Heredity

Basic features of heredity

Prescientific conceptions of heredity

Heredity was for a long time one of the most puzzling and mysterious phenomena of nature. This was so because the sex cells, which form the bridge across which heredity must pass between the generations, are usually invisible to the naked eye. Only after the invention of the microscope early in the 17th century and the subsequent discovery of the sex cells could the essentials of heredity be grasped. Before that time, ancient Greek philosopher and scientist Aristotle (4th century BC) speculated that the relative contributions of the female and the male parents were very unequal; the female was thought to supply what he called the "matter" and the male the "motion." The *Institutes of Manu*, composed in India between 100 and 300 AD, consider the role of the female like that of the field and of the male like that of the seed; new bodies are formed "by the united operation of the seed and the field." In reality both parents transmit the heredity pattern equally, and, on average, children resemble their mothers as much as they do their fathers. Nevertheless, the female and male sex cells may be very different in size and structure; the mass of an egg cell is sometimes millions of times greater than that of a spermatozoon.

The ancient Babylonians knew that pollen from a male date palm tree must be applied to the pistils of a female tree to produce fruit. German botanist Rudolph Jacob Camerarius showed in 1694 that the same is true in corn (maize). Swedish botanist and explorer Carolus Linnaeus in 1760 and German botanist Josef Gottlieb Kölreuter, in a series of works published from 1761 to 1798, described crosses of varieties and species of plants. They found that these hybrids were, on the whole, intermediate between the parents, although in some characteristics they might be closer to one parent and in others closer to the other parent. Kölreuter compared the offspring of reciprocal crosses—i.e., of crosses of variety *A* functioning as a female to variety *B* as a male and the reverse, variety *B* as a female to *A* as a male. The hybrid progenies of these reciprocal crosses were usually alike, indicating that,

Carolus Linnaeus.

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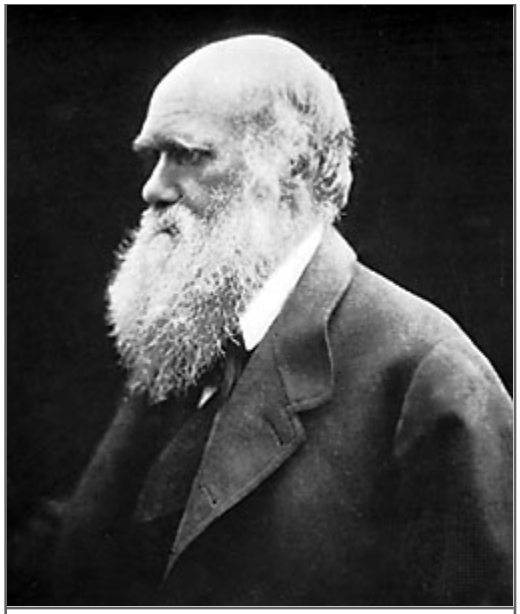
contrary to the belief of Aristotle, the hereditary endowment of the progeny was derived equally from the female and the male parents. Many more experiments on plant hybrids were made in the 1800s. These investigations also revealed that hybrids were usually intermediate between the parents. They incidentally recorded most of the facts that later led Gregor Mendel (*see* below) to formulate his celebrated rules and to found the theory of the gene. Apparently, none of Mendel's predecessors saw the significance of the data that were being accumulated. The general intermediacy of hybrids seemed to agree best with the belief that heredity was transmitted from parents to offspring by "blood," and this belief was accepted by most 19th-century biologists, including English naturalist Charles Darwin.



Charles Darwin, carbon-print photograph by Julia Margaret Cameron, 1868.

Courtesy of the International Museum of Photography at George Eastman House, Rochester, New York

The blood theory of heredity, if this notion can be dignified with such a name, is really a part of the folklore antedating scientific biology. It is implicit in such popular phrases as "half blood," "new blood," and "blue blood." It does not mean that heredity is actually transmitted through the red liquid in blood vessels; the essential point is the belief that a parent transmits to each child all its characteristics and that the hereditary endowment of a child is an alloy, a blend of the endowments of its parents, grandparents, and more-remote ancestors. This idea appeals to those who pride themselves on having a noble or remarkable "blood" line. It strikes a snag, however, when one observes that a child has some characteristics that are not present in either parent but are present in some other relatives or were present in more-remote ancestors. Even more often, one sees that brothers and sisters, though showing a family resemblance in some traits, are clearly different in others. How could the same parents transmit different "bloods" to each of their children?

Mendel disproved the blood theory. He showed (1) that heredity is transmitted through factors (now called genes) that do not blend but segregate, (2) that parents transmit only one-half of the genes they have to each child, and they transmit different sets of genes to different children, and (3) that, although brothers and sisters receive their heredities from the same parents, they do not receive the same heredities (an exception is identical twins). Mendel thus showed that, even if the eminence of some ancestor were entirely the reflection of his genes, it is quite likely that some of his descendants, especially the more remote ones, would not inherit these "good" genes at all. In sexually reproducing organisms, humans included, every individual has a unique hereditary endowment.

Lamarckism—a school of thought named for the 19th-century pioneer French

Jean-Baptiste Lamarck.

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biologist and evolutionist Jean-Baptiste de Monet, chevalier de Lamarck—assumed that characters acquired during an individual's life are inherited by his progeny, or, to put it in modern terms, that the modifications wrought by the environment in the phenotype are reflected in similar changes in the genotype. If this were so, the results of physical exercise would make exercise much easier or even dispensable in a person's offspring. Not only Lamarck but also other 19th-century biologists, including Darwin, accepted the inheritance of acquired traits. It was questioned by German biologist August Weismann, whose famous experiments in the late 1890s on the amputation of tails in generations of mice showed that such modification resulted neither in disappearance nor even in shortening of the tails of the descendants. Weismann concluded that the hereditary endowment of the organism, which he called the germ plasm, is wholly separate and is protected against the influences emanating from the rest of the body, called the somatoplasm, or soma. The germ plasm–somatoplasm are related to the genotype–phenotype concepts, but they are not identical and should not be confused with them.

The noninheritance of acquired traits does not mean that the genes cannot be changed by environmental influences; X-rays and other mutagens certainly do change them, and the genotype of a population can be altered by selection. It simply means that what is acquired by parents in their physique and intellect is not inherited by their children. Related to these misconceptions are the beliefs in "prepotency"—i.e., that some individuals impress their heredities on their progenies more effectively than others—and in "prenatal influences" or "maternal impressions"—i.e., that the events experienced by a pregnant female are reflected in the constitution of the child to be born. How ancient these beliefs are is suggested in the Book of Genesis, in which Laban produced spotted or striped progeny in sheep by showing the pregnant ewes striped hazel rods. Another such belief is "telegony," which goes back to Aristotle; it alleged that the heredity of an individual is influenced not only by his father but also by males with whom the female may have mated and who have caused previous pregnancies. Even Darwin, as late as 1868, seriously discussed an alleged case of telegony: that of a mare mated to a zebra and subsequently to an Arabian stallion, by whom the mare produced a foal with faint stripes on his legs. The simple explanation for this result is that such stripes occur naturally in some breeds of horses.

All these beliefs, from inheritance of acquired traits to telegony, must now be classed as superstitions. They do not stand up under experimental investigation and are incompatible with what is known about the mechanisms of heredity and about the

remarkable and predictable properties of genetic materials. Nevertheless, some people still cling to these beliefs. Some animal breeders take telegony seriously and do not regard as purebred the individuals whose parents are admittedly “pure” but whose mothers had mated with males of other breeds. Soviet biologist and agronomist Trofim Denisovich Lysenko was able for close to a quarter of a century, roughly between 1938 and 1963, to make his special brand of Lamarckism the official creed in the Soviet Union and to suppress most of the teaching and research in orthodox genetics. He and his partisans published hundreds of articles and books allegedly proving their contentions, which effectively deny the achievements of biology for at least the preceding century. The Lysenkoists were officially discredited in 1964.

