitution of the organism. This is *genic sterility*. On the other hand, chromosomes may fail to pair and to form bivalents because they have no structurally similar partners. Chromosomes may contain identical genes, but they may be very differently arranged. Sterility due to such structural dissimilarities is *chromosomal sterility*.

Disturbances in the gametogenesis in hybrids may be initiated before, during, or after the meiotic chromosome pairing. Genic sterility does not necessarily involve interference with the meiotic mechanism. On the other hand, where the abnormalities begin with a failure of chromosome pairing, the sterility may be either chromosomal or genic. The sterility of some hybrids may be caused by a combination of the two causes. Indeed, the interbreeding of many species is prevented not by one but by several isolating mechanisms, which reinforce each other's action.

GENIC STERILITY WITHIN SPECIES

Natural populations of *Drosophila* species carry, concealed in heterozygous condition, many recessive mutant genes which cause, when homozygous, sterility either of males or of females, and, more rarely, of both sexes (see Chapter III). In *D. willistoni*, only about 25 percent of the wild flies do not carry at least one such sterility gene in their germ plasm. Sterile mutants are common also in the progeny of X-ray treated flies (Berg 1937, Prabhu 1939). Twelve female sterile mutants in *D. melanogaster* examined by Beatty (1949) proved to be all different from each other in the manner of their action. Recessive sterility genes are quite common also among plants (see Darlington 1937, Levan 1940, and Andersson 1947, for references). They engender most diverse abnormalities at different stages of meiosis. Especially common are "asynaptic" mutants, which prevent the chromosome pairing or the formation of chiasmata at meiosis. Smith (1936) found asynaptic plants among the segregation products from the cross *Triticum monococcum* × *T. aegilopoides* var. *baidaricum*. Here the asynaptic condition is due to a complementary action of two recessive genes contributed by the

respective parents, so that the double recessive homozygotes (*aabb*) are sterile while the heterozygotes are fertile.

The abundance in natural populations of sterility mutants may seem to suggest that such genes are the building blocks from which sterility barriers between species may be constructed by natural selection. This is unlikely. Hybrid sterility is a situation when two forms each of which is fertile *inter se* (e.g., horse and ass) produce a hybrid which is sterile (mule). Hybrid sterility could be produced by a single gene only if this gene would make both homozygotes (AA and aa) fertile and the heterozygotes (Aa) sterile. Alleles at the T locus in mice affect the development of the tail and a number of other characters. Two of these alleles, t^0 and t^1, produce male sterility in the compound t^0t^1 (Dunn 1937b). Klingstedt (1939) supposes that sterility genes which are recessive within a species might become dominant in interspecific hybrids. If, then, individuals of the two parental species crossed are each heterozygous for several recessive sterility genes, the hybrid may be sterile. A wide applicability of Klingstedt's hypothesis may be doubted, since the hybrid sterility so produced would be tremendously variable depending on the strains of the parental species used in the cross.

Stern (1929, 1936) has devised a model of hybrid sterility within

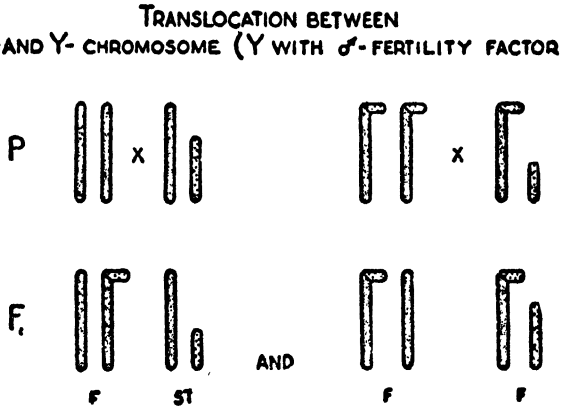


FIG. 15. Two strains of *Drosophila melanogaster* that produce sterile male hybrids when crossed. X chromosome, stippled; Y chromosome, dotted. Upper left, normal female; upper right, male from the translocation strain; below, the hybrids. F, fertile; ST, sterile. (From Stern.)

the species of *Drosophila melanogaster*. Males without a Y chromosome are sterile; at least two different sections of this chromsome are concerned with fertility. Both sections must be present in order that the male may be fertile. Females carrying a whole Y chromosome or a part of it in addition to their X chromosomes are fertile. In a translocation the Y has been broken, and a section containing one of the "fertility genes" has become attached to the X. A strain was obtained (Fig. 15 upper right) in which females have two X chromosomes with sections of the Y attached to them, and males have a similar X and a fragment of the Y that is deficient for just the section that is attached to the X. A male of this strain is fertile because it carries simultaneously both sections of the Y chromosome that are needed for fertility. If normal females are crossed to the males of this strain, the offspring are fertile females and sterile males (Fig. 15, lower left).

Mainland (1942) has described an incipient hybrid sterility in *Drosophila macrospina*, which parallels very closely Stern's model. *D. macrospina limpiensis* is a form known to occur in the Lympia mountain range in Texas. Its relatives, *D. macrospina macrospina* and *D. macrospina ohioensis*, occur elsewhere in Texas and in Ohio respectively. The crosses, *limpiensis* ♀ × *macrospina* ♂ and *limpiensis* ♀ × *ohioensis* ♂ produce fertile daughters and sterile sons; in the reciprocal crosses the F_1 hybrids are fertile. Backcrosses of the hybrid females to *limpiensis* males produce fertile progenies, while if the hybrid females are crossed back to *macrospina* or *ohioensis* males, half of the male offspring are sterile. *Macrospina* and *ohioensis* give fertile hybrids. It follows that males carrying a *limpiensis* X must also carry a *limpiensis* Y chromosome in order to be fertile. Another instance of an incipient sterility barrier has been found by Hadjinov (1937). Two strains of *Sorghum vulgara* derived from India are morphologically similar to other known strains of the same species but, nevertheless, produce semisterile hybrids when outcrossed to the latter. Meiosis in the hybrids is normal, but male gametophytes mostly degenerate soon after the meiotic divisions are completed. The backcrosses to the parental strains have, unfortunately, not been analyzed, but the data as presented suggest that only a few genes are involved in the production of the sterility.

INTERSEXUALITY IN HYBRIDS

The hybrids between some species are sterile because they are intersexual. This is, evidently, a special case of genic sterility, in which the non-production of functional gametes is due to a breakdown of the mechanism of sex determination. The classical example of intersexuality in hybrids is that observed in crosses between geographic races and incipient species of the gypsy moth, *Lymantria dispar*, brilliantly analyzed by Goldschmidt (1931, 1932, 1934, and other works). According to Goldschmidt, the races from the northern island of Japan (Hokkaido) and from Europe have "weak" sex-determining factors. The sex determiners in strains from Russian Turkestan, Manchuria, and southwest Japan are "half weak" or "neutral". Those in the strains from the middle and north Japan are "strong". Crosses weak ♀ × strong ♂ produce in the F_1 generation normal males and intersexual females. The reciprocal cross, strong ♀ × weak ♂, gives normal females and males in F_1 but in the F_2 half of the males are intersexual. Denoting the female determiners by F, the male determiners by M, the weak and strong alleles by the subscripts w and s, the above results have been interpreted by Goldschmidt thus:

F_wM_w (weak ♀) × M_sM_s (strong ♂) = F_wM_s (intersex) and $F_wM_sM_w$ (♂)
F_sM_s (strong ♀) × M_wM_w (weak ♂) = F_sM_w (♀) and $F_sM_wM_s$ (♂)

One F is normally sufficient to suppress the effects of a single M and to produce a female; but an F_w is not strong enough to overpower an M_s, hence an F_wM_s individual is an intersex. Likewise, the individuals of the constitution $F_sM_wM_w$ which appear in the F_2 from the cross strong ♀ × weak ♂ are not males but intersexes. The degree of the intersexuality is very different in different crosses. In some crosses where the "strength" of the sex determiners in the parental races differs only slightly, the intersexes are so much like normal females or males that they are fertile. Where the difference between the parental races is greater, the intersexes have the gonads, the ducts of the reproductive system, the genitalia, the secondary sexual characters, and the sexual behavior patterns modified so extensively that they are sterile. The degenerative processes in the gonads may be

quite extensive, but so far as is known the chromosome behavior at meiosis is unaffected. Finally, crosses between very strong and very weak races give intersexes that are transformed into individuals of the sex opposite to that which they should have had according to their chromosomal constitution (XX instead of XY females, and XY instead of XX males).

The geographic distribution of the *Lymantria* races with weak, intermediate, and strong sex determiners is interesting. Sympatric strains have similar sex genes, and, indeed, a mutation that would change their "strength" would be discriminated against by natural selection, if it were to make some of its carriers intersexual. For similar reasons, populations with sex genes sufficiently different to produce sterile hybrids when crossed never inhabit adjacent and contiguous territories. The "strength" of the sex genes shows geographic gradients. As indicated above, the island of Hokkaido is inhabited by the "weakest" race. If we travel from there through Manchuria, Korea, southwestern Japan, and central Japan, progressively "stronger" races are encountered. The "strongest" race of all lives in the northern parts of the main island of Japan, separated from the "weakest" one in Hokkaido only by the Tsugaru Strait, which is, however, broad enough to prevent the mingling of the races which live on its opposite shores. As shown by Mayr (1942), the races of Hokkaido and of the northern part of the main island of Japan can properly be regarded as incipient species. This conclusion is, however, not accepted by Goldschmidt.

Sterile intersexual hybrids are known in several groups of animals, although in general they do not appear to be very frequent. According to Goldschmidt's analysis (1931) of the data of Keilin and Nuttal, the crosses between the head and the body lice (*Pediculus capitis* × *P. vestimenti*) produce some intersexes in the F_2 and F_3 generations. A similar situation has been observed by Guyénot and Duszynska (1935) in F_2 and F_3 of the cross *Cavia apera* × *C. cobaya* (guinea pigs), and by Crew and Koller (1936) in the F_1 of the cross *Anas* × *Cairina* (ducks). In the latter cross the spermatogenesis in the sterile males has been investigated; meiotic chromosome pairing appears to be normal, but various abnormalities in the second spermatocytes are observed. Sturtevant (1946) found intersexes in the hybrids between *Drosophila repleta* and *D. neorepleta*. Federley

(1949) discovered them in hybrids between some species of the moths *Drepana*.

Sterile intersexes of a very different kind were obtained in the pregenetical days by Standfuss in the cross between the moth species *Saturnia pyri* ♀ × *S. pavonia* ♂. The hybrid males can be backcrossed to *S. pavonia* females; the progeny consists of males and what Standfuss described as "gynandromorphs". The latter have been shown by Pariser (1927) and Goldschmidt (1931) to be intersexes. *S. pavonia* and *S. pyri* have 29 and 30 chromosomes, respectively (haploid). The F_1 hybrid has 59 chromosomes, most of which fail to form bivalents at meiosis. Meiosis in the hybrids proceeds apparently according to the scheme described by Federley for *Pygaera* (see above), and the backcross offspring are subtriploid. The *Saturnia* intersexes are, therefore, comparable to the triploid intersexes in *Drosophila*. Inasmuch as the sterility of some of the backcross individuals in *Saturnia* is due to their intersexuality, this case may be classed as belonging to the genic sterility type. The lack of chromosome pairing in the gametogenesis of the F_1 may, however, be due either to the dissimilarities in the gene arrangements in the chromosomes of the parental species (chromosomal sterility), or to the effects of complementary genetic factors (genic sterility).

GENIC STERILITY IN THE HYBRIDS OF *Drosophila pseudoobscura* × *D. persimilis*

Drosophila pseudoobscura and *D. persimilis* are very closely related species which are very similar in external morphology (sibling species, see Chapter IX). As shown first by Lancefield (1929), the cross *D. persimilis* ♀ × *D. pseudoobscura* ♂ gives F_1 hybrid males with small testes; the reciprocal cross, *D. pseudoobscura* ♀ × *D. persimilis* ♂, produces hybrid males with testes of normal size; in either case the males are completely sterile. The backcrosses of the F_1 hybrid females to *D. persimilis* or to *D. pseudoobscura* males give sons with testes of variable size, ranging from normal to very small. Males with small testes are always sterile, those with large ones are sometimes fertile (Lancefield 1929). The sterility is due to a profound modification of the process of spermatogenesis. The meiotic chromosome pairing is variable; no univalents, some univalents, or only univalents may be present at the first meiotic division. Irrespec-

tive of the numbers of the bivalents and univalents formed, only a single very abnormal meiotic division takes place. The spermatids degenerate (Dobzhansky 1934). The disturbances in spermatogenesis are in general greater the smaller are the testes in a hybrid. Testis size is, therefore, a measure of the degree of departure from the normal course of the spermatogenesis. The disturbances in the hybrids are confined to the gonads, while the rest of the reproductive system (the sexual ducts and external genitalia) is normal. The sterile males are not intersexual. Some real intersexes have been found in *Drosophila pseudoobscura* and they are quite distinct from the hybrid males.

Since *D. pseudoobscura* and *D. persimilis* differ in the gene arrangement in their chromosomes, one might have surmised that the sterility of their hybrids is chromosomal. The differences in the gene arrangement involve however only three, or even only two, inversions. A more conclusive evidence that the sterility of *D. pseudoobscura* × *D. persimilis* hybrids is not chromosomal is afforded by observations on the chromosome behavior in tetraploid spermatocytes (Dobzhansky 1933b). Groups of such spermatocytes are frequently encountered in the testes of hybrid males. Tetraploid spermatocytes contain two full sets of chromosomes of *D. pesudoobscura* as well as of *D. persimilis*. Each chromosome has, consequently, a partner exactly similar to it in the gene arrangement. It is known that, in some plant hybrids in which no chromosome pairing is observed in the diploid, the reduplication of the chromosome complement enables all chromosomes to pair and to form bivalents, and the hybrid to become fertile (see below). The proportion of the chromosomes that become paired in the tetraploid spermatocytes of *D. pseudoobscura* × *D. persimilis* hybrids is however no greater than in the diploid ones. Moreover, after the meiotic divisions the cells derived from the tetraploid spermatocytes undergo the same degenerative changes as the diploid ones.

The hypothesis that the sterility of the hybrids between *D. persimilis* and *D. pseudoobscura* is genic may now be considered. Assume that the genetic constitution of *D. persimilis* is *SStt*, and that of *D. pseudoobscura ssTT;* the hybrids are *SsTt*. *S* and *T* are genes or groups of genes; males which carry *S* alone, or *T* alone, are fertile, but simultaneous presence of *S* and *T* makes a male sterile. This hy-

pothesis can be tested experimentally. In the progenies of F_1 hybrid females backcrossed to males of either parental species, individuals appear that carry various combinations of chromosomes of the two species (Figs. 16 and 17). Some have all chromosomes of one spe-

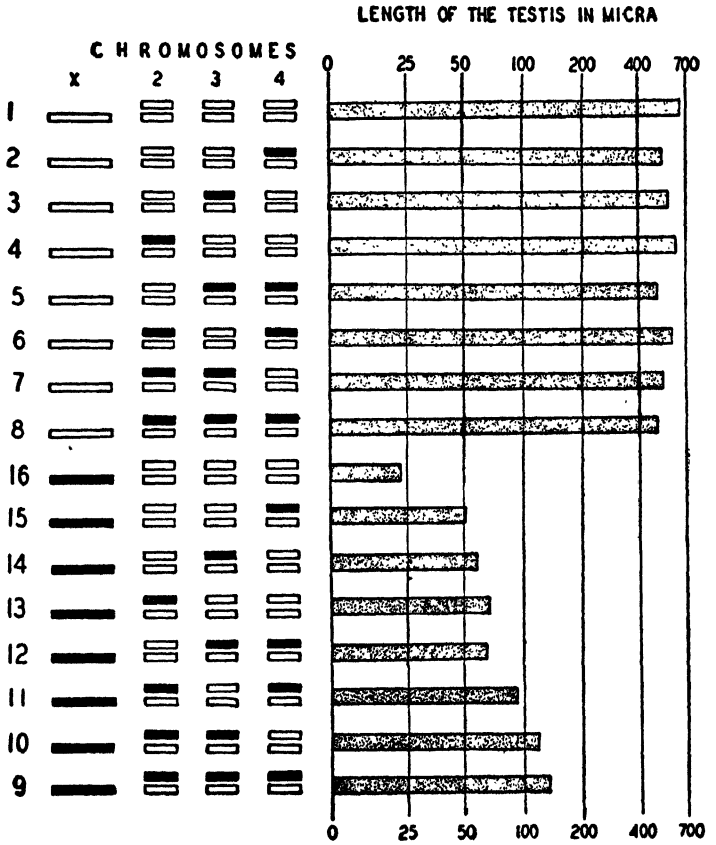


FIG. 16. Testis size in backcross hybrids between *Drosophila pseudoobscura* and *D. persimilis*. Chromosomes of *D. pseudoobscura* are represented in white, and those of *D. persimilis* in black.

cies; others have an X chromosome of one species and autosomes of the other; still others carry various mixtures of the chromosomes of both species. Experiments can be so arranged that every chromosome (with the exception of the very small fifth) is marked with a mutant gene; the constellation of the chromosomes present in a given

backcross individual is, then, recognizable by inspection of its external appearance. It is a simple matter to determine which combinations of chromosomes cause a male to have small testes and to be sterile, and which permit fertility. Moreover, if the original cross is

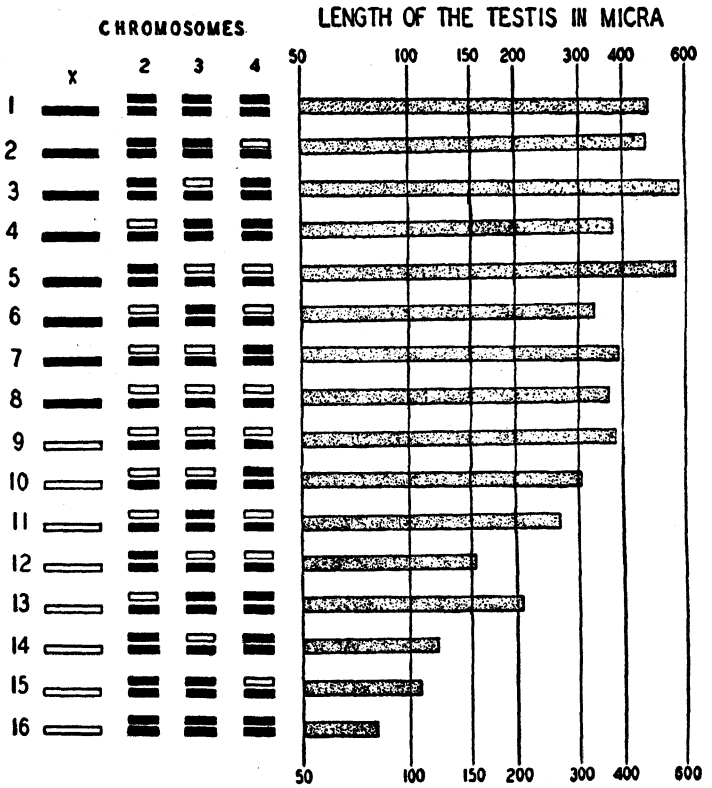


FIG. 17. Testis size in backcross hybrids between *Drosophila pseudoobscura* and *D. persimilis*. Chromosomes of *D. pseudoobscura* are represented in white, and those of *D. persimilis* in black.

made by using *D. pseudoobscura* as a female, the entire offspring has *D. pseudoobscura* cytoplasm, while the cross *D. persimilis* ♀ × *D. pseudoobscura* ♂ gives a progeny with *D. persimilis* cytoplasm. Several crosses in which the chromosomes of the parents were marked as indicated above have been studied by Dobzhansky (1936a). The fertility or sterility in the backcross males depends upon their chromosomal constitution, not upon the ultimate sources of their cyto-

plasm. Males whose grandmother was a *D. pseudoobscura* female are similar to those descended from a *D. persimilis* grandmother, provided they have similar chromosome complements.

Backcross males with X chromosome and autosomes of the same species have large testes and are usually fertile (Figs. 16 and 17). The more dissimilar the X and the autosomes become in species origin the smaller the testis size. The smallest testes are observed in males with the X of one species and all autosomes of the other. With a single exception,[1] all chromosomes act alike, and their action is cumulative. Thus, individuals carrying *D. pseudoobscura* X and *D. persimilis* autosomes have very small testes (class 16, Fig. 16). The introduction of one fourth, or one third, or one second chromosome of *D. pseudoobscura* increases the testis size (classes 13–15, Fig. 16). The simultaneous introduction of the fourth and third (class 12), or second and third (class 10), or second and fourth (class 11), or second, third, and fourth (class 9) chromosomes of *D. pseudoobscura* increases the testis size more than each of these chromosomes does alone. Males having all chromosomes of the same species, or having one third or one fourth chromosome of the opposite species from the rest of the chromosomes, are fertile (classes 2 and 3). But if both the third and fourth chromosomes disagree in origin with the rest of the complement, the male is sterile.

With the exception of the Y and of the small fifth chromosome, all chromosomes of *D. pseudoobscura* and *D. persimilis* carry genes concerned with the sterility of the species hybrids. Moreover, the X, the second, the third, and the fourth chromosomes have each at least two such genes. The minimum number of genes concerned with the sterility is, therefore, eight, but the actual number is almost certainly greater. What the physiological reactions are through which these genes produce their effects culminating in the disturbance of spermatogenesis and in sterility is unknown. The only information is that the fate of the testis is determined by its own genetic constitution and not by that of the body in which it develops (the transplantation experiments of Dobzhansky and Beadle 1936; see above).

[1] The exception is that, in backcrosses to *D. persimilis* males, the sons having *D. pseudoobscura* third chromosome and *D. persimilis* X chromosome have larger testes than their brother homozygous for the *D. persimilis* third. This curious relation is due to a maternal effect, cf. Dobzhansky (1936b).

THE "STRONG" AND "WEAK" RACES OF *Drosophila pseudoobscura* AND *D. persimilis*

The cross *D. persimilis* ♀ × *D. pseudoobscura* ♂ produces in F_1 sterile sons with small testes. Dobzhansky and Boche (1933) showed that certain strains of *D. persimilis*, when crossed to the same *D. pseudoobscura* strain, the environmental conditions being kept constant, produce hybrids with markedly larger testes than other strains. Likewise, certain *D. pseudoobscura* strains produce much larger testes in the hybrids than others when crossed to the same *D. persimilis* strain. Strains that give relatively large testes are designated "weak" and those decreasing the testis size "strong". Although the F_1 hybrid males from crosses between *D. pseudoobscura* and *D. persimilis* are always sterile, the hybrids between weak strains display a complete chromosome pairing at meiosis, only bivalents being present, while in crosses between strong strains the meiotic pairing fails entirely, and not a single bivalent is formed. The expressions "strength" and "weakness" as applied to *D. pseudoobscura* and *D. persimilis* should not be confused with the similar terminology applied to *Lymantria* races (see above), for in the latter the "strength" of the sex-determining factors is what is being referred to.

The strong and weak races differ in their geographic distribution. In the region inhabited by *D. pseudoobscura*, the strength increases as one moves from northwest to southeast. British Columbia and Washington are populated chiefly by very weak or weak races, while in Mexico very strong variants are encountered. In *D. persimilis* the geographic regularity is less clear than in *D. pseudoobscura*, although the strongest strains seem to come from the coastal regions of Oregon and Washington, and the weakest from the Sierra Nevada mountains. Strains coming from the same locality may differ in strength rather widely. Thus, both interpopulational and intrapopulational variations are present. The genetic basis of the differences in strength is a polygenic one, genes modifying this character being found in all the chromosomes studied. Crosses between strains of the same species often produce in the F_2 generation some segregants that are weaker or stronger than either parental strain. Wild populations are evidently quite variable with respect to the genes which determine strength.

The importance of the above facts is revealed by observations that the genes which determine strength are similar to, or identical with, the sterility genes. If *D. pseudoobscura* × *D. persimilis* hybrid females are backcrossed to males of one of the parental species, one may obtain, in the first or in the later backcross generations, individuals that have most of the chromosomes of one species but carry one chromosome or a section of a chromosome of the other species. Parts of chromosomes, or whole chromosomes, of *D. pseudoobscura* may be "transferred" by this method to *D. persimilis*, or vice versa. If the transferred chromosome section is long, or carries powerful sterility genes, the male possessing it may be sterile; other sections do not interfere with fertility to an appreciable extent. The lines of *D. pseudoobscura* and *D. persimilis* known to carry certain chromosome parts of the other species may then be tested for strength with the aid of the same method that is used for testing the wild strains coming from nature, i.e., the size of the testes is determined in the F_1 males from the crosses *D. persimilis* ♀ × *D. pseudoobscura* ♂. Experiments of this type have thus far given consistent results: the strength of a line of *D. pseudoobscura* or of *D. persimilis* is decreased by the introduction of chromosomes or chromosome sections of the other species.

It has been shown that the sterility of the hybrids between *D. pseudoobscura* and *D. persimilis* is due to the effects of a complex of sterility genes. Now it is known in addition that, by interspecific hybridization, this complex can be dismembered into elements, and, what is especially important, these elements prove to have the same action as the genes determining the differences in strength between the different lines of the same species. The gap between the species differences causing the sterility of hybrids and the intraspecific variations is thus bridged. The conclusion is obvious. Within a species we find the genetic elements, the building stones, from which a mechanism causing hybrid sterility could be built. As the situation stands now the analysis is, of course, far from complete. We have not yet succeeded in synthesizing from the genetic elements encountered within a species two strains producing sterile hybrids—a feat that is not beyond the range of possibility in theory. Moreover, the variations in "strength" encountered within a species may be interpreted either as the remains of the store of building materials

from which the species differences had been built in the phylogeny, or else as a result of occasional breakdowns of the separation between the species. The latter interpretation would involve the assumption that *D. pseudoobscura* and *D. persimilis* sometimes produce hybrids in nature, and that through such hybrids some of the genes of *D. pseudoobscura* are transfused into *D. persimilis*, and vice versa. This possibility cannot be entirely excluded, although the fact that the distinction between the species has never been found blurred, even in the regions where their geographical distribution overlap argues against it.

GENIC STERILITY IN THE HYBRIDS *Drosophila virilis* × *D. americana*

An analysis of the sterility in the hybrids between the oriental species *D. virilis* and its American analogues *D. americana* and *D. americana* subsp. *texana* has been made by Patterson et al. (1940, 1942) and Stone (1947). The crosses between *D. virilis* and either race of *D. americana* produce hybrids of both sexes; the fertility of these hybrids varies depending upon the strains of the parental species used, but on the whole it is lower than in the pure species. Hybrids in the F_2 and in the backcrosses are likewise semisterile. If *Drosophila virilis* females are crossed to *D. americana texana* males, and the male hybrids are backcrossed to *D. virilis* females, only about 25 percent of the male progeny are fertile; if the initial cross is made using *D. americana texana* females, some 82 percent of the backcross males are fertile. The two series of crosses may be represented schematically as follows (X^v and X^t, and Y^v and Y^t, being X and Y chromosomes of *D. virilis* and *D. americana texana* respectively):

P *virilis* (X^vX^v) ♀ × *texana* (X^tY^t) ♂	*texana* (X^tX^t) ♀ × *virilis* (X^vY^v) ♂
Backcross *virilis* (X^vX^v) ♀ × X^vY^t ♂	*virilis* (X^vX^v) ♀ × X^tY^v ♂
X^vY^t males (25% fertile)	X^vY^v males (82.5% fertile)

The backcross males in both series are similar in that they carry the *Drosophila virilis* X chromosome, but in the series represented on the left they have the *D. americana* Y, and in that on the right *D. virilis* Y chromosome. Since the chromosomes of *D. virilis* and *D.*

americana are distinguishable cytologically, owing to the inversions and translocation (see below), it has been possible to determine the constitution of the fertile backcross males by examining the chromosomes in their offspring. The fertile males with *D. americana* Y chromosome invariably possess also the second and the fifth chromosomes of the same species. The Y, second, and fifth chromosomes of *D. americana* carry complementary genes which must be simultaneously present to enable a male to be fertile. Whether a single or several genes in each of these chromosomes are concerned has not yet been determined.

MATERNAL AND CYTOPLASMIC EFFECTS IN HYBRIDS

A hybrid inherits its chromosomes from both parents, but its cytoplasm chiefly from the mother. This may be expected to result in differences in the outcome of the reciprocal crosses between the same pair of species. Such differences are indeed not rare. In organisms with separate sexes, these differences are due, however, mostly not to cytoplasmic effects but to the combinations of the X chromosomes of one species, the Y of another, and the autosomes of both (cf. the discussion of Haldane's rule, Chapter VII). Thus, Federley (1929) found that the females from the cross *Chaerocampa elpenor* ♀ × *Metopsilus porcellus* ♂ have a combination of the X chromosome of the latter and the Y chromosome of the former species which acts as a lethal; the reciprocal cross gives rise to viable females that carry the X of *C. elpenor* and the Y of *M. porcellus*. An analogous situation obtains in the cross *Drosophila melanogaster* ♀ × *D. simulans* ♂, which gives females but no males, while the reciprocal cross produces male, but few or no female hybrids (Sturtevant 1920–1921). For further examples, see White (1945).

Differences between the products of reciprocal crosses occur, however, also in hermaphroditic organisms, which have no heterochromosomes. In these, as well as in some bisexual forms, the cytoplasm is probably the causative agent. It must, however, be kept in mind that the characteristics of the cytoplasm of an egg may be determined, first, by its intrinsic properties, independent of the chromosomes it carries or has carried, and, second, by the properties of the chromosomes that were present in the egg before the meiotic divisions and fertilization. The former mechanism is spoken of as cyto-

plasmic inheritance, while the latter, the predetermination of the cytoplasm by the chromosomes, is known as a maternal effect.

A clear case of a maternal effect is observed in the hybrids between *D. pseudoobscura* and *D. persimilis*. As stated above, the cross *D. persimilis* ♀ × *D. pseudoobscura* ♂ normally gives F_1 hybrid males with small testes, while the reciprocal cross gives F_1 hybrids with testes of normal size. The evidence (Dobzhansky 1935b, 1936a) which shows that this difference in testis size is due to a maternal effect can be summarized under two headings. (1) The F_1 hybrid females from either cross can be backcrossed to males of the parental species. The testis size, and the fertility, of the backcross males are known to depend upon the combination of the chromosomes of the two species, and are independent of the source of the cytoplasm in the hybrids (cf. Figs. 16 and 17). In other words, the difference between the reciprocal crosses does not extend beyond the F_1 generation. (2) Treating females of the parental species with X rays, some exceptional eggs may be obtained (through the so-called nondisjunction) which carry no X chromosomes. Such eggs may be fertilized by X-bearing spermatozoa, and give rise to males devoid of the Y chromosome. F_1 hybrid males from *D. persimilis* mothers have small testes regardless of whether they do or do not carry a Y chromosome, and regardless of whether their X chromosome is descended from the *D. persimilis* or the *D. pseudoobscura* parent. F_1 hybrid sons of *D. pseudoobscura* mothers have small testes if they carry an X chromosome of *D. persimilis*, but large ones when the X is derived from *D. pseudoobscura*. The role of the cytoplasm in the production of the differences between the reciprocal crosses is, thus, evident, but it is likewise evident that the properties of the cytoplasm of an egg are determined by the chromosomes that have been present in the body of the mother in which the egg had developed. It has been shown above that the sterility of the hybrids between *D. pseudoobscura* and *D. persimilis* is due to the action of complementary genes contributed by the parental species. To put it more precisely: the sterility of these hybrids is due to interactions between the chromosomal constitution of the hybrid itself and the properties of the cytoplasm of the egg from which it develops, always keeping in mind that the properties of the latter are determined by the chromosomal constitution of the mother.

