12

The Genetical Theory of Natural Selection

Natural selection is the most important concept in the theory of evolutionary processes. It is surely the explanation for most of the characteristics of organisms that we find most interesting, ranging from the origin of DNA as the genetic material to the complexities of the human brain. In its elementary form, natural selection—differential reproductive success—is a very simple concept. But its explanatory power is much greater if we take into account the many ways in which it can act and the ways in which its outcome is affected, especially in sexual organisms, by genetic factors such as recombination and the relationship between phenotype and genotype. When we take into account these complexities, we can begin to address a great variety of questions: Why are some characteristics, but not others, variable within species? How great a difference can we expect to see among different populations of a species, such as our own? Do populations of a species always evolve the same adaptation to a particular environmental challenge? How do cooperative and selfish behaviors evolve? Why do some species reproduce sexually and others asexually? How can we explain the extraordinary display feathers of the peacock, the immense fecundity of elms and oysters, the brevity of a mayfly's life, the pregnancy of the male seahorse, the abundance of transposable elements in our own genome?

Maximizing reproduction. The copious fruits of the rowan tree (*Sorbus aucuparia*) will be eaten by birds, which will then disperse the undigested seeds. Only a small percentage of the seeds will take root and grow to reproductive age. (Photo © Geoff Dore/naturepl.com.)

Darwin fully realized that a truly complete theory of evolutionary change would require understanding the mechanism of inheritance. That understanding began to develop only in 1900, when Mendel's publication was discovered. Modern evolutionary theory started to develop as the growing understanding of Mendelian genetics was synthesized with Darwin's theory of selection. The "genetical theory of natural selection" (as the pioneering population geneticist R. A. Fisher entitled his seminal 1930 book) is the keystone of contemporary evolutionary theory, on which our understanding of adaptive evolution depends.

As we delve into the genetical theory of natural selection, we should keep the following important points about natural selection in mind:

- *Natural selection is not the same as evolution.* Evolution is a two-step process: the origin of genetic variation by mutation or recombination, followed by changes in the frequencies of alleles and genotypes, caused chiefly by genetic drift or natural selection. Neither natural selection nor genetic drift accounts for the origin of variation.
- *Natural selection is different from evolution by natural selection.* In some instances, selection occurs—that is, in each generation, genotypes differ in survival or fecundity—yet the proportions of genotypes and alleles stay the same from one generation to another.
- Although natural selection may be said to exist whenever different phenotypes vary in average reproductive success, *natural selection can have no evolutionary effect unless phenotypes differ in genotype.* For instance, selection among genetically identical members of a clone, even though they differ in phenotype, can have no evolutionary consequences. Therefore, it is useful to describe the reproductive success, or fitness, of genotypes, even though genotypes differ in fitness only because of differences in phenotype.
- Because natural selection is variation in average reproductive success (which includes survival), a feature cannot evolve by natural selection unless it makes a positive contribution to the reproduction or survival of individuals that bear it. The long-haired tail of a horse, used as a fly-switch, could not have evolved merely because it increases horses' comfort; it must have resulted in increased reproductive success, perhaps by lowering mortality caused by fly-borne diseases.

Unlike genetic drift, inbreeding, and gene flow, which act at the same rate on all loci in a genome, the allele frequency changes caused by natural selection in a sexually reproducing species proceed largely independently at different loci. Moreover, different characteristics of a species evolve at different rates (mosaic evolution), as we would expect if natural selection brings about changes in certain features while holding others constant (see Chapter 2). Thus we are justified in beginning our analysis of natural selection with a single variable locus that alters a phenotypic character.

Fitness

Unless otherwise specified, the subsequent discussion of natural selection concerns selection at the level of individual organisms within populations. The consequences of natural selection depend on (1) the relationship between phenotype and fitness, and (2) the relationship between phenotype and genotype. These relationships, then, yield (3) a relationship between fitness and genotype, which determines (4) whether or not evolutionary change occurs.

Modes of selection

The relationship between phenotype and fitness can often be described as one of three MODES OF SELECTION (Figure 12.1). For a quantitative (continuously varying) trait, such as size, selection is **directional** if one extreme phenotype is fittest, **stabilizing** (NORMALIZING) if an intermediate phenotype is fittest, or **diversifying** (**disruptive**) if two or more phenotypes are fitter than the intermediates between them. Which *genotype* has the highest fitness under a given selection regime depends on the relationship between phenotype and genotype. For example, under directional selection for large size, genotype A_1A_1 would be most fit if it were largest, but A_1A_2 would be favored if it were larger than either homozygote. As we will soon see, this difference would have important evolution-