Mendelian genetics

DISCOVERY AND REDISCOVERY OF MENDEL’S LAWS

Gregor Mendel published his work in the proceedings of the local society of naturalists in Brünn, Austria (now Brno, Czech Republic), in 1866, but none of his contemporaries appreciated its significance. It was not until 1900, 16 years after Mendel’s death, that his work was rediscovered independently by botanists Hugo de Vries in Holland, Carl Erich Correns in Germany, and Erich Tschermak von Seysenegg in Austria. Like several investigators before him, Mendel experimented on hybrids of different varieties of a plant; he focused on the common pea plant (*Pisum sativum*). His methods differed in two essential respects from those of his predecessors. First, instead of trying to describe the appearance of whole plants with all their characteristics, Mendel followed the inheritance of single, easily visible and distinguishable traits, such as round versus wrinkled seed, yellow versus green seed, purple versus white flowers, and so on. Second, he made exact counts of the numbers of plants bearing each trait; it was from such quantitative data that he deduced the rules governing inheritance.

Since pea plants reproduce usually by self-pollination of their flowers, the varieties Mendel obtained from seedsmen were “pure” —i.e., descended for several to many generations from plants with similar traits. Mendel crossed them by deliberately transferring the pollen of one variety to the pistils of another; the resulting first-generation hybrids, denoted by the symbol F_1, usually showed the traits of only one parent. For example, the crossing of yellow-seeded plants with green-seeded ones gave yellow seeds, and the crossing of purple-flowered plants with white-flowered ones gave purple-flowered plants. Traits such as the yellow-seed colour and the purple-flower colour Mendel called dominant; the green-seed colour and the white-flower colour he called recessive. It looked as if the yellow and purple “bloods” overcame or consumed the green and white “bloods.”

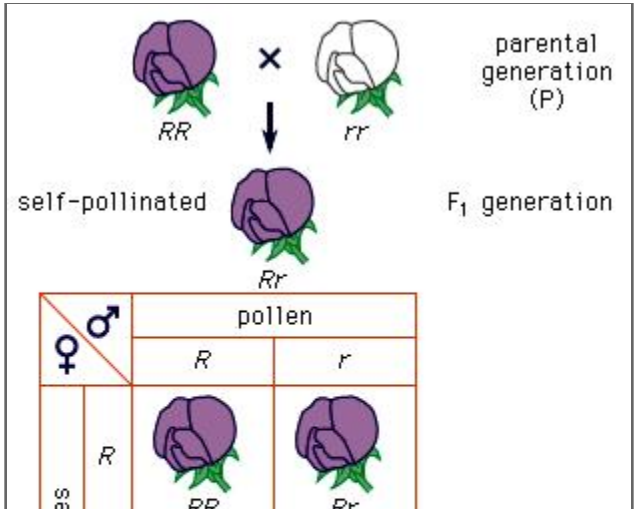
That this was not so became evident when Mendel allowed the F_1 hybrid plants to self-pollinate and produce the second hybrid generation, F_2. Here, both the dominant and the recessive traits reappeared, as pure and uncontaminated as they were in the original parents (generation P). Moreover, these traits now appeared in constant proportions: about $^3/_4$ of the plants in the

second generation showed the dominant trait and $^{1}/_{4}$ showed the recessive, a 3 to 1 ratio.

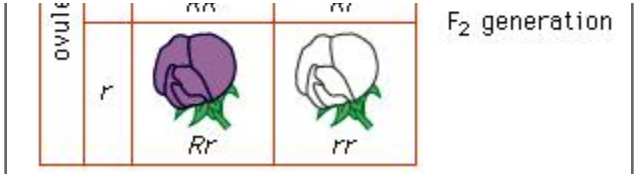
Pea plants with dominant and recessive characters obtained by Mendel in the second generation of hybrids

number dominant		number recessive		ratio
round seed	5,474	wrinkled seed	1,850	2.96:1
yellow seed	6,022	green seed	2,001	3.01:1
purple flowers	705	white flowers	224	3.15:1
tall plants	787	short plants	277	2.84:1

Mendel concluded that the sex cells, the gametes, of the purple-flowered plants carried some factor that caused the progeny to develop purple flowers, and the gametes of the white-flowered variety had a variant factor that induced the development of white flowers. In 1909 the Danish biologist Wilhelm Ludvig Johannsen proposed to call these factors genes.



An example of one of Mendel's experiments (*see*) will illustrate how the genes are transmitted and in what particular ratios. Let *R* stand for the gene for purple flowers and *r* for the gene for white flowers (dominant genes are conventionally symbolized by capital letters and recessive genes by lowercase letters). Since each pea plant contains a gene endowment half of whose set is derived from the mother and half from the father, each plant has two genes for flower colour. If the two genes are alike—for instance, both having come from white-flowered parents (*rr*)—the plant is termed a homozygote. The union of gametes with different genes gives a hybrid plant, termed a heterozygote (*Rr*). Since the gene *R*, for purple, is dominant over *r*, for white, the F_1 generation hybrids will show purple flowers. They are phenotypically purple, but their genotype contains both *R* and *r* genes, and these alternative (allelic or allelomorphic) genes do not blend or contaminate each other. Mendel inferred that, when a heterozygote forms its



Mendel's law of segregation

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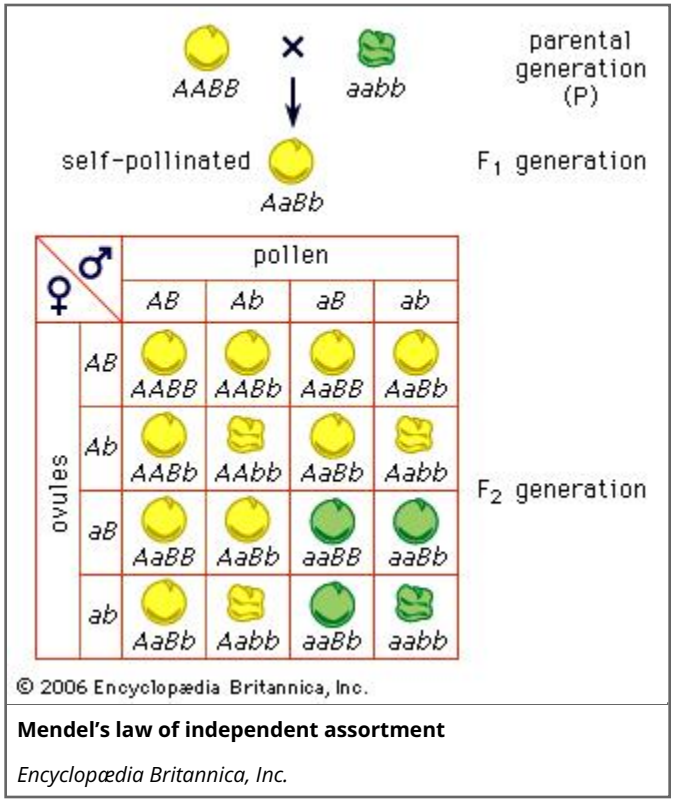
sex cells, the allelic genes segregate and pass to different gametes. This is expressed in the first law of Mendel, the law of segregation of unit genes. Equal numbers of gametes, ovules, or pollen grains are formed that contain the genes *R* and *r*. Now, if the gametes unite at random, then the F_2 generation should contain about $^1/_4$ white-flowered and $^3/_4$ purple-flowered plants. The white-flowered plants, which must be recessive homozygotes, bear the genotype *rr*. About $^1/_3$ of the plants exhibiting the dominant trait of purple flowers must be homozygotes, *RR*, and $^2/_3$ heterozygotes, *Rr*. The prediction is tested by obtaining a third generation, F_3, from the purple-flowered plants; though phenotypically all purple-flowered, $^2/_3$ of this group of plants reveal the presence of the recessive gene allele, *r*, in their genotype by producing about $^1/_4$ white-flowered plants in the F_3 generation.