Kaufmann (1940) has shown that the sterility of the female hybrids between *D. pseudoobscura* and *D. miranda* is almost certainly due to a maternal effect. The male hybrids between these species are absolutely sterile, but the females deposit numerous eggs which, as a rule, give no larvae. The meiotic divisions in these eggs display no striking irregularities, although it has not been possible to ascertain whether the chromosomes always form regular bivalents. However that may be, a random distribution of the chromosomes at the hybrid meiosis must produce some pronuclei with only *Drosophila pseudoobscura* and other pronuclei with only *D. miranda* chromosomes. Since all the eggs of the hybrid females degenerate, causes other than numerical or qualitative irregularities in the chromosome complements must be responsible. The failure of the development regardless of the chromosomal constitution of the zygote indicates that the chromosomes are unable to function normally in the cytoplasm of an egg produced by a hybrid female.

True cytoplasmic inheritance, caused by the presence of self-reproducing entities in the cytoplasm, occurs in some plants and microorganisms, as well as in a few animals (an excellent review by Caspari, 1948). The spores formed after meiosis in the hybrids between the mosses *Funaria hygrometrica* × *Physcomitrium piriforme*, and *Physcomitrium eurystomum* × *Physcomitrella patens* are, in part, inviable. Wettstein (1937a, b) showed that the spores which receive all or most of the chromosomes of the maternal species survive, while presence of the chromosomes of one species in the cytoplasm descended from the other acts as a lethal. Michaelis (1948, 1949), Lehmann, and others proved that the viability and fertility of hybrids between certain species of *Epilobium* plants are determined by interaction of the chromosome complement with the cytoplasm.

INTRASPECIFIC CHROMOSOMAL STERILITY

Suppose that two chromosomes of a species carry the genes ABCD and EFGHI, respectively. A translocation results in two "new" chromosomes, ABFE and DCGHI. Homozygous normals and the translocation homozygotes produce sex cells which carry every gene once and only once. But in a translocation heterozygote at least six classes of sex cells can be produced: (1) ABFE, DCGHI, (2) ABCD, EFGHI, (3) ABFE, EFGHI, (4) ABCD, DCGHI, (5) ABFE,

ABCD, and (6) DCGHI, EFGHI. Classes 1 and 2 carry normal gene complements, but in classes 3 to 6 certain genes are deficient and other genes are present in duplicate; 1 and 2 are termed regular or orthoploid, and 3 to 6 exceptional or heteroploid.

The fate of the heteroploid gametes is different in animals and in plants. In animals, sex cells with grossly unbalanced gene complements retain their functional ability (Muller and Settles 1927, Dobzhansky 1930b, and others). A part of the offspring of a translocation heterozygote is, thus, inviable or abnormal. In plants, the meiotic divisions give rise to gametophytes which undergo several cell divisions before the generative cells, the gametes proper, are produced. Gametophytes with deficiencies and duplications are usually aborted before fertilization can take place. Only small duplications and, even more rarely, deficiencies pass through the gametophytes in non-polyploid species.

In animals, as well as in plants, translocation heterozygotes are semisterile. The degree of sterility evidently depends upon the relative frequency of the regular and exceptional gametes. If the six classes of the gametes should be equally frequent, the regular ones would amount to 33.3 percent of the total, and the translocation would be 66.7 percent sterile. The origin of the exceptional gametes involves, however, the passing of certain sections of chromosomes carrying homologous genes to the same pole of the spindle at the meiotic division; if all homologous sections should disjoin and pass to the opposite poles at the meiotic divisions, only regular gametes would be produced. The meiotic disjunction of chromosome sections depends, in part, on the frequency of chiasma formation, and of crossing over, in these sections (Dobzhansky 1931, 1932, 1933a, Glass 1935, Pipkin 1940, Brown 1940, White 1945, Stebbins 1950, and others). In translocation heterozygotes, the frequency of crossing over is reduced, especially in the vicinity of the points at which the chromosomes have been broken and reattached. If in a translocation a short section of one chromosome has been transposed to another chromosome, the crossing over in that section is suppressed relatively more than in a long transposed section. The chromosomes and sections that suffer the greatest reduction of the frequency of crossing over undergo non-disjunction at meiosis more frequently than sections in which crossing over remains more nearly normal.

In normal, structurally homozygous, individuals every chromosome has one and only one homologue with an identical gene arrangement. In translocation heterozygotes, some chromosomes consist of sections that are homologous to parts of two or more other chromosomes. In inversion heterozygotes, certain chromosomes have homologues containing the same genes arranged in a different linear sequence. The meiotic pairing is due to a mutual attraction between homologous loci rather than between chromosomes as such. In structural heterozygotes, parts of the same chromosome may be pulled in different directions simultaneously. Pairing of some chromosome sections may be delayed or not attained at all. The lack of pairing results in failure of the chiasma formation, reduction of the crossing over, and failure of chromosome disjunction. The more extensive the differences in gene arrangement between the chromosomes of the parents, the greater is the competition for pairing at meiosis, the more frequent are the failures of pairing and disjunction. Other things being equal, a structural heterozygote having chromosomes with more differences in the gene arrangement will produce more gametes with abnormal gene complements than a heterozygote with more nearly similar chromosomes. In different organisms the conditions of the meiotic pairing are, however, not necessarily alike; thus, the translocation heterozygotes in *Oenothera* produce relatively fewer exceptional gametes than the translocations in *Drosophila* (see also Thompson and Thompson 1937, and Thompson 1940).

A special case of chromosomal sterility is that due to cryptic structural hybridity (Stebbins 1945, 1950, Stebbins et al. 1946, Stephens 1950). Translocation of small blocks of genes may give rise to chromosomes which are homologous except for some small segments (for example, chromosomes ABCDEF and GHIJKLM giving rise to ABCDLF and GHIJKEM). A hybrid which carries such chromosomes is, of course, a translocation heterozygote. And yet, because of the competition for pairing, this hybrid will have apparently normal bivalents at meiosis (ABCDEF/ABCDLF and GHIJKLM/GHIJKEM). Fifty percent of the gametes of such a hybrid will contain duplications and deficiencies. Accumulation of cryptic structural differences in several, or in all, chromosomes of a set might give virtually complete chromosomal sterility, despite regular formation of

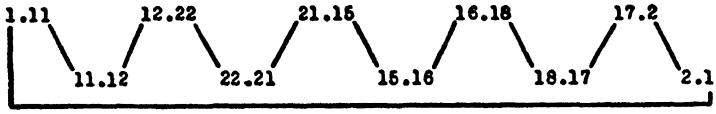
bivalents at meiosis in the hybrid. As shown below, sterility of this type is actually observed.

TRANSLOCATIONS AND INVERSIONS IN SPECIES HYBRIDS

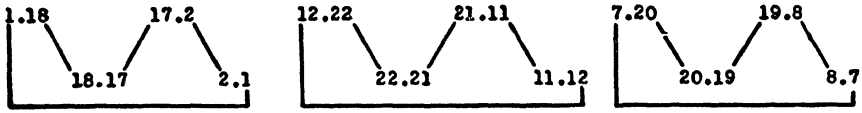
Cytology has amassed a great store of information on the morphology of the chromosomal complements (karyotype) in various organisms. Related species may or may not differ in chromosome number, size, shape, location of the centromeres, presence or absence of satellites, or in combinations of these traits. Such differences may be caused by genic changes altering the general physiology of the cells (the "genotypic control," Darlington 1937). Nawashin (1934) found that the appearance under the microscope of certain chromosomes in species hybrids in *Crepis* is different from that of the same chromosomes in the parental species. Mann and Frost (1927) in *Matthiola*, and Håkansson (1943) in *Godetia* found strains of the same species which differ in chromosome size. In *Matthiola* the difference is due to a single gene, and in the hybrids the chromosomes of both lines look alike, while in *Godetia* they preserve their size differences in the hybrid as well. Fujii (1940) found a strain of *Drosophila virilis*, in which one of the chromosomes differed in its staining capacity from the norm, and Bauer (1945) described a similar condition in the midge *Sergentia*. In a species of *Sciara*, a certain chromosome which is single in sex cells is represented by two separate bodies in salivary gland cells (Crouse 1947). Federley (1943 and previous work) believes that the differences in chromosome numbers in certain species of moths are due to gene-controlled union and separation of chromosomes; Bauer (1941) has, however, challenged this interpretation.

However, the working hypothesis that has amply demonstrated its fruitfulness is that karyotype differences between races and species arise mostly through numerical and structural changes, such as duplications, deficiencies, translocations, and inversions. Blakeslee (1932), and Bergner and Blakeslee (1932, 1935), have compared the gene arrangements in the chromosomes of several species of the Jimson weed, *Datura*. All these species have the same chromosome numbers, 12 haploid, 24 diploid. The chromosomes of the best-known species, *D. stramonium*, are taken as the standard. Each of the chromosomes has its ends indicated by a number, so that the chromosome

"formula" of this species may be written thus: 1.2, 3.4, 5.6, 7.8 . . . 19.20, 21.22, 23.24. Among the chromosomes of *D. discolor*, seven appear similar and five are different from *D. stramonium*. The chromosomes that are thus characteristic for *D. discolor* are 1.11, 2.17, 12.22, 15.21, and 16.18. In the *D. stramonium* × *D. discolor* hybrid seven bivalents and a circle or a chain of ten chromosomes appear. The structure of the circle is as follows:



In this scheme the *D. discolor* chromosomes are shown in the upper line and those of *D. stramonium* in the lower. In *D. quercifolia*, six chromosomes are similar and six are different from *D. stramonium*. The chromosomes that differentiate *D. quercifolia* are 1.18, 2.17, 12.22, 11.21, 7.20, and 8.19. The *D. stramonium* × *D. quercifolia* hybrid has six bivalents and three circles of four chromosomes each. The structure of the circles is as follows (writing the *D. quercifolia* chromosomes in the upper and those of *D. stramonium* in the lower line):



These are the chromosome configurations found in crosses between the standard line of *D. stramonium* on one hand and *D. discolor* and *D. quercifolia* on the other. But we have seen that within the species *D. stramonium* there exist also races that differ from each other in the chromosome structure. Thus, in Peru and Chile the population of *D. stramonium* has chromosomes 1.18, 2.17, 11.21, and 12.22 instead of the chromosomes 1.2, 11.12, 17.18, and 21.22 present in the standard. It may be noticed, however, that all the chromosomes peculiar for the population of *D. stramonium* from Peru and Chile exist also in *D. quercifolia*, and two of them (2.17 and 12.22) also in *D. discolor*. If, then, one compares the Chilean *D. stramonium* with *D. quercifolia*, they prove to differ in only two chromosomes (7.20

and 8.19 in *D. quercifolia* instead of 7.8 and 19.20 in *D. stramonium*), and give a single circle of four chromosomes and ten bivalents at meiosis. The chromosomal difference between the two species, *D. stramonium* and *D. quercifolia*, seems to be no greater than the racial differences within *D. stramonium*.

A study on species of *Nicotiana* has been published by Avery (1938). Three species, *N. alata*, *N. langsdorfii*, and *N. bonariensis*, all have n = 9 chromosomes. The hybrid *alata* × *langsdorfii* has at meiosis usually a complex of five chromosomes, six bivalents, and one univalent; the *alata* × *bonariensis* hybrid has one quadrivalent, two trivalents, and four bivalents; in *bonariensis* × *langsdorfii* one complex of seven chromosomes, two trivalents, two bivalents, and a univalent are seen. If the ends of the nine chromosomes are denoted by numbers from 1 to 18, the make-up of the chromosomes of the three species is judged to be as follows:

Nicotiana alata: 1.2, 3.4, 5.6, 7.8, 9.10, 11.12, 13.14, 15.16, 17.18
N. langsdorfii: 2.12, 3.4, 1.5.6, 7.8, 9.10, 11.5, 13.14, 15.16, 17.18
N. bonariensis: 1.18, ? .4, 5.6, 7.3, 9.10, 11.12, 13.8, 15.16, 17.2

Babcock and his school have analyzed the karyotype of the plant genus *Crepis* (see Babcock 1947 and Stebbins 1950 for further references). The chromosome numbers in this genus vary from 3 to 48 pairs. Among these, the numbers 7 and 8 are regarded as primitive. The higher numbers arose chiefly through polyploidy, and the lower ones through translocations and losses of superfluous centromeres. Tobgy (1943) has studied this process through detailed comparison of two related species, *C. fuliginosa* and *C. neglecta*. These species have three and four chromosome pairs respectively. All the chromosomes are recognizable by their sizes and structures. In the hybrids, the chromosomes of the two species undergo intimate pairing in meiotic prophase (pachytene), indicating that they carry fairly long sections with similarly arranged genes. A great deal of gene rearrangement has, nevertheless, taken place in the phylogeny, as shown by the great variability of the chromosome association at the meiotic metaphase. Some cells had only unpaired chromosomes (univalents), others had 2 or 3 bivalents and 3 or 1 univalents, still others 2 bivalents and 1 trivalent, or 1 quadrivalent with 1 bivalent and 1 uni-

valent, etc. A painstaking analysis of these associations led Tobgy to the conclusion that the chromosomes B and C of *C. fuliginosa* gave rise to the chromosome B of *C. neglecta* by translocations which combined most of the material located in the *C. fuliginosa* B and C into a single chromosome. The centromere of the C chromosome of *C. fuliginosa* was lost. The A and D chromosomes of *C. neglecta* have also exchanged, by translocation, blocks of genes, giving rise to the A and D of *C. fuliginosa*. Furthermore, at least three major inversions have taken place in the phylogeny in the chromosomes A, D, and B–C; because of this, about 15 percent of the meiotic prophases in the hybrid between these species show chromatid bridges at meiosis (cf. Chapter V). Sherman (1946) has given a similar evidence of the occurrence of at least six translocations in the descent of *Crepis kotschyana*, with 4 pairs of chromosomes, from the ancestors which had 5 chromosome pairs.

Translocations and inversions have occurred frequently in the phylogeny of species of peas, *Pisum* (Håkansson 1934, Sansome 1938, Rosen 1944), and in wheats, *Triticum*, and their relatives (a review in Sears 1948). For evidence of chromosomal reconstructions in other organisms, see the works of Darlington (1937), White (1940, 1941, 1945), Lang (1940), Matthey (1949), Stebbins (1950), and others.

GENE ARRANGEMENTS IN DROSOPHILA SPECIES HYBRIDS

If species of *Drosophila* can be hybridized, the giant chromosomes in the salivary gland cells permit more precise comparison of the chromosome structures in the species crossed than is attainable by any other method. Although the sterility of interspecific hybrids in *Drosophila* is mostly genic, rather than chromosomal, understanding of the processes of chromosomal differentiation in evolution is obviously important for studies on chromosomal sterility.

Drosophila melanogaster and *D. simulans* are morphologically very similar, but males can easily be distinguished by their genitalia. The hybrids between these species are completely sterile. Sturtevant (1929) found the genetic maps of the chromosomes of the two species much the same, except for a long inversion in the third chromosome. Pätau (1935), Kerkis (1936), and Horton (1939) studied the salivary gland chromosomes in the hybrids. Aside from the inversion in the third chromosome, these authors found about 24 very short chro-

mosome sections, mostly involving a few stainable discs each, which differ in the two species. Among these, 6 sections seem to be minute inversions. The remainder are undefined changes which may be minute inversions, translocations, or qualitative changes in the chromosomal materials.

D. pseudoobscura and *D. persimilis* are morphologically almost indistinguishable (cf. Chapter IX); their hybrids are sterile as males but fertile as females. The species differ in at least two moderately long inversions in the X and in the second chromosomes. Usually there is also a second inversion in the X, and one or more inversions in the third chromosome, i.e., a total of four or more inversions. The variations in the numbers of the inversions which distinguish the species are due to differences between the strains of the parental species (cf. Chapter V). No small undefined differences, like those in the hybrids between *D. melanogaster* and *D. simulans*, are present (Tan 1935, Dobzhansky and Epling 1944).

D. guaru and *D. subbadia* are morphologically close but distinguishable; the female hybrids are fertile. The metaphase chromosome configurations differ in that the dotlike autosomes of *D. guaru* are replaced by a pair of rods in *D. subbadia*. This difference is produced by a translocation of a heterochromatic segment, presumably from the Y chromosome, onto the dots, which are transformed into rods. The salivary gland chromosomes show numerous inverted sections; but since inversions occur also within the parental species, it is difficult to tell how many of them are constant species differentials. Most interesting is the finding within the species *D. guaru* of two gene arrangements differing in a double overlapping inversion. According to the theory of overlapping inversion (see Chapter V), a third gene arrangement must have existed in the phylogeny, which differed from the two others by single inversions. This "predicted" gene arrangement has not been found in *D. guaru*, but it is present in *D. subbadia*. No small undefined differences exist between the chromosomes of *D. guaru* and *D. subbadia*. However, when the F_1 female hybrids between these species are outcrossed to a third species, *D. guarani* (cf. Chapter VII), the triple hybrids show many inversions, unpaired regions, and small undefined differences in the salivary gland chromosomes (King 1947a).

Patterson et al. (1940, 1942), Stone and Patterson (1947), Pat-

terson and Stone (1949), and others have made a penetrating analysis of the chromosome structure in a group of morphologically closely related species: *D. virilis* (native in the Orient, now living as a scavenger in many parts of the United States), *D. americana* (north central United States), *D. americana texana* (southern United States), and *D. novamexicana* (southern New Mexico). All these species can be intercrossed, and the hybrids produced are more or less fertile (see above). *D. virilis* and *D. novamexicana* are alike in metaphasic chromosome configurations, which consist of five pairs of rod-shaped and one pair of dotlike chromosomes (Fig. 18). The gene arrangements in the X chromosomes differ, however, in a triple inversion, while those in the second, third, and fourth chromosomes differ in one inversion each. In *D. americana texana* the second and the third chromosomes of *D. virilis* have become united, by a translocation, into a V-shaped autosome with a median centromere (Fig. 18). These species differ, thus, in the metaphasic chromosome configuration. The gene arrangements in the second and the third chromosomes differ in a single inversion from *D. virilis* and in two inversions from *D. novamexicana;* in the X chromosome the difference from *D. virilis* is in two inversions, and from *D. novamexicana* in one; and in the

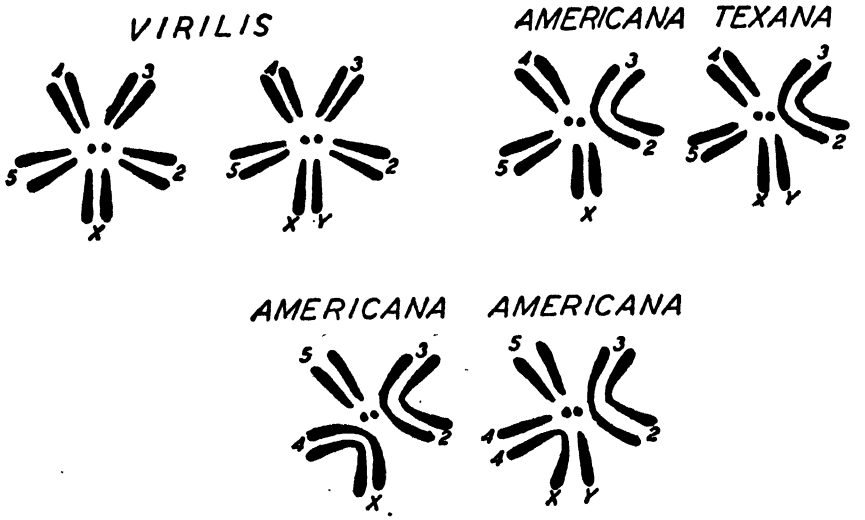


FIG. 18. Chromosome homologies in *Drosophila virilis* and *D. americana*. (After Patterson, Stone, and Griffen.)

fifth chromosome *D. americana texana* differs from both *D. virilis* and *D. novamexicana* in two inversions.

In *D. americana americana* the X and the fourth chromosomes underwent a translocation and became united into a V-shaped chromosome. Females of this species have, accordingly, two V-shaped chromosome pairs, while males have a V-shaped autosome, a V-shaped X chromosome, and rodlike Y and fourth chromosomes (Fig. 18). The gene arrangements in the chromosomes of *D. americana ameri-*

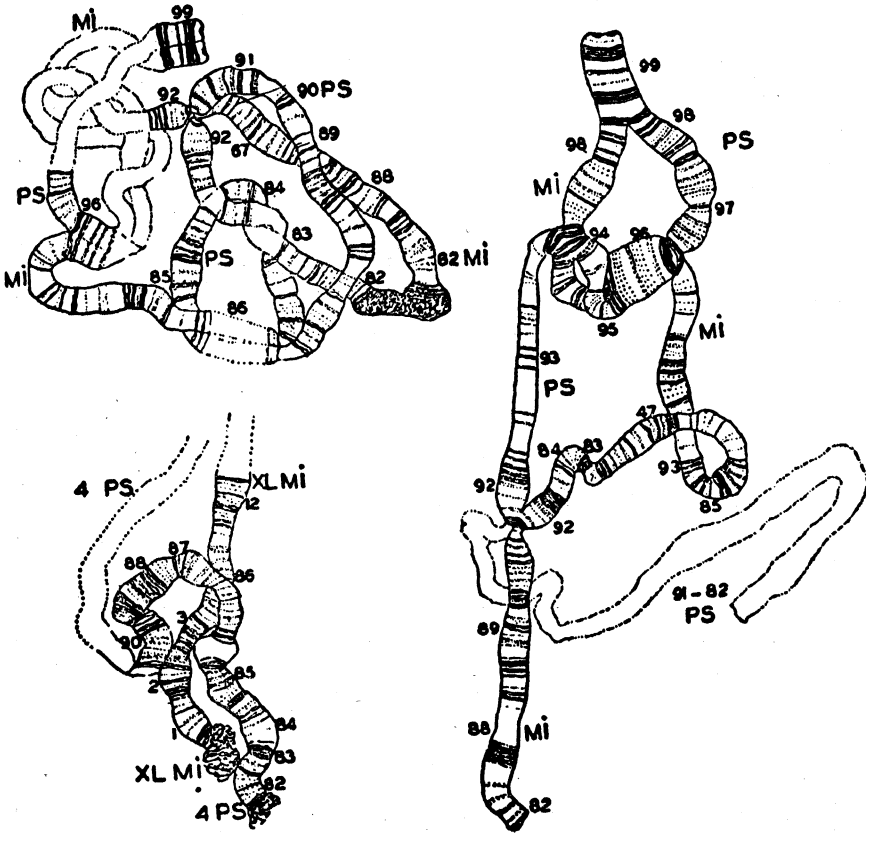


FIG. 19. Chromosome pairing in the salivary gland cells in the hybrid *Drosophila pseudoobscura* × *D. miranda*. Upper left, the fourth chromosomes; lower left, the fourth chromosome of *D. pseudoobscura* partly paired with the left limb of the X chromosome of *D. miranda;* right, the fourth chromosomes. (After Dobzhansky and Tan.)

cana are a combination of the inversions present separately in *D. americana texana* and *D. novamexicana*. One may, consequently, imagine that *D. americana americana* arose as a result of hybridization and recombination of the hereditary materials of these two forms. This does not, however, mean that *D. americana texana* and *D. novamexicana* are older as distinct species than *D. americana americana*. The three forms may as well have differentiated at the same time from the population of an ancestral species which contained all the gene arrangements which now have become restricted to some of derived species. It may be noted that *D. americana americana* and *D. americana texana* are at present only subspecies which interbreed in the zone of the overlap of their geographic distributions (from Arkansas to Tennessee). Stone (1949) showed that the chromosome disjunction in their hybrids is so regular that these hybrids, despite being translocation heterozygotes, show no loss of fertility.

The morphological resemblance between *D. pseudoobscura* and *D. persimilis* on one hand and *D. miranda* on the other is at least as close as, and probably closer than, that between *D. melanogaster* and *D. simulans*. Their metaphase chromosomes are identical, except that one of the autosomes of *D. pseudoobscura* is present only once in the chromosome group of the *D. miranda* male; *D. pseudoobscura* is XX and XY in the female and the male respectively, while *D. miranda* female is $X^1X^1X^2X^2$ and male X^1X^2Y (Dobzhansky 1935a). MacKnight (1939) has shown that the Y chromosome of *D. miranda* harbors some material which is homologous to that borne in the X^2 of that species and to that in the corresponding autosomal pair of *D. pseudoobscura*. The origin of *D. miranda* must have involved a translocation of that particular autosome onto the Y chromosome, with the subsequent rearrangement of the autosomal material by repeated inversions. Dobzhansky and Tan (1936) have compared the gene arrangements in the *D. pseudoobscura* and *D. miranda* chromosomes in the salivary glands of hybrid larvae. The differences are so profound that the chromosomes fail to pair entirely, or form extremely complex pairing configurations, examples of which are shown in Fig. 19. Because of the occurrence of inversions in the phylogenetic development of *D. pseudoobscura* and *D. miranda*, genes that in one species lie adjacent, in the other species may be far apart in the same chromosome. Some genes which in one species are located in the same

chromosome are borne in different chromosomes in the other. Such differences are apparently due to the occurrence of translocations. Finally, homologues of certain chromosome sections in *D. pseudoobscura* have not been detected at all in *D. miranda*, and vice versa. It seems, then, that some chromosome sections have been so thor-

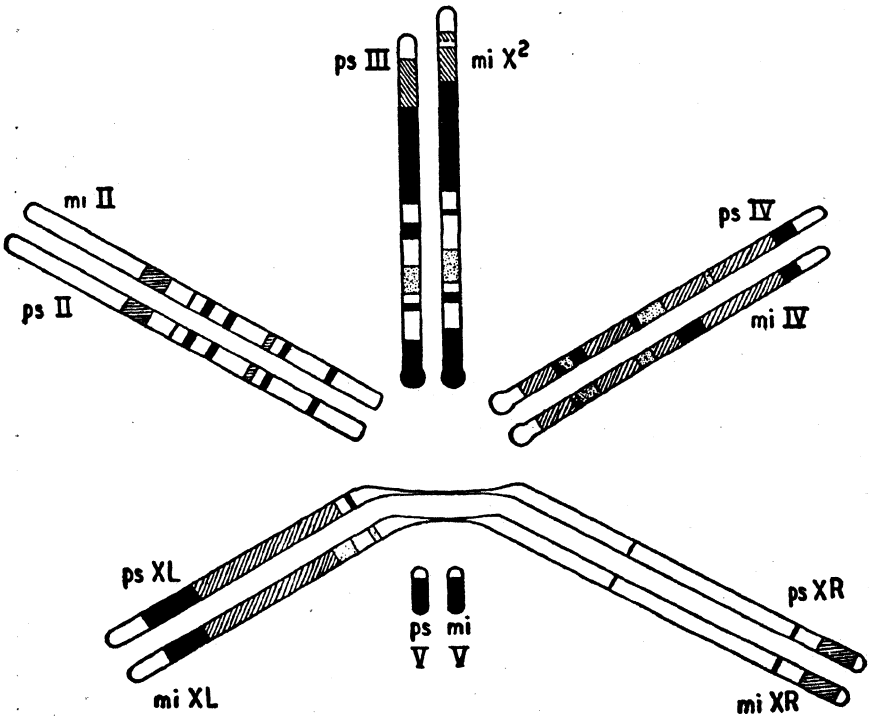


FIG. 20. A comparison of the gene arrangements in *Drosophila pseudoobscura* and *D. miranda*. Sections having the same gene arrangements in the two species are white; inverted sections, cross-hatched; translocations, stippled; sections of which the homologues are not detectable in the other species, black.

oughly rebuilt by repeated inversions and translocations that their disc patterns in the salivary gland chromosomes no longer resemble each other, and no pairing of the homologous genes takes place.

A comparison of the chromosomes of *D. pseudoobscura* and *D. miranda* is shown in Fig. 20. If the chromosome sections that seem to be present in one species only are disregarded, the differences between these species appear to be due chiefly to repeated inversions

of blocks of genes. Translocations are less numerous and involve very small gene blocks. To visualize the derivation of the chromosome structure observed in one species from that in the other, the chromosomes must be broken into fragments, and then reconstructed by placing the fragments in new linear series. A minimum of 49 breakages are necessary for such a process. The sections the homologues of which are not identifiable in the other species suggest, however, that the actual number of breakages must have been at least twice as large; 100 breakages is a conservative estimate.

As stated above, *D. pseudoobscura* and *D. persimilis* differ in several inversions in their chromosomes. Although the chromosome structure in *D. miranda* is widely removed from either of the other two species, careful comparison shows that the gene arrangement in *D. miranda* is closer to that in *D. pseudoobscura* than to that in *D. persimilis*.

COMPARISON OF GENE ARRANGEMENTS IN SPECIES OF DROSOPHILA WHICH CANNOT BE HYBRIDIZED

It is clear from the foregoing discussion that no correlation is discernible between the amount of morphological divergence and of divergence in chromosome structure in species of *Drosophila* which are sufficiently close for hybrids between them to be obtainable (cf., Spencer 1940a and b). Comparison of more remote species discloses, however, that some positive correlation exists.

D. willistoni, *D. paulistorum*, *D. tropicalis*, and *D. equinoxialis* are barely distinguishable morphologically, but, nevertheless, are incapable of producing hybrids. Their metaphasic chromosome configurations are alike. Their salivary gland chromosomes can be compared by microscopic inspection in the pure species (Burla et al. 1949). This is a far less precise method than comparison in hybrids, where the pairing of the stainable discs furnishes a guide to their homologies. Four of the five chromosome strands present in the salivary gland cells have patterns of the stainable discs similar enough for the strands to be identified as largely homologous. To be sure, a more careful inspection suggests that some inversions have taken place in certain of these strands. But the fifth strand, corresponding to the genetic third chromosome, underwent much alteration in the phylogeny. The arrangement of the discs in this strand in *D. willistoni*

is entirely different from that found in *D. paulistorum*. Neither of these species resembles *D. tropicalis* or *D. equinoxialis*. The two last named species are, however, alike in the structure of the third chromosome.

D. capricorni, *D. fumipennis*, and *D. nebulosa* are species fairly closely related to the preceding four, but easily distinguishable from the latter and from each other in externally visible characters. Their metaphase configurations of chromosomes are alike. The disc patterns in the salivary gland chromosomes are, however, so distinct that no strands at all can any longer be identified as homologous by inspection. The amount of rebuilding of the gene order by inversions and translocations has evidently been too great. All of the above species are a natural group (the "*willistoni*" species group), which differs from the "*obscura*" species group (*D. pseudoobscura*, *D. persimilis*, *D. miranda*, and certain other species), and from the "*melanogaster*" species group. The metaphasic configurations of chromosomes differ in these species groups, and the disc patterns in the salivary gland chromosomes are wholly unlike.