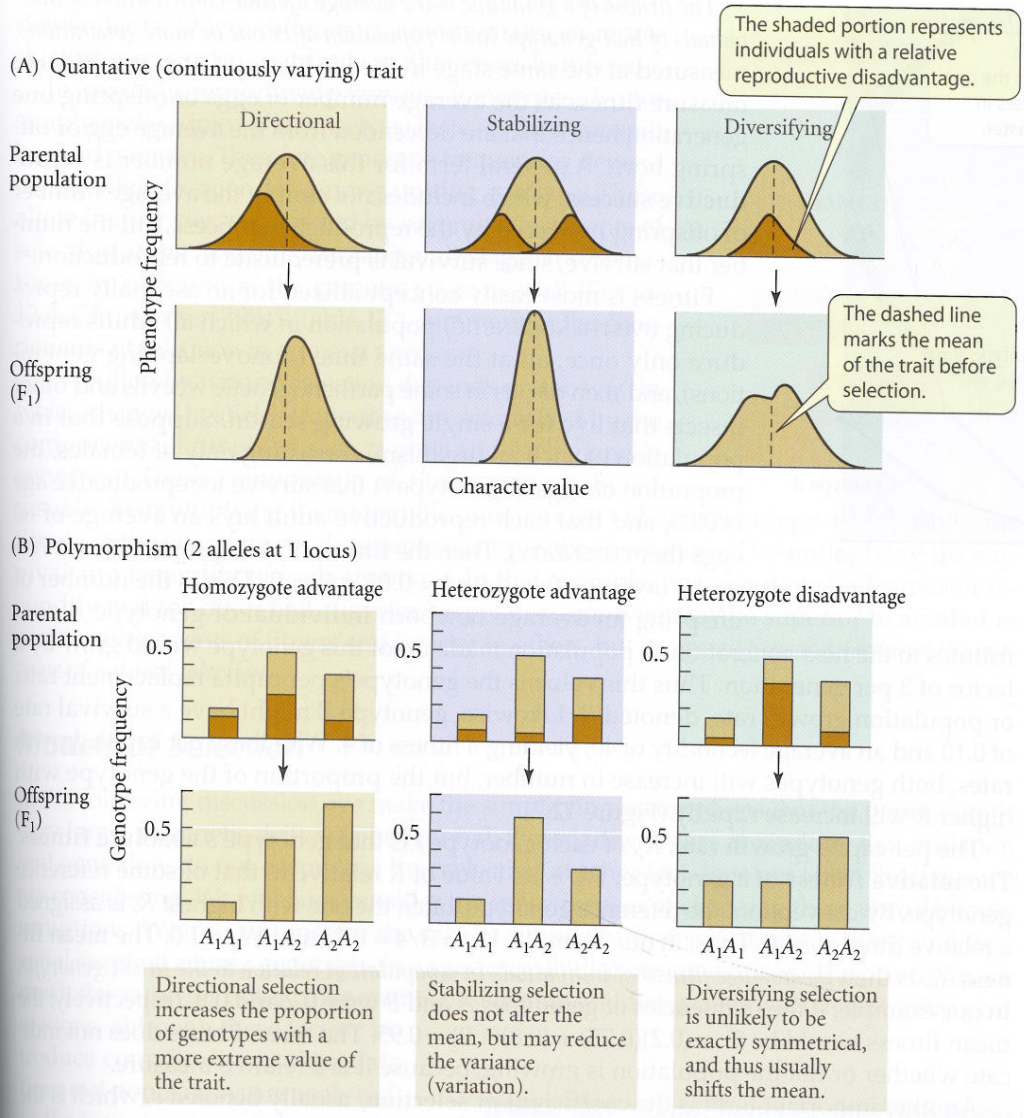

Figure 12.1 Modes of selection on (A) a heritable quantitative (continuously varying) character and (B) a polymorphism consisting of two alleles at one locus. The upper graphs in both (A) and (B) show the distribution in the parental generation, before selection occurs. The shaded portions represent individuals with a relative disadvantage (lower fitness). The dashed line in A represents the mean character value in the parental generation. The lower graphs in both (A) and (B) show the frequency distribution in the F_1 generation, after selection has occurred. (After Endler 1986.)

ary results: the population would become fixed for the largest phenotype if the homozygote were largest, but not if the heterozygote were largest.

The relationship between phenotype and fitness can depend on the environment, since different environmental conditions can favor different phenotypes. It also depends on how the mean and variation in a character are distributed relative to the fitness/phenotype relationship. Thus, if the mean body size is below the optimum, it will be directionally selected until it corresponds to the optimum (at least approximately); after that, it is subject to stabilizing selection.

Defining fitness

Because we are concerned with only those effects of selection that depend on inheritance, we will use models in which an average fitness value is assigned to each genotype. A genotype is likely to have different phenotypic expressions as a result of environmental influences on development, so the fitness of a genotype is the mean of the fitnesses of its several phenotypes, weighted by their frequencies. For example, a particular genotype of *Drosophila pseudoobscura* has a variable number of bristles, depending on the temperature at which the fly develops (see Figure 9.18). Thus, if fitness depended on bristle number, the fitness of a given genotype would depend on the proportions of flies that developed at each temperature.

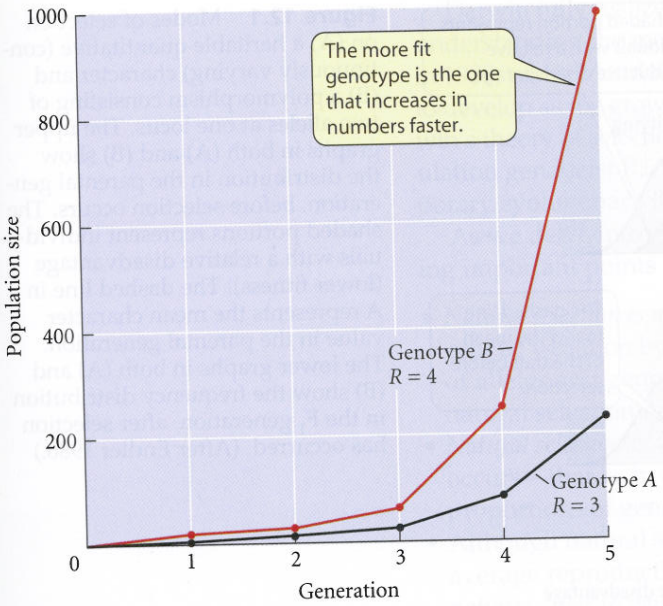

Figure 12.2 The growth of two genotypes with different per capita growth rates in an asexually reproducing population with nonoverlapping generations.

The fitness of a genotype is the average lifetime contribution of individuals of that genotype to the population after one or more generations, measured at the same stage in the life history. Often it suffices to measure fitness as the average number of eggs or offspring one generation hence that are descended from the average egg or offspring born. A general term for this average number is **reproductive success**, which includes not simply the average number of offspring produced by the reproductive process, but the number that survive, since survival is prerequisite to reproduction.

Fitness is most easily conceptualized for an asexually reproducing (PARTHENOGENETIC) population in which all adults reproduce only once, all at the same time (nonoverlapping generations), and then die, as in some parthenogenetic weevils and other insects that live for a single growing season. Suppose that in a population of such an organism, consisting only of females, the proportion of eggs of genotype A that survive to reproductive age is 0.05, and that each reproductive adult lays an average of 60 eggs (her FECUNDITY). Then the fitness of A is (proportion surviving) × (average fecundity) = 0.05 × 60 = 3. This is the number of offspring an average newborn individual of genotype A contributes to the next generation. A population made up of this genotype would grow by a factor of 3 per generation. Thus this value is the genotype's per capita replacement rate, or population growth rate, denoted R. Likewise, genotype B might have a survival rate of 0.10 and an average fecundity of 40, yielding a fitness of 4. With these per capita growth rates, both genotypes will increase in number, but the proportion of the genotype with higher R will increase rapidly (Figure 12.2).

The per capita growth rate, R_i, of each genotype i is that genotype's **absolute fitness**. The **relative fitness** of a genotype, W_i, is its value of R relative to that of some reference genotype. By convention, the reference genotype, often the one with highest R, is assigned a relative fitness of 1.0. Thus, in our example, $W_A = 3/4 = 0.75$ and $W_B = 1.0$. The **mean fitness**, $\bar{w}$, is then *the average fitness of individuals in a population relative to the fittest genotype.* In our example, if the frequencies of genotypes A and B were 0.2 and 0.8, respectively, the mean fitness would be $\bar{w} = (0.2)(0.75) + (0.8)(1.0) = 0.95$. The mean fitness does not indicate whether or not the population is growing, because it is a relative measure.

Another important term is the **coefficient of selection**, usually denoted s, which is the amount by which the fitness of one genotype is reduced relative to the reference genotype. In our example, $W_A = 0.75$, so $s = 0.25$. The coefficient of selection measures the **selective advantage** of the fitter genotype, or the intensity of selection against the less fit genotype.

It is easy to show mathematically that *the rate of genetic change under selection depends on the relative,* not the absolute, *fitnesses of genotypes.* The rate at which a population would become dominated by genotype B in our hypothetical example would be the same, whether genotypes A and B had R values of 0.6 versus 0.8, or 15 versus 20, or 300 versus 400.