Mendel also crossbred varieties of peas that differed in two or more easily distinguishable traits. When a variety with yellow round seed was crossed to a green wrinkled-seed variety (*see*), the F_1 generation hybrids produced yellow round seed. Evidently, yellow (*A*) and round (*B*) are dominant traits, and green (*a*) and wrinkled (*b*) are recessive. By allowing the F_1 plants (genotype *AaBb*) to self-pollinate, Mendel obtained an F_2 generation of 315 yellow round, 101 yellow wrinkled, 108 green round, and 32 green wrinkled seeds, a ratio of approximately 9 : 3 : 3 : 1. The important point here is that the segregation of the colour (*A*–*a*) is independent of the segregation of the trait of seed surface (*B*–*b*). This is expected if the F_1 generation produces equal numbers of four kinds of gametes, carrying the four possible combinations of the parental genes: *AB*, *Ab*, *aB*, and *ab*. Random union of these gametes gives, then, the four phenotypes in a ratio 9 dominant–dominant : 3 recessive–dominant : 3 dominant–recessive : 1 recessive–recessive. Among these four phenotypic classes there must be nine different genotypes, a supposition that can be tested experimentally by raising a third hybrid generation. The predicted genotypes are actually found. Another test is by means of a backcross (or testcross); the F_1 hybrid (phenotype yellow round seed; genotype *AaBb*) is crossed to a double recessive plant (phenotype green wrinkled seed; genotype *aabb*). If the hybrid gives four kinds of gametes in equal numbers and if all the gametes of the double recessive are alike (*ab*), the predicted progeny of the backcross are yellow round, yellow wrinkled, green



Mendel's law of independent assortment

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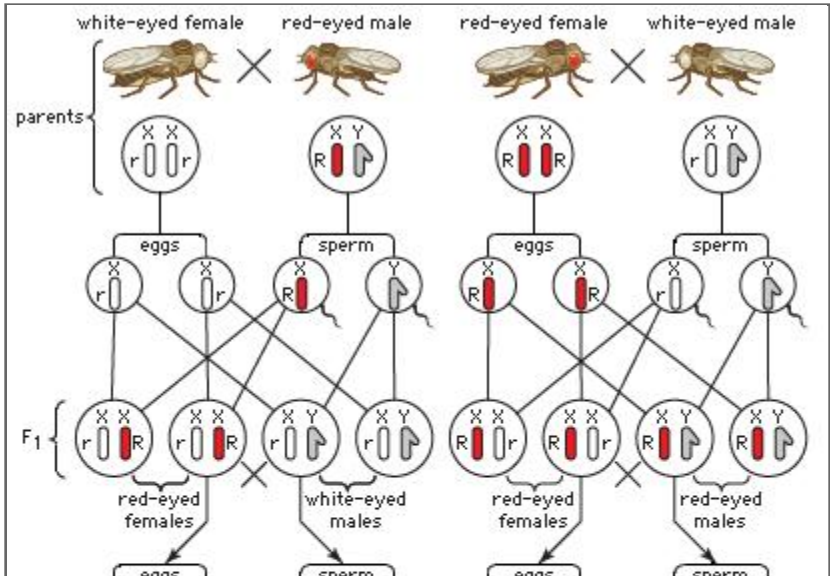
round, and green wrinkled seed in a ratio 1 : 1 : 1 : 1. This prediction is realized in experiments. When the varieties crossed differ in three genes, the F_1 hybrid forms 2^3, or eight, kinds of gametes (2^n = kinds of gametes, *n* being the number of genes). The second generation of hybrids, the F_2, has 27 (3^3) genotypically distinct kinds of individuals but only eight different phenotypes. From these results and others, Mendel derived his second law: the law of recombination, or independent assortment of genes.

UNIVERSALITY OF MENDEL'S LAWS

Although Mendel experimented with varieties of peas, his laws have been shown to apply to the inheritance of many kinds of characters in almost all organisms. In 1902 Mendelian inheritance was demonstrated in poultry (by English geneticists William Bateson and Reginald Punnett) and in mice. The following year, albinism became the first human trait shown to be a Mendelian recessive, with pigmented skin the corresponding dominant.

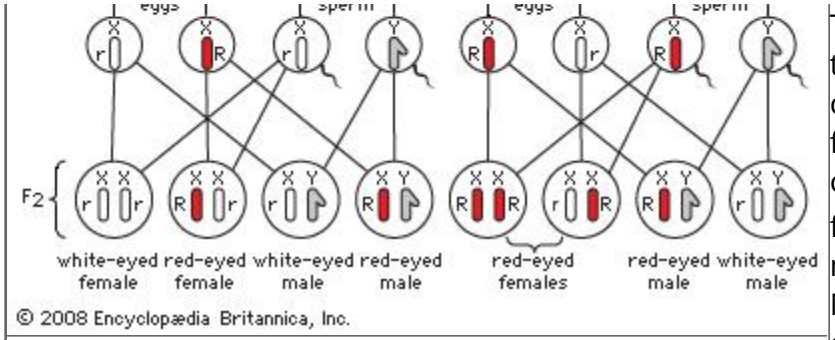
In 1902 and 1909, English physician Sir Archibald Garrod initiated the analysis of inborn errors of metabolism in humans in terms of biochemical genetics. Alkaptonuria, inherited as a recessive, is characterized by excretion in the urine of large amounts of the substance called alkapton, or homogentisic acid, which renders the urine black on exposure to air. In normal (i.e., nonalkaptonuric) persons the homogentisic acid is changed to acetoacetic acid, the reaction being facilitated by an enzyme, homogentisic acid oxidase. Garrod advanced the hypothesis that this enzyme is absent or inactive in homozygous carriers of the defective recessive alkaptonuria gene; hence, the homogentisic acid accumulates and is excreted in the urine. Mendelian inheritance of numerous traits in humans has been studied since then.



In analyzing Mendelian inheritance, it should be borne in mind that an organism is not an aggregate of independent traits, each determined by one gene. A "trait" is really an abstraction, a term of convenience in description. One gene may affect many traits (a condition termed pleiotropic). The white gene in *Drosophila* flies is pleiotropic; it affects the colour of the eyes and of the testicular envelope in the males, the fecundity and the shape of the spermatheca in the females, and the longevity of both sexes. In humans many diseases caused by a single defective gene will have a variety of symptoms, all pleiotropic manifestations of the gene.

ALLELIC INTERACTIONS

DOMINANCE RELATIONSHIPS



Sex-linked inheritance of white eyes in *Drosophila* flies.

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The operation of Mendelian inheritance is frequently more complex than in the case of the traits recorded by Mendel. In the first place, clear-cut dominance and recessiveness are by no means always found. When red- and white-flowered varieties of four-o'clock plants or snapdragons are crossed, for example, the F_1 hybrids have flowers of intermediate pink or rose colour, a situation that seems more explicable by the blending notion of inheritance than by Mendelian concepts. That the inheritance of flower colour is indeed due to Mendelian mechanisms becomes apparent when the F_1 hybrids are allowed to cross, yielding an F_2 generation of red-, pink-, and white-flowered plants in a ratio of 1 red : 2 pink : 1 white. Obviously the hereditary information for the production of red and white flowers had not been blended away in the first hybrid generation, as flowers of these colours were produced in the second generation of hybrids.

The apparent blending in the F_1 generation is explained by the fact that the gene alleles that govern flower colour in four-o'clocks show an incomplete dominance relationship. Suppose then that a gene allele R_1 is responsible for red flowers and R_2 for white; the homozygotes R_1R_1 and R_2R_2 are red and white respectively, and the heterozygotes R_1R_2 have pink flowers. A similar pattern of lack of dominance is found in Shorthorn cattle. In diverse organisms, dominance ranges from complete (a heterozygote indistinguishable from one of the homozygotes) to incomplete (heterozygotes exactly intermediate) to excessive or overdominance (a heterozygote more extreme than either homozygote).