Construction of genetic chromosome maps is the only, though very laborious, method of comparison of the gene arrangements in the chromosomes of species which neither can be crossed nor show visible similarities in their salivary gland chromosomes. Mutants which arise in different species frequently produce very similar phenotypic changes. This leads to the inference that the genes which produce similar mutations are homologous. The reliability of this method is obviously low, since phenotypically similar mutants ("mimic" mutants) are often produced at different gene loci in the same species. Nevertheless, the comparison of the genetic maps of *D. melanogaster* and *D. simulans* made by Sturtevant (1929) has been later confirmed by cytological studies in the hybrids between these species (see above). Crew and Lamy (1935), Donald (1936), and Sturtevant and Tan (1937) have compared the mutants, and the genetic maps of *D. melanogaster* and *D. pseudoobscura*. Let the chromosomes of *D. melanogaster* be designated X, IIL.IIR, IIIL.IIIR, and IV, and those of *D. pseudoobscura* XL.XR, II, III, IV, and V (IIL.IIR, IIIL.IIIR, and XL.XR refer to the respective limbs of the V-shaped chromosomes present in these species, X is the X chromosome, and IV and V are the dotlike autosomes; the periods

between the symbols of the chromosome limbs indicate that they are united into V-shaped chromosomes). The distribution of the homologous genes is as follows (the corresponding chromosome parts are in the same vertical columns):

melanogaster	X	IIL	IIR	IIIL	IIIR	IV
pseudoobscura	XL	IV	III	XR	II	V

The gene arrangements within the corresponding limbs are, however, very different indeed. Sturtevant (1940) and Sturtevant and Novitski (1941) have generalized these results. They believe that inversions within a chromosome limb (paracentric inversions) have occurred frequently in the phylogeny of the flies, Diptera, while inversions which include the centromere (pericentric inversions) and translocations have not occurred at all (except those involving heterochromatic sections). The karyotype composed of five pairs of rod-shaped and one pair of dotlike chromosomes is apparently the primitive one in the genus *Drosophila* (see Fig. 21), since it recurs in quite

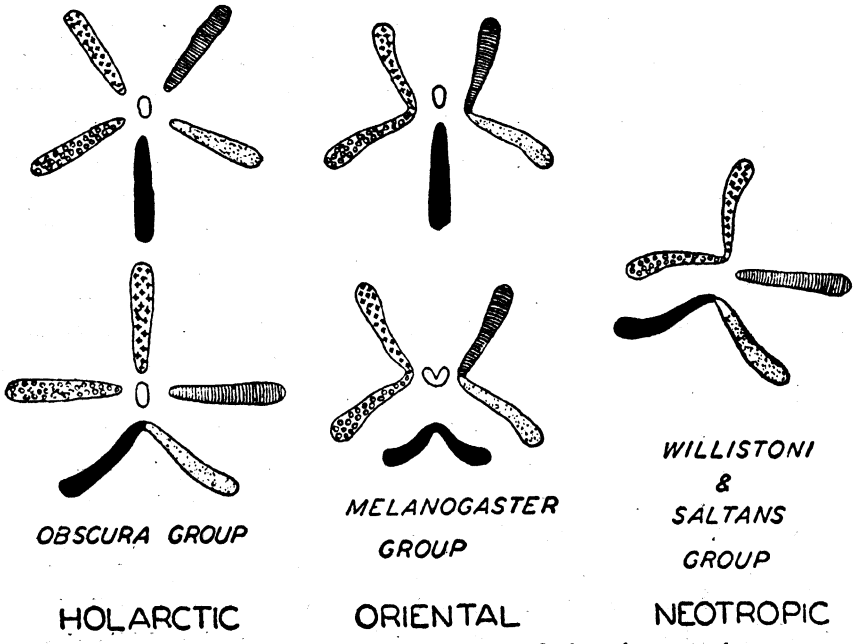


FIG. 21. Chromosome homologies in species of the *obscura*, *melanogaster*, *willistoni*, and *saltans* species groups of the genus *Drosophila*.

unrelated forms which belong to different subgenera and species groups. Other karyotypes found in *Drosophila* and its relatives are derived from the primitive one, through fusion, or separation, of the intact chromosome limbs or "elements".

It is, indeed, clear that paracentric inversions are most common in natural populations of many species of *Drosophila*, while pericentric inversions and translocations are rare. This is a consequence of the fact that heterozygosis for paracentric inversions is less prone to make its carriers semisterile than that for pericentric inversions and translocations (cf. Chapter V). The chromosome "limbs" are, accordingly, retained quite tenaciously in the phylogeny. According to Spassky and Dobzhansky (1950), the X chromosomes carry mostly the same genes in the representatives of the *willistoni*, *saltans*, and a majority of the *obscura* species groups of the genus *Drosophila* (Fig. 21). This kind of X chromosome does not occur at all in species of the *melanogaster* group. However, most species of the *melanogaster*, *willistoni*, and *saltans* groups have apparently similar second chromosomes, which do not occur in the *obscura* group. The dotlike autosome is present in the *melanogaster* and *obscura*, but not in the *willistoni* and *saltans* groups. It may be noted that the *willistoni* and *saltans* species groups are native chiefly in the Neotropical zoogeographic region, *obscura* in the Holarctic, and *melanogaster* in the Oriental region. The Neotropical species, thus, share chromosome structures separately present in Holarctic and Oriental species, but it would be rash to conclude that the former arose by hybridization of the latter.

Pericentric inversions and translocations which break the integrity of the chromosome "limbs" did occur in the phylogeny of *Drosophila* and of other insects, although far less often than did paracentric inversions. Spencer (1949) found that some of the mutants in the third chromosome of *D. hydei* resemble those in the second, and some those in the third, chromosomes of *D. melanogaster*. In *D. prosaltans*, and probably in *D. willistoni*, the genes located in *D. melanogaster* in the dotlike autosome are divided between the X chromosome and one of the autosomes (Spassky et al. 1950). Wharton (1943) and Dobzhansky and Pavan (1943) in *Drosophila*, and Bauer (1945) in Chironomids have found variations in the numbers of euchromatic chromosome "limbs" in related species. Lerche (1941) in the fly *Phryne*,

Dickler (1943) in *Lucilia*, and Tate (1947) in *Calliphora* found autosomal mutants which resemble the well-known sex-linked white eye and yellow body colors in *Drosophila*. An euchromatic translocation has taken place in the phylogeny of two very similar species of the beetle, *Agrilus* (Smith 1949).

CHROMOSOMAL STERILITY IN SPECIES HYBRIDS

The species *Drosophila pseudoobscura* and *D. persimilis*, and the species related to *D. virilis*, are known to differ in the gene arrangement in their chromosomes. The gene arrangement in *D. pseudoobscura* is rather radically different from that in *D. miranda*. And yet, the sterility of the hybrids between these species is, as shown above, genic rather than chromosomal. The fact that some species differ in the gene arrangement does not permit the inference that the sterility of the hybrids between these species is caused by the chromosomal differences. Nevertheless, the existence of chromosomal sterility in certain plant hybrids is rather well established. The principal evidence is, in these cases, the behavior of the allopolyploid hybrids. One of the classical examples of such hybrids is that studied by Karpechenko (1927, 1928).

Radish (*Raphanus sativus*) and cabbage (*Brassica oleracea*) have the same chromosome numbers—eighteen diploid. The F_1 hybrids have 18 chromosomes, 9 from the radish and 9 from the cabbage parent. No chromosome pairing takes place, 18 univalents are present at the metaphase of the first meiotic division, and are distributed at random to the poles. At the second division the univalents split, giving rise to cells with a varying number of chromosomes, mostly from 6 to 12. In some of the pollen mother cells, however, the first division is abortive, and nuclei are formed that include all of the 18 univalents. The F_1 hybrids are nearly sterile; most plants produce no seeds at all, but some do produce a few. Most of the F_2 hybrids (213 out of 229) have 36 chromosomes in their somatic cells. Their origin is due to the union of the exceptional gametes possessing the full chromosome complement of the F_1 hybrid. The F_2 plants contain, therefore, 18 radish and 18 cabbage chromosomes. They are allotetraploid. The meiotic divisions in these plants are very regular, in striking contrast with the abnormalities observed at meiosis in the

F_1 hybrids. Eighteen bivalents are formed, the chromosome disjunction is normal, and the resulting cells, with few exceptions, contain 18 chromosomes each.

The tetraploid plants are fully fertile, and they are morphologically distinct both from radish and from cabbage. Some traits are intermediate, in others the influence of one of the parents predominates. The fruit structure in the tetraploids is very interesting. The fruit of radish is spindle-shaped and nondehiscent; that of cabbage is elongate and dehisces in two valves. The base of the radish fruit is, however, homologous to the two-valved part of the cabbage, and the cabbage fruit has an apical part resembling the radish fruit. The fruits of the hybrids are clearly compromise structures, resembling cabbage in the lower, and radish in the upper, part. The tetraploid resembles the F_1 diploid, but in the former the size of the fruit is appreciably greater than in the latter. The tetraploids are luxuriant plants, true breeding, and obviously different from either parental species. They represent an experimentally created species, to which Karpechenko gave the name *Raphanobrassica.*

The lack of the bivalent formation in the diploid hybrids might be caused either by dissimilarities of the gene arrangement in the chromosomes of radish and cabbage, or by the genetic constitution of the hybrids. What is, however, the most likely explanation of the restoration of the normal bivalent formation in the tetraploid *Raphanobrassica*? The simplest hypothesis is that no chromosome of radish is sufficiently similar in the gene arrangement to any cabbage chromosome to insure bivalent formation; the presence of the two sets of radish and of the two sets of cabbage chromosomes in the tetraploid *Raphanobrassica* creates, on the other hand, a situation when every chromosome in the nucleus has one and only one partner with an identical gene arrangement. The sterility of the diploid hybrid is chromosomal. The doubling of the chromosomes does not induce bivalent formation in hybrids the sterility of which is genic. The gene combination the physiological effect of which is a suppression of the chromosome pairing persists unaltered in the diploid as well as in the tetraploid hybrid. Thus, in the tetraploid spermatocytes in the hybrids of *Drosophila pseudoobscura* × *D. persimilis* the proportions of bivalents and univalents are no different from those in the

adjacent diploid cells; the spermatids which arise in the tetraploid section of the gonad degenerate, and the hybrids are completely sterile (see above).

Darlington (1937) has established a rule applicable to many plant hybrids, which seems inexplicable except as a corollary of chromosomal sterility. Sterile diploid hybrids with little or no chromosome pairing at meiosis give rise to allopolyploids that are fertile and display mostly or only bivalents at the meiotic division. Conversely, the allopolyploids derived from the diploids with many bivalents show an irregular chromosome pairing and disjunction. The fertility of an allopolyploid tends to be inversely proportional to that of its diploid ancestor. The occurrence of pairing in a diploid hybrid indicates that the gene arrangement in the chromosomes of the parental species is similar enough for some or all chromosomes of one species to find approximate homologues among those of the other. The doubling of the chromosome complement gives rise to a situation in which each chromosome has three potential mates that are more or less similar to it. In the competition for pairing that arises in the prophase of meiosis, the pairing of the chromosomes of the same species is interfered with by the presence of the partial homologues. As a result, bivalents, trivalents, quadrivalents, and univalents are formed in proportions that are inconstant from cell to cell; gametes with unbalanced chromosome complements are produced; and the hybrid is more or less sterile. Where the chromosomes of the parental species fail to pair in the diploid on account of extensive dissimilarities in the gene arrangement, every chromosome in the allotetraploid has only one mate, with which it can pair with little or no interference from the chromosomes of the other species. Hence, only bivalents are produced, meiosis is regular, and fertility is restored.

Where chromosome pairing in a diploid hybrid is suppressed by the genetic constitution rather than by dissimilarities in the gene arrangement, the same suppression should be encountered in the allotetraploid derived from it. Moreover, the greater the suppression in a diploid hybrid of such a kind, the greater it will be in the tetraploid. In other words, Darlington's rule is expected not to apply to the sterility which is genic. It does not. As stated above, in certain hybrids between *Drosophila pseudoobscura* and *D. persimilis* only bivalents may be present in diploid spermatocytes; the tetraploid

spermatocytes formed in such hybrids contain bivalents and multivalents. Hybrids between certain other strains of the same species show little or no chromosomal pairing either in diploid or in tetraploid spermatocytes.

Primula kewensis is an allotetraploid hybrid between the diploid species *P. verticillata* and *P. floribunda*. Newton and Pellew (1929) and Upcott (1939) found that the diploid hybrid between these species has mostly bivalents at meiosis, and yet it is nearly sterile. The tetraploid has again bivalents (with an occasional quadrivalent), and is fertile. The hypothesis of chromosomal sterility, caused by cryptic structural hybridity (see above), furnishes the most plausible explanation of the situation.

The gene arrangements in the chromosomes of *P. verticillata* and *P. floribunda* are probably different, but not different enough to prevent their pairing in the diploid hybrid. In the tetraploid hybrid each chromosome has a homologue with an exactly similar gene arrangement, and also two partial homologues. Due to the competition for pairing, the complete homologues will unite to form bivalents more frequently than the partial ones. In a few cells, quadrivalents may, however, arise owing to the chance occurrence of chiasmata between parts of chromosomes of the two species. Now, the meiotic disjunction in the tetraploid gives rise to cells, most of which contain a full haploid set of *verticillata* and a full set of *floribunda* chromosomes. Cells resulting from the meiosis in the diploid have the same numbers of chromosomes, but a majority of them will include some *verticillata* and some *floribunda* chromosomes. Cells with a pure chromosome complement of one species will be produced only rarely. If the cells with mixtures of chromosomes of the two species have deficiencies and duplications for blocks of genes, such cells are aborted, and the hybrid will be sterile. Stebbins (1950) gives a long list of hybrids between species of plants, the sterility of which is probably caused by a mechanism similar to that encountered in *Primula kewensis*.

CHROMOSOMAL STERILITY IN HYBRIDS BETWEEN POLYPLOID SPECIES

In hybrids between polyploid and diploid species, or in those between polyploid ones, several chromosome sets of different origin are brought together. Such hybrids may show at meiosis only bivalents, or both bivalents and univalents, or only univalents. Pairing may

take place between chromosomes of different parents (allosyndesis) or between those of the same parent (autosyndesis).

The relationships of species of tobacco, *Nicotiana*, have been studied by many investigators (see Clausen 1928a and b, 1941, Greenleaf 1941, 1942, and Goodspeed 1945 for further references). Some species of this genus are diploid (n = 12), others tetraploid (n = 24), and still others hexaploid (n = 36). The tetraploid species are probably derivatives from natural crossing of pairs of diploid species, followed by chromosome doubling. The cross *N. tabacum* (2n = 48) × *N. sylvestris* (2n = 24) gives a triploid hybrid with 36 chromosomes. In this hybrid, 12 bivalents and 12 univalents are formed at meiosis, and considerable sterility results. The crosses *N. tabacum* × *N. tomentosa* (2n = 24) and *N. tabacum* × *N. tomentosiformis* (2n = 24) also give triploid hybrids which form 12 bivalents and 12 univalents at meiosis. The problem is whether these bivalents are formed by pairing of the chromosomes of *N. tabacum* (autosyndetically), or between those of *N. tabacum* and of the other species (allosyndetically). For the solution of this problem, two sets of facts are relevant. First, by a form of parthenogenesis, a "haploid" *N. tabacum* can be obtained, which has 24 chromosomes in its somatic cells. Few or no bivalents are formed in such plants at meiosis, showing that the two sets of 12 chromosomes in *N. tabacum* are too different to pair. Secondly, the crosses of the diploid species, *N. sylvestris* × *N. tomentosa* and *N. sylvestris* × *N. tomentosiformis* form almost completely sterile hybrids with little or no chromosome pairing. Hence, the chromosomes of *N. tabacum* consist of two groups of 12 chromosomes each, which resemble, in at least the gene arrangements, the chromosomes of *N. sylvestris* on one hand, and of *N. tomentosa* and *N. tomentosiformis* on the other. The obvious inference is that *N. tabacum* had arisen through hybridization of these, or similar, species.

This inference has been tested by crossing *Nicotiana sylvestris* to *N. tomentosiformis*, obtaining the sterile F_1 diploid hybrid, and inducing in it a doubling of the chromosome complement by artificial means. The resulting allotetraploid hybrid has a fair external resemblance to some strains of *N. tabacum*, and, what is more important, has normal bivalent formation at meiosis, and a high proportion of functional pollen grains. But it forms no seed, either with its own or

with any other pollen, because the embryo sacs are aborted at an early stage of development. Greenleaf concludes that the sterility of the *N. sylvestris* × *N. tomentosiformis* hybrids is partly chromosomal but in part genic. The chromosomal sterility is removed in the tetraploid hybrid, but the genic sterility persists. The strains of *N. sylvestris* and *N. tomentosiformis* used in these experiments are evidently different from those which gave rise to *N. tabacum* in the past. Indeed, Kostoff (1938) has obtained an allotetraploid that was fertile both as a female and as a male. When the "raw", or synthetic, *N. tabacum* is crossed to the natural one, the hybrid has normal bivalent formation at meiosis.

The situation in cottons (*Gossypium*) is remarkably parallel to that in *Nicotiana*. The New World tetraploid cottons (*G. hirsutum* and *G. barbadense*) have 26 pairs of chromosomes. These represent two sets of 13 chromosomes each, homologous, respectively, to those of the New World and of the Old World diploid cottons. The hybrids between the New World and the Old World diploids have mostly univalents at meiosis; those between either group of diploids and the tetraploids have up to 13 bivalents, and the remainder of the chromosomes form univalents and multivalents. Harland and also Beasley (1942) have crossed the Asiatic diploid, *G. arboreum* with the American diploid *G. thurberi*, and caused a chromosome doubling to occur in the hybrids. The allotetraploid derivative produced functional ovules, but its pollen was mostly degenerate. This male sterility is, presumably, genic, like the female sterility in the "raw" *N. tabacum*. The "raw" tetraploid cotton crosses readily, as a female, to the common tetraploid American cottons. The hybrids prove fairly fertile, the chromosome forming mostly bivalents at meiosis. Hutchinson et al. (1947) and Stephens (1947) consider that the American diploid species which is the most probable ancestor of the American tetraploids is not *G. thurberi* but the Peruvian *G. raimondii*. Allotetraploid hybrids of *G. raimondii* × *G. arboreum* have not yet been tested.

The extensive studies of many authors on species of wheats (*Triticum*) and of the related genus *Aegilops*, are revealing a fascinating story of evolution of the chromosome structure in a diversified and agriculturally important group of plants (see Sears 1948, McFadden and Sears 1947, Kihara 1949, and Kihara and Lilienfeld 1949 for

further references). The basic chromosome number in these plants is 7; diploid, tetraploid, and hexaploid species, with somatic chromosome numbers of 14, 21, and 42, occur. The so-called "einkorn" wheats, *T. monococcum* and *T. aegilopoides* are diploid, and are supposed to possess the "genome" (chromosome set) designated A. The tetraploid, or emmer, wheats carry also the genome A, and, in addition, the genome B (*T. durum*, *T. dicoccum*, etc.), or the genome G (*T. timopheevi*). The emmer × einkorn hybrids are triploid, and form up to 7 bivalents and 7 univalents at meiosis. The hexaploid (bread) wheats (*T. vulgare*, *T. spelta*, etc.) have three genomes: A, B, and D. When crossed to the emmers, they give pentaploid hybrids, with up to 14 bivalents and 7 univalents at meiosis.

An attractive hypothesis is that the bread wheats arose by hybridization of an emmer, contributing the genomes A and B, with some other plant, contributing D, followed by chromosome doubling. Thompson et al. (1943), McFadden and Sears (1946), and Kihara and Lilienfeld (1949) found that the D genome is present in some species of *Aegilops*, particularly in the diploid *A. squarrosa*. This latter, it may be noted, is an agriculturally useless grass, growing wild around the Caspian Sea and in Middle Asia, where its distribution area overlaps that of a wild emmer, *T. dicoccoides*. Artificially induced hexaploid hybrids between these forms have about 21 bivalents at meiosis, are fertile, and give fertile hybrids with the hexaploid bread wheats. It is fair to say that the process which gave rise to the bread wheats in the past has been reproduced in controlled experiments.

Other species of *Aegilops* are supposed to have various combinations of several genomes—S, C, D, M, C^u, M^c, M^b, etc. It should be kept in mind that this classification of genomes is arrived at through observations on the amount of chromosome pairing in the hybrids which carry these sets of chromosomes. When the chromosome sets produce mostly or only bivalents, they are denoted by the same letter; when few or no bivalents are found, the chromosomes are symbolized by different letters. Unfortunately, all degrees of relationship are observed in actual experiments; not only bivalents and univalents but also multivalent associations are often observed. The chromosomes composing a "genome" have not remained constant, but have undergone changes by translocations and inversions.

Furthermore, the pairing properties of chromosomes in heterozygotes are determined more by the arrangement of the genes which they carry than by the quality of these genes. The conclusions reached regarding the similarities and dissimilarities of the genomes are very likely oversimplifications.

The examples of genic sterility discussed in this chapter are concerned mostly with animals, and those of chromosomal sterility mostly with plant hybrids. It would, however, be premature to conclude that the two kingdoms differ in the prevailing types of hybrid sterility. The apparent high frequency of chromosomal sterility among plants may simply reflect the fact that it is usually inferred from experiments on allopolyploids, which are more often met with in plants than in animals.

IX: Species as Natural Units

THE GENETIC BASIS OF CLASSIFICATION

IT HAS BEEN POINTED out in Chapter I, and repeatedly elsewhere in this book, that the organic diversity may be considered an outcome of the adaptation of life to the diversity of the environments on our planet. This is, in fact, the cardinal working hypothesis of the modern evolutionary thought. The evidence furnished by genetics and by other biological disciplines bears out, in the opinion of most evolutionists, the validity of the hypothesis. The symbolic representation devised by Wright (1932) of the relationships between the environment and the genetic systems of its inhabitants (Fig. 1) suggests certain further corollaries of the basic hypothesis.

Let us suppose, following Wright, that an organism has 1,000 genes, each capable of producing, by mutation, 10 different alleles. The number of homozygous gene combinations which such an organism is potentially capable of producing is 10^{1000}. This number is vastly greater than the estimated number of electrons and protons in the visible Universe. Nothing can be more certain than that only an infinitesimal fraction of the possible gene combinations can ever be realized in organisms the genotypes of which consist of hundreds or thousands of genes. The potentially possible gene combinations constitute, however, the "field" within which evolutionary changes may occur. The adaptive values of the different gene combinations in the existing environments are, of course, not alike. Some gene combinations which actually appear from time to time, and probably the vast majority of the potentially possible ones, are discordant and unfit for survival. Others are suitable for the occupation of the existing ecological niches. The adaptive values of the gene combinations are symbolized in Fig. 1 by the contour lines which resemble those on topographic maps. Fig. 1 gives, of course, a much simplified representation of the situation, since an exact representation would require

a number of dimensions greater by one than the number of the genes involved.

As pointed out in Chapter I, gene patterns which differ in only a few genes usually have more or less similar adaptive values. The patterns with superior adaptive values form the "adaptive peak"; the peaks are separated by the "adaptive valleys" which symbolize the gene combinations that are unfit for survival and perpetuation. The reproductive isolating mechanisms, as well as the geographic isolation, interdict promiscuous formation of the gene combinations corresponding to the adaptive valleys, and keep the existing genotypes more or less limited to the summits of the adaptive peaks (Chapter VII). The observed discontinuity in the body structures and in the ways of life is a result of adaptation to the discontinuity of the secular environments on our planet.

The discontinuity of the organic variation is being made use of by systematic zoologists and botanists to name and to classify the organisms. But it must be stressed that this discontinuity exists regardless of whether it is or is not used by the systematists for their purposes, and for that matter whether it is studied at all. The discontinuity, the absence of immense multitudes of potentially possible gene combinations, is an objectively ascertainable fact. In some cases, it is possible to produce certain of these gene combinations artificially, by hybridization of organisms which do not cross in the state of nature. The discontinuity may, however, be viewed from different angles and investigated with the aid of different methods and operational procedures. Geneticists, ecologists, and other experimentalists endeavor to learn the causes, intrinsic to the organisms as well as residing in the environments, which maintain the existing arrays of genotypes attached to certain adaptive peaks, as well as the mechanisms which produce new gene combinations, some of which may be fit to occupy new adaptive peaks. The primary task of systematists is, in the words of Simpson (1945), "simply to provide a convenient, practical means by which zoologists [and botanists] may know what they are talking about and others may find out. It is helpful for this purpose and it is also a secondary but still essential aim that classification should be consistent with the most important thing that evolutionary taxonomists have to talk about, that is, with animal affinities."

There is obviously no conflict between these aims and endeavors of systematists and of geneticists. In fact, they are complementary. It should, nevertheless, be made explicit that what a systematist is operating with are categories of classification. A category of classification is a group concept. Its adequacy is judged by the accuracy with which it describes the characteristics of the things classified. A population geneticist is, on the other hand, concerned with mating and parentage bonds and reproductive relationships which unite certain organisms into breeding communities. The most important and most highly integrated form of breeding communities, are Mendelian populations (Chapter III). Categories of classification are constructs devised by the student for his convenience; in this sense, they are sometimes called "arbitrary" or "subjective". Mendelian populations are spatio-temporal objects, and hence can be designated as "real" or "objective". But some taxonomic groupings, particularly species and races, are, by a deliberate effort of the systematists, made to coincide as closely as possible with Mendelian populations of different orders. This fact is often overlooked in discussions of the "reality" of species and other "natural" entities (Hatch 1941, 1946, Gregg 1950).

THE NATURAL SYSTEM

The existing biological classification is not the only possible one. Books in a library may be classified according to contents, name of the author, year of publication, size, or color of the cover; which of these methods is selected depends on convenience. The same principle applies to the classification of organisms. In fact, Pliny did reject the system of animals proposed before him by Aristotle, which happened to be relatively similar to the modern one, and divided the animals into those living in water, on land, and in the air. One might just as well classify by such characters as usefulness or harmfulness to man, or occurrence in different climates. The reason why the modern classification is more "natural" than that of Pliny is that being told that an organism belongs to the genus *Drosophila* we know that its body consists of segments, that it respires with the aid of tracheae, has a legless larva, certain wing veins, bristles on the thorax, a branched arista, a short period of development, a low number of chromosomes, etc. The position of an organism in the system

of Pliny would not define so many of its characteristics. A knowledge of the position of an organism in an ideal natural system would permit the formation of a sufficient number of deductive propositions for its complete description. A system based on the empirically existing discontinuous arrays, conveys to the student the greatest possible amount of information.

On the other hand, since the time of Darwin the term "natural classification" has meant one based on common descent of organisms. The forms united together in a species, genus, class, or phylum are supposed to have descended from a common ancestor. The lines of separation between the systematic categories are adjusted, at least in theory, to the branching of the phylogenetic trees. And yet the classification continues to be based chiefly on morphological studies of existing organisms rather than of series of fossils. The difficulty thus incurred is circumvented with the aid of an hypothesis according to which the similarity between organisms is a function of their descent. Fortunately, this difficulty is more theoretical than real. The classification of organisms that existed before the advent of evolutionary theories underwent surprisingly little change in the times following it. Such changes as have been made have depended only to a trifling extent on the elucidation of the actual phylogenetic relationships through paleontological evidence. The phylogenetic interpretation was simply superimposed on the existing classification. The subdivisions of the animal and plant kingdoms established by Linnaeus are, with few exceptions, retained, and this despite the enormous number of discovered new forms. The new forms were either included in the Linnaean groups, or new groups have been created to accommodate them. There has been no necessity for a basic change in the classification. This fact is taken for granted by systematists, and frequently overlooked by the representatives of other biological disciplines (Simpson 1945, 1949).

To avoid misunderstanding, it is necessary to define in what sense the classification may be said to have remained constant. The system of Linnaeus recognized only five systematic categories: species, genus, order, class, and kingdom. Two categories were added very early: the family and the phylum. The number of categories now used is large: species, subspecies, subgenera, sections, tribes, subfamilies, families, superfamilies, suborders, etc. Among insects, for

example, most of the Linnaean genera are now treated as families. It is possible that Linnaeus intended that the number of generic names should be kept low enough, so that the first name in the binomial nomenclature would at once convey to a biologist a general idea about what kind of organism is being referred to. If such was his intention, it was frustrated by his successors, since no human memory can now keep all the generic names of either animals or plants. In fact, some taxonomists have multiplied the genera, especially in mammals and birds, to the point where most of them contain single species. This, of course, defeats the purpose of the binomial nomenclature (Mayr 1942).

What remained unaltered through all these metamorphoses is the recognition that a given complex of forms represents a natural group. The evaluation of a group either as a genus, or a tribe, subfamily, or family is a matter of convenience; an investigator is, within limits, free to exercise his choice. The number of different orders of discontinuities in the organic world is so large that more and more categories could be created to describe them, just as branches of a tree can be classified only into major and minor ones, or else into primary, secondary, tertiary, and the rest.

There is, however, a systematic category which, in contrast to others, has withstood the changes in the nomenclature with a singular tenacity. This is the species. To be sure, some of the species described by Linnaeus have been split into two or more new ones, and yet a majority of the Linnaean species are still treated as species, not as subgenera, genera, or anything else. In animal and plant groups which are taxonomically well understood, and excepting the so-called "difficult" ones (which constitute a special problem to be discussed below), the delimitation of species usually is subject to no dispute at all (Mayr 1942, 1948, 1949). Simpson (1945) points out that, with modern methods of species recognition, a most inveterate "splitter" seldom recognizes twice as many species as does an extreme "lumper," although the former might recognize five times as many families as the latter.

To be sure, at the beginning of our century, some taxonomists succumbed for a time to the temptation of assigning species rank to every local race distinct enough to permit most specimens to receive determination labels. This occurred chiefly in the well studied groups,

such as mammals, birds, and some genera of insects, where most species were already known, and the taxonomic specialists were tempted to overestimate infraspecific differences. A veritable pandemonium of splitting still prevails in the study of fossil man, where some hunters of human remains describe almost every new fragment of bone as a new species, when they do not make it a new genus. A salutary reaction has, however, set in with the introduction of the polytypic species concept, which recognizes that allopatric populations of a species often become genetically differentiated into systems of races. The book of Mayr (1942) which has been very effective in dissemination of the polytypic species concept in the last decade, contains an excellent account of this reform in modern systematics. Modern systematics has vindicated the intuitive conviction which workers in this field always had, and which was expressed concisely by Bateson (1922): "Though we cannot strictly define species, they yet have properties which varieties have not, and...the distinction is not merely a matter of degree."