Components of fitness

Survival and female fecundity are only two of the possible components of fitness. The components of fitness are more complex if a species reproduces sexually and if it reproduces repeatedly during the individual's lifetime. When generations overlap, as in humans and many other species that reproduce repeatedly, the absolute fitness of a genotype may be measured in large part by its per capita rate of population increase per unit time, r (see Chapter 17). This rate of increase depends on the proportion of individuals surviving to each age class and on the fecundity of each age class. Moreover, r is strongly affected by the age at which females have offspring, not just by their number; that is, genotypes may differ in the length of a generation. If females of genotypes A and B have the same number of offspring when they are 6 months and 12 months old, respectively, the rate of increase (the fitness) of A is about twice that of B, because A will have two generations of de-

scendants by the time B has produced one generation of descendants. Often, differences among males in reproductive success also contribute to differences in fitness.

In sexually reproducing species, genotypes do not simply make copies of themselves; instead, they transmit haploid gametes. Therefore genotype frequencies depend on the allele frequencies among uniting gametes. These allele frequencies are affected by several components of selection at the "zygotic" (organismal) stage, and sometimes by selection at the gametic stage as well (Figure 12.3; Christiansen 1984). Table 12.1 summarizes the components of selection in a sexual species.

Evolution by natural selection depends on the way in which changes in allele frequencies are determined by the components of fitness of each zygotic and each gametic genotype. These components of fitness are combined (usually by multiplying them) into the overall fitness of each genotype. For instance, the fitness of the genotypes in the simple example above was found by multiplying the survival and fecundity of each genotype. In that example, one genotype had superior fecundity and the other had superior survival: a genotype may be superior to another in certain components of fitness and inferior in others, but its *overall fitness determines the outcome of natural selection.*

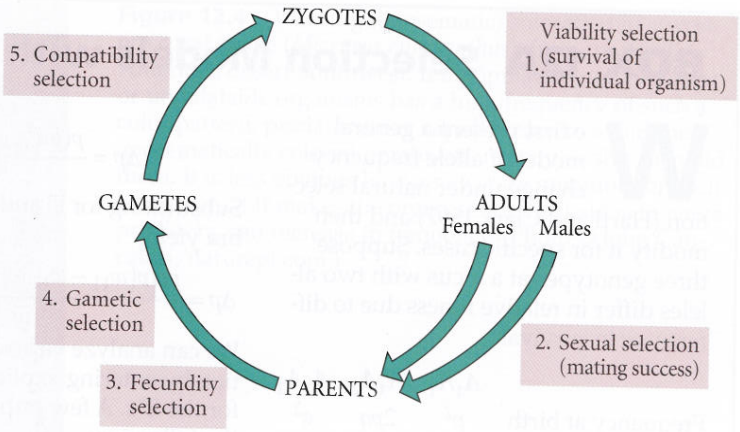

Figure 12.3 Components of natural selection that may affect the fitness of a sexually reproducing organism over the life cycle. Beginning with newly formed zygotes, (1) genotypes may differ in survival to adulthood; (2) they may differ in the numbers of mates they obtain, especially males; (3) those that become parents may differ in fecundity (number of gametes produced, especially eggs); (4) selection may occur among the haploid genotypes of gametes, as in differential gamete viability or meiotic drive; and (5) union of some combinations of gametic genotypes may be more compatible than others. (After Christiansen 1984.)

Models of Selection

In the following discussion, we make the simplifying assumptions that the population is very large, so genetic drift may be ignored; that mating occurs at random; that mutation and gene flow do not occur; and that selection at other loci does not affect the locus we are considering. We will later consider the consequences of changing these unrealistic assumptions. We also assume, for the sake of simplicity, that selection acts through differential survival among genotypes in a species with discrete generations. The principles are much the same for other components of selection and for species with overlapping generations, although these factors introduce complications when data from real populations are analyzed.

If a locus has two alleles (A_1, A_2) with frequencies p and q, the change in frequency from one generation to the next is expressed by Δp, which is positive if the allele is increasing in frequency, negative if it is decreasing, and 0 if p is at an equilibrium. In any model of selection, the change in allele frequencies depends on the relative fitnesses of the different genotypes and on the allele frequencies themselves. Box A provides a mathematical framework for several models of selection.

Directional selection

THEORY. The replacement of relatively disadvantageous alleles by more advantageous alleles is the fundamental basis of adaptive evolution. This replacement occurs

TABLE 12.1 *Components of selection in sexually reproducing organisms*

I. Zygotic selection

A. *Viability.* The probability of survival of the genotype through each of the ages at which reproduction can occur. After the age of last reproduction, the length or probability of survival does not usually affect the genotype's contribution to subsequent generations, and so does not usually affect fitness.

B. *Mating success.* The number of mates obtained by an individual. Mating success is a component of fitness if the number of mates affects the individual's number of progeny, as is often the case for males, but less often for females, all of whose eggs may be fertilized by a single male. Variation in mating success is the basis of sexual selection.

C. *Fecundity.* The average number of viable offspring per female. In species with repeated reproduction, the contribution of each offspring to fitness depends on the age at which it is produced (see Chapter 17). The fertility of a mating may depend only on the maternal genotype (e.g., number of eggs or ovules), or it may depend on the genotypes of both mates (e.g., if they display some reproductive incompatibility).

II. Gametic selection

D. *Segregation advantage* (meiotic drive or segregation distortion). An allele has an advantage if it segregates into more than half the gametes of a heterozygote.

E. *Gamete viability.* Dependence of a gamete's viability on the allele it carries.

F. *Fertilization success.* An allele may affect the gamete's ability to fertilize an ovum (e.g., if there is variation in the rate at which a pollen tube grows down a style).

BOX 12A Selection Models with Constant Fitnesses

We first present a general model of allele frequency change under natural selection (Hartl and Clark 1997) and then modify it for specific cases. Suppose three genotypes at a locus with two alleles differ in relative fitness due to differences in survival:

	A_1A_1	A_1A_2	A_2A_2
Frequency at birth	p^2	$2pq$	q^2
Relative fitness	w_{11}	w_{12}	w_{22}

The ratio of A_1A_1: A_1A_2: A_2A_2 among surviving adults is

$$p^2w_{11}:2pqw_{12}:q^2w_{22}$$

and the ratio of the alleles (A_1: A_2) among their gametes is

$$[p^2w_{11} + \tfrac{1}{2}(2pqw_{12})]:[\tfrac{1}{2}(2pqw_{12}) + q^2w_{22}]$$

which simplifies to

$$p(pw_{11} + qw_{12}):q(pw_{12} + qw_{22})$$

The gamete frequencies, which are the allele frequencies among the next generation of offspring, are found by dividing each term by the sum of the gametes, which is

$$\begin{aligned} &p(pw_{11} + qw_{12}) + q(pw_{12} + qw_{22}) \\ &= p_2w_{11} + 2pqw_{12} + q_2w_{22} \\ &= \overline{w} \end{aligned}$$

Thus the allele frequencies after selection (p', q') are the gamete frequencies, or

$$p' = \frac{p(pw_{11} + qw_{12})}{\overline{w}}$$

$$q' = \frac{q(pw_{12} + qw_{22})}{\overline{w}}$$

The change in allele frequency between generations is $\Delta p = p' - p$, or

$$\Delta p = \frac{p(pw_{11} + qw_{12}) - p\overline{w}}{\overline{w}}$$

Substituting for $\overline{w}$ and doing the algebra yields

$$\Delta p = \frac{pq[p(w_{11} - w_{12}) + q(w_{12} - w_{22})]}{\overline{w}} \quad \text{(A1)}$$