Another form of dominance is one in which the heterozygote displays the phenotypic characteristics of both alleles. This is called codominance; an example is seen in the MN blood group system of human beings. MN blood type is governed by two alleles, *M* and *N*. Individuals who are homozygous for the *M* allele have a surface molecule (called the M antigen) on their red blood cells. Similarly, those homozygous for the *N* allele have the N antigen on the red blood cells. Heterozygotes—those with both alleles—carry both antigens.

MULTIPLE ALLELES

The traits discussed so far all have been governed by the interaction of two possible alleles. Many genes, however, are represented by multiple allelic forms within a population. (One individual, of course, can possess only two of these multiple alleles.) Human blood groups—in this case, the well-known ABO system—again provide an example. The gene that governs ABO blood types has three alleles: I^A, I^B, and I^O. I^A and I^B are codominant, but I^O is recessive. Because of the multiple alleles and

their various dominance relationships, there are four phenotypic ABO blood types: type A (genotypes I^AI^A and I^AI^O), type B (genotypes I^BI^B and I^BI^O), type AB (genotype I^AI^B), and type O (genotype I^OI^O).

GENE INTERACTIONS

Many individual traits are affected by more than one gene. For example, the coat colour in many mammals is determined by numerous genes interacting to produce the result. The great variety of colour patterns in cats, dogs, and other domesticated animals is the result of different combinations of complexly interacting genes. The gradual unraveling of their modes of inheritance was one of the active fields of research in the early years of genetics.

Two or more genes may produce similar and cumulative effects on the same trait. In humans the skin-colour difference between so-called blacks and so-called whites is due to several (probably four or more) interacting pairs of genes, each of which increases or decreases the skin pigmentation by a relatively small amount.

EPISTATIC GENES

Some genes mask the expression of other genes just as a fully dominant allele masks the expression of its recessive counterpart. A gene that masks the phenotypic effect of another gene is called an epistatic gene; the gene it subordinates is the hypostatic gene. The gene for albinism (lack of pigment) in humans is an epistatic gene. It is not part of the interacting skin-colour genes described above; rather, its dominant allele is necessary for the development of any skin pigment, and its recessive homozygous state results in the albino condition regardless of how many other pigment genes may be present. Albinism thus occurs in some individuals among dark- or intermediate-pigmented peoples as well as among light-pigmented peoples.

The presence of epistatic genes explains much of the variability seen in the expression of such dominantly inherited human diseases as Marfan syndrome and neurofibromatosis. Because of the effects of an epistatic gene, some individuals who inherit a dominant, disease-causing gene show only partial symptoms of the disease; some in fact may show no expression of the disease-causing gene, a condition referred to as nonpenetrance. The individual in whom such a nonpenetrant mutant gene exists will be phenotypically normal but still capable of passing the deleterious gene on to offspring, who may exhibit the full-blown disease.

Examples of epistasis abound in nonhuman organisms. In mice, as in humans, the gene for albinism has two variants: the allele for nonalbino and the allele for albino. The latter allele is unable to synthesize the pigment melanin. Mice, however, have another pair of alleles involved in melanin placement. These are the agouti allele, which produces dark melanization of the hair except for a yellow band at the tip, and the black allele, which produces melanization of the whole hair. If melanin cannot be formed (the situation in the mouse homozygous for the albino gene), neither agouti nor black can be expressed. Hence,

homozygosity for the albinism gene is epistatic to the agouti/black alleles and prevents their expression.

COMPLEMENTATION

The phenomenon of complementation is another form of interaction between nonallelic genes. For example, there are mutant genes that in the homozygous state produce profound deafness in humans. One would expect that the children of two persons with such hereditary deafness would be deaf. This is frequently not the case, because the parents' deafness is often caused by different genes. Since the mutant genes are not alleles, the child becomes heterozygous for the two genes and hears normally. In other words, the two mutant genes complement each other in the child. Complementation thus becomes a test for allelism. In the case of congenital deafness cited above, if all the children had been deaf, one could assume that the deafness in each of the parents was owing to mutant genes that were alleles. This would be more likely to occur if the parents were genetically related (consanguineous).

POLYGENIC INHERITANCE

The greatest difficulties of analysis and interpretation are presented by the inheritance of many quantitative or continuously varying traits. Inheritance of this kind produces variations in degree rather than in kind, in contrast to the inheritance of discontinuous traits resulting from single genes of major effect (*see* above). The yield of milk in different breeds of cattle; the egg-laying capacity in poultry; and the stature, shape of the head, blood pressure, and intelligence in humans range in continuous series from one extreme to the other and are significantly dependent on environmental conditions. Crosses of two varieties differing in such characters usually give F_1 hybrids intermediate between the parents. At first sight this situation suggests a blending inheritance through "blood" rather than Mendelian inheritance; in fact, it was probably observations of this kind of inheritance that suggested the folk idea of "blood theory."

It has, however, been shown that these characters are polygenic—i.e., determined by several or many genes, each taken separately producing only a slight effect on the phenotype, as small as or smaller than that caused by environmental influences on the same characters. That Mendelian segregation does take place with polygenes, as with the genes having major effects (sometimes called oligogenes), is shown by the variation among F_2 and further-generation hybrids being usually much greater than that in the F_1 generation. By selecting among the segregating progenies the desired variants—for example, individuals with the greatest yield, the best size, or a desirable behaviour—it is possible to produce new breeds or varieties sometimes exceeding the parental forms. Hybridization and selection are consequently potent methods that have been used for improvement of

agricultural plants and animals.

Polygenic inheritance also applies to many of the birth defects (congenital malformations) seen in humans. Although expression of the defect itself may be discontinuous (as in clubfoot, for example), susceptibility to the trait is continuously variable and follows the rules of polygenic inheritance. When a developmental threshold produced by a polygenically inherited susceptibility and a variety of environmental factors is exceeded, the birth defect results.

Heredity and environment

PREFORMISM AND EPIGENESIS

A notion that was widespread among pioneer biologists in the 18th century was that the fetus, and hence the adult organism that develops from it, is preformed in the sex cells. Some early microscopists even imagined that they saw a tiny homunculus, a diminutive human figure, encased in the human spermatozoon. The development of the individual from the sex cells appeared deceptively simple: it was merely an increase in the size and growth of what was already present in the sex cells. The antithesis of the early preformation theories was theories of epigenesis, which claimed that the sex cells were structureless jelly and contained nothing at all in the way of rudiments of future organisms. The naive early versions of preformation and epigenesis had to be given up when embryologists showed that the embryo develops by a series of complex but orderly and gradual transformations (*see* animal development). Darwin's "Provisional Hypothesis of Pangenesis" was distinctly preformistic; Weismann's theory of determinants in the germ plasm, as well as the early ideas about the relations between genes and traits, also tended toward preformism.

Heredity has been defined as a process that results in the progeny's resembling his parents. A further qualification of this definition states that what is inherited is a potential that expresses itself only after interacting with and being modified by environmental factors. In short, all phenotypic expressions have both hereditary and environmental components, the amount of each varying for different traits. Thus, a trait that is primarily hereditary (e.g., skin colour in humans) may be modified by environmental influences (e.g., suntanning). And conversely, a trait sensitive to environmental modifications (e.g., weight in humans) is also genetically conditioned. Organic development is preformistic insofar as a fertilized egg cell contains a genotype that conditions the events that may occur and is epigenetic insofar as a given genotype allows a variety of possible outcomes. These considerations should dispel the reluctance felt by many people to accept the fact that mental as well as physiological and physical traits in humans are genetically conditioned. Genetic conditioning does not mean that heredity is the "dice of destiny." At least in principle, but not invariably in practice, the development of a trait may be manipulated by changes in the environment.