MENDELIAN POPULATIONS AS PRODUCTS OF ADAPTIVE EVOLUTION

The relative stability of the genes results from their ability to reproduce themselves (Chapter II). The self-reproduction is what distinguishes the living from the nonliving. But absolute stability, even if it were physically possible to attain, would preclude any progress in the utilization by life of its old environments and expansion into new ones. Mutation limits the stability of the gene, and has as its corollary the process of natural selection, and, hence, of the evolutionary development. Most organisms possess, however, many genes which mutate independently. A mutant gene which on a certain genotypic background has adaptively unfavorable effects may be favorable in combination with other genes. The evolutionary potentialities of an organism depend upon how great a variety of gene combinations it is capable of producing. The larger the part of the field of gene combination which is available, the greater is the chance that a new adaptive peak may be discovered (Fig. 1). The formation of favorable gene combinations is, however, difficult in organisms which reproduce asexually. It requires the occurrence of a series of mutations in the same line of descent. If each mutation is favorable *per se*, this may eventually be accomplished, though the time lost may

be immense. But if an adaptive change requires a combination of several mutational steps each of which taken separately is unfavorable, the adaptation may never become realized.

Weismann had pointed out as early as 1892 that sexual reproduction increases the genetic variability. Genetics has confirmed this prophetic view. Sexuality brings forth innumerable gene combinations that are tested for fitness by natural selection. Hybridization of carriers of different genotypes, and gene segregation and recombination in the hybrids, permit life to "experiment" with new genotypes and to "explore" greater and greater portions of the field of potentially possible gene combinations. Some of the "experiments" result in evolutionary "inventions"—formation of genotypes fit to occupy new adaptive peaks. Darlington (1939) and Darlington and Mather (1949) have pointed out that the integration of the genes into chromosomes, development of the whole complex machinery of the chromosome and cell division, meiotic pairing, crossing over, and reduction division may be regarded as a series of adaptations to secure the evolutionary advantages of gene recombination.

In organisms which reproduce asexually, the individual is the only organismic unit. For example, the individuals in a clone of bacteria are genotypically alike, unless mutation has intervened. But these individuals have no biological bond, except retrospectively by virtue of descent from a common ancestor. Sexual reproduction has brought about a new form of biological integration. Individuals are combined into reproductive communities, Mendelian populations. These supra-individual entities are considered supraorganisms by some authors (Allee et al. 1949). In any case, they owe their cohesion, as pointed out above, not only to common descent, but, and primarily, to mating and to parentage bonds. The sexual unions and the gene segregations occur in every generation in Mendelian populations, and determine both the continuity and the changeability of their collective genotypes, gene pools. For example, every human population, from a clan or a tribe to mankind as a whole, is a continuous network of individuals connected by parentage and marriage relationships. No less important is the fact that, in sexual organisms, Mendelian populations, rather than individuals, have become the units of the adaptively most decisive forms of natural selection (Chapter V, also Dobzhansky 1950d).

It must be reiterated that Mendelian populations are not synonymous with any groupings or categories of systematics. A systematist recognizes the existence of two or more groups only if their members are genetically, or at least phenotypically, distinct. Mendelian populations may or may not be genetically distinct, but they are more or less segregated reproductively. To establish taxonomic groups, a sample of their representatives must be obtained, and their morphological or other characteristics examined. Mendelian populations may be apprehended from demographic data. For example, examination of marriage and birth registration data for several generations would undoubtedly disclose that mankind is broken up into Mendelian populations of various orders. Nevertheless, it is certainly true that some systematic categories, races, subspecies, and species, would be, and usually are, coincident with Mendelian populations. For Mendelian populations tend to diverge in their genetic constitution in response to environmental differences. The systematists perceive and record the results of that divergence.

The evolutionary advantages brought about by the appearance of sex and the emergence of new organismic entities, Mendelian populations, are immense. A far greater proportion of the field of gene combinations has been explored by life than could have happened without sex, and consequently numerous adaptive peaks have been discovered. These "discoveries" have given rise to the organic diversity which we observe around us. But the adaptive peaks are separated by adaptive valleys. As pointed out in Chapter VII, unrestricted hybridization would produce too many ill-adapted gene combinations. The arrays of genotypes which inhabit the adaptive peaks must be protected from disintegration. This biological problem has been solved by the development of reproductive isolating mechanisms. Mendelian populations have become integrated into complexes within which interbreeding is possible, but between which it is limited or eliminated entirely. These complexes are the biological species. The species of the systematists usually, but not always, correspond to the biological species.

DEFINITION OF SPECIES IN SEXUALLY REPRODUCING ORGANISMS

There has been no shortage of attempts to define what constitutes a species. The lack of morphological intergrades between species and

their presence between races has frequently been depended upon, but there are some very distinct species apparent intergrades between which occasionally occur, and there are races and even mutants produced by changes in single genes that are discrete. Among insects, differences in the genitalia were assumed to mark species, but such differences may be present in races and absent in species. Species are frequently sympatric while races are allopatric, but many species are strictly allopatric. The failure of species to produce fertile hybrids is again by no means universal (Chapter VIII). Writers inclined toward eclecticism believe that none of the above criteria are sufficient when taken singly, but that a satisfactory result may be obtained by combining them. The futility of attempts to find a valid criterion of species as a static entity has become rather generally recognized (Mayr 1942).

An interesting trial was made by Lotsy (1931), who regarded a "syngameon" (which he defined as "an habitually interbreeding community of individuals") to be the fundamental unit among systematic categories. Syngameons are, however, not species but any kind of Mendelian populations. Lotsy's attempt had, nevertheless, the merit of directing the attention to interbreeding communities, Mendelian populations in our present terminology, as the fundamental realities of the living world. Dobzhansky (1935c, 1937a, and the first edition of this book) pointed out that the process of speciation, as distinct from the race formation, consists in the development of reproductive isolating mechanisms. The species is not a static unit, but a stage in the process of evolutionary divergence. Species are formed when a once actually or potentially interbreeding array of Mendelian populations becomes segregated in two or more reproductively isolated arrays.[1] Species are, accordingly, groups of populations the gene exchange between which is limited or prevented in nature by one, or by a combination of several, reproductive isolat-

[1] In the early papers just quoted, the bars to the interbreeding of species were described as "physiological," that is genotypically conditioned, in contrast to the geographical isolation which is extrinsic to the organism. Although a list of "physiological" isolating mechanisms, substantially identical with that appearing on p. 181 was given, and any notion that species must always be "intersterile" was explicitly disclaimed, several critics so misconstrued the definition. To avoid misunderstanding, Mayr (1942) suggested the term "reproductive," in place of "physiological" isolating mechanisms. Whereupon at least two critics accused both Mayr and the present writer of defining species by "intersterility".

ing mechanisms. In short, a species is the most inclusive Mendelian population.

To quote only some names, Allee et al. (1949), Bates (1949), Bauer and Timofeeff-Ressovsky (1943), Cain (1944), Darlington and Mather (1949), Emerson (1938), Epling (1939), Huxley (1942), Mayr (1940, 1942, 1948, 1949), Muller (1942), Patterson (1942), Schmalhausen (1949), Simpson (1943), Stebbins (1950), Thorpe (1940) and Timofeeff-Ressovsky (1940a) have adopted the idea that the development of reproductive isolation constitutes the essence of the process of speciation. In fact, the only voices raised against it have been those of Gates (1948) and Sturtevant (1942), who insist on the retention of the morphological species concept of classical taxonomy.

BIOLOGICAL SPECIES AND TAXONOMIC SPECIES

The genetic discontinuity between Mendelian populations becomes fixed by reproductive isolation. The stage of the evolutionary process at which this fixation occurs is fundamentally important. The attainment of this stage constitutes the advent of the species distinction. Species are tangible natural phenomena. Interbreeding, gene exchange, and the presence or absence of reproductive isolation between Mendelian populations can, however, be studied directly only with the aid of the methods of experimental genetics and ecology. Systematists are rarely able to use any of these methods in describing or studying species, and this situation is not likely to undergo substantial change in a predictable future. The question arises, to what extent do the species based on the criteria of reproductive isolation coincide with the species established by systematists ? The balance of the present Chapter will be devoted to the demonstration that, in sexual and cross-fertilizing organisms, in other words, in the organisms which form Mendelian populations, the correspondence is usually quite close.

Simpson (1943) has stated the relationships between the taxonomic and the biological species in a most lucid way: "a taxonomic species is an inference as to the most probable limits of the morphological species from which a given series of specimens has been drawn." A morphological species, which in turn is an inference as to the most probable limits of the biological (genetic) species, is "a

group of individuals that resemble each other in most of their visible characters, sex for sex and variety for variety, and such that adjacent local populations within the group differ only in variable characters that intergrade marginally." What a working taxonomist describes as a species is a sample of specimens, usually dead ones, drawn from a certain natural population at a certain time. Only very rarely is he acquainted with the totality of individuals which constitute the breeding community of the biological species; and he never observes more than an infinitesimal fraction of the time dimension of that population.

Provided that the sample of specimens is really representative of the status of the species population at a given time, a study of the morphology and the geographic origin of these specimens is usually capable of producing indirect evidence on the genetic limits of this population. The systematists have intuitively grasped the existence of the biological species. The definition of species as reproductively isolated groups of populations does not claim to furnish an inflexible yardstick with the aid of which the systematists could always decide whether their samples of specimens represent one or more species. The value of this definition to the systematists lies in that it substitutes an analytical judgment for the less communicable intuition.

Mayr (1942) has pointed out the fundamental differences between the methods used in recognition of sympatric and of allopatric species in sexual and cross-fertilizing organisms. Two or more Mendelian populations can be sympatric, i.e., can coexist indefinitely in the same territory, only if they are reproductively isolated, at least to the extent that the gene exchange between them can be kept under control by natural selection. The genetic gaps between sympatric species are, as a rule, absolute. Now, genetic differences are usually reflected in the morphology of the organism. The consequence is the presence of a greater or lesser morphological hiatus between most species. "If a taxonomist receives a series of specimens from a particular locality, he is almost never in doubt as to whether they belong to one or to several species." This does not mean that the morphological differences between sympatric species are always great. In some groups they may be small and recondite (sibling species, see below). The important fact is that once the difference is detected, any individual can be assigned to one or the other species without ambiguity. "The

difficulties in delimiting sympatric species...are of a technical and temporary nature," according to Mayr.

But "the gaps between allopatric species are often gradual and relative, as they should be, on the basis of the principle of geographic speciation" (Mayr). Allopatric populations do not directly exchange genes simply because they are allopatric. Whether such populations are isolated also reproductively, so that they could maintain their genetic differences if they were to become sympatric, is often a moot point. In many cases the problem can be resolved by observing that the populations in question are united by a continuous chain of intermediate populations in the geographically intervening localities. The presence of such a chain of intermediate populations is the *prima facie* evidence that unimpeded gene exchange is at least potentially possible between the populations by diffusion through the intervening space. This is, for example, clearly the case between human races, and history has shown that whenever any two races become sympatric they eventually become a single interbreeding population, and this despite the social and economic bars to interbreeding. There is only a single human species, *Homo sapiens*. But very often allopatric populations are separated by extrinsic gaps—marine straits, mountain ranges, expanses of deserts, etc. How is one to find out whether or not these populations are reproductively isolated, especially if genetic experimentation with them is impracticable ? Mayr has pointed out that, in well-known groups of organisms, uncertain and debatable cases of species distinction involve allopatric populations. He has proposed that such doubtful cases should be resolved by a convention: when the morphological differences between the allopatric populations are about as great as, or greater than, the average difference between sympatric species in the same group of organisms, these populations should be regarded as distinct species. Otherwise, they should be catalogued as races (Mayr 1942, 1948). An analogous convention is the only possible one for the allochronic populations of the paleontologists (Simpson 1943, Newell 1947, Kühn 1948). Indeed, reproductive isolation between populations separated in time can have no other than inferential meaning. Stebbins (1950) has pointed out the evident pitfalls in such inferences; these same pitfalls were also clearly recognized by both Mayr and Simpson.

SPECIES, INCIPIENT SPECIES, AND RACES

Linnaeus and his immediate successors dealt mainly with faunas and floras of relatively small territories. The facility with which sympatric species could be delimited did not contradict the view that species arose through separate acts of creation. If every species is a primordial entity, the investigator must learn only to discriminate between true species and their secondary subdivisions. As more and more lands were explored, systematists had to deal with allopatric populations. Eventually it was realized that the impossibility of distinguishing certain species from races is not an accident but is inherent in the living beings themselves. The explanation of the phenomenon offered by Darwin and his successors is still valid today: species evolve from races through accumulation of genetic changes. Races, species, genera, and families are nothing more than different degrees of phylogenetic divergence. This divergence being a gradual one, instances must be found, and are found, when two or more races have become so distinct as to approach, but not to attain completely, the species rank. Once the process of speciation is accomplished, species can no longer be mistaken for races. What to systematists has been a source of vexation has become the keystone of evolutionary theory.

The gradualness of the divergence is a fact which could not be postulated *a priori*. Goldschmidt (1940) believes that species do not evolve from races but arise through sudden "systemic" mutations. Lamprecht (1948) also believes that species differ from each other in special species genes. A method, namely polyploidy, is indeed known whereby new species arise from ancestral ones by sudden changes (Chapter X). But this method, although very important in some groups, especially among plants, is certainly not a general occurrence. For this reason, examples of populations which stand at the boundary between race and species can be given by systematists working with almost any group of organisms (except the groups which are old and relictual, in which formation of new species is no longer going on).

On the other hand, it must be emphasized that, despite the occurrence of these "borderline cases," a vast majority of populations can be recognized either as distinct species or as races without any

hesitation at all. It is for this reason that the category of species has on the whole shown a remarkable stability from Linnaeus to our day (see above). There is no question that the cat and the lion, the horse and the ass, the Norway rat and the black rat belong to different species. There is likewise no question that the Siamese and the alley cats, the Arabian charger and the draft horse, or the maize of Iowa and that of Mexico are distinct races and not distinct species. The same is true of the human races, although the eccentric idea that they are species appealed to some scientists. The reason why biologists are apt to spend far more time discussing the doubtful borderline cases than the doubtless species and the doubtless races is not that the former are very common. It is rather that the borderline cases are interesting to evolutionists: the relative rarity of borderline cases indicates that, although the process of divergence is a gradual one, the speciation in the strict sense, i.e., the development of reproductive isolation, is a crisis which is passed relatively rapidly.

SIBLING SPECIES

It may be well to consider at this point the species variously referred to as sibling, cryptic, biological, physiological, or ecological species, or phenons, which may seem to belong to the category of borderline cases, although in reality they do not. Sibling species are reproductively isolated Mendelian populations, the members of which show few or no easily visible differences in the bodily structures. Although any change in the bodily structures is of necessity a sequel to physiological developmental processes, some physiological differences are not accompanied by detectable changes in the visible morphology. A museum systematist is perforce confined to describing the structural differences in his materials. The assumption implicit in his work is that a certain fraction of genetic differences between populations are reflected in morphological traits, and, hence, the morphological descriptions reflect reasonably accurately the magnitude of the genetic differences between the races, species, genera, etc. This assumption is on the whole justified, but some groups are known in which the genetic divergence may be accompanied by little morphological divergence.

Drosophila pseudoobscura and *D. persimilis* have different geographic distribution areas, but they are sympatric in a territory

which extends from British Columbia to California. In this territory these species differ in ecological preferences, but sometimes they occur together, and may be found feeding side by side (Carson 1951). They show a pronounced sexual isolation, but in laboratory experiments some hybrids are invariably produced whenever the adults of the two species are placed together (Chapter VII). No hybrids have, nevertheless, been found in nature in localities where the species are sympatric; the cause which prevents the appearance of hybrids in these localities is obscure. The artificially produced hybrids are sterile as males but fertile as females; backcrosses to the parental species suffer from a breakdown of the viability (Chapter VII). The absence, or extreme rarity, of the gene exchange between these species in nature is finally attested by the fact that the genetic variants, such as chromosomal inversions, for which one of the species is polymorphic do not diffuse into sympatric populations of the other species (Dobzhansky and Epling 1944). Mather and Dobzhansky (1939) and Reed and Reed (1948a) found very slight average differences in body morphology between the species, but the variations are too broadly overlapping to permit classification of single specimens. Rizki (1951) found, however, differences in the male genitalia with the aid of which the males can now be classified. The females remain, however, morphologically indistinguishable. Needless to say, crossing experiments, or cytological examination, always permit quite unambiguous distinction of the species to be made. *D. willistoni*, *D. paulistorum*, *D. equinoxialis*, and *D. tropicalis* are a group of sibling species which differ in the structure of their chromosomes, in physiological traits, and in some slight and recondite morphological differences. The reproductive isolation between these species is absolute: the strong sexual isolation permits cross-insemination to occur only rarely, and no hybrids at all are produced (Burla et al. 1949, see also Chapters V and VII above). Sibling species are rather common in the genus *Drosophila;* for further examples see Patterson 1942, 1943, King 1947a and b, and other works of Patterson and his collaborators.

Groups of sibling species are a common occurrence among mosquitoes (see Bates 1940 and 1949 for a review and references). *Anopheles maculipennis*, *A. atroparvus*, *A. messeae*, *A. labranchiae*, *A. sacharovi*, and *A. subalpinus* have all been confused under the

name "*maculipennis*" because the adult insects are very similar in morphology. But they differ in geographic distribution, feeding habits, breeding places, mating habits, ability to transmit malaria, and in some instances, in the visible characters of their eggs, The evidence appears sufficient to show that the reproductive isolation between these species is complete. Sibling species are known also in other genera of mosquitoes.

The "species" names of the infusorians *Paramecium bursaria* (Jennings 1939, Chen 1946a and b), *P. aurelia* (Sonneborn and Dippell 1946, Sonneborn 1947) and *Euplotes patella* (Kimball 1939) refer each to a group of sibling species, referred to as "varieties" by the authors just quoted. The species are reproductively isolated; conjugation between them occurs with difficulty, and if it does the participants die (Chen 1946b) or produce inviable hybrids (Sonneborn and Dippell 1946). Sibling species in the parasitic wasps *Trichogramma* have been described by Harland and Atteck (1933), in termites by Emerson (1935), in the grain beetles *Calandra* by Birch (1944). For other examples see Thorpe (1940), and Hoare (1943), Mayr (1948), and Allee et al. (1949).

Some authors have argued that sibling species should not be considered species because museum taxonomists cannot distinguish them in materials preserved by time-honored methods. Species are, however, phenomena of nature which exist regardless of our ability to distinguish them. The techniques of investigation of the species change with time. Cultural and biochemical tests are at present used routinely to classify some microorganisms. Is it really necessary to have *Drosophila* pinned, dried, and shriveled before classifying them as to species ? In organisms which are studied exclusively with the aid of classical museum techniques sibling species can not be distinguished. But a student of evolution can hardly ignore the fact of species distinction between *Drosophila pseudoobscura* and *D. persimilis*, and students of public health and preventive medicine will want to discriminate between the species of *Anopheles* which do and those which do not transmit malaria.

Species of some genera differ strikingly enough to be distinguished by a layman, while in other groups the visible species distinctions appear trifling or absent. If reproductive isolation were the consequence of accumulation of a certain amount of genetic differences

between populations, one would have to conclude that in some organisms the proportion of genetic changes which produce visible external effects is higher than in others. On the other hand, it is possible that the amount of genetic change which precedes the development of reproductive isolation varies from group to group. In this case, species would comprise much larger units in some groups than in others, in the sense that, to put it crudely, the numbers of genes differentiating related species would be variable. It is also possible that in some groups of organisms the external morphology has reached so high an adaptive level that changes are discriminated against by natural selection. Further adaptive specialization would then proceed by way of physiological modification unaccompanied by morphological change.

BORDERLINE CASES BETWEEN RACES AND SPECIES

The most striking instances of borderline cases, in which the populations have diverged almost too much to be considered races but not quite enough to be regarded good species, are the so-called "rings of races". Sympatric populations which share the same territory without intergradation behave like distinct species, and yet they may be united by a chain of allopatric races which imperceptibly grade into each other and into the extreme members of the series. The Asiatic titmouse *Parus minor* occurs from Amur and Japan to southern China, where it intergrades with *P. bokharensis*. The latter inhabits southern Asia from Indonesia, through India, to Turkestan, and in Iran intergrades with the European *P. major*. The distribution of *P. major* extends across Siberia, and in the Amur region meets that of *P. minor;* in that region both forms occur in the same territory without intergradation (Stegmann 1931, Rensch 1933; see Fig. 22). If the species were to die out in India, for example, or anywhere along the "ring" of countries it occupies, the forms *major* and *minor* would doubtless be considered separate species. As the situation actually stands, a systematist is confronted with the impossibility of drawing the "line" anywhere between the two. The nomenclatorial difficulty need not, however, obscure the evolutionary importance of the fact that the end members of the series have attained the stage at which interbreeding no longer takes place. For other examples of

"rings of races," see Rensch 1933, Mayr 1942, Allee et al .1949, and Stebbins 1950.

As might be expected, different authors have made different evaluations of the phenomenon of racial rings. To Kinsey (1936, 1937) the nomenclatorial difficulties seemed important enough so that he

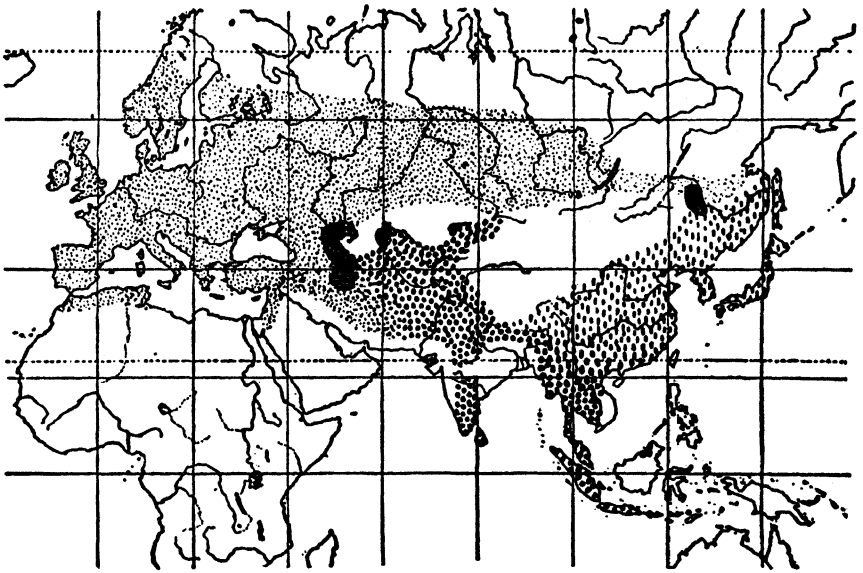


FIG. 22. The geographical distribution of *Parus major* and its relatives. *Parus major*, finely stippled; *P. bokharensis*, coarsely stippled; *P. minor*, vertical dashes; the area in which both *P. major* and *P. minor* occur side by side is shown in black (From Rensch.)

proposed that the term species be applied only to the smallest distinguishable population units (Mendelian populations ?). Goldschmidt (1940) ascribes no importance to the lack of interbreeding between the extreme members of the rings of races: "As a taxonomist, do with them what appears to be practical. But as an evolutionist, treat them as members of one species, which they most clearly are, though they do not interbreed in some localities, just as the Brahmin does not interbreed with a Pariah, his own near biological relative." We agree with the first part of Goldschmidt's advice, but not with the second; as evolutionists we must treat the end members of the racial rings as different species, which they most clearly are.

The borderline cases take, of course, many forms other than the rings of races. The work of Moore on *Rana pipiens*, reviewed in Chapter VII, has shown that the populations of New England and of Florida or Texas could not exchange genes directly, because the hybrids between them are inviable. And yet, these populations are united by geographically and genetically intermediate ones. An adaptively valuable trait appearing in New England presumably could in time diffuse into Florida and Texas populations under the impetus of natural selection. *Rana pipiens* is rightly considered a single species. And yet if the populations intervening between New England and Florida were destroyed by some means, the extreme populations would become reproductively isolated species. Blair's work on the toads, also reviewed in Chapter VII, has disclosed, in a sense, an opposite situation. *Bufo americanus* and *B. fowleri* had evolved enough reproductive isolation to become sympatric. But since this isolation was chiefly ecological, man's interference with the habitats of the toads may conceivably lead to eventual obliteration of the species separation. This example shows that the species differentiation is potentially reversible until the reproductive isolation has become absolute.

ECOSPECIES AND CENOSPECIES

Some reproductive isolating mechanisms seem to be more dependent upon the environment, and therefore more easily modified by external influences, than others. Indeed, ecological, seasonal, mechanical, and even sexual isolation between species can be overcome in experiments more easily than hybrid inviability or hybrid sterility. It would appear, then, that the species differentiation based on, for example, seasonal isolation is less final and irreversible than that based on inviability or sterility of the hybrids. These considerations seemed important enough to certain students of evolution, particularly in plants, to induce them to distinguish two kinds of species—namely ecospecies and cenospecies (Turesson 1922, 1925, Clausen, Keck, and Hiesey 1940, 1945). Ecospecies are groups of populations which "are able to exchange genes freely without loss of fertility or vigor in the offspring"; cenospecies consist of ecospecies which "may exchange genes among themselves to a limited extent through hybridization." Hybrids between cenospecies are partially or com-

pletely inviable or sterile. Among zoologists, Blair (1943, 1950) has endorsed the distinction between ecospecies and cenospecies.

The practical difficulty met with in attempts to apply these concepts is evident enough. If two sexual populations are sympatric and yet preserve their distinctions, the conclusion is justified that they are reproductively isolated. But what reproductive isolating mechanisms are operative is only rarely known, and when it is, one usually finds not a single mechanism but a combination of several cooperating ones. More importantly, the distinction of ecospecies and cenospecies implies that the former is a stage of the evolutionary divergence which precedes the latter. There is, however, no basis for the assumption that the diverging populations become isolated first ecologically, seasonally, or mechanically, and then hybrid inviability and sterility are added to make the reproductive isolation complete. On the contrary, it is arguable that at least some hybrid inviability or hybrid breakdown appears first, and serves as a stimulus for the development of other forms of reproductive isolation (cf. Chapter VII). However that may be, any form of reproductive isolation is potentially capable of blocking the gene exchange between populations entirely, and thus making the species separation irreversible. Conversely, any form of reproductive isolation is in principle reversible, inasmuch as any genotypic change compounded of mutational steps may be undone by reverse mutations.

"SPECIES" IN ASEXUAL ORGANISMS

An occasional or regularly periodic occurrence of self-fertilization, apogamy, or asexual reproduction in an organism need not cause any essential alteration in its evolutionary pattern (Chapter X). A species remains a group of populations which are actually or potentially able to exchange genes, and the gene pool of the species continues to be a reality. The situation changes when selfing, apogamy, or asexual reproduction become obligatory instead of facultative or periodic. Pure lines or clones do not exchange genes, as such an exchange is precluded by their very method of reproduction. The genotype of each line is a closed system isolated from other similar ones and capable of changing only through mutation or through reversal to sexuality. It is not surprising that the groups of organisms recognised as being uncommonly "difficult" from the standpoint of

delimiting species have proved to be mainly those in which asexual reproduction, apogamy, or self-fertilization are the only, or the chief, modes of propagation. The standard examples of such "difficult" groups are the plant genera *Crataegus*, *Hieracium*, and *Rubus* (Gustafsson 1946b, 1947b, 1948). The opinions of different authorities on what constitutes a species in these genera vary so widely that it is not uncommon to find that one investigator unites under a single specific name a complex of forms that is divided by others into numerous "species". The subdivision of the mass of clones into species *Escherichia coli*, *Salmonella typhosa*, and *S. enteritidis* is purely a matter of taste; one might just as well regard all of them as a single species (Baur 1930, van Niel 1946). The same is true for the lichen genus *Cladonia* and the related ones, in which a clear separation of species is impossible (but in which, nevertheless, a tremendous number of "species" have been described).

The above statements should not be misunderstood as implying that the variation in asexually reproducing groups is absolutely continuous. On the contrary, we find there aggregations of numerous more or less clearly distinct genotypes, each of which is constant and reproduces its like if allowed to breed. These constant genotypes are sometimes called elementary species, but they are not united into integrated groups that are known as species in the cross-fertilizing forms. The term "elementary species" is therefore misleading and should be discarded. The existing genotypes obviously do not embody all the potentially possible combinations of genes. As in cross-fertilizing organisms, the genotypes in the asexual ones are clustered around some "adaptive peaks" in the field of gene combinations while the "adaptive valleys" remain more or less uninhabited. Furthermore, the clusters are arranged in an hierarchical order, in a way which is again analogous to that encountered in sexual forms. The different clusters may, then, be designated some as species, others as subgenera, still others as genera, and so on. Which one of these ranks is ascribed to a given cluster is, however, decided by considerations of convenience, and the decision is in this sense purely arbitrary. In other words, the species as a category which is more fixed and therefore less arbitrary than the rest is lacking in asexual and obligatory self-fertilizing organisms. All the criteria of species distinction utterly break down in such forms.

The binominal system of nomenclature, which is applied universally to all living things, has forced systematists to describe "species" in the sexual as well as in the asexual organisms. Two centuries have rooted this habit so firmly that a radical reform is beyond practical possibility. Nevertheless, systematists themselves have come to the conclusion that sexual species and asexual ones or "agamospecies" must be distinguished (Du Rietz 1930). All that is saved by this method is the word "species". As pointed out by Babcock and Stebbins (1938), "The species, in the case of a sexual group, is an actuality as well as a human concept; in an agamic complex it ceases to be an actuality."

X: Patterns of Evolution

INTRODUCTION

THE PROCEDURE of science is to dismember natural phenomena into their constituent parts, and, after duly examining the parts and assaying their properties, to reconstruct the original order. It is hoped that by so doing a more communicable, if not a more profound, insight into the nature of things may be gained than it is possible to secure with the aid of other than scientific methods. Some scientists obtain the greatest satisfaction from analysis and examination of parts, and others from synthesis of the whole from the parts; the former are attracted by the diversity and the latter by the unity of things. In the field of evolution, some investigators strive to discover the most widespread mechanisms of evolutionary changes, and others to detect the peculiarities of the evolutionary patterns in the separate lines of descent. It behooves us to recognize the legitimacy of both methods of approach.

Gene mutation, chromosome changes, restriction of the population size, natural selection, and development of isolating mechanisms are the known common denominators of many, if not all, evolutionary histories. Different phylogenetic lines vary, however, in that one or the other of these evolutionary agents may become limiting at different stages of the process. Polyploidy, self-fertilization, apogamy, and asexual reproduction create very special conditions, to which some references have been made in the foregoing chapters. In the present chapter the subject will be considered more systematically.

THE TYPES OF EVOLUTIONARY CHANGES

Let us return again to Wright's symbolic picture of the field of gene combinations with its "adaptive peaks" and "adaptive valleys" (Chapters I and IX, Figs. 1 and 23). The peaks, it will be remembered, symbolize groups of related gene combinations which make

their carriers fit to survive and reproduce in a given ecological niche; the valleys symbolize the gene combinations the adaptive values of which are low in the existing environments. Every living species, or any other group of organisms above the level of elementary Mendelian population, may be thought of as occupying one of the available peaks, or a group of adjacent peaks, in the field of gene combinations.