We can analyze various cases of selection by entering explicit fitness values for the $\overline{w}$'s. A few important cases are the following:

1. Advantageous dominant allele, disadvantageous recessive allele ($w_{11} = w_{12} > w_{22}$).

For w_{11}, w_{12}, and w_{22}, substitute 1, 1, and $1 - s$ respectively in Equation A1. The mean fitness is $p^2(1) + 2pq(1) + q^2(1 - s) = 1 - sq^2$ (bearing in mind that $p^2 + 2pq + q^2 = 1$). The equation for allele frequency change is

$$\Delta p = \frac{spq^2}{1 - sq^2}$$

or, equivalently,

$$\Delta q = \frac{-spq^2}{1 - sq^2} \quad \text{(A2)}$$

2. Advantageous allele partially dominant, disadvantageous allele partially recessive ($w_{11} > w_{12} > w_{22}$).

Let h, lying between 0 and 1, measure the degree of dominance for fitness, and substitute 1, $1 - hs$, and $1 - s$ for w_{11}, w_{12}, and w_{22}. (If $h = 0$, allele A_2 is fully recessive.) After sufficient algebra, we find that

$$\Delta p = \frac{-spq[h(1 - 2q) + sq]}{1 - 2pqhs - sq^2} \quad \text{(A3)}$$

which is positive for all $q > 0$, so allele A_1 increases to fixation. If $h = \frac{1}{2}$, Equation A3 reduces to $\Delta p = spq/[2(1 - sq)]$.

$$\Delta p = \frac{spq}{[2(1 - sq)]}$$

3. Fitness of heterozygote is greater than that of either homozygote ($w_{11} < w_{12} > w_{22}$).

Using s and t as selection coefficients, let the fitnesses of A_1A_1, A_1A_2, and A_2A_2 be $1 - s$, 1, and $1 - t$ respectively. Substituting these in Equation A1, we obtain

$$\Delta p = \frac{pq(-sp + tq)}{1 - sp^2 - tq^2} \quad \text{(A4)}$$

There is a stable "internal equilibrium" that can be found by setting $\Delta p = 0$; then $sp = tq$. Substituting $1 - p$ for q, the equilibrium frequency p is $t/(s + t)$. Thus the frequency of A_1 is proportional to the relative strength of selection against A_2A_2.

4. Fitness of heterozygote is less than that of either homozygote (that is, $w_{11} > w_{12} < w_{22}$).

As this is the reverse of the preceding case, let $1 + s$, 1, and $1 + t$ be the fitnesses of A_1A_1, A_1A_2, and A_2A_2. The equation for allele frequency change is

$$\Delta p = \frac{pq(sp - tq)}{1 + sp^2 + tq^2} \quad \text{(A5)}$$

Δp is positive if $sp > tq$, and negative if $sp < tq$. Setting $\Delta p = 0$ and solving for p, we find an internal equilibrium at $p = t/(s + t)$, but this is an unstable equilibrium. For example, if $s = t$, the unstable equilibrium is $p = 0.5$, but then Δp is positive if $p > q$ (i.e., if $p > 0.5$), and negative if $p < q$. The allele frequency therefore arrives at either of two stable equilibria, $p = 1$, or $p = 0$.

when the homozygote for an advantageous allele has a fitness equal to or greater than that of the heterozygote or of any other genotype in the population.

An advantageous allele may initially be fairly common if under previous environmental circumstances it was selectively neutral or was maintained by one of several forms of balancing selection (see page 280). However, an advantageous allele is likely to be initially very rare if it is a newly arisen mutation or if it was disadvantageous before an environmental change made it advantageous.

An advantageous allele that increases from a very low frequency is often said to INVADE a population. *Unless an allele can increase in frequency when it is very rare, it is unlikely to be-*

Figure 12.4 Warning (aposematic) coloration in a western coral snake (*Micrurus euryxanthus*), from the North American desert Southwest. If a population of dangerous or unpalatable organisms has a high frequency of such a color pattern, predators may rapidly learn to avoid the aposematically colored organisms, or may evolve to avoid them. It is less obvious how a new, rare mutation for such coloration, if it makes the organisms conspicuous to naive predators, can increase in frequency. (Photo © John Cancalosi/naturepl.com.)

come fixed in the population. According to this principle, some conceivable adaptations are unlikely to evolve because they could not increase if they were initially very rare. For instance, venomous coral snakes (*Micrurus*) are brilliantly patterned in red, yellow, and black (Figure 12.4). This pattern is presumed to be APOSEMATIC (warning) coloration, which is beneficial because predators associate the colors with danger and avoid attacking such snakes. How this coloration initially evolved has long been a puzzle, however, since the first few mutant snakes with brilliant colors would presumably have been easily seen and killed by naive predators. Given that all coral snakes are aposematically colored, it is understandable that predators might evolve an aversion to them (and, indeed, some predatory birds seem to have an innate aversion to coral snakes)—but how the snake's adaptation "got off the ground" is uncertain. (One possibility is that predators generalized from other brilliantly colored unpalatable or dangerous organisms, such as wasps, and avoided aposematic snakes from the beginning.)

A simple example of directional selection occurs if the fitness of the heterozygote is precisely intermediate between that of the two homozygotes (i.e., neither allele is dominant with respect to fitness). The frequencies and fitnesses of the three genotypes may be denoted as follows:

Genotype	A_1A_1	A_1A_2	A_2A_2
Frequency	p^2	$2pq$	q^2
Fitness	1	$1-(s/2)$	$1-s$

These fitnesses may be entered into Equation A1 in Box A, which, when solved, shows that the advantageous allele A_1 increases in frequency, per generation, by the amount

$$\Delta p = \frac{\frac{1}{2}spq}{1-sq} \qquad (12.1)$$

where $(1-sq)$ equals the mean fitness, $\bar{w}$.

Equation 12.1 tells us that Δp is positive whenever p and q are greater than zero. Therefore allele A_1 increases to fixation ($p = 1$), and $p = 1$ is a *stable equilibrium*. The rate of increase (the magnitude of Δp) is proportional to both the coefficient of selection s and the allele frequencies p and q, which appear in the numerator. Therefore the rate of evolutionary change increases as the variation at the locus increases. (It is approximately proportional to $2pq$, the frequency of heterozygotes, when selection is weak.)

Another important aspect of Equation 12.1 is that Δp is positive as long as s is greater than zero, even if it is very small. Therefore, as long as no other evolutionary factors intervene, *a character state with even a minuscule advantage will be fixed by natural selection*. Hence

Figure 12.5 A cryptic katydid (*Mimetica crenulata*) from Costa Rica. The irregular outline, twisted form, and conspicuous vein of the wing provide extraordinary resemblance to a dry, chewed, dead leaf. (Courtesy of P. Naskrecki.)

even very slight differences among species, in seemingly trivial characters such as the distribution of hairs on a fly or veins on a leaf, could conceivably have evolved as adaptations. This principle explains the extraordinary apparent "perfection" of some features. Some katydids, for example, resemble dead leaves to an astonishing degree, with transparent "windows" in the wings that resemble holes and blotches that resemble spots of fungi or algae (Figure 12.5). One might suppose that a less detailed resemblance would provide sufficient protection against predators, and some species are indeed less elaborately cryptic; but if an extra blotch increases the likelihood of survival by even the slightest amount, it may be fixed by selection (providing, we repeat, that no other factors intervene).