HERITABILITY

Although hereditary diseases and malformations are, unfortunately, by no means uncommon in the aggregate, no one of them occurs very frequently. The characteristics by which one person is distinguished from another—such as facial features, stature, shape of the head, skin, eye and hair colours, and voice—are not usually inherited in a clear-cut Mendelian manner, as are some hereditary malformations and diseases. This is not as strange as it may seem. The kinds of gene changes, or mutations, that produce morphological or physiological effects drastic enough to be clearly set apart from the more usual phenotypes are likely to cause diseases or malformations just because they are so drastic.

The variations that occur among healthy persons are, as a general rule, caused by polygenes with individually small effects. The same is true of individual differences among members of various animal and plant species. Even brown-blue eye colour in humans, which in many families behaves as if caused by two forms of a single gene (brown being dominant and blue recessive), is often blurred by minor gene modifiers of the pigmentation. Some apparently blue-eyed persons actually carry the gene for the brown eye colour, but several additional modifier genes decrease the amount of brown pigment in the iris. This type of genetic process can influence susceptibility to many diseases (e.g., diabetes) or birth defects (e.g., cleft lip—with or without cleft palate).

The question geneticists must often attempt to answer is how much of the observed diversity between persons or between individuals of any species is because of hereditary, or genotypic, variations and how much of it is because of environmental influences. Applied to human beings, this is sometimes referred to as the nature-nurture problem. With animals or plants the problem is evidently more easily soluble than it is with people. Two complementary approaches are possible. First, individual organisms or their progenies are raised in environments as uniform as can be provided, with food, temperature, light, humidity, etc., carefully controlled. The differences that persist between such individuals or progenies probably reflect genotypic differences. Second, individuals with similar or identical genotypes are placed in different environments. The phenotypic differences may then be ascribed to environmental induction. Experiments combining both approaches have been carried out on several species of plants that grow naturally at different altitudes, from sea level to the alpine zone of the Sierra Nevada in California. Young yarrow plants (*Achillea*) were cut into three parts, and the cuttings were replanted in experimental gardens at sea level, at mid-altitude (4,800 feet [1,460 metres]), and at high altitude (10,000 feet [3,050 metres]). It was observed that the plants native at sea level grow best in their native habitat, grow less well at mid-altitudes, and die at high altitudes. On the other hand, the alpine race survives and develops better at the high-altitude transplant station than it does at lower altitudes.

With organisms that cannot survive being cut into pieces and placed in controlled environments, a partitioning of the observed variability into genetic and environmental components may be attempted by other methods. Suppose that in a certain population individuals vary in stature, weight, or some other trait. These characters can be measured in many pairs of parents and in their progenies raised under different environmental conditions. If the variation is owing entirely to environment and not at all to heredity, then the expression of the character in the parents and in the offspring will show no correlation (heritability = zero). On the other hand, if the environment is unimportant and the character is uncomplicated by dominance, then the means of this character in the progenies will be the same as the means of the parents; with differences in the expression in females and in males taken into account, the heritability will equal unity. In reality, most heritabilities are found to lie between zero and one.

Some heritability estimates

trait	correlation
Cattle	
butterfat percentage	0.6
milk yield	0.3
Pigs	
body length	0.5
weight at 180 days	0.3
litter size	0.15
Poultry	
egg weight	0.6
annual egg production	0.3
body weight	0.2
viability	0.1
Drosophila melanogaster	
abdominal bristle number	0.5
body size	0.4
ovary size	0.3
egg production	0.2

It is important to understand clearly the meaning of heritability estimates. They show that, given the range of the environments in which the experimental animals lived, one could predict the average body sizes in the progenies of pigs better than one could predict the average numbers of piglets in a litter. The heritability is, however, not an inherent or unchangeable property of each character. If one could make the environments more uniform, the heritabilities would rise, and with more-diversified environments they would decrease. Similarly, in populations that are more variable genetically, the heritabilities increase, and in genetically uniform ones, they decrease. In humans the situation is even more complex, because the environments of the parents and of their children are in many ways interdependent. Suppose, for example, that one wishes to study the heritability of stature, weight, or susceptibility to tuberculosis. The stature, weight, and liability to contract tuberculosis depend to some extent on the quality of nutrition and generally on the economic well-being of the family. If no allowance is made for this fact, the heritability estimates arrived at may be spurious; such heritabilities have indeed been claimed for such things as administrative, legal, or military talents and for social eminence in general. It is evident that having socially eminent parents makes it easier for the children to achieve such eminence also; biological heredity may have little or nothing to do with this.

A general conclusion from the evidence now available may be stated as follows: diversity in almost any trait—physical, physiological, or behavioural—owes in part to genetic variables and in part to environmental variables. In any array of environments, individuals with more nearly similar genetic endowments are likely to show a greater average resemblance than the carriers of more diverse genetic endowments. It is, however, also true that in different environments the carriers of similar genetic endowments may grow, develop, and behave in different ways.

Heredity and evolution

At the centre of the theory of evolution as proposed by Charles Darwin and Alfred Russell Wallace were the concepts of variation and natural selection. Hereditary variants were thought to arise naturally in populations, and then these were either selected for or against by the contemporary environmental conditions. In this way, subsequent generations either became enriched or impoverished for specific variant types. Over the long term, the accumulation of such changes in populations could lead to the formation of new species and higher taxonomic categories. However, although hereditary change was basic to the theory, in the 19th-century world of Darwin and Wallace, the fundamental unit of heredity—the gene—was unknown. The birth and proliferation of the science of genetics in the 20th century after the discovery of Mendel's laws made it possible to consider the process of evolution by natural selection in terms of known genetic processes.

Population genetics

Because the processes of variation and selection take place at the population level, the basic theory of the genetics of evolutionary change is contained in the general area known as population genetics.

A simple way of viewing evolutionary change at the genotypic level would be to invent some hypothetical ancestral genotype, such as *AAbbccDDEE*, and an "evolved" derivative, such as *aaBBccddee*. (For illustrative purposes, only five genes are used, and these are assumed to be all homozygous.) Also, for simplicity it can be assumed that in both the ancestral and the evolved populations all individuals are identical. Clearly for all the genes except *cc*, a new allele completely replaces the original allele, and the new alleles can be either dominant or recessive. For example, in the case of the first gene, in the ancestral population all alleles are *A*, and in the evolved population all are *a*. For *a* to replace *A*, the population must go through stages in which there are mixtures of *A* and *a* alleles present in the population at the same time. In population genetics, allele frequency is the measurement of the commonness of an allele. The convention is to let the frequency of a dominant allele be *p* and that of a recessive allele *q*. Both are generally expressed as decimal fractions. In the above example, *p* changes from 1 to 0, and *q* changes from 0 to 1. Since there are only two alleles in this example, $p + q$ must always equal 1. In the intermediate stages, there must be times when there are intermediate allele frequencies, for example when $p = 0.4$ and $q = 0.6$.

What can be said about genotype frequencies in the intermediate populations? In the ancestral and derived populations there must have been the following genotypic frequencies:

Ancestral *AA* = 1, *Aa* = 0, *aa* = 0

Evolved *AA* = 0, *Aa* = 0, *aa* = 1

Intuitively it seems that, in the intermediate stages, there must be more-complex proportions, including some heterozygotes. One possible intermediate stage is as follows:

AA = 0.30, *Aa* = 0.20, *aa* = 0.50

The allele frequencies at such an intermediate stage can be calculated by "adding up" the alleles. Hence, the frequency of *A* will be 0.30 plus $^{1}/_{2}$ of 0.20 because the heterozygotes only carry one *A* allele. This is written

$$p = 0.30 + {}^{0.20}/_{2} = 0.40$$

Similarly, $q = 0.50 + {}^{0.20}/_{2} = 0.60$

(Noting these values for *p* and *q*, it is possible that this could have been the population discussed earlier, in which these specific values for *p* and *q* were hypothesized.)