The possibilities of adaptive evolution are twofold. First, a change in the environment may make the old genotypes adaptively less valuable than they were before. Symbolically we may say that the "field" had changed, some of the old peaks have been leveled off, and some of the old valleys or pits have risen to become peaks. The environmental change, produced either by geological causes or by man's interference with the habitats of organisms, lowers the adaptive values of some of the genotypes which were favored before the change, and augments the values of other genotypes which were discriminated against in the old environments. The species may become extinct, if no genetic elements (mutations) necessary to produce the new adaptive genotypes are available, or if the requisite constellations of these elements do not appear in time. In order to survive, the species must reconstruct the gene pools of its component populations, and arrive at the gene combinations that represent the new adaptive peaks. Another type of adaptive evolution takes place when a species finds its way from the adaptive peak which it occupies to other and unoccupied adaptive peaks. The first type of change is primarily a response to the secular environmental shifts. The second type may, theoretically, occur in a constant environment; in a most general way, this is referred to as "progressive evolution". In reality, the two types of changes usually occur together.

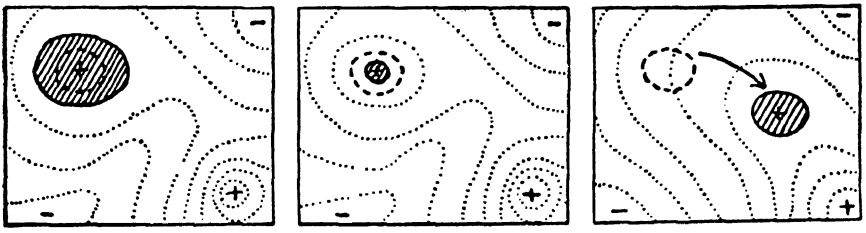
The existence of unoccupied adaptive peaks is a consequence of the fact that innumerable gene combinations have never been formed and tried out—this is obviously so, because the number of possible combinations far exceeds the number of individuals in any species or any group of species (see Chapter IX). There are in the environment unoccupied ecological niches as well as niches the occupants of which are not in a perfect harmony with their environments. The validity of the foregoing statements is rather obvious on a priori grounds—it means essentially nothing more than that the existing world is not the best of all possible ones. A proof is furnished by the

rapid spread of many species of animals and plants introduced from foreign countries. The ability of such invaders not only to take root in a foreign soil but sometimes to displace the native species means that before the invader's arrival there had existed either empty or inefficiently exploited ecological niches. Man-made changes in the earth's biota have led to the extinction of many "wild" species and to manifold increases in the populations of others, some of which became pests, weeds, or commensals. The species that died out were evidently unable to effect the necessary readjustments rapidly enough, while those that spread either evolved new adaptive genotypes or else happened to be "pre-adapted" to the conditions created by man. The availability of an ecological niche does not in itself insure its occupation by an organism. There is no obvious reason why mammals could not have existed in the environment of the Paleozoic time, but actually they did not appear until the Mesozoic era.

Species, genera, and higher groups differ in large numbers of genes. Moreover, the genes are so integrated that the adaptive value of a genotype is a property of the whole rather than of the constituent genes. Evolutionary changes may involve not merely additions and subtractions of genes, but development and integration of gene systems. Hence, a shift from one adaptive peak to another, which may be even higher than the first, may require a thorough rebuilding of the genotype. The difficulty of this process appears to be that the stages intermediate between the two or more adaptive gene systems may represent unbalanced genotypes. Adaptive peaks may be separated by adaptive valleys (Fig. 23), and the transition from peak to peak may require a trial and error mechanism on a grand scale which would enable the species to "explore" the region around its own adaptive peak, in order finally to encounter the gradients leading towards the other peaks.

Such a trial and error mechanism is provided primarily by mutation and sexual reproduction, which are able to generate a practically limitless variety of genotypes (Chapter IX). But this does not mean that the modern theory of evolution is based on a belief in "chance", as is often but groundlessly alleged. "Chance" enters only to the extent that any mutation has a finite probability of happening, and consequently mutations occur regardless of whether they will be immediately, or ever, useful. But the evolutionary changes in Mendel-

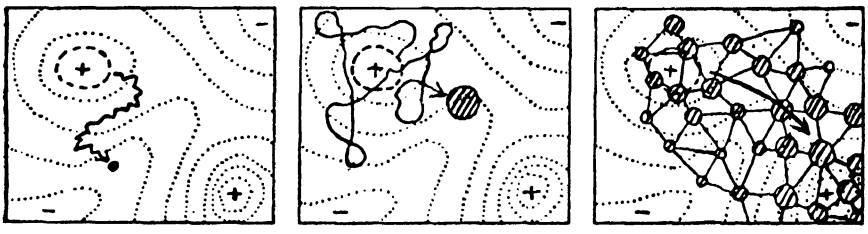
ian populations are far from automatic results of lucky throws of the genetical dice, or even of the demands of the environments. The relations between the genetic system and the external millieu are so complex that the evolutionary process can be described as a creative one. Indeed, this process gives rise to previously nonexistent coherent



A. Increased Mutation or reduced Selection 4Nu, 4Ns very large

B. Increased Selection or reduced Mutation 4Nu, 4Ns very large

C. Qualitative Change of Environment 4Nu, 4Ns very large



D. Close Inbreeding 4Nu, 4Ns very small

E. Slight Inbreeding 4Nu, 4Ns medium

F. Division into local Races 4nm medium

FIG. 23. Fate of populations of different size and under different conditions in the "field" of gene combinations. Further explanation in text. (From Wright.)

entities, new organisms fit to perpetuate themselves in certain habitats. And yet, the process involves risk of failure and miscreation, in other words, partakes of the quality which, in the application to human affairs, is called freedom. Biologists are justly impressed by the convergent formation of similar adaptive types, such as American cacti and the African euphorbias, in similar biota in different parts of the world (Chapter VII). No less impressive is the fact that such adaptive types are often absent in environments where they could be formed. Their absence shows that evolutionary history, like human history, is essentially unrepeatable and irreversible.

THE BALANCE OF EVOLUTIONARY FORCES

Let us consider the evolutionary possibilities of a very large undivided species (Fig. 23 A, B, C), in which the genetically effective population is so large that either the products 4Nu and 4Ns are much larger than unity, or the exchange of individuals between the colonies is so rapid that no isolation obtains (N is the population number, u the mutation rates, and s the selection coefficients). In such a species, each gene ultimately reaches an equilibrium frequency determined by the interaction of the mutation and the selection pressures. An increase of mutation or a relaxation of selection increases the variance in a nonadaptive fashion. The field occupied by the species (Fig. 23A) spreads along the slopes of its adaptive peak. If the spread is sufficiently great, the species may find its way to a neighboring adaptive peak and occupy it as well. A decrease of the mutation rates, or an increase in the stringency of selection (Fig. 23B), will force the species to withdraw to the highest level of its adaptive peak. The variability is reduced, but the average adaptive level of the individuals is increased. The possibility of progressive evolution is curtailed, except through mutations that may be favorable from the start. Since such mutations are probably very rare, this condition leads to an extreme specialization which may prove fatal if the environment changes.

Changes in the environment provoke alterations of the relief of the adaptive field. The relative elevations of the peaks and valleys change (Fig. 23C). In extreme cases the adaptive peak may, figuratively speaking, escape from under the species, which may be left in a valley instead. To avoid extinction, an evolutionary change may become essential. A species with a large variable population will probably undergo a reconstruction consonant with the new demands of the environment and the genes will gradually reach new equilibrium values.

A restriction of the population size which renders the breeding population very small (4Nu and 4Ns less than unity, Fig. 23D) leads to a depletion of the supply of the hereditary variability, and to fixation of genes by genetic drift. Not only neutral but also somewhat deleterious alleles may be fixed, and superior alleles may be lost. The part of the field occupied by the species is much reduced and the

adaptive peak may be abandoned. This is a way to extinction. With an intermediate population size (Fig. 23E), the effect is about the same as with a relaxation of selection or an increase of mutation in a large population; the species begins to wander on the slopes of the adaptive peak, and may find a gradient leading to a new one. The difference is that the chance of extinction is obviously greater when the population is small.

As Wright pointed out (1931a and b, 1932, 1940a and b, 1948, 1949), conditions most favorable for progressive evolution obtain in species subdivided into large numbers of local populations, at least some of which have medium or small effective sizes (Fig. 23F). The behavior of such populations, considered separately, may be similar to that shown in Fig 23D and E, that is, some or most of them may drift off too far from the adaptive peak and face extinction. In some of the populations the store of the variability may be depleted, with the result that only a limited number of gene combinations will occur, while in others the variability may remain intact. Different gene combinations may become established in different colonies. Compared to a large undivided species, the intrapopulational variability will be on the average lower, but, because the separate local populations drift apart, the total variability of the species as such will be high. Perhaps the most important feature is that gene combinations whose adaptive value is somewhat lower than the average of the whole species may be temporarily preserved in some of the colonies, rather than eliminated as they would be in an undivided species. Most of these denizens of the slopes of their adaptive peaks will eventually drift down into the valleys and be lost, but perhaps a small minority may conceivably encounter a gradient leading to a different peak. Once that has happened, the population may climb the new peak relatively rapidly, increase in numbers, and either supplant the old species, or, more likely, form a new one that owes its allegiance to the new peak. Natural selection will deal here not only with individuals of the same population (intragroup selection) but also, and perhaps to a greater extent, with colonies as units (intergroup selection). In case of an environmental change, the colony first reaching the vicinity of the new adaptive peak will obviously have the best chance of being the victorious one. Here, then, conditions are given both for differentiation of a single species into derived ones, and for

a movement of the species as a whole to a new status. At any one time the average adaptive level of a species broken up into small populations is liable to be lower than that of a large undivided one; evolutionary plasticity must be purchased at the price of sacrificing some adaptive uniformity.

RATES OF EVOLUTION

Paleontology has revealed tremendous contrasts between the tempos of evolution, both with respect to the rate of structural change and to the rate of diversifications, in different lines of descent and at different times within the same line. Thus, the evolution of mammals has taken place in the main during the Tertiary Period (although mammals had already appeared in the early Mesozoic). On the other hand, the principal types of mollusks were differentiated in the early Paleozoic, and, with the exception of the cephalopods, have undergone little fundamental change since then. The evolution of the horse tribe involved progression through eight genera during the recent 60 million years. In contrast to this, the opossums which lived some 80 million years ago are hardly distinguishable from the modern ones. Simpson (1944, 1949), Rensch (1947), Schmalhausen (1949), and Stebbins (1950) have reached, largely independently, essentially similar interpretations of the variations in the rates of evolution.

It should be stated at the outset that the frequency of mutation is, though potentially a limiting factor, rarely a decisive determinant of the evolutionary rates (Chapter III). The process of mutation supplies the raw materials of evolution, but the tempo of evolution is determined at the populational levels, by natural selection in conjunction with the ecology and the reproductive biology of the group of organisms. The most important challenge calling forth evolutionary changes is that of unoccupied or inefficiently exploited habitats and living spaces (cf. Chapters V and VII). The abundant proliferation of new and diverse forms from a limited number of kinds of ancestors on oceanic islands and in ancient lakes furnishes a particularly unequivocal illustration of the importance of the stimulus of ecological opportunity (Lack 1947, Amadon 1947, Brooks 1950).

The evolutionary effectiveness of natural selection is determined not only by its intensity but also by the manner of its action. Many organisms are destroyed in large numbers by overpowering enemies

or irresistible physical factors. For example, many plankton organisms are utterly defenseless as individuals before the much larger predators, such as fishes. Survival or destruction of an individual is here a matter of chance rather than of the adaptive merits of its genotype. Such indiscriminate destruction is countered in evolution chiefly by the development of greater fecundity, speeding up of the life cycle, and often by a decrease of the body size. The differentiation of races and species adapted to local conditions (Rensch's "kladogenesis") may go on, but organisms of this sort do not give rise to new types of organization (Rensch's "anangenesis," progressive evolution). Many defenseless forms are among the examples of extreme evolutionary conservatism: nonpathogenic bacteria, diatoms, plankton crustaceans, etc. A similar limitation of the evolutionary perspectives occurs in organisms which adopt passive means of defense —a sedentary mode of life, hard shells or armors, protective colorations, etc.

The opposite situation obtains in organisms which struggle actively to avoid or to resist their natural enemies, and especially in those which occupy the summits of the food pyramids and meet no adversaries stronger than themselves. The populations of such forms grow up to the limit of the food supply. The survival and reproduction of individuals becomes highly selective. This is especially the case in forms with a limited fecundity and a well developed provisioning, protection, or care of the offspring. It is probably no accident that mammals and birds among the vertebrates, and hymenopterans among the insects, in which the parental care is on the whole most developed, seem to have been the most rapidly evolving groups in their respective phyla. The greatest individualization of the natural selection is reached in social organisms, especially in insect societies, in which the genotype selected or discriminated against is that of the sexual members of the colony.

RUDIMENTATION

It has been pointed out that natural selection is opportunistic: genetic changes become established if they confer an advantage on their carriers at a given time and place, regardless of whether such changes might be favorable or otherwise in the long run. Any adaptive peak, however temporary, is occupied by a population, provided

only that the peak is accessible. Adaptation to specialized environments may decrease the importance of certain organs and physiological functions which are vital in other environments. Such organs and functions may become vestigial or disappear altogether. There are two possible ways to account for vestigial structures. Weismann and other classical evolutionists have introduced the idea of the struggle of parts of the body: since it takes energy to build an organ, genetic changes which dispose of a superfluous organ entail a saving of effort and thereby acquire a positive adaptive value. On the other hand, the frequencies of mutations which weaken or destroy an organ are usually much higher than those of mutations which strengthen it. So long as the functioning of an organ remains vital to the species, the destructive mutations are opposed by natural selection; when an organ ceases to be vital, selection is relaxed and the mutation pressure alone might lead to rudimentation.

Some of the best examples of specialization and rudimentation are encountered among cave inhabitants. Reduction and disappearance of the eyes and of the pigmentation of the body, development of the organs with tactile functions and of certain peculiar behavior patterns are observed in cave animals which belong to various subdivisions of the animal kingdom, from the vertebrates to insects, crustaceans, and flatworms. The work of Hubbs (1938), De Lattin (1939), Kosswig (1940, 1946, 1948), Pavan (1946a) and others has shed interesting light on the relations between the subterranean species and their surface relatives. The instances in which the same or closely related species occur in, as well as out of, the caves are particularly important, since here the processes of adaptation to the subterranean life may be studied. The variability of the structure of such organs as the eyes within the population of a single cave may be striking. Some individuals have fully developed eyes, while in others only rudiments are present; some individuals are fully pigmented and others colorless. Aberrant individuals resembling in certain particulars the cave forms may be found in the surface populations as well, but their frequency outside the caves is small. Although some of these variations have been proven to be hereditary, no less important is the extraordinary phenotypic plasticity of certain characters of cave animals. Kammerer (1912) showed that the salamander *Proteus an-*

guinus, which, when kept in the dark, has vestigial eyes and little or no black pigmentation, develops apparently functional eyes and a black pigmentation when grown under light. The genotype of an organism is, in general, so adjusted as to insure a standard development of vital organs and physiological functions in a variety of environments that are likely to be encountered; a deterioration of this adjustment may be one of the first steps of the rudimentation process.

PARASITISM AND MUTUALISM

Different sympatric species may stand to each other in a variety of relationships: disoperation, or mutual harm; exploitation, or benefit to one at the expense of harm to the other participant; toleration, when neither is harmed; and mutualism, or symbiosis, when benefits accrue to both (Allee et al. 1949). Disoperation occurs chiefly when species which have had no common evolutionary history first encounter each other, as in the case of introduced pests which destroy their food supply, only to die out themselves. Exploitation and toleration are very common in the form of parasitism and of predator-prey relationships. Mutualism ranges from facultative to obligatory mutual dependence of different organisms.

It is easy to see that disoperation is a form of relationship which is unstable in the evolutionary sense, and that it will tend to disappear and to be replaced by cooperation and mutualism. Any genetic changes which increase the benefits, or diminish the harm to either associated species will be adaptively advantageous, and, hence, will be encouraged by natural selection. The importance of this consideration has been appreciated especially by some parasitologists. According to Burnet (1945), "once an animal has died of microorganismal infection there is no further possibility of the pathogen being transferred to new hosts except in very special circumstances. An acutely fatal infection is, therefore, disadvantageous for the survival of the parasite. Conversely, a low-grade infection with no more than trivial symptoms but with free liberation of the pathogen over a considerable period of time will usually provide the maximum opportunity for dissemination of the parasite. With many sorts of qualification and limitation the normal end result of long-period interaction under approximately constant conditions between host and parasite is a

state in which the host suffers no significant disability and the parasite persists long enough to ensure transfer by one or other method to a new susceptible host."

According to Huff (1938) malarial plasmodia were originally associated with insects, to which they cause no harm, and have invaded vertebrates relatively recently, giving rise to fatal infections in the latter. Similarly, rickettsiae are old associates of ticks to which they cause no harm, and in which they are transmitted from generation to generation through the egg cytoplasm. *Rickettsia prowazeki* has invaded man, in whom it causes the epidemic typhus; it is transmitted through lice, to which it is likewise pathogenic, but to which it is transmitted only through man. According to Burnet (1945), psittacosis occurs regularly in some parrots and other birds, in which it seldom causes fatal disease, which it does when transferred to man. On the other hand, the virus of *Herpes simplex* has accomplished an almost perfect evolutionary adjustment to the human host, in whom it causes only trifling discomfort, and yet it infects "about 90 percent of its possible hosts for about 90 percent of their lives." The "Killer" strains of *Paramecium aurelia* usually carry in their cytoplasm self-perpetuating inclusions, which perhaps resemble some rickettsiae (Sonneborn 1947, Preer 1948). It is interesting that the Killer strains differ from non-Killer ones in a single gene K, and that the cytoplasmic inclusions do not reproduce successfully except in animals which carry this gene. And yet, Infusoria with the gene K may be artificially freed from the Killer cytoplasmic particles. It is not surprising that the Killer particles were at first described as plasmagenes (cf. Chapter II), and indeed the plasmagenes may well be symbiotic organisms which have become integral parts of the cells of the host as a result of a long association.

Although the normal evolutionary development is from disoperation, through exploitation, toleration, and facultative to obligatory mutualism, genetic changes may bring also reversals of this process. Burnet (1945) considers it possible that the poliomyelitis virus in man has in general reached the toleration stage, but that occasional mutations in the virus cause it to relapse to the status of a fatal pathogen. Darlington and Mather (1949) and other authors have evolved a theory according to which plasmagenes occasionally change

by mutation to "proviruses," some of which cause neoplastic diseases, or to true viruses which can be transmitted by infection.

POLYPLOIDY AS A METHOD OF THE ORIGIN OF SPECIES

Since the differences between species, and often also between races, involve numerous genes and chromosomal structures, the origin of races and species is usually a slow process of compounding of mutational steps. The opinion of some early geneticists that new species arise by mutation is false as a general proposition. And yet, alongside this slow method of species formation, there exists a mechanism of rapid emergence of new species by multiplication of the chromosome complement, by polyploidy. In the wide sense of the term "mutation" (cf. Chapter II), polyploidy is a kind of mutational change. The species formation through concatenation of gene and chromosomal changes entails gradual reconstruction of the genotype of the ancestral species to give rise to the genotypes of the derived ones. Species formation through polyploidy occurs either through doubling of the chromosome complement in the hybrid between two previously existing species (allopolyploidy), or through multiplication of the chromosomes of a single species (autopolyploidy). In either case, the polyploid possesses all the genes which were present in its ancestors and no new ones. Since, however, the ancestral species may continue to exist side by side with the polyploid, the organic diversity is augmented by chromosome doubling.

Although species formation through polyploidy is restricted to certain groups of organisms, mainly in the plant kingdom, its importance is very considerable. It is known to have occurred in all major groups of plants, with the possible exception of the fungi. Stebbins (1950) estimates that among the angiosperms the proportion of polyploid species (of recent and ancient origin) is about 30 to 35 percent. The proportion of polyploids is highest among perennial herbs, smaller in annuals, and the lowest in woody plants. Some large and widespread families are free of polyploids, while others contain many polyploid species and even genera. Polyploidy is rare among the gymnosperms, although the redwood (*Sequoia sempervirens*) is a polyploid. Some of the most important crop plants, such as wheat, oats, cotton, tobacco, potato, banana, sugar cane, and coffee are polyploids.

Since most or all individuals in sexual and cross-fertilizing organisms are more or less complex heterozygotes, no sharp distinction can be drawn between auto- and allopolyploids (Stebbins 1940, 1950, Clausen, Keck, and Hiesey 1945). As a convention, one may take the doubling of the chromosomes within a Mendelian population to produce autopolyploids, while hybrids between reproductively isolated populations are allopolyploids. Müntzing (1936) argued that autopolyploidy is an evolutionary factor of some consequence, and indeed some natural polyploids are known (*Sedum pulchellum*, Baldwin 1943, Smith 1946; some blueberries, *Vaccinium*, Camp 1944, Darrow and Camp 1945; some mosses of the genus *Mnium*, Lowry 1948). Nevertheless, more and more forms which were regarded as autopolyploids are being shown by more careful studies to have been of hybrid origin.

An example of this is a group of species and races related to *Biscutella laevigata*, a representative of the Cruciferae (Manton 1934, 1937, Stebbins 1950). The distribution area of the tetraploid forms is a continuous one, including the Alps, Carpathians, and the mountains of Italy and of the northern part of the Balkan peninsula. The area of the diploids is much smaller and is sharply discontinuous. The diploids are confined to the valleys of the Rhine, Elbe, Oder, upper Danube, and some of their tributaries. The diploids may be regarded as relics of the ancestral polytypic species or a group of species, and the tetraploids as their successors. Such interpretation agrees with the known facts of the recent geological history of Europe. The diploids are confined to regions not covered by the ice sheet during the glacial period and consequently open to habitation by plants for a long time. On the other hand, the tetraploids occur almost exclusively in the territory which was ice-covered until a geologically more recent time and must therefore be regarded as immigrants from elsewhere. Manton concludes that the diploids represent interglacial, if not preglacial, relics.

The doubling of the chromosome complement often produces physiological changes which are comparable with those produced by gene mutations. The cell size in polyploids is usually greater, and the body size is frequently, although by no means always, increased. The water contents, the osmotic pressure, vitamin contents, etc., may be changed (Noggle 1946). Such changes occur, of course, in auto- as

well as in allopolyploids. Allopolyploids have the gene complements of both parental species, and consequently, have a reaction norm which may be either intermediate between, or a combination of various properties of the parental forms. The combination may possess a high adaptive value, particularly if, as sometimes but by no means always happens, the allopolyploid possesses the environmental tolerances of both parents. Such allopolyploids are, of course, favored by natural selection. There is a considerable literature dealing with geographic regularities in the incidence of polyploids (the work of Tischler 1934, Hagerup 1940, Gustafsson 1948, Löve and Löve 1943, Clausen et al. 1945, Stebbins 1950, and others). It seems to be generally agreed that in the floras of arctic, subarctic, and recently glaciated lands the proportions of polyploid species tend to be greater than in warmer and geologically more ancient lands; unfortunately no data are available on the incidence of polyploidy in the tropics. Since the formation of species through polyploidy is a process incomparably more rapid than the more general process of race divergence, polyploids are likely to be most suitable for colonization of newly opened lands, such as those recently freed from the continental ice sheets (Babcock and Stebbins 1938, Stebbins 1950). Secondly, the floras of high latitudes include many perennial herbs, and relatively few woody species; the incidence of polyploidy among the former is known to be higher than among the latter (see above).

The phylogenetic development is customarily symbolized by a tree, the branching of which represents the differentiation of a group of organisms. A better image would have the trunk and the branches of the phylogenetic tree pictured as cables consisting of numerous strands, and running on the whole parallel to each other but occasionally branching or coming to an end (Anderson 1936). In groups where allopolyploidy is not encountered, the cables will preserve their independence from each other. They may go parallel, or diverge, or converge somewhat, or branch further, but only in rare cases can they coalesce or intertwine where a hybridization of the separate species takes place. The emergence of an allopolyploid signifies that one or several strands have been torn away from two cables, these strands fuse, and presently become subdivided again into a number of new ones, forming a new cable of the polyploid species. Where the species formation through allopolyploidy is frequent, the phylogenetic "tree"

will tend to lose its treelike appearance on account of the fusion of its branches, and will come to resemble, according to the metaphor of Epling (1939), "a gigantic and ragged *Hydrodictyon* floating in time."

RE-CREATION OF NATURAL POLYPLOID SPECIES OF PLANTS

The production of polyploids is the most powerful tool yet available to geneticists for molding living matter into new shapes. This is especially true since Blakeslee and Avery (1937) discovered, and other investigators perfected, techniques for artificial chromosome doubling by the alkaloid colchicine and other chemicals. The creation of a new species, *Raphanobrassica*, in the experiments of Karpechenko has been discussed in Chapter VIII. It should be emphasized that a polyploid species is reproductively isolated from its parents from the moment of its origin. Indeed, the crosses of the tetraploid *Raphanobrassica* to either radish or cabbage give triploid hybrids which are largely sterile on account of meiotic abnormalities (Karpechenko 1927, 1928). The evidence presented above indicates that, at least in some parts of the plant kingdom, polyploidy has been resorted to on a grand scale for the production of species in nature. The almost instantaneous character of the origin of new species through polyploidy makes possible experimental re-creation of naturally existing species from their putative ancestors. The relatively successful attempts to re-create the species of tobacco, cotton, and wheat have also been discussed in Chapter VIII. Some examples in which the experimentally obtained polyploids are virtually identical with existing wild species are presented below.

Six out of the eight species of the mint *Galeopsis* investigated by Müntzing (1930, 1932, 1936) have the haploid number of chromosomes, 8, and the two remaining ones have $n = 16$. Among the former are the species *G. pubescens* and *G. speciosa*, and among the latter is *G. tetrahit*. The cross *pubescens* × *speciosa* gives a highly sterile F_1 hybrid. At meiosis varying numbers of bivalents and univalents are formed. In the F_2 generation a single plant was found that proved to be a triploid ($3n = 24$). Its origin was probably due to the union of a gamete with the somatic complement of the F_1 hybrid (i.e., 8 chromosomes of *pubescens* and a like number from *speciosa*) with a gamete carrying 8 chromosomes, the proportions of the chromosomes

of the two parental species in the latter gamete not being clear. This triploid plant was backcrossed to a pure *pubescens*. A single seed resulted from the backcross. It gave rise to a tetraploid (4n = 32) plant which was fertile, and became the progenitor of a strain named "artificial Tetrahit." The origin of the tetraploid was due to a union of an unreduced gamete of the triploid with a normal one of *G. pubescens*.

The hybrids between *G. pubescens* and *G. speciosa* exhibit a striking resemblance to *G. tetrahit*. The latter species has however taken no part in the production of these hybrids. The resemblance, which according to Müntzing reaches in some individuals an apparent identity, suggests that the true *G. tetrahit* arose as an allotetraploid from the cross *G. pubescens* × *G. speciosa*, or types similar to these species. The artificial *tetrahit* is like the real *Galeopsis tetrahit* in possessing 32 chromosomes in somatic cells and 16 bivalents at meiosis. The meiotic divisions are, with few exceptions, normal. A cross between the artificial and the natural *tetrahit* gives normal offspring which are externally similar to either parents. The fertility is complete in some individuals, while others are partially sterile; it must be taken into consideration that a partial sterility has been observed by Müntzing in some lines of the pure *G. tetrahit* as well. The meiotic divisions are normal; 16 bivalents are formed which undergo a regular disjunction. In short, the artificial and the natural *G. tetrahit* are similar both morphologically and in their genetic and cytological behavior.

An even more clear-cut case is the synthesis of the species *Madia citrigracilis* from *M. gracilis* and *M. citriodora* by Clausen et al. (1945). *M. citrigracilis* was at first considered a race of *M. gracilis*, but the existence between them of reproductive isolation became evident with the discovery that the former species has the gametic chromosome number n = 24 and the latter n = 16. *M. citriodora* has n = 8. The cross *M. citriodora* × *M. gracilis* produces a highly sterile triploid hybrid with 24 chromosomes in its somatic cells and almost no bivalent formation at meiosis. Artificial doubling of the chromosome complement gave rise to a hexaploid hybrid which resembled closely *M. citrigracilis*, formed 24 bivalents at meiosis, and was fertile. In turn, *M. gracilis* is presumed to be an allotetraploid hybrid between unknown diploid species, each of which has contributed a set of 8 chromosomes.

The genus *Brassica* (cabbage, field mustard) contains, among others, the following species with the gametic chromosome numbers as shown:

B. nigra	(n = 8)	*B. carinata*	(n = 17)
B. oleracea	(n = 9)	*B. juncea*	(n = 18)
B. campestris	(n = 10)	*B. napus*	(n = 19)

Frandsen (1943, 1947) has shown experimentally that *B. carinata* may be re-created from hybrids of *B. nigra* and *B. oleracea* (8+9 =17), *B. juncea* from *B. nigra* and *B. campestris* (8+10=18), and *B. napus* from *B. oleracea* and *B. campestris* (9+10=19). For further examples of synthesis of natural allopolyploid species, as well as for instances in which the putative parents of natural species can be identified with a reasonable degree of certainty, see Stebbins (1950).

POLYPLOIDY IN ANIMALS AND IN DIOECIOUS PLANTS

The prevalence of polyploids among plants and their relative scarcity among animals is the most striking known difference between the evolutionary patterns in the two kingdoms. Muller (1925) surmised that this difference is correlated with a preponderance of hermaphroditism (monoecy) among plants, and the separation of sexes (dioecy) among animals. Where the sex of an individual is determined by a mechanism like that known to exist in *Drosophila*, polyploidy may result in the production of intersexes and other abnormal and sterile types. In *Drosophila*, the X chromosome is female-determining, while the autosomes carry an excess of male-determining genes. Zygotes which carry equal numbers of X chromosomes and sets of autosomes develop into haploid, diploid, triploid, tetraploid, etc., females. When X chromosomes are only half as numerous as sets of autosomes the result is a male; diploid, tetraploid, hexaploid, etc. males are possible. But if the ratio of the numbers of X chromosomes and of sets of autosomes is intermediate between that found in females (1 : 1) and that in males (1 : 2), the result is a sterile intersex. Imagine, then, the appearance in a natural population of a tetraploid mutant female, or of a tetraploid male. Such mutants will almost certainly cross to normal diploid individuals of

the opposite sex, and their offspring will probably consist of triploid females and of intersexes.

Muller's argument has lost much of its force with the discovery by Warmke and Blakeslee (1940) and by Westergaard (1940, 1948) that in the dioecious plant *Melandrium album* the male-determining genes lie mainly in the Y, and the female determiners in the X chromosome; the autosomes have only a slight effect, if any, on sex. Tetraploid females and males were obtained with the aid of colchicine and heat treatments. When tetraploid males are crossed to diploid females, they give mostly triploid individuals, with three sets of autosomes, two X chromosomes, and one Y chromosome. These individuals are, however, not intersexes as they would be in *Drosophila* but somatically normal and fertile males, although they occasionally produce some functional hermaphroditic flowers. It may be noted that, in *Melandrium*, diploid individuals with an extra Y chromosome (XXY individuals) are self-fertile hermaphrodites, not females, as they are in *Drosophila*.