The same equations that describe the increase of an advantageous allele describe the fate of a disadvantageous allele: If A_1 and A_2 are advantageous and disadvantageous alleles, respectively, with frequencies p and q, and if $p + q = 1$, then $\Delta p = -\Delta q$. Selection that reduces the frequency of a deleterious mutation or eliminates it is referred to as **purifying selection**, which is simply directional selection in favor of the prevalent, advantageous homozygous genotype.

The number of generations required for an advantageous allele to replace one that is disadvantageous depends on the initial allele frequencies, the selection coefficient, and the degree of dominance (Figure 12.6). An advantageous allele can increase from low frequency more rapidly if it is dominant than if it is recessive because it is expressed in the heterozygous state, and until it reaches a fairly high frequency, it is carried almost entirely by heterozygotes. After a dominant advantageous allele attains high frequency, the deleterious recessive allele is eliminated very slowly, because a rare recessive allele occurs mostly in heterozygous form, and is thus shielded from selection.

One more theoretical conclusion can be drawn from Equation 12.1. The denominator is the mean relative fitness of individuals in the population, $\bar{w}$, which increases as the frequency (q) of the deleterious allele decreases. The mean fitness therefore increases as natural selection proceeds. In a graphical representation of this relationship (Figure 12.7A), we may think of the population as climbing up a "hillside" of increasing mean fitness until it arrives at the summit.

Equation 12.1, finally, can be used to draw an interesting inference from data. If we have data on the frequencies of genotypes at a locus (and therefore also have estimates of the frequencies of alleles, p and q), and if we also have data on allele frequencies in successive generations (i.e., an estimate of Δp), we can solve for s in the equation. This is one way of estimating the strength of natural selection. Several other methods are used to estimate selection coefficients,

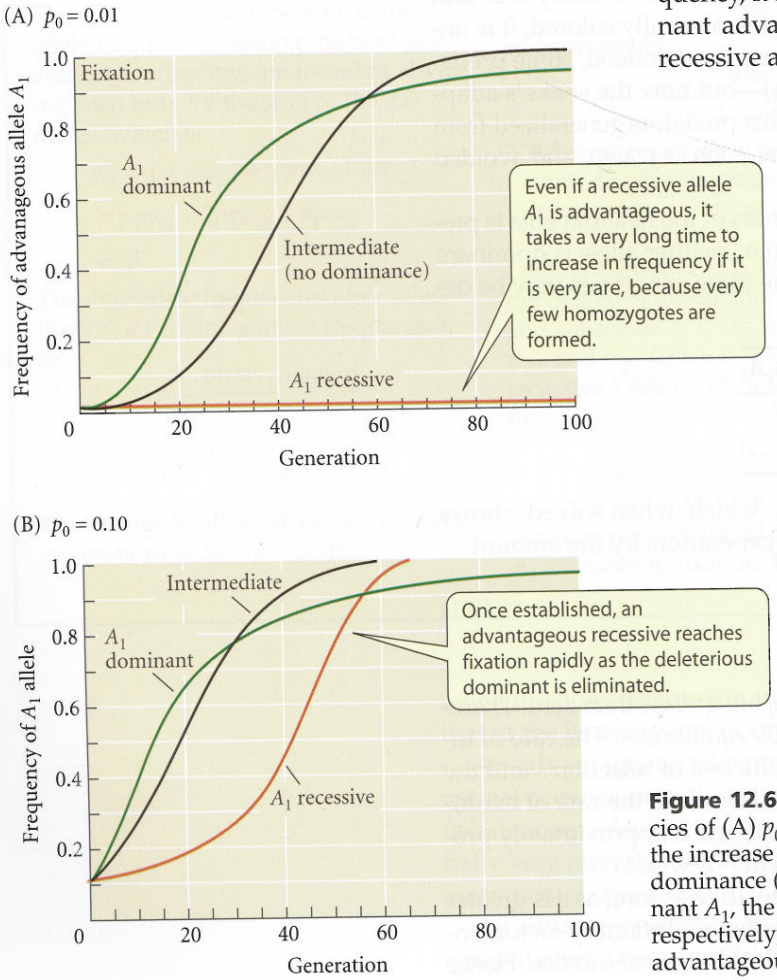

Figure 12.6 Increase of an advantageous allele (A_1) from initial frequencies of (A) $p_0 = 0.01$ and (B) $p_0 = 0.10$. The three curves in each graph show the increase of a fully dominant allele (green), an allele with intermediate dominance (black), and a recessive allele (red). For the advantageous dominant A_1, the fitnesses of genotypes A_1A_1, A_1A_2, and A_2A_2 are 1.0, 1.0, and 0.8 respectively; for the "intermediate" case they are 1.0, 0.9, and 0.8; for the advantageous recessive A_1, they are 1.0, 0.8, and 0.8.