In general, if D = frequency of homozygous dominants, R = frequency of homozygous recessives, and H = frequency of heterozygotes, then

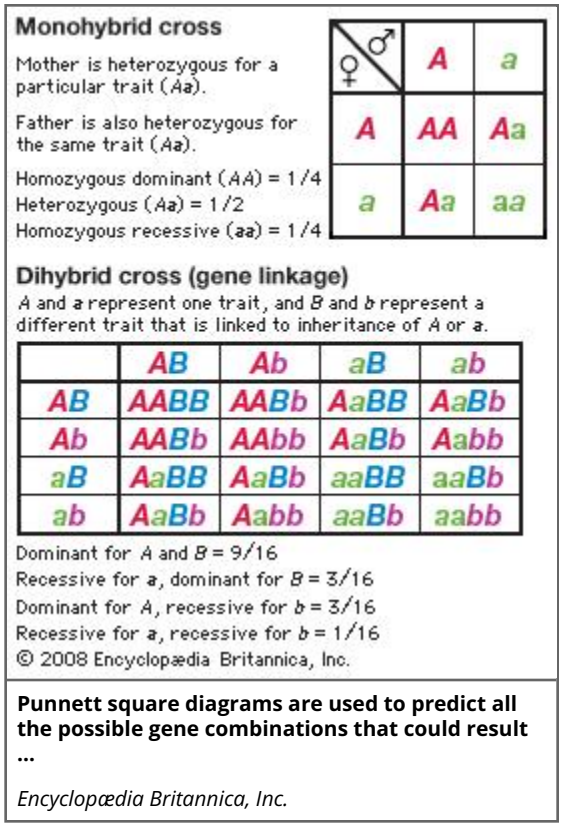
$$p = D + {}^{H}/_{2}$$

and

$$q = R + {}^{H}/_{2}$$

This section has shown the importance of the concepts of allele frequency and genotype frequency in describing the genetic structure of populations. Of these, allele frequency is the simpler descriptor, and it forms the central tool of population genetics. Hence, the genetic basis of evolutionary change at the population level is described in terms of changes of allele frequencies.

HARDY-WEINBERG EQUILIBRIUM



Punnett square diagrams are used to predict all the possible gene combinations that could result ...

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It is a curious fact that populations show no inherent tendency to change allele or genotype frequencies. In the absence of selection or any of the other forces that can drive evolution, a population with given values of p and q will settle into a special stable set of genotypic proportions called a Hardy-Weinberg equilibrium. This principle was first realized by Godfrey Harold Hardy and Wilhelm Weinberg in 1908. The Hardy-Weinberg equilibrium of a population with allele frequencies p and q is defined by the set of genotypic frequencies p^2 of AA, $2pq$ of Aa, and q^2 of aa.

When such a population reproduces itself to make a new generation, the lack of change is made apparent. It is intuitive that the allele frequencies p and q in the population are also measures of the frequencies of eggs and sperm used in creating a new generation (represented in the formula below). The new generation produced from the zygotes has exactly the same genotypic proportions as the first generation (the parents of the zygote).

Some specific allele frequencies, 0.7 for p and 0.3 for q, can be used to illustrate the calculation of the genotypic frequencies that constitute the Hardy-Weinberg equilibrium:

$$p \times p = 0.7 \times 0.7 = 0.49 \text{ of } AA$$

$$2 \times p \times q = 2 \times 0.7 \times 0.3 = 0.42 \text{ of } Aa$$

$$q \times q = 0.3 \times 0.3 = 0.09 \text{ of } aa$$

When this population reproduces, there will be 0.49 + 0.21 = 0.7 of *A* gametes and 0.09 + 0.21 = 0.3 of *a* gametes (*see* the formulas in the previous section), and, when these gametes combine, the population in the next generation will clearly have the same genotypic proportions as the previous one.

These simple calculations rely on several underlying assumptions. Perhaps the most crucial one is that there is random mating, or mating regardless of the genotype of the partner. In addition, the population must be large, and there can be no other pressures, such as selection, that can change allele frequencies. Despite these stringent requirements, many natural populations that have been studied are in Hardy-Weinberg equilibrium for the genes under investigation. The Hardy-Weinberg equilibrium constitutes an important benchmark for population genetic analysis.

If the Hardy-Weinberg principle of population genetics shows that there is no inherent tendency for evolutionary change, then how does change occur? This is considered in the following sections.

CHANGES IN GENE FREQUENCIES

SELECTION

One assumption behind the calculation of unchanging genotypic frequencies in Hardy-Weinberg equilibrium is that all genotypes have the same fitness. In genetics, fitness does not necessarily have to do with muscles; fitness is a measure of the ability to produce fertile offspring. In reality, the fitnesses of different genotypes are highly variable. The genotype with the greatest fitness is given the fitness value (*w*) of 1, and the lesser fitnesses are fractions of 1. For example, if snails of genotypes *AA* and *Aa* were to have an average of 100 offspring but those of genotype *aa* only 70, then the fitnesses of these three genotypes would be 1, 1, and 0.7, respectively. The proportional difference from the most fit is called the selection coefficient, *s*. Hence, $s = 1 - w$.

Alleles carried by less-fit individuals will be gradually lost from the population, and the relevant allele frequency will decline. This is the fundamental way in which natural selection operates in a population. Selection against dominant alleles is relatively efficient, because these are by definition expressed in the phenotype. Selection against recessive alleles is less efficient, because these alleles are sheltered in heterozygotes. Even though populations under selection technically are not in Hardy-Weinberg equilibrium, the proportions of the formula can be used as an approximation to show the relative proportions of homozygous recessives and heterozygotes. If a rare deleterious recessive allele is of frequency $^{1}/_{50}$ in the population, then $(^{1}/_{50})^{2}$, or 1 out of 2,500, individuals will express the recessive phenotype and be a candidate for negative selection. Heterozygotes will be at a frequency of $2pq = 2 \times {}^{49}/_{50} \times {}^{1}/_{50}$, or about 1 in 25. In other words, the heterozygotes are 100 times more common than recessive homozygotes; hence, most of the recessive alleles in a population will escape selection.

Because of the sheltering effect of heterozygotes, selection against recessive phenotypes changes the frequency of the recessive allele slowly. Even if the most severe level of selection is imposed, giving the recessive phenotype a fitness of zero (no fertile offspring), the recessive allele frequency (expressed as a fraction of the form $^1/_x$) will increase in denominator by 1 in every generation. Therefore, to halve an allele frequency from $^1/_{50}$ to $^1/_{100}$ would proceed slowly from $^1/_{50}$ to $^1/_{51}$, $^1/_{52}$, $^1/_{53}$, and so on and would take 50 generations to get to $^1/_{100}$. For lower intensities of selection, the progress would be even slower.

A different type of natural selection occurs when the fitness of a heterozygote exceeds the fitness of both homozygotes. The maintenance in human populations of the severe hereditary disease sickle cell anemia is owing to this form of selection. The disease allele (Hb^S) produces a specific type of hemoglobin that causes distortion (sickling) of the red blood cells in which the hemoglobin is carried. (Normal hemoglobin is coded by another allele, Hb^A). Accordingly, the possible genotypes are $Hb^A Hb^A$, $Hb^A Hb^S$, and $Hb^S Hb^S$. The latter individuals are homozygous for the sickle cell allele and will develop severe anemia because the oxygen transporting property of their blood is compromised. While the condition is not lethal before birth, such individuals rarely survive long enough to reproduce. On these grounds it might be expected that the disease allele would be selected against, driving the allele frequency to very low levels. However, in tropical areas of the world, the allele and the disease are common. The explanation is that the $Hb^A Hb^S$ heterozygote is fitter and capable of leaving more offspring than is the homozygous normal $Hb^A Hb^A$ in an environment containing the falciparum form of malaria. This extra measure of protection is evidently provided by the sickle cell hemoglobin, which is detrimental to the malaria parasite. In malarial environments, therefore, populations that contain the sickle cell gene have advantages over populations free of this gene. The former populations are in less danger from malaria, although they “pay” for this advantage by sacrificing in every generation some individuals who die of anemia.