Polyploidy as a method of species formation occurs commonly only in self-fertile hermaphrodites (as most plants), or in organisms which reproduce by parthenogenesis. This is manifestly not because chromosome reduplication is a rare form of mutation in dioecious forms. Fankhauser (1938, 1939, 1945) found 4 triploids among 100 examined larvae of the newt *Triturus viridescens*, and 13 triploids and 2 tetraploids among 134 larvae of the salamander *Eurycea bislineata*. Nevertheless, no polyploid races of these species are known. In contrast to this, among the 17 parthenogenetic species of weevils (Curculionidae) examined by Suomalainen (1940a and b, 1945, 1947), only one is diploid, eleven are triploid, four tetraploid, and one is pentaploid. A single meiotic division takes place in the eggs of these beetles, at which the chromosomes divide equationally, whereupon the eggs develop without fertilization. All the related bisexual species that were examined proved to be diploid, and to have normal meiosis in both sexes. When diploid (bisexual) and triploid (parthenogenetic) races are present in the same species, the former tend to occur in territories that were not covered by the Pleistocene ice sheets, and the latter in the areas which underwent glaciation (Suomalainen 1947). A similar correlation between the glacial history of a territory and the presence in it of parthenogenetic polyploid

races of otherwise bisexual diploid insects has also been found by Seiler (1946, 1947). Further examples of diploid bisexual and polyploid parthenogenetic strains are known in the moth *Solenobia triquetrella*, the sow bug *Trichoniscus elisabethae*, the shrimp *Artemia salina*, the ostracod *Heterocypris incongruens*, and in certain other invertebrates. The pertinent literature has been lucidly and exhaustively reviewed by Suomalainen (1950).

The opinion that polyploidy has played an appreciable role in the phylogeny of some dioecious and obligatorily cross-fertilizing forms is revived from time to time in the literature. Large variations in the chromosome numbers found in related organisms make the hypothesis of polyploidy appear attractive. For example, Svärdson (1945) has found species with somatic chromosome numbers, 58, 60, 80, 84, and 102 among salmonid fishes. He believes, then, that these forms are descended from ancestors which had 10 chromosomes as the basic number. If so, the modern representatives are hexaploid, octaploid, or decaploid. Some authors went so far as to suggest that the eutherian mammals are old polyploids, since their chromosome numbers (24 to 86) are higher than those of the marsupials (12 to 28). White (1945, 1946) and Mathey (1949) have justly pointed out that the chromosome numbers recorded in these groups are not usually exact multiples of any particular basic number, and the supposed basic numbers are hypothetical and not actually observed in any living species. Moreover, processes of translocation which can change the chromosome numbers are well known, making the hypothesis of polyploidy superfluous. Perhaps the only bisexual group of animals in which the polyploidy is established beyond reasonable doubt are certain earwigs, Dermaptera (Bauer 1947).

MUTATION IN POLYPLOIDS AND THE ORIGIN OF NEW GENES

Whether a species is an auto- or an allopolyploid, it has at least a part of its genes represented more than twice in the somatic cells and more than once in the gametes. Thus, an einkorn wheat is A^1A^1, an emmer $A^1A^1A^2A^2$, and a bread wheat $A^1A^1A^2A^2A^3A^3$, where A^1, A^2, and A^3 are the alleles of the same gene located in the different semihomologous sets of chromosomes. A mutation from A to a recessive allele a can easily manifest itself in the einkorn wheat, since a heterozygote A^1a^1 will produce on inbreeding one quarter of the offspring

homozygous for $a^1(a^1a^1)$. A similar mutation in an emmer wheat will not be detectable. An individual $a^1a^1A^2A^2$, despite being homozygous for a^1, carries two dominant alleles A^2 which suppress the effects of a^1. The same argument is applicable *a fortiori* to the hexaploid *vulgare* wheats. The manifestation of recessive mutant genes in the emmer and *vulgare* wheats becomes possible only if similar mutations take place in the two or three chromosome sets.

The mutation frequencies in related species with different chromosome numbers have been compared by Stadler (1929, 1932). The diploid oats *Avena brevis* and *A. strigosa* (n=7) and the hexaploid *A. byzantina* and *A. sativa* (n=21) were given similar amounts of X-ray treatments. Fourteen recessive mutations were obtained in the former and none in the latter in approximately equally large samples. The experiments with wheat species gave comparable results. Stadler expresses the mutation frequency in terms of the number of mutations obtained per unit of the X-ray treatment (r-unit). The resulting figures are 10.4×10^{-6} for the diploid *Triticum monococcum*, 2.0×10^{-6} and 1.9×10^{-6} for the tetraploids *T. dicoccum* and *T. durum*, respectively. No mutations were obtained in the hexaploid *T. vulgare*. In diploid species, deleterious mutations are kept down in frequency by natural selection. In a polyploid, an unfavorable recessive mutation, even a lethal or a gene deficiency, is "sheltered" from natural selection by the presence of normal alleles in the other chromosome sets. Only dominant mutations, or such recessives as have appeared in all the chromosome sets, can be kept under control by selection.

Hutchinson et al. (1947) have, however, pointed out that polyploids may show actually a greater variety of phenotypes than diploids with respect to the dominants and some semidominant genes. A diploid may carry either one or two dominant alleles, while genotypes with one, two, three, and four dominants may be formed in a tetraploid. Since genetic changes which affect polygenic traits are usually neither dominant nor recessive, Hutchinson et al. are of the opinion that "the evolutionary potentialities of a young polyploid will rapidly approach those of a diploid." The sheltering of the destructive recessive mutations produces, however, at least a temporary effect which is virtually equivalent to a sharp reduction of the mutation rates. This drying up of a major source of variability is bound to

have profound effects on the evolutionary perspectives of a polyploid species. In the opinion of Stebbins (1940, 1950) "polyploidy is a 'short cut' by which a species or a genus may adapt itself easily to a rapidly changing environment," and "in every example in which its immediate effects have been analyzable, polyploidy has appeared as a complicating force, producing innumerable variations on old themes, but not originating any major new departures."

Harland (1936) and others have put forward the suggestion that the initially homologous genes lying in the different chromosome sets will mutate in different directions, and will gradually become so distinct as to be no longer allelic. Such a differentiation eventually transforms a polyploid into a species that has most genes represented only once in the gametes and twice in the zygotes, and thus in effect restores the diploid status despite the altered chromosome numbers. Polyploidy is thus a mechanism whereby both the gene number and the gene variety are increased.

It must be emphasized that the phenomena of gene duplication are not restricted to polyploids. Some genes and blocks of genes are carried in duplicate, or even in triplicate, in the haploid chromosome complements. Such "repeats" are known cytologically in *Drosophila* and in *Sciara*, which are not suspected of being either recent or ancient polyploids (cf. Chapter II). An opportunity for a gradual divergence of the reduplicated genes thus exists also in diploids. This is clearly a process of major importance, since the formation of new genes in evolution can be visualized only through radical modification of preexisting ones. Otherwise one would have to postulate recurrent spontaneous generation of life from inert matter. Unfortunately, little is known about the kinds of mutational changes which transform allelic genes into non-allelic ones. Significant findings, which may shed light on this difficult problem, have been made in recent years through the discovery of the so-called "partial alleles" or "semi-allelic" genes. Partial alleles are known, or suspected, to exist in organisms as diverse as *Drosophila* (Lewis 1945, Bonnier et al. 1947, Green and Green 1949), maize (Stadler 1946, Laughnan 1948, 1949), mice (Dunn and Caspari 1945, Dunn and Schoenheimer 1950), cotton (Stephens 1948), *Harmonia* beetles (Tan 1946a), and perhaps man (Fisher 1947, Komai 1950). In all these cases one is dealing with absolutely or very closely linked genes, which produce

by mutation series of variants which behave in a manner resembling multiple alleles of a single locus. The decision whether one deals in these cases with single complex genes or with groups of very similar genes is often ambiguous or a matter of contention. This ambiguity is, however, very suggestive in itself of distinct but related units in the chromosome caught in the process of differentiation.

INTROGRESSIVE HYBRIDIZATION

The conflict between sexual reproduction on one hand and reproductive isolating mechanisms on the other has repeatedly been pointed out in the foregoing chapters. The biological function of sexual reproduction is formation of an immense variety of genotypes, some of which prove to be adaptively valuable and are established by natural selection. Conversely, reproductive isolation prevents the gene exchange between populations which occupy different adaptive peaks. In so doing, reproductive isolation prevents the appearance of great masses of disharmonious gene patterns, and thus preserves the integrity of the historically evolved arrays of genotypes which are the existing species. The conflict is resolved by a compromise. The freedom of the gene exchange between Mendelian populations is so regulated by natural selection that adaptive plasticity is preserved at the price of destruction and elimination of the smallest possible numbers of ill-adapted individuals. Reproductive isolation between diverging species may not become absolute if an occasional gene exchange between their populations confers adaptive versatility on these species. It is, consequently, not surprising that we find the reproductive isolation between closely related species varying in rigidity in different groups of organisms. The genetic rift between species of *Drosophila* is usually absolute; the gene exchange between species in many plant genera is frequent enough to be easily detected.

Numerous species hybrids recorded in the botanical literature were used by Lotsy (1916) as the foundation of his theory of evolution by hybridization. According to this theory, mutation does not occur or is unimportant, and evolutionary changes arise owing to recombination of a finite number of preexisting gene alleles. This theory stands as a warning to scientists not to succumb to the temptation of imputing universality to their special discoveries. Du Rietz (1930), Camp (1944, 1945) and others have recorded many instances of

"hybrid swarms" formed in territories where the geographic areas of certain plant species meet and overlap. Among recent authors, Anderson (1949) has ascribed the greatest evolutionary significance to introgressive hybridization, which is a term coined by Anderson and Hubricht (1938) for infiltration of genes of one species into the gene pool of another. Stebbins (1950) has given a balanced and moderate account of the occurrence and importance of species hybridization and introgression.

An excellent example of introgression has been described by Riley (1938) in the populations of *Iris fulva* and *Iris hexagona* var. *gigantocaerulea* which inhabit the Mississippi Delta region. The former species grows by preference on clay soils and in partial shade, while the latter prefers the tidal marshes and full sun. This ecological isolation has suffered a breakdown owing to the destruction of the forests and the drainage of the swamps for pastures. It is especially in such man-made habitats that hybrids between these *Iris* species are found; the F_1 hybrids are partially sterile, but backcrosses to the parental species occur, giving rise to numerous populations of *I. hexagona* which carry genes derived from *I. fulva*. Heiser (1947) has described an equally striking case of introgression in the sunflowers *Helianthus annuus*, *H. bolanderi*, and *H. petiolaris*. Abundant sunflower populations now exist as weeds growing on disturbed soils. These populations very often show signs of origin by hybridization of two or more wild ancestral species. For a review of other instances of introgression see Stebbins 1950.

Wiegand (1935), Anderson (1949), and others have pointed out that introgressive hybridization is observed most frequently in habitats modified by man, and in plants that are weeds or are otherwise associated with man. Now, man creates extensive new habitats in all parts of the world. The sudden appearance of these new habitats has the consequences, first, of breaking down the ecological isolation between many species, and, secondly, of putting a prize on the ability to undergo adaptive genetic changes quickly. Adaptive changes involve substitution of some gene alleles, or chromosome structures, for others. Such substitutions may occur within a species by mutation. But if the adaptively valuable alleles are readily available in a related sympatric species, they may be acquired even more easily by hybridization with the latter. It has been pointed out in

Chapter VII that one of the very few securely established cases of introgressive hybridization in animals, namely that described by Blair (1941) in species of toads, occurs chiefly in man-modified territories.

There is hardly any doubt that introgressive hybridization is not completely confined to man-modified environments, but it is difficult to decide how widespread it may prove to be. The existing data are both scanty and often uncritically collected. Suppose that one finds that the populations of a species A show certain characteristics of a species B in regions where both species are sympatric. This resemblance may be due to parallel selection of similar gene alleles by similar environments, or it may be due to introgression. Of course, the hypothesis of introgression becomes more probable if groups of traits not due to manifold effects, rather than a single trait or small groups of them, are involved (Anderson 1949, Stebbins 1950). More important still is the necessity to distinguish between what Mayr (1942) has called primary and secondary intergradation. Allopatric populations, races, of the same species are often connected by geographic gradients in phenotypic traits and in gene frequencies (Chapters V and VI). This is primary intergradation. On the other hand, reproductively isolated populations, species, may show some gene exchange when they become sympatric and their reproductive isolation proves to be incomplete. This is secondary intergradation or introgression. Applying the term introgression to primary intergradation would make this term meaningless.

Excellent examples of primary intergradation are the transition zones between the human races. Extensive and very carefully collected data on geographic gradients in traits which distinguish the subspecies of the butterfly weed, *Asclepias tuberosa*, in the southeastern and central United States have been reported by Woodson (1947). There is, however, nothing in these data as published to show that the situation in the butterfly weed is different from that in the human species. On the other hand, Sweadner (1937) has described the species and subspecies of the moth *Platysamia* in North America. This seems to be a typical "borderline case" of uncompleted speciation (cf. Chapter IX), but the occurrence in nature of hybrids between populations which are known to be partly isolated reproductively suggests an introgressive hybridization.

Although much remains to be learned about the frequency of introgressive hybridization, it seems to be more prevalent among plants than among animals. Its incidence varies also in different groups of plants. Stebbins (1950) has advanced some brilliant working hypotheses that may explain these variations. He points out that the length of life of an individual is, by and large, greater in plants than in animals. In many plants which are capable of vegetative reproduction an individual, or a clone, may exist for hundreds, or even thousands, of years. In such forms the maintenance and the spreading capacity of the populations are guaranteed largely through asexual means, and sexual reproduction, by seeds, serves chiefly to maintain the evolutionary plasticity. Wide hybridization and production of diversified genotypes in the seeds are expected to be more frequent in such plants than in animals, in which the maintenance of the species is entirely dependent on cross-fertilization. The open system of growth and the relative simplicity of the plant tissues, as contrasted with the closed system of growth and the great complexity of the tissues and the organ systems in animals, are also important. The adaptive value of the genotype in an animal is likely to depend upon the entire constellation of genes, as an integrated whole, while in plants the genes may affect the fitness more nearly independently of each other. Hybridization of species, is, then, less likely to lead to formation of valuable gene recombination products in animals than in plants. Indeed, the rigidity of reproductive isolation between animal species tends to be greater than between plant species.

RETROGRESSION OF SEXUALITY

The appearance of sexual reproduction was perhaps the most important advance in the evolution of life. This advance has made other evolutionary advances more easily accessible. And yet, the sexuality has been permitted in some phylogenetic lines, especially in the plant kingdom, to degenerate to the point where its basic evolutionary function is lost. Moreover, this retrogression has taken place in a variety of ways.

The simplest form of retrogression of sexuality is self-fertilization. The outward appearance of sexual reproduction is retained, the chromosome cycle is normal, functional gametes are formed, but a union of gametes of a single hermaphrodite individual, instead of the

fusion of gametes produced by different individuals, takes place. The danger of self-fertilization is inherent in hermaphroditism, and many hermaphrodites have developed various devices to prevent selfing: separation of female and male sexual ducts, flower structure making self-pollination difficult or impossible, gametes of one sex maturing earlier than those of the other, and, finally, genic self-sterility. Nevertheless, some hermaphrodites reproduce facultatively or obligatorily through self-fertilization. Facultative selfing, if it occurs rarely, has the same effect on a population as an occasional close inbreeding: homozygotes become more frequent than they would be under random mating, recessive genes with deleterious effects are eliminated more rapidly, and the supply of the hereditary variability is somewhat reduced in local populations. On the whole, the breeding structrue is not materially different from that obtaining under panmixia. If, however, self-fertilization becomes the predominant or the only method of reproduction, populations of a species consist mostly of homozygotes. Mutations, whether dominant or recessive, manifest themselves in the phenotype soon after their origin, and those among them that are deleterious in the given genetic or secular environment are eliminated. If the effects of a mutation are favorable, the new type will successfully compete with the old ones. The formation of favorable gene combinations is, however, made difficult, for this requires the occurrence of a series of mutations in the same line of descent. If each mutation is favorable *per se*, the task may be accomplished at the expense of a great loss of time; otherwise the potentially possible evolutionary change may never become realized. Obligatory or habitual selfing robs the species of evolutionary plasticity, transforming it into a complex of genetically homogeneous strains (pure lines) which do not exchange their genes.

Apomixis is a common name for several methods of procreation in which the sexual structures (sexual ducts, genitalia, flowers) may be retained, but in which development is initiated without fertilization. Where the specialized reproductive cells—eggs in animals and macrospores in plants—give rise to the embryo, we are dealing with parthenogenesis. Diploid parthenogenesis, in which the reproductive cells contain the diploid chromosome complement, is most frequent. In plants the sporophyte may arise without fertilization from a vegetative cell of the gametophyte (apogamy), or the gametophyte may

develop from a cell other than a spore (apospory), or from somatic cells of the nucellus (nucellar embryogony). Apomixis and related phenomena have been reviewed very adequately by White (1945) for animals and by Gustafsson (1946b, 1947b) and Stebbins (1950) for plants.

The point which is important for us here is that the meiotic chromosome pairing in most apomicts is suppressed; the eggs come to possess the same chromosome complement which is present in the mother, and therefore the genotype of the entire progeny resembles that of the progenitor. Binary fission, procreation through adventitious buds, sprouts, stolons, bulbs, and other forms of asexual reproduction are in this respect analogous to apomixis. Apomixis and asexual reproduction, like self-fertilization, eventually lead to formation of groups of individuals having identical genotypes and not exchanging genes with other similar groups; such groups are termed clones. But in another respect the effects of apomixis and asexual reproduction are the antithesis of self-fertilization. Prolonged selfing may give rise to a virtually completely homozygous pure line; apomictic or asexual clones retain whatever heterozygosis may be present in their ancestors.

In many protozoans, coelenterates, some worms, crustaceans (Cladocera), insects (aphids and others), and in certain plants, sexually reproducing generations alternate more or less regularly with asexual or diploid parthenogenetic generations. In many other plants, sexual, apomictic, and asexual reproduction are facultative and occur side by side. So long as cross-fertilization takes place not too infrequently in the pedigree of any given strain composing the species, the evolutionary situation remains rather similar to that in purely cross-fertilizing forms. Omission of the sexual process in some generations entails a certain loss of the opportunity to form novel gene patterns; the patterns that have been formed are, however, multiplied and thoroughly tested by natural selection before they are returned to the melting pot of sexual reproduction (cf. Banta and Wood 1939). The species remains a unit, since all strains composing it are at least potentially capable of exchanging genes with each other.

Where apomixis or asexual reproduction are the rule, very peculiar evolutionary situations may be created. Many genetic conditions that are known to arise by mutation in the wide sense of that term can-

not become established with cross-fertilization. Here belong polyploids with odd numbers of chromosome complements (triploids, pentaploids, etc.) which cannot breed true sexually, owing to the impossibility of forming only bivalents and no univalents at meiosis. Autopolyploids and allopolyploids coming from hybridization between closely related species may have even numbers of chromosome sets, and yet variable multivalent associations at meiosis may lead to production of gametes with various deviations from the standard chromosome number. Reduplications and losses of certain chromosomes of a single set may give rise to aneuploids, monosomics, and polysomics; individuals carrying such chromosome complements, if reproducing sexually, form more than one type of gametes, and a segregation is observed in their offspring. Nevertheless, such unbalanced chromosome complements may create reaction norms which are favorable in certain environments. Retention and fixation of an inherently unstable chromosomal or genic condition is a problem the solution of which is difficult with sexual reproduction; apomixis and asexuality offer, according to Darlington's (1939) figure of speech, an "escape". This escape has, indeed, been made use of by many plants and by some animal species.

There can be no doubt that some apomictic and asexual types are successful in the struggle for existence: in some plant genera, diploid species occur as relics while larger territories are populated by swarms of apomicts. Each apomictic type taken separately displays, however, a limited individual variability and appears narrowly specialized to fit a certain restricted environment. According to Babcock and Stebbins (1938), "An agamic complex is a 'closed system', whose ultimate fate is bound up in the fate of its sexual members. It can give rise to nothing new, and can keep abreast of changing conditions only through the activity of the latter forms." Retrogression of sexuality is a striking example of evolutionary opportunism, an escape, according to Darlington, in a phylogenetic blind alley.

BIOLOGICAL AND CULTURAL VARIABLES OF HUMAN EVOLUTION

Ostensibly there is a basic clash in human nature. Mankind is a biological species which belongs to the animal kingdom. But man is also the creator and the creature of his society and of his cultural heritage. And, finally, the inspiration of the mystics sees man in still

a third light—that of the Son of God. The intellectual history of mankind can be written in terms of shifting emphasis on one or the other of these aspects of the human nature. And the history of human error could well be portrayed in terms of attempts to understand everything, instead of something, about man by investigation of only one of these aspects to the exclusion of the others. In particular, the study of human evolution has often been handicapped by this purblindness. Darwin's affirmation that man is a part of nature seemed to many of his contemporaries, and still seems to some misguided souls, downright blasphemy. Ninety years after the publication of the *Origin of Species* a school of dialectical materialism has proclaimed a dogma that considering man a biological species "degrades him to the level of beasts." To this nonsense, some thoughtless biologists replied in kind by the asseveration that man is "nothing but an ape with a few extra tricks." This is not merely bad biology but a dangerous deceit, which has become the pseudo-scientific foundation of the vicious obsession of racialism. It is a demonstrable fact that human biology and human culture are parts of a single system, unique and unprecedented in the history of life. Human evolution cannot be understood except as a result of interaction of biological and of social variables. The only known processes which could have transformed the genotype of the pre-human apelike animal into the present human genetic endowment are mutations, sexual reproduction, natural selection, genetic drift, geographic isolation, and social regulation of marriage. And it is evidently the human genetic endowment which has made, and is making, possible the development of culture. Apes, monkeys, and other animals are genetically incapable of using symbols and hence of assimilating human culture. The substitution of a single gene allele in an otherwise "normal" human genotype may result in an idiot wholly unable to perform the functions expected in any human society. Human genetics has not been superseded by human culture; the former remains the foundation which enables man to manifest the kinds of behavior which are called social and cultural. An insight into the workings of the human genotype, and of the human gene pool, are indispensable for understanding man.

The interrelationships between biology and culture are, however, reciprocal. Social life, and especially the development of civilizations,

have influenced the evolutionary patterns of the human species so decisively that human biology is incomprehensible apart from the human frame of reference. The ancestors of the human species have gradually evolved a highly developed brain. The human brain proved to be an adaptive mechanism of matchless power and efficiency. With the aid of this mechanism man has gained a mastery of the environments on earth never before even approached by any species. This biological adaptation has determined, and doubtless will continue to determine, all subsequent evolutionary history of the human species.

Despite the numerous specific and generic names scattered over the literature dealing with fossil man, all the available evidence is consistent with the view that at any one time level mankind represented always one and only one species (Weidenreich 1946, Dobzhansky 1944a, Mayr 1951). Mankind was and is an organic entity, a system of Mendelian populations integrated by the bonds of descent and of intermarriage. But this system has reached a singular degree of complexity in the human species. The gene exchange between races of a sexual and cross-fertilizing species is normally limited by distance or by geographic barriers. Races are allopatric populations. In man, the marriage regulation by social customs has made possible at least a temporary sympatric existence of races. Races of sexually reproducing animals and plants usually form a single geographic hierarchy culminating in the species. Mankind contains several overlapping hierarchies of Mendelian populations, conditioned by geographic, linguistic, religious, national, economic, and occupational variables.

The importance of geography in the restriction of the gene exchange between populations is evident, even in the era of motorships and airplanes. But it is also evident that the probability of marriage is influenced by the ability to speak the same language, and by belonging to the same religious denomination, or the same economic or occupational group. The basic racial differentiation of the human species is, as in other biological species, geographic. This differentiation arose long ago, possibly still on the prehuman, or the subhuman, level. It is undoubtedly adaptive, and owes its origin to natural selection in different geographic environments. Nevertheless, next to nothing is known with certainty about the adaptive significance of the racial traits in man. Classical anthropologists assumed

that racial traits are adaptively neutral, and some of them even made this assumption a part of their definitions of race (for examples see Count 1950). Medical science also gave little attention to the physiological consequences of the human genetic variability outside the realm of pure pathology. It is no overstatement to say that the progress in the understanding of the mechanisms of human evolution will depend on the investigation of the adaptive values of the race differentials. Some working hypotheses which will be useful in such investigations may be found in the remarkable book of Coon et al. (1950). Are the relatively short trunks and extremities which characterize the body build of many people in the Arctic regions adaptive in cold climates? Are the tall, slender bodies and the long extremities of the inhabitants of some hot deserts adaptive because of the great body surface in relation to the body bulk? Is the Mongoloid face with its abundant fat "padding" adaptive in the continental climates of the interior of Asia? Is it possible that these traits are neutral in the environments provided by the industrial civilization, but that they were important for the survival under primitive conditions?

The genetic connotations of the social barriers to the gene flow between human populations are also far from understood. Although in the primitive societies bachelors and spinsters are rare, and all sexually mature individuals are potential parents, little is known about the possible differential fertility of individuals in different social situations. More important still is the problem of the genetic differentiation of social groups in civilized societies. History records many cases in which the descendants of foreign conquerors formed the upper classes, and the conquered natives the lower classes of a society. Different trades and professions may also be monopolized by people of different geographic origin, and hence with different gene pools. If the gene exchange between the classes or professional groups is limited by any social factors, these classes and groups may exist for a time as sympatric Mendelian populations. The castes of India are the most extreme examples in recorded history of the retention of genetic differences between sympatric populations. And yet, even in India there has been enough diffusion of genes between the gene pools of the different castes to cause a gradual genetic convergence. An aristocracy very often becomes a group of people with

foreign sounding names but with a gene pool similar to that of the plebeians.

It has frequently been suggested that a genetic difference between social classes may arise through natural selection within a society. The full implications of such an hypothesis of sympatric race differentiation are, however, not always realized. The basis of this hypothesis is, of course, the unproven assumption that the qualities which make persons fit for the occupation of different social positions are genetically determined. Even if this be taken for granted, the consequences are by no means simple. In aristocratic societies, the social position is inherited regardless of the personal merits or weaknesses of the heirs. The gene segregation causes, however, variations in the genetic endowments of members of the same family. This being the case, the aristocratic social organization could, at most, perpetuate for a time the genetic differences present at the inception of the social stratification.

The situation will, of course, be different in societies which allow an equality of opportunity to their members. Here an individual is free to become a member of a class, group, or a profession for which he is best fitted by his genotype, and regardless of the social stations occupied by his parents and relatives. Suppose that such a faultless choice should occur. The profession of musicians will then include all individuals whose genetic endowments make them good musicians, and the profession of farmers will claim all good agriculturists. The social structure will, then, accurately reflect the genetic variability present in the gene pool of the population. Persons genetically endowed to be musicians do not constitute, however, a Mendelian population, just as persons who belong to the O, or to the A, blood groups do not constitute such populations. Occupational groups in a society with a perfect equality of opportunity would not be genetic entities; they would be social categories.[1]

In reality, the social position of an individual is determined in all existing societies partly by the merit of the individual himself and partly by the station occupied by his parents or relatives. An indi-

[1]Such groups could become Mendelian populations only in the absence of intermarriage between the groups, and only provided that they would be uniformly homozygous for the genes which determine the group membership. This certainly does not occur in any human society.

vidual may move up to a more privileged station by overcoming a greater or lesser resistance of a class barrier. The degradation to the less privileged situations is slowed down by the accident of birth in a higher stratum. Social and occupational groups may, then, temporarily differ in their genetic endowments, but it is extremely doubtful that these differences could ever become integrated and crystallized into anything resembling biological race differentials.

The critical problem is, of course, to what extent the social fitness of an individual is determined by his genetic endowment (pathological cases, of course, excluded). The adaptation to the environment is achieved in animals and in plants by changing their genotypes; man alone responds to the challenges of the environment chiefly through discovery, invention, and the forms of behavior which constitute culture. Now, cultural evolution is a process which is vastly more rapid and more efficient than biological evolution. A valuable gene can be transmitted only to some of the descendants of the individual in which it has first appeared, and it can displace and supplant other genes only by the slow process of outbreeding them. A scientific discovery or a technological invention can be transmitted to any number of contemporary individuals, and, since the invention of writing, it can be communicated to the future generations regardless of the parentage bonds. We can "inherit" the wisdom of our intellectual "ancestors" who died, thousands of years ago, or who live anywhere in the world and are unaware of our existence.

Because the social and cultural attainments proved to confer on man unrivaled adaptive advantages in most diverse environments, the capacity to acquire and to transmit cultural traits became selectively very important in the human species. The fitness of individuals and populations is to a considerable extent determined by their educability, i.e., by the aptitude to learn from experience and to modify one's behavior accordingly (Dobzhansky and Ashley Montagu 1947, Dobzhansky 1950e). The educability has had, and continues to have, a high adaptive value in all human cultures, from the most primitive to the most highly advanced ones. It has given to all normal human beings the capacity to acquire any one of the existing cultural patterns. And yet, the genetically conditioned educability favors diversity of human personalities and cultures. Indeed, students of culture are in substantial agreement that the interper-

sonal relationships established in a given culture are the most important determinants of individual's personality (see, for example, Kluckhohn and Murray 1949). Since these relationships are highly variable, the more so the more advanced becomes a culture, an endless diversity of human personalities is the outcome. The biological meaning of the diversity among humans, like that of the organic diversity on the biological level, is adaptation to the variety of the environments which the organism encounters or creates. The evolution of life has only one discernible goal, and that is life itself.