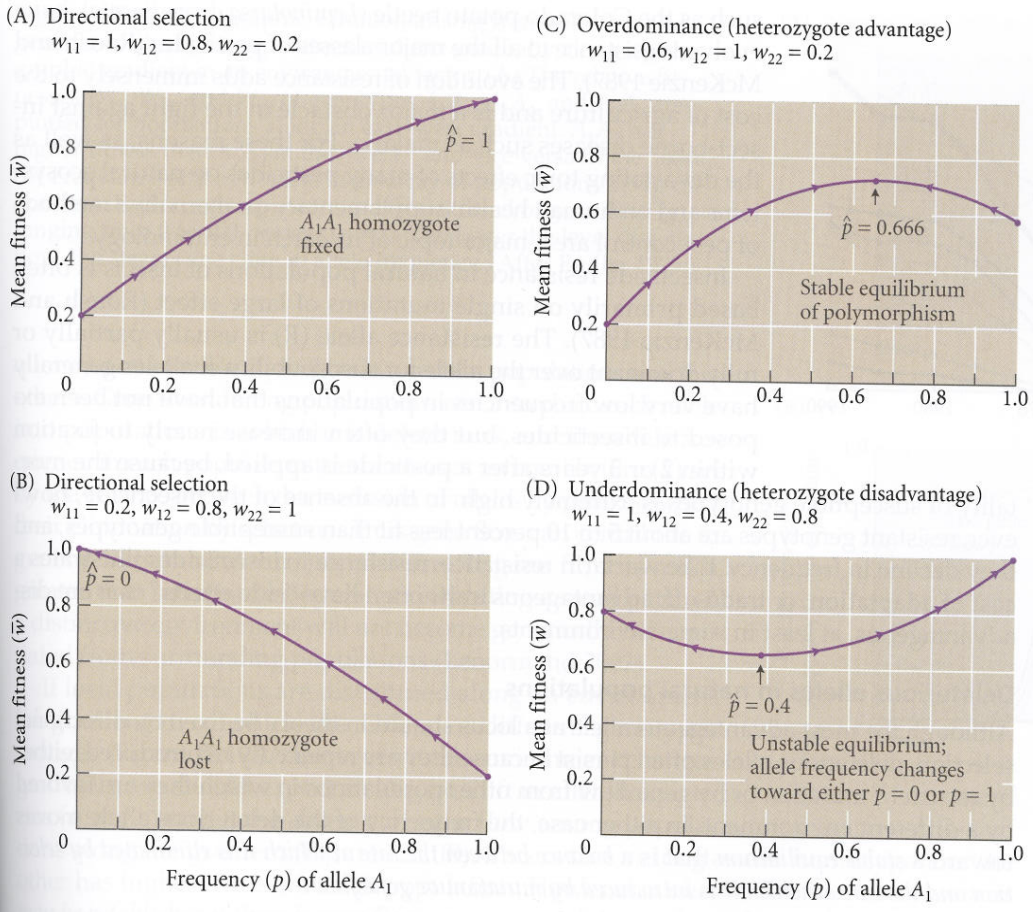

Figure 12.7 Plots of mean fitness ($\bar{w}$) against allele frequency (p) for one locus with two alleles when genotypes differ in survival. Each of these plots represents an "adaptive landscape," and may be thought of as a surface, or hillside, over which the population moves. From any given frequency of allele A_1 (p), the allele frequency moves in a direction that increases mean fitness ($\bar{w}$). The arrowheads show the direction of allele frequency change. (A) Directional selection. Here, A_1A_1 is the favored genotype. The equilibrium ($\hat{p} = 1$) is stable: the allele frequency returns to $p = 1$ if displaced. (B) Directional selection, in which the relative fitnesses are reversed compared with graph A, perhaps because of changed environmental conditions. A_2A_2 is now the favored genotype. (C) Overdominance (heterozygote advantage). From any starting point, the population arrives at a stable polymorphic equilibrium ($\hat{p}$). (D) Underdominance (heterozygote disadvantage). The interior equilibrium ($\hat{p} = 0.4$ in this example) is unstable because even a slight displacement initiates a change in allele frequency toward one of two stable equilibria: $\hat{p} = 0$ (loss of A_1) or $\hat{p} = 1$ (fixation of A_1). Therefore this curve represents an adaptive landscape with two peaks. (After Hartl and Clark 1989.)

such as estimating the survival rates (or other components of fitness) of different genotypes in natural populations (Endler 1986).

EXAMPLES OF DIRECTIONAL SELECTION. If a locus has experienced consistent directional selection for a long time, the advantageous allele should be near equilibrium—that is, near fixation. Thus the dynamics of directional selection are best studied in recently altered environments, such as those altered by human activities. Many examples of rapid evolution under such circumstances have been observed. Many are changes in polygenic traits, described in the next chapter.

An example of rapid evolution of a single-locus trait is the case of warfarin resistance in brown rats (*Rattus norvegicus*) (Bishop 1981). Warfarin is an anticoagulant: it inhibits an enzyme responsible for the regeneration of vitamin K, a necessary cofactor in the production of blood-clotting factors. Susceptible rats poisoned with warfarin often bleed to death from slight wounds. A mutation confers resistance by altering the enzyme to a form that is less sensitive to warfarin, but also less efficient in regenerating vitamin K, so that a higher dietary intake of the vitamin is necessary.

Warfarin has been used as a rat poison in Britain since 1953, and by 1958 resistance was reported in certain rat populations. Under exposure to warfarin, resistant rats have a strong survival advantage, and the frequency of the mutation has been known to increase rapidly to nearly 1.0 (Figure 12.8). Resistant rats suffer a strong disadvantage compared with susceptible rats, however, because of their greater need for vitamin K, and the frequency of the resistance allele drops rapidly if the poison is not administered.

Resistance to insecticides has evolved in many insects and mites (Metcalf and Luckmann 1994; Roush and Tabashnik 1990). Resistance appeared in many species in the 1940s, when synthetic pesticides came into wide use. By 1990, populations of more than 500 species were known to be resistant to one or more insecticides (Figure 12.9). Some species,

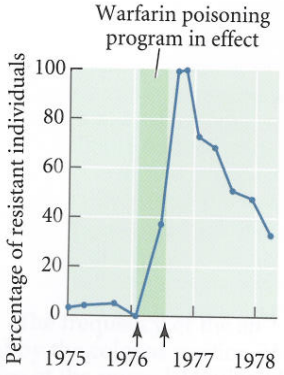

Figure 12.8 The proportion of warfarin-resistant individuals in a population of rats in Wales. The proportion increased when warfarin poisoning was practiced in 1976, but decreased after the poisoning program ended. (After Bishop 1981.)

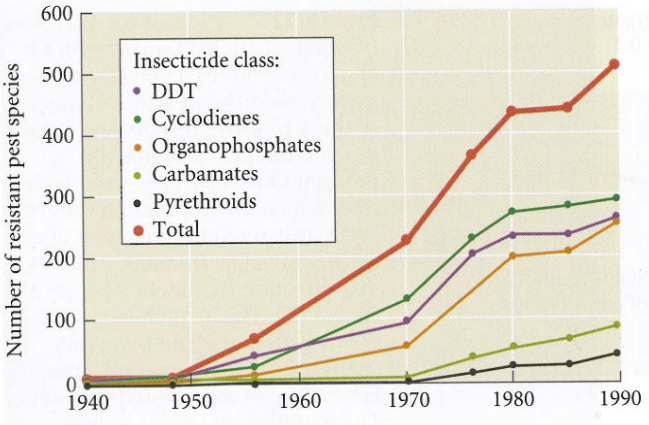

Figure 12.9 The cumulative numbers of arthropod pest species known to have evolved resistance to five classes of insecticides. The upper curve provides the total number of insecticide-resistant species. (After Metcalf and Luckmann 1994.)

such as the Colorado potato beetle (*Leptinotarsa decemlineata*), have evolved resistance to all the major classes of pesticides (Roush and McKenzie 1987). The evolution of resistance adds immensely to the cost of agriculture and is a major obstacle in the fight against insect-borne diseases such as malaria. For these reasons, as well as the devastating toxic effects of many pesticides on natural ecosystems and on human health, supplementary or alternative methods of pest control are a major topic of research in entomology.

Insecticide resistance in natural populations of insects is often based primarily on single mutations of large effect (Roush and McKenzie 1987). The resistance allele (R) is usually partially or fully dominant over the allele for susceptibility. R alleles generally have very low frequencies in populations that have not been exposed to insecticides, but they often increase nearly to fixation within 2 or 3 years after a pesticide is applied, because the mortality of susceptible genotypes is extremely high. In the absence of the insecticide, however, resistant genotypes are about 5 to 10 percent less fit than susceptible genotypes, and they decline in frequency. Like warfarin resistance, resistance to insecticides illustrates a **cost of adaptation**, or **trade-off**: advantageous traits often have "side effects" that are disadvantageous, at least in some environments.