MUTATION

Genetics has shown that mutation is the ultimate source of all hereditary variation. At the level of a single gene whose normal functional allele is *A*, it is known that mutation can change it to a nonfunctional recessive form, *a*. Such “forward mutation” is more frequent than “back mutation” (reversion), which converts *a* into *A*. Molecular analysis of specific examples of mutant recessive alleles has shown that they are generally a heterogeneous set of small structural changes in the DNA, located throughout the segment of DNA that constitutes that gene. Hence, in an example from medical genetics, the disease phenylketonuria is inherited as a recessive phenotype and is ascribed to a causative allele that generally can be called *k*. However, sequencing alleles of many independent cases of phenylketonuria has shown that this *k* allele is in fact a set of many different kinds of mutational changes, which can be in any of the protein-coding regions of that gene.

Recessive deleterious mutations are relatively rare, generally in the order of 1 per 105 or 106 mutant gametes per generation. Their constant occurrence over the generations, combined with the even greater rarity of back mutations, leads to a gradual

accumulation in the population. This accumulation process is called mutational pressure.

Since mutational pressure to a deleterious recessive allele and selection pressure against the homozygous recessives are forces that act in opposite directions, another type of equilibrium is attained that effectively sets the value of *q*. Mathematically, *q* is determined by the following expression in which *u* is the net mutation rate of *A* to *a*, and *s* is the selection coefficient presented above:

$$q^2 = (u/s), \text{ or } q = \sqrt{(u/s)}$$

NONRANDOM MATING

Many species engage in alternatives to random mating as normal parts of their cycle of sexual reproduction. An important exception is sexual selection, in which an individual chooses a mate on the basis of some aspect of the mate's phenotype. The selection can be based on some display feature such as bright feathers, or it may be a simple preference for a phenotype identical to the individual's own (positive assortative mating).

Two other important exceptions are inbreeding (mating with relatives) and enforced outbreeding. Both can shift the equilibrium proportions expected under Hardy-Weinberg calculations. For example, inbreeding increases the proportions of homozygotes, and the most extreme form of inbreeding, self-fertilization, eventually eliminates all heterozygotes.

Inbreeding and outbreeding are evolutionary strategies adopted by plants and animals living under certain conditions. Outbreeding brings gametes of different genotypes together, and the resulting individual differs from the parents. Increased levels of variation provide more evolutionary flexibility. All the showy colors and shapes of flowers are to promote this kind of exchange. In contrast, inbreeding maintains uniform genotypes, a strategy successful in stable ecological habitats.

In humans, various degrees of inbreeding have been practiced in different cultures. In most cultures today, matings of first cousins are the maximal form of inbreeding condoned by society. Apart from ethical considerations, a negative outcome of inbreeding is that it increases the likelihood of homozygosity of deleterious recessive alleles originating from common ancestors, called homozygosity by descent. The inbreeding coefficient *F* is a measure of the likelihood of homozygosity by descent; for example, in first-cousin marriages, $F = {}^1/_{16}$. A large proportion of recessive hereditary diseases can be traced to first-cousin marriages and other types of inbreeding.

RANDOM GENETIC DRIFT

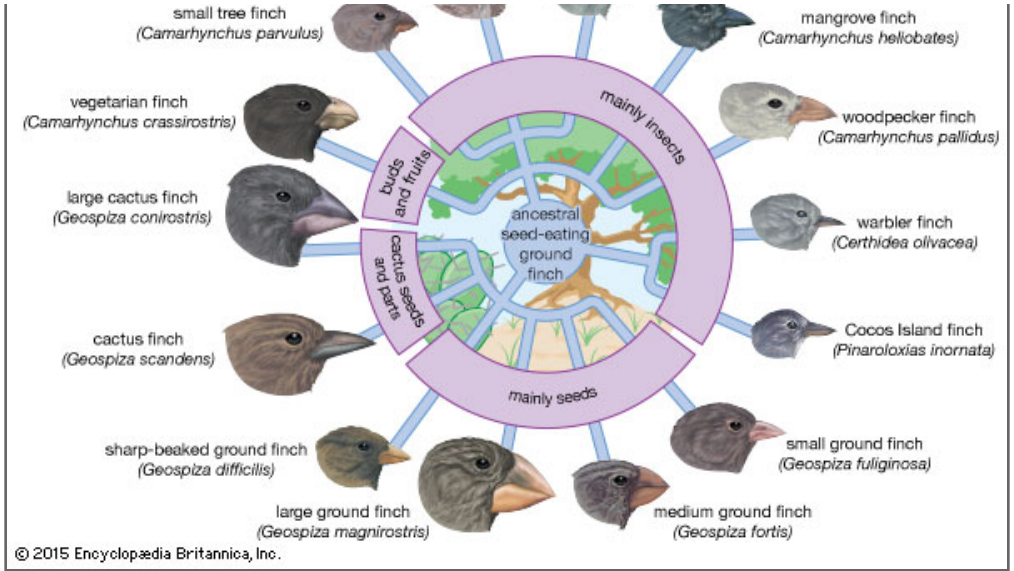
In populations of finite size, the genetic structure of a new generation is not necessarily that of the previous one. The explanation lies in a sampling effect, based on the fact that a subsample from any large set is not always representative of the larger set. The gametes that form any generation can be thought of as a sample of the alleles from the parental one. By chance the sample might not be random; it could be skewed in either direction. For example, if $p = 0.600$ and $q = 0.400$, sampling "error" might result in the gametes having a p value of 0.601 and a q of 0.399. If by chance this skewed sampling occurs in the same direction from generation to generation, the allele frequency can change radically. This process is known as random genetic drift. As might be expected, the smaller the population, the greater chance of sampling error and hence significant levels of drift in any one generation. In extreme cases, drift over the generations can result in the complete loss of one allele; in these occurrences the other is said to be fixed.

Other cases of sampling error occur when new colonies of plants or animals are founded by small numbers of migrants (founder effect) and when there is radical reduction in population size because of a natural catastrophe (population bottleneck). One inevitable effect of these processes is a reduction in the amount of variation in the population after the size reduction. Two species that have gone through drastic bottlenecks with the associated reduction of genetic variation are cheetahs (Africa) and northern elephant seals (North America).

Microevolution

There is ample evidence that the processes described above are at work in natural populations. Together, these changes are called microevolution—in other words, small-scale evolution. Even within the relatively short period of time since Darwin, it has been possible to document such processes. Allelic variation has been found to be common in nature. It is detected as polymorphism, the presence of two or more distinct hereditary forms associated with a gene. Polymorphism can be morphological, such as blue and brown forms of a species of marine mussel, or molecular, detectable only at the DNA or protein level. Although much of this polymorphism is not understood, there are enough examples of selection of polymorphic forms to indicate that it is potentially adaptive. Selection has been observed favouring melanic (dark) forms of peppered moths in industrial areas and favouring resistance to toxic agents such as the insecticide DDT, the rat poison warfarin, and the virus that causes the disease myxomatosis in rabbits.

More-complex genetic changes have been documented, leading to special locally adapted "ecotypes." Anoles (a type of lizard) on certain



Fourteen species of Galapagos finches that evolved from a common ancestor. The different shapes of ...