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A.N.—American Naturalist
B.Z.—Biologisches Zentralblatt
B.Zh.—Biologichesky Zhurnal (Moscow)
C.—Cytologia
E.—Evolution
G.—Genetics
Hs.—Hereditas
Hy.—Heredity
J.E.Z.—Journal of Experimental Zoology
J.G.—Journal of Genetics
J.H.—Journal of Heredity
P.N.A.S.—Proceedings of the National Academy of Sciences
S.—Science
U. Texas P.—University of Texas Publications
Z.i.A.V.—Zeitschrift für induktive Abstammungs-und Vererbungslehre

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INDEX

INDEX

Aberrations, chromosomal, 28–29; produced by mustard compounds, 43
Achatinella, 170
Achatinella mustellina, 170
Adalia bipunctata: cyclic seasonal changes in, 130
Adaptation: diversity in relation to, 3–4; natural selection in relation to, 77; of animal races, 148–52; of plant races, 145-48
Adaptively neutral traits, 155–58
"Adaptive peaks" in gene combinations, 9 (*fig.*), 255, 276 ff.
"Adaptive valleys" in gene combinations, 9 (*fig.*), 255, 277
Adaptive value: concept, 77–79; environmental modification of, 82–86; of chromosomal forms to environment, 115–16
Aegilops, 251 f.
Aegilops squarrosa, 252
Agamic complex, 303
Agamospecies, 275
Agrilus, 246
Akdik, S., 70
Allee, W. C., 15, 78, 109, 165, 182, 205, 260, 263, 269, 271, 285
Alleles, partial, 296–97
Allelism, 174, 176
Allen's rule, 153, 154
Allium: chromosome breakage in, 40
Allopatric organisms, 135–36
Allopatric theory of species formation, 204–6
Allopolyploidy, 18, 287, 288, 289
Allosyndesis, 250
Alopecurus myosuroides, 70
Altschuler, V., 83
Amadon, D., 282
Anangenesis, 283
Anas, 219
Anderson, E., 20, 289, 298, 299
Anderson, E. H., 88
Andersson, E., 215
Aneuploids, 303
Animal populations: historical changes in composition, 94–97
Anopheles atroparvus, 268
Anopheles culicifacies: dispersion rates, 168
Anopheles labranchiae, 268
Anopheles maculipennis, 268
Anopheles messeae, 268
Anopheles sacharovi, 268
Anopheles subalpinus, 268
Antirrhinum majus, 86, 103; mutations, 27
Aonidiella aurantii: distribution of resistant and nonresistant races, 94 (*fig.*), 94–95
Aphids, 302
Apogamy, 92, 273 f., 301
Apomixis, 301, 302
Apomotis cyanellus, 103
Apospory, 302
Arctostaphylos mariposa, 183
Arctostaphylos patula, 183
Aristogenesis, 17
Aristotle's system of classification, 256
Artemia salina, 294
Asclepias tuberosa, 299
Asexual reproduction, 92, 273 f., 301, 302
Ashley-Montagu, M. F., 79, 308
Asiatic beetle: geographic distribution of color patterns, 142 (*tab.*), 143 (*fig.*)
Aspergillus, 43
Atteck, O. M., 104
Auerbach, Ch., 43
Autopolyploidy, 287, 288
Autosyndesis, 250
Avena brevis, 295
Avena byzantina, 295
Avena sativa, 295
Avena strigosa, 295
Avery, A. G., 290
Avery, O. T., 46, 48
Avery, Priscilla, 235

Babcock, E. B., 235, 275, 289, 303
Babers, F. H., 95
Bacteria: resistance to bacteriophage, 87–88
Bacteriophage, 87, 88
Baker, W., 187, 201
Baldi, E., 166
Baldwin, J. T., Jr., 288
Baluzac, John, 64
Banana, 287
Banta, A. M., 83, 302
Bar eye, mutant, 25

Barigozzi, C., 30
Barley, 94
Bateman, A. J., 187, 188
Bates, Marston, 168, 186, 263, 268
Batesian mimicry, 102
Bateson, W., 259
Bauer, H., 110, 124, 143, 233, 245, 263, 294
Baur, E., 27, 274
Beadle, G. W., 30, 213, 224; work on metabolism in *Neurospora*, 13
Beale, G. H., 45
Beasley, J. O., 251
Beatty, R. A., 215
Beetle, 246; variations in Mediterranean species of *Carabus*, 153; *see also* Asiatic beetle; Ladybird beetle
Berg, R. L., 60, 215
Bergmann's rule, 153
Bergner, A. D., 127, 233
Berry, R. O., 193
Bertani, G., 44
Binomial square law, *see* Hardy-Weinberg law
Biological species, 261, 263–65, 267
Birch, L. C., 269
Birds: differences between races in various climates, 153; species known, 6; territoriality, 166
Birdsell, J. B., 140, 171
Biscutella laevigata: distribution of diploids and tetraploids, 288
Biston betularia, 132
Black scale, 95
Blair, A. P.: studies of toad species, 183–84, 272, 299
Blair, W. F., 151, 165, 167, 273
Blakeslee, A. F., 127, 193, 233, 290, 293
Blending theory of heredity, 51–52
Blood groups, human: genotypic nature, 23
Blossom, P. M., 151
Boche, R. D., 225
Bogert, C. M., 167
Bonnier, G., 296
Bovey, P., 133
Boyd, W. C., 140, 143, 176, 178
Brachycephalic skull, 97
Brassica: synthesis of natural allopolyploid species, 292
Brassica campestris, 292
Brassica carinata, 292
Brassica juncea, 292
Brassica napus, 292
Brassica nigra, 292
Brassica oleracea, 292; hybridized with *Raphanus sativa*, 246–47
Braun, W., 87
Bread wheat, 294
Brehme, K., 103
Brewbaker, H. E., 69
Bridges, C. B., 37, 103
Brooks, J. L., 206, 282
Brooks, W. K., 156
Brücher, H., 86
Buchholz, J. T., 192
Bufo americanus, 184, 272
Bufo fowleri, 184, 272
Bufo terrestris, 184
Bufo woodhousii, 184
Bunting, M. I., 62
Burla, H., 167, 242, 268
Burnet, F. McF., 285, 286
Burt, W. H., 167
Butterflies, 143; effects of temperature on racial characters, 154
Butterfly weed, 299
Buzzati-Traverso, A., 60, 64, 69

Cabbage, *see Brassica; Brassica oleracea*
Cactus mouse, *see Peromyscus eremicus*
Cain, A. J., 170
Cain, S. A., 263
Cairina, 219
Calandra, 269
Calhoun, J. B., 97
Calliphora, 246
Camouflage, 102
Camp, W. H., 20, 288, 297
Carabus beetles: variations in Mediterranean species, 153
Carson, H. L., 114, 120, 121, 124, 268
Carvalho, A., 35
Caspari, E., 14, 132, 230, 296
Cat, 5, 6
Catcheside, D. G., 37, 39
Cavalcanti, A. G. L., 69, 114
Cavalli, L. L., 64
Cave animals: specialization and rudimentation, 284
Cavia apera, 219
Cavia cobaya, 219
Cenospecies, 272–73
Center of origin hypothesis, 134
Centromere: importance in cell division, 41
Cepaea hortensis, 170
Ceres, 98
Chaerocampa elpenor, 189, 228
Chamaea fasciata: territoriality, 166
Chemical mutagens, 43–45
Chemomorphoses, 23
Chen, T. T., 269
Chevais, S., 25
Chironomidae, 124, 245
Chorthippus bicolor, 214
Chorthippus biguttulus, 214
Chromosomal aberrations, 28–29; produced by mustard compounds, 43
Chromosomal sterility: caused by cryptic structural hybridity, 232–33; defined, 215; distinguished from genic sterility, 214–15; in hybrids between polyploid species, 249–52; in *Saturnia*, 220; in

species hybrids, 246–49; intraspecific, 230–33
Chromosome: changes affecting gene arrangement, 28; changes affecting number of, 28; fragmentation induced by chemicals, 45; giant, 29; structural changes, 40–41; subvital, 67; supervital, 67
Chromosome homologies: in *Drosophila americana* and *D. virilis*, 238–39, 238 (*fig.*); in *Drosophila* species groups, 244 (*fig.*)
Chromosome pairing: in salivary gland cells of *Drosophila* hybrids, 239 (*fig.*), 240–41
Citricola scale, 95
Cladocera, 302
Cladonia, 274
Clark, A. R., 69
Classification: Aristotle's system, 256; biological, 5; fundamental to study of organic diversity, 10; genetic basis, 254–56; Linnaeus' system, 257; natural system, 256–59; of birds, 6; Pliny's system, 256
Clausen, J., 145, 146, 199, 250, 272, 288, 289, 291
Clay, T., 205
ClB method, 31–32, 56
Cleland, R. E., 129
Clematis, 125
Clematis fremontii riehlii, 166
Coccidae, 94
Coccus pseudomagnoliarum, 95
Cockroach, 129
Coffea arabica, 35
Coffee, 287
Colchicine, 290
Coleman, L. C., 126
Colias, 143
Colletotrichum circinans, 99
Coloration, protective, 101–3, 132–33
Consanguinity, 69
Continuous racial variability, *see* Racial variability, polygenic
Continuous variability, *see* Variability, continuous
Coon, C. S., 140, 306
Coprinus, 43
"Corky" genetic complex: as isolating mechanism in cotton, 210; syndrome in cotton (*Gossypium*), 200–201
Cosmic rays: mutations caused by, 39
Cott, H. B., 102, 103
Cotton, 104, 287; partial alleles, 296 f.; sterile hybrids, 251; *see also Gossypium barbadense; Gossypium hirsutum*
Count, E. W., 108, 306
Craig, R., 95
Crampton, H. E., 143, 170
Crataegus, 274
Crenichtys, 83
Crepis: karyotype studies, 233, 235
Crepis bursifolia, 200
Crepis capillaris, 200
Crepis fuliginosa, 235, 236
Crepis kotschyana, 236
Crepis leontodontoides, 200
Crepis neglecta, 235
Crepis setosa, 200
Crepis taraxacifolia, 200
Crepis tectorum, 200
Crew, F. A. E., 219, 243
Cricetus cricetus: color phases, 120; frequencies of occurrence of black phase in Russia, 140, 141 (*fig.*)
Crombie, A. C., 109
Crosby, J. L., 98
Crossing over: effect of translocation on, 126; in inversion heterozygotes, 125 (*fig.*)
Crouse, H., 233
Crow, J. F., 201
Cruciferae, 288
Cryptic species, 267
Csik, L., 83
Cunha, A. B. da, 78, 114, 130, 131, 133
Curculionidae, 293
Cyprinidin fish, 153
Cytoplasmic inheritance, 228–30

Dactylis glomerata, 70
Dandelion, *see Taraxacum officinale*
Daphnia longispina, mutant, 83
Darlington, C. D., 38, 43, 71, 123, 126, 129, 215, 233, 236, 248, 260, 263, 303
Darrow, G. M., 288
Darwin, Charles, 12, 51–52, 76, 179, 266, 304
Darwin's finches, 206
Datura: crossability of different species, 192, 193
Datura discolor: chromosome configurations in hybrids, 234
Datura quercifolia: chromosome configurations in hybrids, 234
Datura stramonium: chromosomal constitution in various geographical regions, 128; chromosome configurations in hybrids, 234; translocations, 128–29, 129 (*fig.*)
Dawson, M. H., 46
Deer, 100
Deer mouse, *see Peromyscus*
Deficiency: cause of mutational change, 28; lethal effect on cells in *Drosophila*, 34
Delaporte, B., 88
Delbrück, M., 14, 87
Demerec, M., 34, 44, 60, 62, 87, 89, 192
Dempster, E. R., 81
Dermaptera, 294

Desert plants: adaptations, 152
Deoxyribonucleic acid: chromosome constituent, 48,
Developmental genetics: defined, 13
Dice, L. R., 103, 151, 165, 171
Dickey, F. H., 44
Dickler, H., 246
Dickson, R. C.: experiments with red scale, 95
Dicranomyia, 124
Digitalis, 213
Dioecy, 292
Diplococcus pneumoniae, 46
Diplontic sterility, 214
Dippell, R. V., 269
Diptera, 124, 244
Discontinuity, 4–8; useful in classification, 255
Disoperation: in sympatric species, 285
Di Stefano, H., 25
Diver, C., 170
Diversity, organic, 3–18; distinction between sympatric and allopatric, 135–36
Dobzhansky, Theodosius, 19, 20, 36, 66, 68, 72, 78, 114, 115, 117, 118, 122, 123, 129, 133, 136, 137, 142, 152, 164, 167, 168, 174, 175, 176, 180, 187, 188, 191, 195–96,208, 210,214, 221, 224, 225, 231, 237, 240, 245, 260, 262, 268, 305, 308; studies of evolutionary changes in *Drosophila pseudoobscura*, 90–91; studies of inversion in *Drosophila*, 112; studies of lethals in *Drosophila*, 56, 57, 58; studies of manifold effects in *Drosophila melanogaster*, 34; studies of Mendelian populations, 15, 79; studies of mutant stubbloid, 33; viability studies in *Drosophila pseudoobscura*, 84–85, 85 (*tab.*)
Dominance: causes of variation in, 105; origin of, 103–7
Dominance modifiers, 105, 106
Donald, H. P., 243
Dowdeswell, W. H., 165
Drepana, 220
Dreyfus, A., 129
Drosophila: behavior of mutations in, 27; characteristics of genus, 256; concealed recessive mutants, 171–76; crosses between individuals of different body sizes, 189; gene duplication, 296; genetics of isolating mechanisms, 201; giant chromosomes, 29; insemination reaction, 191; laboratory experiments in natural selection, 90–91; mechanism of sex determination, 292; mutants in wild populations, 63–64; partial alleles, 296; potential genetic variability in populations of, 65–69; primitive karyotype in, 244; recessive mutants in, 66; recessive mutant sterility genes, 215; sexual isolation between various species, 186; translocation heterozygotes, 232; viability of mutants, 84
Drosophila affinis, 191
Drosophila aldrichi, 201
Drosophila algonquin, 114
Drosophila americana: chromosome homologies in *D. virilis* and, 238 ff., 238 (*fig.*); cross-inseminations with related species, 191; genic sterility in hybrids between *D. virilis* and, 227–28
Drosophila americana texana, 227
Drosophila ananassae, 114, 129
Drosophila athabasca, 114, 191
Drosophila azteca, 112, 114
Drosophila capricorni, 243
Drosophila equinoxialis, 133, 242, 243, 268
Drosophila fumipennis, 243
Drosophila funebris, 114, 119–20, 121; viability of mutants, 83–84, 84 (*tab.*); viability of strains of different geographic origin, 148–49, 149 (*tab.*)
Drosophila guarani, 114, 237; sexual isolation between related species and, 210
Drosophila guaru: gene arrangements in hybrids, 237; sexual isolation between related species and, 210
Drosophila hydei, 64, 105, 114, 245
Drosophila immigrans: mutant gene frequencies, 173–74
Drosophila lacicola: cross-inseminations with related species, 191
Drosophila macrospina, 217
Drosophila macrospina limpiensis, 217
Drosophila macrospina macrospina, 217
Drosophila macrospina ohioensis, 217
Drosophila melanogaster, 114, 213, 245; artificial selection experiments, 101; dispersion rates, 167; effect of formalin on mutation rate, 44; frequencies of lethals, 173; hybrid sterility, 214, 215, 216–17, 216 (*fig.*); inversions, 110; lethal mutations, 56–58, 57 (*tab.*); lethals in second chromosome, 68; mutability, 61; mutable genes in, 63; mutants, 64, 103; mutation affected by temperature, 42; mutation rates, 60; mutations, 29–31; norm of reaction, 25; origin of spontaneous lethal mutations in X chromosomes, 57 (*tab.*); phenotypic variations in, 25; sex-linked lethals produced by mustard gas, 43; translocations in, 37; variability of normal strains and mutants, 24; viability of *D. funebris* compared with, 148–50; viability of mutants, 83
Drosophila miranda, 191, 246; chromosome pairing in salivary gland cells of hybrid between *D. pseudoobscura* and, 239 (*fig.*), 240–41; maternal effect in hybrids, 230; sexual isolation between *D. pseudoobscura* and, 210; viability

of hybrids from crosses with *D. pseudoobscura*, 195–96
Drosophila montana: cross-inseminations with related species, 191
Drosophila mulleri, 201
Drosophila nebulosa, 114, 243
Drosophila neorepleta, 219
Drosophila pallidipennis centralis, 188
Drosophila pallidipennis pallidipennis, 187
Drosophila paulistorum, 133, 134, 242, 243, 268
Drosophila persimilis, 115, 116, 191, 240, 246, 247, 248, 267–68; crosses with *D. pseudoobscura*, 196–99; effects of hybridization with *D. pseudoobscura*, 212–13; gene arrangements, 112–13, 113 (*fig.*); gene arrangements in hybrids, 237; genic sterility in hybrids of *D. pseudoobscura* and, 220–24; hybrid sterility, 214; insemination, experimental results, 186–87; mutability, 61; sexual isolation between *D. pseudoobscura* and, 201, 209; "strong" and "weak" races, 225–27; testis size in backcross hybrids between *D. pseudoobscura* and, 222 (*fig.*), 223 (*fig.*)
Drosophila polymorpha, 78; color patterns of abdomen, 130 (*fig.*), 130–31
Drosophila prosaltans, 69, 114, 188, 245
Drosophila pseudoobscura, 68, 78, 105, 112, 118, 191, 246, 247, 248, 267–68; chromosomal polymorphism, 122–23; chromosomal races, 136–38; chromosome pairing in salivary gland cells of hybrid between *D. miranda* and, 239 (*fig.*), 240–41; crosses with *D. persimilis*, 196–99; dispersion rates, 167; effects of hybridization with *D. persimilis*, 212–13; frequency of chromosomes with Standard gene arrangement, 114–15, 115 (*fig.*); frequencies of lethals, 173; gene arrangements, 112–13, 113 (*fig.*), 136–38, 138 (*fig.*); gene arrangements at different altitudes, 120–21, 121 (*tab.*); gene arrangements compared with those of *D. miranda*, 240–42, 241 (*fig.*); gene arrangements in hybrids, 237; genic sterility in hybrids of *D. persimilis* and, 220–24; heterosis in, 122–23; hybrid sterility, 214; insemination, experimental results, 186–87; laboratory experiments on selection, 90–91; lethals, 56, 58, 174; maternal effect in hybrids, 230; mutation rate, 175; polymorphism, 116–20; racial distinction, 139–40; seasonal changes in gene arrangements, 118–19, 119 (*fig.*); sexual isolation between *D. miranda* and, 210; sexual isolation between *D. persimilis* and, 201, 209; "strong" and "weak" races, 225–27; studies of spontaneous structural changes in chromosomes, 40; testis size in backcross hybrids between *D. persimilis* and, 222 (*fig.*), 223 (*fig.*); viability of hybrids from crosses with *D. miranda*, 195–96; viability studies, 72–73, 84–85, 85 (*tab.*)
Drosophila repleta, 114, 219
Drosophila robusta, 114, 115, 120, 121
Drosophila simulans, 213; gene arrangements in species hybrids, 236–37; hybrid sterility, 214
Drosophila subbadia: gene arrangements in hybrids, 237; sexual isolation between related species and, 210
Drosophila subobscura, 69
Drosophila tropicalis, 133, 134, 242, 243, 268
Drosophila virilis, 114, 233, 246; chromosome homologies in *D. americana* and, 238–39, 238 (*fig.*); chromosome structure, 238; cross-inseminations with related species, 191; genic sterility in hybrids between *D. americana* and, 227–28; mutable genes in, 62–63
Drosophila willistoni, 114, 133, 134, 215, 242, 268; concealed mutants in, 173; dispersion rates, 167; lethal mutations, 56; studies of genetic effects in homozygotes, 66 (*tab.*), 66–67
Drygalski, U. V., 213
Dubinin, N. P., 37, 56, 60, 64, 65, 66, 68, 114, 119, 121, 156, 157, 159, 173
Dubovskij, N. V., 60
Duck, 219
Dulbecco, R., 88
Dunn, L. C., 35, 65, 105, 216, 296
Duplication, in chromosomes, 28
Du Reitz, G. E., 275, 297
Durfour, Leon, 189
Duszynska-Wietrykowska, 219
Dynamics, evolutionary, 17–18

Earwig, 294
Ecological isolation, 181
Ecological species, 267
Ecological variables: population size in relation to, 164–68
Ecospecies, 272–73
Ecotypes: defined, 147; of *Hieracium umbellatum*, 148; of *Solidago virgaurea*, 148
Einkorn wheat, 252, 294
Eisentraut, M., 167
Elementary species, 274
Elodea canadensis, 86
Elton, C. S., 165, 167
Elymus, 125
Emerson, A. E., 269
Emerson, S., 14, 48, 89, 165, 263
Emmer wheat, 252, 294, 295
English sparrow, 96

Environment: effect on developmental processes, 20; influence on phenotype, 21; moulder of human personality, 23
Enzyme production by genes, 13, 35
Ephestia, 132
Ephestia kühniella, 14, 84
Ephrussi, B., 48, 213
Epilachna chrysomelina, 69, 195
Epilobium, 213, 230
Epling, Carl, 112, 136, 137, 168, 183, 237, 263, 268, 290; estimates of known plant species, 7
Erickson, M. M., 166
Erickson, R. O., 166
Escherichia coli, 274; mutants resistant to bacteriophage, 87–88; mutation rate affected by chemicals, 45; mutations, 58; strains resistant to ultraviolet and X rays, 88–89; streptomycin-resistant mutants, 89
Ethological isolation, 181
Euglena gracilis, 48
Euplotes patella, 269
Eurycea bislineata, 293
Eurygaster integriceps, 190
Eversae mutant, 83
Evolution, 10–12; a change in genetic composition of populations, 16; agencies of, 50; biological and cultural variables of human, 303; defined, 21; Fisher's definition, 77; genetics in relation to, 12–14; Lamarckian interpretation, 23; Lotsy's hybridization theory, 297; natural selection a factor in, 77; patterns of, 276–309; rates of, 282–83; relation of mutation to, 282; stages in process, 18
Evolutionary changes, 276–79
Evolutionary dynamics, 17–18
Evolutionary statics, 17–18
Exploitation, in sympatric species, 285

Fankhauser, G., 293
Fano, U., 39, 87
Federley, H., 189, 214, 219, 228, 233; studies of hybrid sterility in moths, 213
Fedorov, V. S., 70
Felis domestica, 5, 6
Felis leo, 5, 6
Fertilization, in species crosses, 190–92
Festuca pratensis, 70, 213
Field mustard, 292
Finalism, 17
Fish: difference between races in various climates, 153
Fisher, J., 165
Fisher, R. A., 79, 116, 132, 155, 156, 158, 208, 296; definition of evolution, 77; theory of origin of dominance, 106
Fission, binary, 302
Ford, E. B., 116, 132, 133, 155
Frandsen, K. J., 292
Frankel, O. H., 125
Fregata, 99
Fritillaria, 125
Frizzi, G., 124
Frog: isolating mechanisms in North American species, 193, 194 (*tab.*); studies of physiological traits in various species, 150–51; *see also Rana; Rana catesbeiana; Rana pipiens; Rana sylvatica*
Frog, leopard, *see Rana pipiens*
Frost, H. B., 233
Fujii, S., 233
Funaria hygrometrica, 230

Gadkari, P. D., 104
Gahan, J. B., 95
Galeopsis, 290
Galeopsis pubescens, 290 f.
Galeopsis speciosa, 290 f.
Galeopsis tetrahit, 290 f.
Galtsoff, P. S., 184
Gambusia partuelis, 103
Gametic isolation, 181
Gametic sterility, 214
Gametophytic isolation, 181
Gammarus chevreuxi, 69
Garn, S. M., 140
Gasterosteus: fresh-water and migratory forms, 182–83
Gasterosteus aculeatus: breeding habits, 184–85
Gasterosteus pungitius: breeding habits, 184–85
Gates, R. R., 263
Gause, G. F., 109, 155
Gause's principle, 109–10
Geitler, L., 124
Gene: action in development, 13, 14, 35; chromosomes as carriers, 12; deficiency in chromosome, 28; defined, 38; duplication in chromosome, 28; enzyme production, 13; evidence of existence, 27; inversion, 29; location and size, 14; manifold effects of, 33–35; molecular nature, 38; mutant, in *Drosophila*, 70; origin of new, 294–97; position effects, 36–38; reduplication of, 19; specificity, 14; stability, 19, 20; synthesis, 19; translocation, 28
Gene arrangements: in *Drosophila persimilis*, 112–13, 113 (*fig.*); in *Drosophila pseudoobscura*, 112–13, 113 (*fig.*), 136–37, 138 (*fig.*); in *Drosophila pseudoobscura* at different altitudes, 120–21, 121 (*tab.*); in *Drosophila pseudoobscura* compared with *D. miranda*, 240, 241 (*fig.*); in *Drosophila* species hybrids, 236–42; in nonhybridizing species of *Drosophila*,

242–46; seasonal changes in *Drosophila pseudoobscura*, 118–19, 119 (*fig.*)
Gene changes, *see* Mutation
Gene combinations: represented in a topographic map, 8–9, 9 (*fig.*); Wright's symbolic picture, 276–77
Gene frequencies, 53, 79–82; distribution in populations of different size, 160 (*fig.*), 161–63; relation between effective population size and variance of, 157
Genetic drift, 156; in relation to concealed genetic variability, 171–76; interrelations between selection and, 159, 161; role in evolutionary process, 164–65
Genetic equilibrium, 163; Hardy-Weinberg formula, 53; influenced by mutation, 54–55
Genetics: defined, 12; evolution in relation to, 12–14; geography in relation to, 135–36; of populations, 14–17; subdivisions, 14–15
Genetic variability, *see* Variability, genetic
Genic sterility: defined, 215; distinguished from chromosomal sterility, 214–15; in hybrids of *Drosophila pseudoobscura* × *D. persimilis*, 220–24; in hybrids of *Drosophila virilis* × *D. americana*, 227–28; in *Saturnia*, 220; within species, 215–17
Genotype: adaptive value of, 78; constitution of, 20; determiner of fixity and plasticity of traits, 24; distinguished from phenotype, 20; environmental influence on, 21; norm of reaction, 20; of Mendelian populations, 15; relation to environment, 20
Genotypic control, 233
Geographic isolation, 180–82; distinguished from reproductive isolation, 182; relation to species formation, 204
Geographic variation, 152–55
Geospizinae, 206
Gerhardt, U., 186
Germ plasm, 12
Gershenson, S., 70, 120, 140
Giles, N., 40
Gloger's rule, 152, 154
Gloor, H., 31
Godetia, 233
Godetia whitneyi, 129
Goldschmidt, R., 16, 61, 77, 143, 151, 219, 220, 271; analysis of intersexuality in *Lymantria dispar*, 218–19; interpretation of gene mutations, 29; theory of evolution by systemic mutations, 203; theory of species formation, 266; work on phenotypic variations, 24–25
Goldstein, M. S., 143
Goodspeed, T. H., 250
Gordon, C., 25, 69
Gordon, M., 201
Gossypium, 104; sterile hybrids, 251
Gossypium arboreum, 251
Gossypium barbadense, 199, 200, 251; inheritance of petal spots, 104; isolating mechanisms in, 209–10
Gossypium hirsutum, 199, 200, 251; inheritance of petal spots, 104; isolating mechanisms in, 209–10
Gossypium raimondii, 251
Gossypium thurberi, 251
Gossypium tomentosum, 199
Grain beetle, 269
Grant, V., 190
Grasshopper, 126; color polymorphism, 131–32
Green, K. C., 296
Green, M. M., 296
Greenleaf, W., 250
Gregg, J. R., 256
Gregor, J. W., 145
Gregory, P. W., 65
Griffen, A. B., 238
Griffith, F., 46
Gross, A. O., 166
Grüneberg, H., 35
Guinea pig, 219
Guirard, B. M., 14
Gussev, S. N., 90
Gustafsson, A., 86, 122, 130, 274, 289, 302
Guyénot, E., 219
Gynandromorphs, 220
Gypsy moth, *see Lymantria dispar*

Haas, F. L., 44
Haase-Bessell, G., 213
Hadjinov, M. J., 217
Hadorn, E., 31, 35, 44
Hagedorn, A. C., 156
Hagedorn, A. L., 156
Hagerup, O., 289
Håkansson, A., 129, 213, 233, 236
Haldane, J. B. S., 79, 106, 116, 195
Haldane's rule, 195
Hamster: color phases, 120; frequencies of black phase in Russia, 140, 141 (*fig.*)
Haploidy, 28, 70
Haplontic sterility, 214
Hardman, N. F., 95
Hardy, G. H., 53
Hardy-Weinberg law, 53–54
Harlan, H. V., 93
Harland, S. C., 104, 199, 207, 251, 296
Harmonia: partial alleles, 296
Harmonia axyridis: geographic distribution of color patterns, 142 (*tab.*), 143 (*fig.*)
Harrison, B. J., 58, 72, 101
Hasebroek, K., 132
Haskins, C. P., 188, 211
Haskins, E. F., 188, 211
Hatch, M. H., 256

Hayes, H. K., 69
Heidelberger, M., 46
Heiser, C. B., 298
Heitz, E., 31, 110
Helfer, R. G., 105
Helianthus annuus, 298
Helianthus bolanderi, 298
Helianthus petiolaris, 298
Heptner, M. A.: studies of mutation rates in relation to gene position, 63
Heredity: blending theory, 51–52; mutation in relation to, 19–49; particulate theory, 51–52; self-reproduction the basis of, 19–21
Héritier, Ph. L', 90, 114
Hermaphroditism, 292, 301
Herpes simplex, 286
Herring gull: Kent Island breeding grounds of, 166
Herskowitz, I., 44; studies of mutant Hexaptera, 30
Hertwig, P., 193
Heterocypris incongruens, 294
Heterosis: relation to balanced polymorphism, 121–23
Heuts, M. J., 118
Hieracium, 274
Hieracium umbellatum: ecotypes, 148
Hiesey, W. M., 145, 146, 272, 288
Hoare, C. A., 269
Hollingshead, L., 200
Hologenesis, 17
Holz, A. M., 34
Homeosis, 30
Homeostasis, 22
Homing phenomena, 167
Homo sapiens, 265
Horowitz, N. H., 13, 30
Horse: evolution of, 282
Horton, I. H., 236
Hosino, Y., 142
Housefly: resistance to DDT, 95–96
Hovanitz, W., 143
Howard, H. W., 125
Howard, W. E., 167
Hsu, T. C., 124
Hubbs, C. L., 284
Hubricht, L., 298
Huff, C. G., 286
Hughes-Schrader, S., 41
Human races, 140
Hutchinson, J. B., 96, 104, 199, 251, 295
Huxley, J. S., 100, 132, 143, 182, 185, 205, 263
Hybrid breakdown, 181, 196–99
Hybrid inviability, 181, 192–96, 204
Hybridization, introgressive, 297–300
Hybrids: intersexuality, 218–20; maternal and cytoplasmic effects in, 228–30; translocations in, 233–36
Hybrid sterility, 181, 204, 212–53
Hybrid vigor, *see* Heterosis
Hydrodictyon: phylogenetic tree compared to, 290
Hymenoptera, haploid males, 70

Ignatiev, M. V., 60, 73
Inbreeding: effects on offspring in various animals and plants, 69–70
Insemination reaction: in *Drosophila* species, 191
Intersexes: variability of phenotypes, 24
Intersexuality in hybrids, 218–20
Introgressive hybridization, *see* Hybridization, introgressive
Inversion, 29; chromosomal polymorphism resulting from, 110–15; chromosome pairing in heterozygous individuals, 111 (*fig.*); genetic effect, 123; in *Drosophila*, 36, 134; in experimental populations of *Drosophila*, 114–16; in plants, 124–25; in species hybrids, 233–36; overlapping, 111–12; paracentric, 244–45; pericentric, 244–45
Inversion heterozygotes, 124–25 (*fig.*), 232
Invertebrates: estimated number of species, 7
Inviability, hybrid, *see* Hybrid inviability
Iris, 20
Iris fulva, 298
Iris hexagona gigantocaerulea, 298
Isolating mechanisms, 179–211; ecological, 182–84; genetic analysis of, 199–202; geographic, 180–82, 204; mechanical, 189–90; reproductive, 18, 180–82, 202–4, 206–11, 263; seasonal, 182–84; sexual, 181, 184–89; term, 180
Ives, P. T., 56, 58, 60, 68, 114, 173