Deleterious alleles in natural populations

Although the most advantageous allele at a locus should in theory be fixed by directional selection, deleterious alleles often persist because they are repeatedly reintroduced, either by recurrent mutation or by gene flow from other populations in which they are favored by a different environment. In either case, the frequency of the deleterious allele moves toward a *stable equilibrium* that is a *balance between the rate at which it is eliminated by selection and the rate at which it is introduced by mutation or gene flow.*

SELECTION AND MUTATION. Suppose that a deleterious recessive allele A_2, with frequency q, arises at a mutation rate u from other alleles that have a collective frequency of $p = 1 - q$. The increase in frequency of A_2 due to mutation in each generation is up, whereas the decrease in its frequency due to selection (from Equation A2 in Box A) is $-spq^2/\bar{w}$. At equilibrium, the rate of increase equals the rate of decrease:

$$up = \frac{spq^2}{\bar{w}}$$

where $\bar{w} = 1 - sq^2$.

Let us assume that A_2 is rare, so that $\bar{w}$ is approximately equal to 1, and solve for q. The result is the equilibrium frequency, denoted $\hat{q}$. We find that $\hat{q}^2 = u/s$, and

$$\hat{q} = \sqrt{\frac{u}{s}}$$

The equilibrium frequency of a deleterious recessive allele, therefore, is directly proportional to the mutation rate and inversely proportional to the strength of selection. Thus, if s is much greater than u, the allele will be very rare. For example, if $s = 1$ (i.e., A_2 is a recessive lethal allele) and the mutation rate is 10^{-6}, the equilibrium frequency will equal 0.001, but almost all the zygotes with this allele will be heterozygous. If the deleterious allele is partly or entirely dominant, its equilibrium frequency will be even lower because of selection against both homozygous and heterozygous carriers. Such MUTATION-SELECTION BALANCE explains why many chromosomes in *Drosophila* populations (as well as in humans and many other species) carry rare mutations that slightly reduce fitness in heterozygous condition and are lethal when homozygous (Crow 1993; see Figure 9.9).

SELECTION AND GENE FLOW. Very often, different environmental conditions favor different alleles in different populations of a species. Thus, in the absence of gene flow, the fre-

broken down the strong association between an advantageous *G6PD* mutation and the microsatellite variants with which it was linked at first. When Tishkoff and collaborators performed computer simulations of various possible histories of change, they found that in simulations involving genetic drift, but not selection, levels of microsatellite variation were much higher that those observed, and levels of linkage disequilibrium were lower. The observed data on variation among A^- copies are best predicted by a simulation model in which the A^- allele has a selective advantage (s) of 0.044, and in which this allele has increased rapidly within the last 6357 years (with a range from 3840 to 11,760 years ago). The *Med* allele, likewise, has had a selective advantage of about 0.034, and increased within the last 3330 (range 1600–6640) years. Furthermore, low levels of synonymous nucleotide variation in *Plasmodium falciparum*, the malaria-causing protozoan, imply that its population size has increased greatly within the last 10,000 years (Volkman et al. 2001; Joy et al. 2003). The genetic data from both human and *Plasmodium* populations are consistent with archaeological and historical evidence that malaria has become a significant source of human mortality only within the last 10,000 years. The probable cause of this change is the spread of slash-and-burn agriculture and clearing of forests, land use practices that increase breeding habitats for the anopheline mosquitoes that carry *Plasmodium*.

The Strength of Natural Selection

Until the 1930s, most evolutionary biologists followed Darwin in assuming that the intensity of natural selection is usually very slight. By the 1930s, however, examples of very strong selection came to light. One of the first examples was INDUSTRIAL MELANISM in the peppered moth (*Biston betularia*). In some parts of England, a black form of the moth carrying a dominant allele increased in frequency after the onset of the Industrial Revolution. Museum collections dating since the mid-nineteenth century in England, after the onset of the Industrial Revolution, show that in less than a century, the "typical" pale gray form declined and the black (melanic) form increased from about 1 percent to more than 90 percent in some areas. The rate of change is so great that it implies a very substantial selective advantage, possibly as high as 50 percent, for the melanic form (Haldane 1932). There is considerable evidence, obtained by several independent researchers, that birds attack a greater proportion of gray than black moths where tree trunks, due to air pollution, lack the pale lichens that would otherwise cover them (Figure 12.25A); however, other factors also appear to affect the allele frequencies (Majerus 1998).

As air pollution has become regulated, conditions have reverted to favor the typical gray phenotype, and the frequency of the melanic form has declined very rapidly in Great Britain, Europe, and the United States (Figure 12.25B; Grant and Wiseman 2002; Cook 2003). By applying the appropriate equation for allele frequency change (see Box A) to the

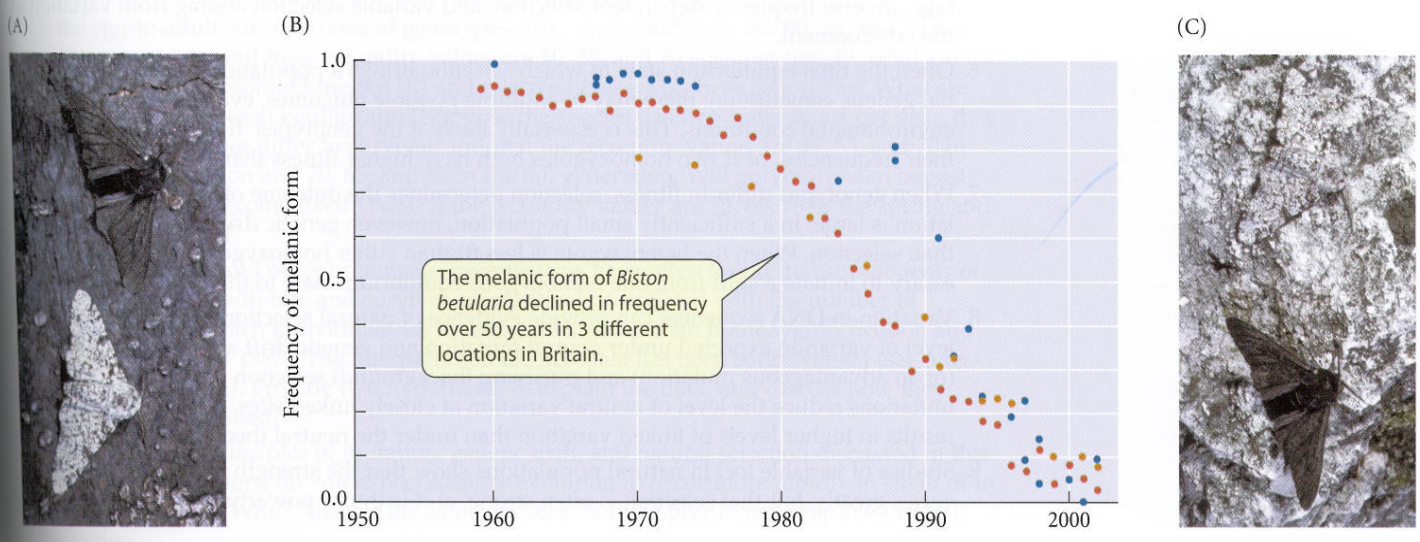

Figure 12.25 (A) The pale "typical" form and the dark melanic form of the peppered moth (*Biston betularia*) on a dark tree trunk. The British biologist H. B. D. Kettlewell pinned these and other freshly killed specimens to both dark and pale trunks, and determined that birds took a higher proportion of the more conspicuous phenotype in each situation. (B) The decline in the frequency of the melanic form in three British localities, indicated by different symbols. (C) The "typical" and melanic forms of the moth on a pale tree trunk covered with lichens, which grow in areas with clean air. (A, C, © photolibrary.com; B after Cook 2003.)