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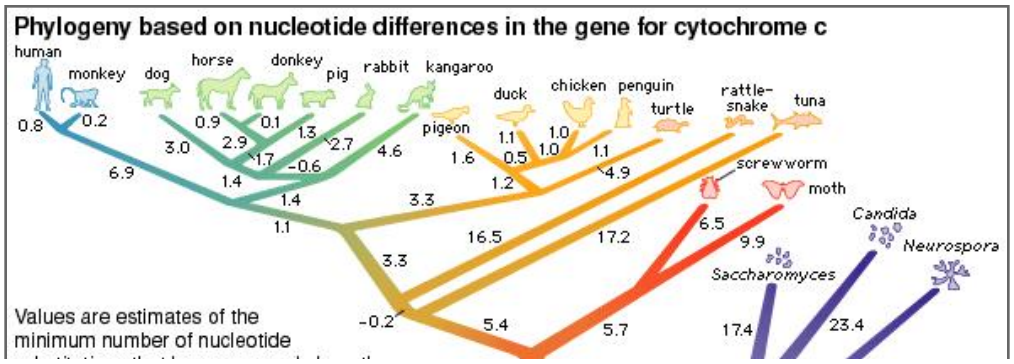
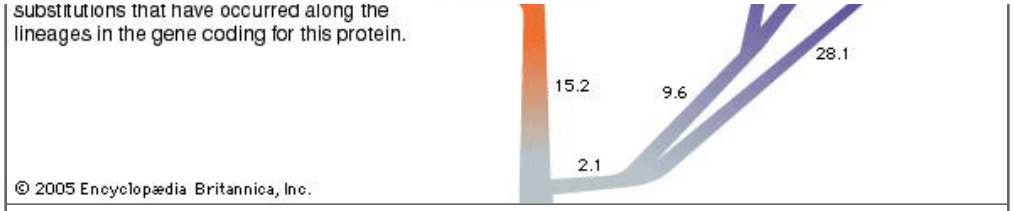
Caribbean islands show convincing examples of adaptations to specific habitats, such as tree trunks, tree branches, or grass. Introductions of lizards onto uncolonized islands result in demonstrable microevolutionary adaptations to the various vacant niches. On the Galapagos Islands, studies over several decades have documented adaptive changes in the beaks of finches. In some studies, documented changes have led to incipient new species. An example is the apple maggot, the larva of a fly in North America that has evolved from a similar fly living on hawthorns—all in the period since the introduction of apples. The formation of new species was a key component of Darwin's original theory. Now it appears that the accumulation of enough small-scale genetic changes can lead to the inability to mate with members of an ancestral population; such reproductive isolation is the key step in species formation.

It is reasonable to assume that the continuation of microevolutionary genetic changes over very long periods of time can give rise to new major taxonomic groups, the process of macroevolution. There are few data that bear directly on the processes of macroevolution, but gene analysis does provide a way for charting macroevolutionary relationships indirectly, as shown below.

DNA PHYLOGENY



The ability to isolate and sequence specific genes and genomes has been of great significance in deducing trees of evolutionary relatedness. An important discovery that enables this sort of analysis is the considerable evolutionary conservation between organisms at the genetic level. This means that different organisms have a large proportion of their genes in common, particularly those that code for proteins at the central core of the chemical machinery



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of the cell. For example, most organisms have a gene coding for the energy-producing protein cytochrome C, and furthermore, this gene has a very similar nucleotide sequence in all organisms (that is, the sequence is conserved). However, the sequences of cytochrome C in different organisms do show differences, and the key to phylogeny is that the differences are proportionately fewer between organisms that are closely related. The interpretation of this observation is that organisms that share a common ancestor also share common DNA sequences derived from that ancestor. When one ancestral species splits into two, differences accumulate as a result of mutations, a process called divergence. The greater the amount of divergence, the longer must have been the time since the split occurred. To carry out this sort of analysis, the DNA sequence data are fed into a computer. The computer positions similar species together on short adjacent branches showing a relatively recent split and dissimilar species on long branches from an ancient split. In this way a molecular phylogenetic tree of any number of organisms can be drawn.

DNA difference in some cases can be correlated with absolute dates of divergence as deduced from the fossil record. Then it is possible to calculate divergence as a rate. It has been found that divergence is relatively constant in rate, giving rise to the idea that there is a type of "molecular clock" ticking in the course of evolution. Some ticks of this clock (in the form of mutations) are significant in terms of adaptive changes to the gene, but many are undoubtedly neutral, with no significant effect on fitness.

One of the interesting discoveries to emerge from molecular phylogeny is that gene duplication has been common during evolution. If an extra copy of a gene can be made, initially by some cellular accident, then the "spare" copy is free to mutate and evolve into a separate function.

Molecular phylogeny of some genes has also pointed to unexpected cases of, say, a plant gene nested within a tree of animal genes of that type or a bacterial gene nested within a plant phylogenetic tree. The explanation for such anomalies is that there has been horizontal transmission from one group to another. In other words, on rare occasions a gene can hop laterally from one species to another. Although the mechanisms for horizontal transmission are presently not known, one possibility is that bacteria or viruses act as natural vectors for transferring genes.

SYNTENY

Genomic sequencing and mapping have enabled comparison of the general structures of genomes of many different species. The general finding is that organisms of relatively recent divergence show similar blocks of genes in the same relative positions in the genome. This situation is called synteny, translated roughly as possessing common chromosome sequences. For example,

many of the genes of humans are syntenic with those of other mammals—not only apes but also cows, mice, and so on. Study of synteny can show how the genome is cut and pasted in the course of evolution.

POLYPLOIDY

Genomic analysis also has shown that one of the important mechanisms of evolution is multiplication of chromosome sets, resulting in polyploidy ("many genomes"). In plants and animals, spontaneous doubling of chromosomes can occur. In some plants, the chromosomes of two related species unite via cross-pollination to form a fusion product. This product is sterile because each chromosome needs a pairing partner in order for the plant to be fertile. However, the chromosomes of the fusion product can accidentally double, resulting in a new, fertile species. Wheat is an example of a plant that evolved by this means through a union between wild grasses, but a large proportion of plants went through similar ancestral polyploidization.

Human evolution

Many of the techniques of evolutionary genetics can be applied to the evolution of humans. Charles Darwin created a large controversy in Victorian England by suggesting in his book *The Descent of Man* that humans and apes share a common ancestor. Darwin's assertion was based on the many shared anatomical features of apes and humans. DNA analysis has supported this hypothesis. At the DNA sequence level, the genomes of humans and chimpanzees are 99 percent identical. Furthermore, when phylogenetic trees are constructed using individual genes, humans and apes cluster together in short terminal branches of the trees, suggesting very recent divergence. Synteny too is impressive, with relatively minor chromosomal rearrangements.

Fossils have been found of various extinct forms considered to be intermediates between apes and humans. Notable is the African genus *Australopithecus*, generally believed to be one of the earliest hominins and an intermediate on the path of human evolution. The first toolmaker was *Homo habilis*, followed by *Homo erectus* and finally *Homo sapiens* (modern humans). *H. habilis* fossils have been found only in Africa, whereas fossils of *H. erectus* and *H. sapiens* are found throughout the Old World. Phylogenetic trees based on DNA sequencing of all peoples have shown that Africans represent the root of the trees. This is interpreted as evidence that *H. sapiens* evolved in Africa, spread throughout the globe, and outcompeted *H. erectus* wherever the two cohabited.

Variations of DNA, either unique alleles of individual genes or larger-sized blocks of variable structure, have been used as markers to trace human migrations across the globe. Hence, it has been possible to trace the movement of *H. sapiens* out of Africa and into Europe and Asia and, more recently, to the American continents. Also, genetic markers are useful in plotting human migrations that occurred in historical time. For example, the invasion of Europe by various Asian conquerors can be followed using blood-type alleles.

As humans colonized and settled permanently in various parts of the world, they differentiated themselves into distinct groups called races. Undoubtedly, many of the features that distinguish races, such as skin colour or body shape, were adaptive in the local settings, although such adaptiveness is difficult to demonstrate. Nevertheless, genomic analysis has revealed that the concept of race has little meaning at the genetic level. The differences between races are superficial, based on the alleles of a relatively small number of genes that affect external features. Furthermore, while races differ in allele frequencies, these same alleles are found in most races. In other words, at the genetic level there are no significant discontinuities between races. It is paradoxical that race, which has been so important to people throughout the course of human history, is trivial at the genetic level—an important insight to emerge from genetic analysis.

> *Anthony J.F. Griffiths*