Jenkins, M. T., 69
Jennings, H. S., 269
Jimson weed, *see Datura stramonium*
Johannsen, W., 27; distinction between genotype and phenotype, 20
Johnsson, H., 70
Jones, D. F., 192
Jones, H. A., 99
Jordan, D. S., 204
Jordan, K., 189, 204

Kalmus, H., 83
Kammerer, P., 284
Kaplan, W. D., 44
Karpechenko, G. D., 246, 290
Karyotype, 233
Kaston, B. J., 185
Kaufmann, B. P., 230
Keck, D. D., 145, 146, 272, 288
Kerkis, J., 31, 189, 214, 236
Kerr, W. E., 70
Khvostova, V. V., 60, 68
Kihara, H., 251, 252
Kikkawa, H., 114
Kimball, R. F., 269

King, J. C., 114, 210, 268
King, W. V., 95
Kinsey, A. C., 271
Kladogenesis, 283
Klingstedt, H., 214; hypothesis concerning hybrid sterility, 216
Kluckhohn, C., 309
Koller, P. C., 43, 125, 126, 210, 219
Kölmark, G., 45
Komai, T., 142, 296
Kondakova, A. A., 43
Koopman, K. F.: experiments on reproductive isolation, 209
Korjinsky, S. Y.: mutation theory of, 26
Kosiupa, D. E., 43
Kossikov, K. V., 37
Kosswig, C., 201, 284
Kostoff, D., 200
Kramer, G., 171
Krug, C. A., 35
Kühn, A., 84
Kuhn, E., 265

Lack, D. L., 109, 205, 206, 211, 282
La Cour, L. F., 129
Ladybird beetle: cyclic seasonal changes in, 130; pigmentation, 152–53; *see also Epilachna chrysomelina*
Laibach, F., 193, 212
Lamarck, J. B. P. A. de Monet, 23, 179
Lamm, R., 125
Lamprecht, H., 266
Lamy, R., 60, 243
Lancefield, D. E., 220
Landauer, Walter, 35, 86, 105
Lang, A., 236
Larus argentatus: Kent Island breeding grounds, 166
Lasiocampa quercus, 195
Lattin, G. de, 284
Laughnan, J. R., 296
Law, L. W., 43
Lea, D. E., 39
Lebistes reticulatus, 188
Lederberg, J., 30, 87, 88
Lefevre, G., 40
Lehmann, E., 230
Leiner, M.: studies of *Gasterosteus*, 184
Leopard frog, see *Rana pipiens*
Lerche, W., 245
Lerner, M. M., 69, 79, 81, 157
Lethals: allelic, 174–75; chromosome deficiencies act as, 34; ClB chromosome, 31–32; dominant, 41; equilibrium values for recessive autosomal, 172; produced by mustard gas, 43; rate of origin, 56–58; recessive, 55; studies of, in *Drosophila*, 56–58; value in studies of mutation, 56
Levan, A., 45, 215
Levene, M., 118
Levitan, M., 114, 115
Lewis, E. B., 36, 296
Li, C. C., 79, 81, 157
Lice: intersexuality, 219
Lilienfeld, F., 251, 252
Lillie, F. R., 190
Linanthus parryae, distribution of white- and blue-flowered phases, 168–69, 169 (*fig.*)
Linnaeus, Carolus: species of animals known by, 6; system of classification, 257
Linum austriacum, 193
Linum perenne, 193
Lion, 5
Liriomyza, 124
Liu, T. T., 124
Lobashov, M. E., 43
Lolium perenne, 213
Lotsy, J. P., 262; theory of evolution by hybridization, 297
Löve, A., 125, 289
Löve, D., 125, 289
Lowry, R. J., 288
Loxia, 86
Lucilia, 246
Lüers, H., 83
Lundman, B., 143
Luria, S. E., 87, 88
Lymantria: geographic distribution of races, 219
Lymantria dispar, 151; intersexuality in hybrids, 218–20

Maas, A. H., 25
McAtee, W. L., 103
McCarty, M., 46, 47
McClintock, B., 34, 37
McEwen, R. S., 30
McFadden, E. S., 251, 252
MacKnight, R. H., 240
Macroevolution, 16, 17
Madia citrigracilis, 291
Madia citriodora, 291
Madia gracilis, 291
Magrzhikovskaja, K. V., 43
Mainland, G. B., 217
Mainx, F., 124
Maize, 127; chlorophyll defects, 69; crosses between sugary and nonsugary, 192; genotypic control of mutability in, 62; partial alleles, 296 f.
Malarial plasmodia, 286
Malthus, T. R., 77
Mammals: anatomical differences between races in various climates, 153; evolution 282; territoriality, 167; *see also* names of individual mammals, e.g., Cat; Hamster; Lion
Mampell, K., 61
Mangelsdorf, P. C., 69–70, 192
Manifold effects of genes, 33–35

Mann-Lesley, M., 233
Manning, M. L., 96
Man-o'-war bird, 99
Manton, I., 288
Marsh, F. L., 11
Marshall, W. H., 171
Martini, M. L., 93
Maternal effect in hybrids, 228–30
Mather, Kenneth, 14, 58, 71, 72, 101, 105, 123, 190, 260, 263, 268
Matthey, R., 236, 294
Matthiola, 233
Mayr, Ernst, 6, 7, 109, 143, 147, 152, 166, 171, 181, 182, 186, 187, 188, 205, 206, 210, 211, 219, 258, 259, 262, 263, 264, 265, 269, 271, 305
Mechanical isolation, 181
Melandrium, 125
Melandrium album, 293
Melanin, 152
Melanism, industrial, 132–33
Melanogaster species group of *Drosophila*, 243 ff., 244 (*fig.*)
Melospiza melodia: territoriality, 166
Mendel, Gregor, 177
Mendelian population, 79, 256; as product of adaptive evolution, 259–61; defined, 15, 135; evolutionary advantages of, 261; sympatric, 264
Merrell, D. J., 90, 186, 188
Mertens, R., 171
Metopsilus porcellus, 189, 228
Metrioptera brachyptera, 129
Meurman, O., 125
Mice: partial alleles, 296 f.
Michaelis, P. G., 230
Microevolution, 16, 17
Microgeographic races, 168–71
Microorganisms: mutation and selection in, 86–90; mutation rates, 57
Micropoecilia parae, 188
Midge, 124, 233
Miller, A. H., 144
Miller, D. D., 114
Mimic mutants, 243
Mimicry, 102, 132–33
Mint, 290
Mixodiaptomus laciniatus, 166
Mnium, 288
Modifications, adaptive: distinguished from morphoses, 22; examples of, 22; Lamarckian view of, 23
Mollusks, 282; shell size related to climate, 153
Monoecy, 292
Monosomics, 303
Moody, P. A., 143, 159
Moore, J. A.: studies of isolating mechanisms in *Rana*, 193, 194 (*tab.*); studies of physiological traits in species of *Rana*, 150–51; studies of *Rana pipiens*, 272
Morgan, T. H.: mutation studies in *Drosophila*, 26–28
Mormoniella, 70
Morphoses: distinguished from adaptive modifications, 22; examples of, 22–23
Mosquito, 124; dispersion rates, 168; sibling species, 268–69
Moss, 288
Moth, 294, 299; hybrid sterility, 213; intersexes, 220; melanic variants, 132
Mouse, 143
Mouse, cactus, *see Peromyscus eremicus*
Muller, H. J., 14, 20, 22, 34, 37, 182, 196, 207, 231, 263, 292; production of gene mutations and chromosomal changes by X rays, 39; studies of effect of temperature on mutation, 42
Müllerian mimicry, 102
Multiple factors, *see* Polygenes
Müntzing, A., 70, 129, 214, 288, 290
Murphy, R. C., 99
Murray, H. A., 309
Musca domestica: resistance to DDT, 95–96
Mustard gas: as chemical mutagen, 43
Mutability: genetic control of, 58–63; in *Drosophila persimilis*, 61
Mutable genes, 62–63
Mutant: Bar eye, 25; concealed, 171–76; in *Drosophila funebris*, 83–84, 84 (*tab.*); in wild populations, 63–65; mimic, 243; phenocopy distinguished from, 25; stubbloid, 33; vestigial, 33; white eye, 33
Mutation: classification of types, 28–29; definitions, 25, 26, 28; evolution dependent upon, 25; extent of changes produced by, 31–33; frequency affected by temperature, 42; genetic control of, 58–63; history of theory, 25–28; induced by radiation, 38–41; induced by temperature changes, 41–42; influence on selection, 81–82; in microorganisms, 86–90; in polyploids, 294–97; in populations, 50–75; in relation to environment, 74; in relation to heredity, 19–49; lethal, 56–58, 174, 175; nature of, 27; probability of extinction and of survival of, 159 (*tab.*); produced by mustard compounds, 43; rates, 55–58, 59 (*tab.*); relation to evolution, 76, 282; reproductive isolation produced by, 203; source of evolutionary changes, 18; types of changes produced by, 29–31; viability affected by, 32 (*tab.*)
Mutation pressure: interaction with selection and population size factor, 162
Mutator, 61
Mutualism, 285–287

Nachtsheim, H., 96
Natural selection, *see* Selection

Naumenko, V. A., 43
Nawashin, M. S., 233
Neefs, Y., 90
Neel, J. V., 60
Neurospora, 43, 44, 89; metabolism studies, 13; mutations, 44, 48–49
Neurospora crassa, 45
Newell, N. D., 100, 265
Newton, W. C. F., 249
Nice, M. M., 166
Nichols, Ch., 40
Nicoro, Z., 90
Nicotiana: sterile hybrids, 250–51
Nicotiana alata: chromosomal make-up, 235
Nicotiana bonariensis: chromosomal make-up, 235
Nicotiana glauca, 200
Nicotiana langsdorfii: chromosomal make-up, 235
Nicotiana rustica humilis, 200
Nicotiana rustica texana, 200
Nicotiana sylvestris, 250 f.
Nicotiana tabacum, 250 f.
Nicotiana tomentosiformis, 250 f.
Niggli, H., 44
Nilsson, F., 70
Nilsson-Ehle, H.: principle of multiple factors, 71
Noggle, G. R., 288
Nomogenesis, 17
Norm of reaction, 20, 21–24, 82, 154–55
North, S. B., 105
Novikoff, A. B., 15
Novitski, E., 42, 114, 244
Nucellar embryogony, 302
N value of population size, 163–64

Oats, 125, 287, 295
Obscura species group of *Drosophila*, 243 ff., 244 (*fig.*)
Oenothera, 129; translocation heterozygotes, 232
Oenothera blandina, 37
Oenothera organensis: population estimate, 165
Olenov, J. M., 42
One gene–one enzyme hypothesis, 13, 35
Onion: resistance to smudge fungus, 99–100
Ophiostoma, 43
Opossums, 282
Organic diversity, *see* Diversity, organic
Organic selection, 155
Origin of Species (Darwin), 304
Orthogenesis, 17, 100
Orthoselection, 100
Ostracod, 294

Paeonia, 124
Painter, T. S., 110
Paracentric inversions, 244
Paramecium aurelia, 269; killer strains, 286; serotype classification of, 45
Paramecium bursaria, 269
Parasitism, 285–87
Paratettix texanus, 132
Pariser, K., 220
Paris quadrifolia, 124
Park, T., 15
Parthenogenesis, 92, 301
Partial alleles, 296–97
Particulate theory of heredity, 51–52
Partula, 170
Partula suturalis, 170
Partula taeniata, 170
Parus bokharensis: geographical distribution, 270, 271 (*fig.*)
Parus major: geographical distribution, 270, 271 (*fig.*)
Parus minor: geographical distribution, 270, 271 (*fig.*)
Pätau, K., 236
Patterson, J. T., 114, 182, 186, 187, 188, 191, 201, 227, 237, 238, 263, 268
Pavan, C., 66, 114, 173, 245, 284
Pearson, Karl, 53
Peas, 236
Pediculus capitis: intersexuality, 219
Pediculus vestimenti: intersexuality, 219
Pellew, C., 249
Penicillium, 43
Pericentric inversions, 244
Perognathus intermedius: protective coloration, 151–52
Peromyscus, 69; geographic races, 144
Peromyscus eremicus: protective coloration, 152
Peromyscus maniculatus, 143; protective coloration, 103
Peromyscus maniculatus osgoodi: population estimates of, 165
Peromyscus polionotus leucocephalus: population estimates of, 165
Petersen, B., 153
Peto, F. H., 213
Phenocopies, 24–25
Phenogenetics, defined, 13
Phenons, 267
Phenotype: a by-product of gene reproduction, 21; distinguished from genotype, 20; environment as influence on, 20 ff.
Philiptchenko, Jur., 144
Phleum pratense, 70
Phryne, 245
Phyllodromia germanica, 129
Phylogenetic tree, 289
Phylogeny, 11
Physcomitrella patens, 230
Physcomitrium eurystomum, 230
Physcomitrium piriforme, 230
Physiological species, 267
Pictet, A., 195

Pigmentation: Gloger's rule, 152, 154
Pirschle, K., 86, 130
Pisum, 236
Pittendrigh, C. S., 109, 211
Plant: historical changes in populations, 97–99; number of known species, 7; *see also* names of individual plants and plant groups, e.g., Barley; Oats; Snapdragon; Wheat
Plants, desert, 152
Plasmagene, 14, 46
Platyfish: effects of hybridization with swordtail, 202
Platypoecilus maculatus: effects of hybridization with *Xiphophorus helleri*, 202
Platysamia, 299
Pleiotropic genes, 33
Pleiotropism, 35
Pliny: system of classification, 256
Plough, H. H., 42
Plunkett, C. R., 20, 106
Pneumococci, 47
Pocket mouse, rock, 151
Poecilia vivipara, 188
Poeciliid fishes, 188
Poephila, 132
Poisson series, 158
Poliomyelitis virus, 286
Polygenes, 70–73, 101
Polygenic racial variability, 143–45
Polygenic variability, 71–73
Polygonatum, 125
Polymorphism, adaptive, 108–34; defined, 109; ecological opportunity in relation to, 133–34; origin in natural populations, 132
Polymorphism, balanced: relation of heterosis to, 121–23; theory, 116–18
Polymorphism, chromosomal: biological functions in *Drosophila*, 118–21; detection, 124; function in adaptation to altitude, 120–21, 121 (*tab.*); in *Drosophila*, 110–14; in organisms other than *Drosophila*, 123–29; natural selection applied to, 117–18
Polymorphism, genic, 129–32
Polyommatus icarus: population on isle of Tean, 165
Polyploids: geographic regularities in incidence of, 289; mutation and the origin of new genes, 294–97; production in plants, 290–92
Polyploidy, 28, 266; as method of origin of species, 287–90; in animals, 292–94; in dioecious plants, 292–94
Polysaccharide envelope of pneumococci, 47
Polysomics, 303
Polytypic species concept, 259
Ponomarev, V. P., 43
Popova, O. T., 43
Population dynamics, 51
Population number: defined, 157
Populations: defined, 15; genetics of, 14–17; mutation in, 50–75; organismic attributes, 15; possibilities of evolution in, 279 (*fig.*), 280–82
Population size: ecological variables in relation to, 164–68; estimates of various species, 165–66; relation between selection intensity and, 161–62; value N in, 163–64
Porto Santo rabbit, 96
Position effects of genes, 36–38
Postnikova, E. D., 68
Potato, 287
Potentilla glandulosa: Californian climatic races, 146–47
Poulson, D. F., 31, 34
Poultry: dominant mutants, 103
Power, M. E. 30
Prabhu, S. S., 215
Pravosoli, L., 48
Primrose: polymorphism, 98–99; *see also* the various species of *Primula*
Primula elatior, 183
Primula floribunda, 249
Primula kewensis, 249
Primula verticillata, 249
Primula vulgaris, 183; polymorphism, 98–99
Prokofieva, A. A., 37
Protective coloration, 101–3; in *Perognathus intermedius*, 151–52; in *Peromyscus eremicus*, 152
Protective resemblance, 101–3
Proteus anguinus, 284–85
Provirus, 287
Psittacosis, 286
Psychological isolation, 181
Puccinia graminis tritici, 97 (*tab.*), 97–98
Pygaera, 220
Pygaera anachoreta, 213
Pygaera curtula, 213
Pygaera pigra, 213

Quayle, H. J.: experiments with red scale, 95

Rabbit, Porto Santo, 96
Race: borderline cases between species and, 270–71; defined, 138; genetic conception of, 176–78; in human species, 140; microgeographic, 168–71; relation to species, 266–67
Race differences, 139–40
Race formation, 135–78
Race limits, 139–40
Races, rings of, 270–71
Racial variability, 177–78
Racial variability, polygenic, 143–45
Racial variation: due to single genes, 140–43

Radiation: effects in natural habitats, 40
Radiomorphoses, 23
Radish: hybrids between cabbage and, 246–47
Rana: isolating mechanisms in North American species, 193, 194 (*tab.*)
Rana catesbeiana: embryonic temperature tolerance, 150
Rana pipiens: geographic variation in embryonic temperature tolerance and rate of development, 150 (*tab.*); inviability in hybrids between geographic races, 194; rate of development in northern and southern species, 151
Rana sylvatica: embryonic temperature tolerance, 150
Raphanobrassica, 247, 290
Raphanus sativus: hybridized with *Brassica oleracea*, 246–47
Rapoport, J. A., 14, 25, 37, 44
Reaction norm, *see* Norm of reaction
Red scale: distribution of resistant and nonresistant races, 94 (*fig.*), 94–95
Redwood, 287
Reed, E. W., 90, 268
Reed, S. C., 90, 268
Renner, O., 214
Rensch, B., 17, 97, 100, 152, 154, 204, 205, 206, 270, 282, 283; studies of correlation between racial differences and climate, 153
Rensch's rule, 153
Reproduction: the integrating agent in Mendelian populations, 15
Reproductive isolating mechanisms, 18, 180–82, 202–4, 206–11, 263
Reproductive isolation, 181–82; distinguished from geographic isolation, 182; natural selection in relation to, 206–11; relation to geographic isolation, 205
Resemblance, protective and warning, 101–3
Rhoades, M. M., 62, 127
Rhoeo discolor, 129
Richards, O. W., 77
Ricker, W. E., 183
Rickettsia prowazeki, 286
Riley, H. P., 298
Rings of races, 270–71
Ris, H., 41
Rizki, M. T. M., 268
Roberts, L. M., 37
Robinow, C. F., 88
Robson, G. C., 77
Rodents: aberrations in, 65
Rohm, P. B., 124
Romanes, G. J.: quoted, 179
Romashov, D. D., 157, 159
Rosen, G. von, 236
Rosin, S., 44
Rubus, 274
Rudimentation, 283–85
Rumex, 125
Ryan, F. J., 89
Rye, 125

Sacharov, W. W., 43
Saissetia oleae, 95
Salmon, 183
Salmonella enteritidis, 274
Salmonella typhosa, 274
Salmonid fish: chromosome numbers, 294
Saltans species groups of *Drosophila*, 244 (*fig.*), 245
Saltykovsky, A. I., 70
Salvia apiana, 183
Salvia mellifera, 183
Samjatina, N. D., 43
Sang, J. H., 25
Sansome, E. R., 236
Sargent, M. C., 83
Saturnia pavonia: intersexes in hybrids, 220
Saturnia pyri: intersexes in hybrids, 220
Saxifraga, 213
Scale insects: resistance to hydrocyanic gas, 94–95
Schmalhausen, I. I., 17, 22, 23, 24, 106, 155, 207, 263, 282
Schneider, L. R., 89
Schoenheimer, S. Gluecksohn, 35, 296
Schwab, J. J., 34
Sciara, 124, 233; gene duplication, 296
Sciurus carolinensis, 126
Sears, E. R., 236, 251, 252
Seasonal isolation, 181
Sedum pulchellum, 288
Seiler, J., 294
Selection, 76–107; correlated responses to, 99–101; Darwin's concept, 77; experiments with organisms other than *Drosophila*, 92–94; in *Drosophila*, laboratory experiments, 90–91; influence on development of isolating mechanisms, 208 ff.; in microorganisms, 86–90; interaction of mutation and, 81–82; relation to evolution, 76–77, 282
Selection, stabilizing, 106–7
Selection coefficients, 79–81
Selection intensity: relations between population size and, 161–62
Selectionism, Darwin's: mutation theory of De Vries distinguished from, 26
Self-fertilization, 273 f., 300–301
Self-reproduction, 19–21
Semenov-Tian-Shansky, A., 204
Semi-allelic genes, *see* Partial alleles
Sengün, A., 190
Sequoia sempervirens, 287
Serebrovsky, A. S., 185
Sergentia, 233
Serinus canaria, 97

Serotypes: in *Paramecium aurelia*, 45–46
Settles, F., 231
Sewall Wright effect, 156
Sex: evolutionary advantages, 261
Sexton, E. W., 69
Sexual isolation, 181, 184–89
Sexuality: retrogression of, 300–303
Shapiro, N. J., 60, 73
Sheppard, P. M., 170
Sherman, M., 236
Shrimps, gammarid, 206
Sibling species, 267–70
Sidorov, B. N., 37
Silow, R. A., 104
Simpson, G. G., 3, 17, 78, 100, 205, 255, 257, 258, 263, 265, 282; statement of relationships between biological and taxonomic species, 263–64
Sitko, P., 63
Skovsted, A., 48
Smith, H. E., 288
Smith, H. S., 96
Smith, L., 215
Smith, S. G., 246
Snail: microgeographic variations, 170
Snapdragon, 27, 103
Sokolov, D., 114
Solenobia triquetrella, 294
Solidago virgaurea: ecotypes, 148
Song sparrow, *see Melospiza melodia*
Sonneborn, T. M., 45, 269
Sorghum vulgare, 217
Southern, H. N., 132
Sow bug, 294
Sparrow, English, 96
Spassky, B., 245; studies of evolutionary changes in *Drosophila pseudoobscura*, 90–91; studies of lethals, 56, 58; viability studies in *Drosophila pseudoobscura*, 84–85, 85 (*tab.*)
Spatial isolation, 181
Speciation, *see* Species formation
Species: as biological units, 6; asexual, 275; as natural units, 254–75; as systemic category, 258; borderline cases between races and, 270–71; criteria for distinction, 212; estimated number of plant, 7; evolutionary possibilities, 280–82; experimentally created, 247; in asexual organisms, 273–75; in sexually reproducing organisms, defined, 261–63; methods of distinguishing, 269–70; number of invertebrate, 7; number of vertebrate, 7; proportion of polyploid, 287; relationship between biological and taxonomic, 261, 263–65; relation to races, 266–67; sexual, 275
Species, sibling, *see* Sibling species
Species formation, 204–6, 263
Spencer, Herbert, 110
Spencer, W., 61, 64, 65, 66, 69, 173, 242, 245
Spermatheca: variation in shape caused by manifold effects, 34–35
Sphingidae, 189
Spiders: courtship behavior, 185
Spiegelman, S., 14
Spiess, E., 115
Spieth, H. T., 186, 187, 188
Spooner, G. M., 69
Squirrel, 126
Stabilizing selection, 106–7
Stadler, L. J., 29, 34, 40, 58, 62, 295, 296
Stakman, E. C.: studies of races of *Puccinia graminis tritici*, 97 (*tab.*), 98
Stalker, H. D., 114, 120, 121
Standfuss, M., 154, 189, 212, 219
Staphylococcus aureus: mutation rates increased by irradiated culture media, 44; penicillin-resistant strains, 89
Statics, evolutionary, 17–18
Stebbins, G. L., Jr., 93, 124, 125, 129, 143, 145, 147, 182, 190, 193, 206, 211, 213, 232, 235, 236, 249, 263, 265, 271, 275, 282, 287, 288, 289, 292, 296, 298, 299, 300, 302, 303
Stebbins, R. C., 144
Stegmann, B., 270
Stem rust of wheat, 97
Stephens, S. G., 104, 199, 209, 232, 251, 296
Sterility, chromosomal, *see* Chromosomal sterility
Sterility, genic, *see* Genic sterility
Sterility, hybrid, *see* Hybrid sterility
Stern, C.: studies of hybrid sterility in *Drosophila melanogaster*, 216–17, 216 (*fig.*)
Stickleback, *see Gasterosteus; Gasterosteus aculeatus; Gasterosteus pungitius*
Stone, W. S., 44, 227, 237, 238, 240
Storer, T. J., 65
Strassburger, E. H., 195
Streisinger, G., 187, 188
Strong, L. C., 44
Strongylocentrotus franciscanus, 190–91
Strongylocentrotus purpuratus, 190–91
Stubbe, H., 31, 86, 103, 130
Sturtevant, A. H., 37, 61, 73, 110, 112, 114, 208, 219, 228, 243, 244, 263
Subvital chromosomes, 67
Sugar cane, 287
Sukatschew, W.: experiments on selection in dandelion, 92–93
Sula bassana: population estimates, 165
Sumner, F. B., 69, 83, 144; studies of protective coloration in fish, 102–3
Sunfish, 103
Sunflower, 298
Suomalainen, E., 125, 129, 293, 294
"Supergenes," 123
Supervital chromosomes, 67
Svärdson, G., 294

Swanson, C. R., 125
Sweadner, W. R., 299
Swordtail: effects of hybridization with platyfish, 202
Symbiosis: in sympatric species, 285
Sympatric organisms, 135–36
Sympatric theory of species formation, 204–6
Synapis alba, 70
Syngameon, defined, 262
Syrphidae, 86
Systematics, *see* Classification

Tan, C. C., 142, 237, 240, 243, 296; analysis of genetic mechanisms underlying sexual isolation, 201
Taraxacum officinale: selection experiments, 92–93, 93 (*tab.*)
Tate, P., 246
Tedin, O., 144
Teissier, G., 90, 114
Temperature: mutation rate affected by, 42
Temporal isolation, 181
Territoriality: in birds, 166; in insects, 167; in mammals, 167
Testis size: evidence for dependence on maternal effect, 229; in *Drosophila pseudoobscura* × *D. persimilis* hybrids, 222–24, 222 (*fig.*), 223 (*fig.*), 225 f.
Thayer: studies of protective coloration, 102
Therman, E., 125
Thompson, M. G., 232
Thompson, W. P. 232
Thorpe, W. H., 205, 263, 269
Timofeeff-Ressovsky, H., 65, 69
Timofeeff-Ressovsky, N. W., 31, 39, 56, 60, 65, 83, 130, 143, 148, 167, 263; experiments on mutations affecting viability, 32 (*tab.*); mutation experiments, 61; studies of sex-linked lethals, 42
Tiniakov, G. G., 60, 114, 119, 121
Tischler, G., 289
Titmouse, Asiatic, 270
Tjio, J. H., 45
Toad, *see Bufo americanus; Bufo fowleri*
Tobacco, 287; sterile hybrids, 250–51
Tobgy, H. A.; studies of reduction in chromosome number in *Crepis*, 235–36
Toleration: in sympatric species, 285
Tonissi, M., 30
Tradescantia, 40, 41, 125
Translocation, 28; effects of, 126–27; in *Drosophila* chromosomes, 36, 37; in *Drosophila melanogaster*, 216 (*fig.*); in Jimson weed, 127–28, 128 (*fig.*); in species hybrids, 233–36
Translocation heterozygotes, 230–32
Trichogramma, 269
Trichoniscus elisabethae, 294
Triticum, 236; chromosome structure, evolution of, 251–52
Triticum aegilopoides, 252
Triticum aegilopoides baidaricum, 215
Triticum dicoccoides, 252
Triticum dicoccum, 252, 295
Triticum durum, 252, 295
Triticum monococcum, 215, 252, 295
Triticum spelta, 252
Triticum timopheevi, 252
Triticum vulgare, 252, 295
Triturus viridescens, 293
Tschetwerikoff, S. S., 65
Turesson, G., 145, 147, 148, 272
Turrill, W. B., 145

Uber, F., 40
Ultraviolet radiation: mutations induced by, 39–40

Vaccinium, 20, 288
Valadares, M., 60
Valentine, D. H., 183
Vandel, A., 77, 100
Van Niel, C. B., 274
Variability: controlling factors, 172; scattering of, 158–63
Variability, continuous, 71–73
Variability, genetic: concealed, in relation to genetic drift, 171–76; in *Drosophila*, 65–69; increased by sexual reproduction, 260; in organisms other than *Drosophila*, 69–70
Variability, racial, 177–78
Variation: discontinuity of organic, 255; geographic, 152–55; sources of hereditary, 50
Vavilov, N. I., 134
Vertebrates: estimated number of species, 7
Vestigial structures, 284
Vevers, H. G., 165
Viability: mutations affecting, 32 (*tab.*)
Virchow, R., 108
Vogt, M., 44
Volkova, K. V., 60
Vries, Hugo de: mutation studies in *Oenothera*, 26; mutation theory, 26, 31, 76
Vulgare wheats, 295

Waagen, W., 25–26
Wagner, M., 179
Wagner, R. P., 14, 44
Walker, J. C., 99
Wallace, B., 56, 58, 115, 118
Walters, J. L., 124, 125
Warmke, H. E., 293
Warters, M., 114
Warwick, B. L., 193
Wasps, 152

Weevils, 293
Weidenreich, Franz, 97, 305
Weinberg, W., 53
Weismann, August, 35, 260, 284
Welch, D'Alte A., 143, 170
Westergaard, M., 45, 293
Wettstein, F. von, 31
Wettstein, V. von, 230
Wharton, L., 245
Wheat, 97–98, 236, 287; chromosome structure, evolution of, 251–52
Wheat, bread, 294
Wheat, einkorn, 294
Wheat, emmer, 294
Wheat, *vulgare*, 295
Wheat rust, 97–98
Wheeler, M. R., 187, 201
White, M. J. D., 70, 126, 129, 213, 228, 236, 294, 302
Weigand, K. M., 298
Wigan, L. G., 101
Willistoni species group of *Drosophila*, 243 ff., 244 (*fig.*)
Witkin, E. M., 44, 58
Wolf, E., 124
Wolfenbarger, D. O., 168
Wood, T. R., 83, 302
Woodson, R. E., 299
Wren tit, *see Chamaea fasciata*
Wright, S., 8, 13, 57, 58, 68, 79, 106, 116, 117, 126, 157, 164, 165, 167, 168, 172, 174, 175, 176, 254, 279, 281; studies of interrelations of selection and genetic drift, 159, 161; studies of population dynamics, 51

Xiphophorus helleri: effects of hybridization with *Platypoecilus maculatus*, 202
X rays: mutations induced by, 39, 40

Yeast: transformations in, 48

Zauschneria cana, 199
Zauschneria septentrionalis, 199
Zea mays: crosses between sugary and nonsugary, 192
Zimmermann, K., 152, 195
Zygaena ephialtes, 133
Zygotic sterility, 214