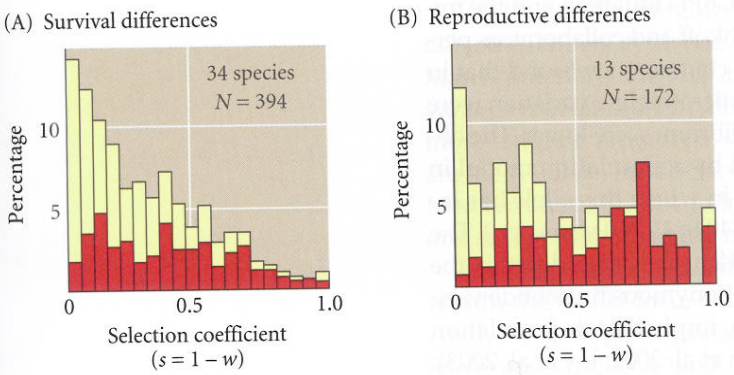

Figure 12.26 A compilation of selection coefficients (s) reported in the literature for discrete, genetically polymorphic traits in natural populations of various species. The total height of each bar represents the percentage of all reported values in each interval, and the red portion represents the percentage shown by statistical analysis to be significantly different from zero. N is the number of values reported, based on one or more traits from each of a number of species. (A) Selection based on differences in survival. (B) Selection based on differences in reproduction (fecundity, fertility, and sexual selection). (After Endler 1986.)

data, Lawrence Cook has estimated selection coefficients (s) against the melanic form of 0.05 to more than 0.20 in various British sites.

In the last few decades, components of fitness have been quantified for polymorphic traits in many species. Although cases in which s is close to zero are probably underrepresented because investigators may not report studies that yielded no evidence of selection, the selection coefficients estimated in natural populations range from low to very high (Figure 12.26). Moreover, selection acting through both survival and reproduction can be very strong. Thus natural selection is a powerful factor in evolution and is often far stronger than Darwin ever would have imagined.

Summary

1. Even at a single locus, the diverse genetic effects of natural selection cannot be summarized by the slogan "survival of the fittest." Selection may indeed fix the fittest genotype, or it may maintain a population in a state of stable polymorphism, in which inferior genotypes persist.
2. The absolute fitness of a genotype is measured by its rate of increase, the major components of which are survival, female and male mating success, and fecundity. In sexual species, differences among gametic (haploid) genotypes may also contribute to selection among alleles.
3. Rates of change in the frequencies of alleles and genotypes are determined by differences in their relative fitness, and are also affected by genotype frequencies and the degree of dominance at a locus.
4. Much of adaptive evolution by natural selection consists of replacement of previously prevalent genotypes by a superior homozygote (directional selection). However, genetic variation at a locus often persists in a stable equilibrium condition, owing to a balance between selection and recurrent mutation, between selection and gene flow, or because of any of several forms of balancing selection.
5. The kinds of balancing selection that maintain polymorphism include heterozygote advantage, inverse frequency-dependent selection, and variable selection arising from variation in the environment.
6. Often the final equilibrium state to which selection brings a population depends on its initial genetic constitution: there may be multiple possible outcomes, even under the same environmental conditions. This is especially likely if the genotypes' fitnesses depend on their frequencies, or if two homozygotes both have higher fitness than the heterozygote.
7. When genotypes differ in fitness, selection determines the outcome of evolution if the population is large; in a sufficiently small population, however, genetic drift is more powerful than selection. When the heterozygote is less fit than either homozygote, genetic drift is necessary to initiate a shift from one homozygous equilibrium state to the other.
8. Variation in DNA sequences can provide evidence of natural selection. Compared with the level of variation expected under neutral mutation and genetic drift alone, positive selection (of an advantageous mutation) and purifying (background) selection against deleterious mutations reduce the level of neutral variation at closely linked sites. Balancing selection results in higher levels of linked variation than under the neutral theory.
9. Studies of variable loci in natural populations show that the strength of natural selection varies greatly, but that selection is often strong, and is thus a powerful force of evolution.

ms and Concepts

lute fitness
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ptive peak/valley
gonistic selection
ciative overdominance
kground selection
ncing selection
fficient of selection
ponents of fitness
of adaptation (trade-off)
ctional selection
uptive selection
ersifying selection
quency-dependent selection (inverse or positive)
heterozygote advantage/disadvantage
mean (average) fitness
multiple stable equilibria
multiple-niche polymorphism
overdominance
peak shift
purifying selection
relative fitness
reproductive success
selective advantage
selective sweep
stabilizing selection
underdominance

ggestions for Further Reading

ural selection in the wild, by J. A. Endler (Princeton University Press, Princeton, NJ, 1986), analyzes methods of detecting and measuring natural selection and reviews studies of selection in natural populations. Textbooks of population genetics, such as D. L. Hartl and A. G. Clark's *Principles of population genetics* (third edition, Sinauer Associates, Sunderland, MA,1997) and P. W. Hedrick's *Genetics of populations* (Jones and Bartlett, Sudbury, MA, 2000), present the mathematical theory of selection in depth.

oblems and Discussion Topics

1. If a recessive lethal allele has a frequency of 0.050 in newly formed zygotes in one generation, and the locus is in Hardy-Weinberg equilibrium, what will be the allele frequency and the genotype frequencies at this locus at the beginning of the next generation? (Answer: q = 0.048; p^2 = 0.9071, $2pq$ = 0.0907; q^2 = 0.0023.) Calculate these values for the succeeding generation. If the lethal allele arises by mutation at a rate of 10^{-6} per gamete, what will be its frequency at equilibrium?
2. Suppose the egg-to-adult survival of A_1A_1 is 80 percent as great as that of A_1A_2, and the survival of A_2A_2 is 95 percent as great. What is the frequency (p) of A_1 at equilibrium? What are the genotype frequencies among zygotes at equilibrium? Now suppose the population has reached this equilibrium, but that the environment then changes so that the relative survival rates of A_1A_1, A_1A_2, and A_2A_2 become 1.0, 0.95, and 0.90. What will the frequency of A_1 be after one generation in the new environment? (Answer: 0.208.)
3. If the egg-to-adult survival rates of genotypes A_1A_1, A_1A_2, and A_2A_2 are 90, 85, and 75 percent, respectively, and their fecundity values are 50, 55, and 70 eggs per female, what are the approximate absolute fitnesses (R) and relative fitnesses of these genotypes? What are the allele frequencies at equilibrium? Suppose the species has two generations per year, that the genotypes do not differ in survival, and that the fecundity values are 50, 55, and 70 in the spring generation and 70, 65, and 55 in the fall generation. Will polymorphism persist, or will one allele become fixed? What if the fecundity values are 55, 65, 75 in the spring and 75, 65, 55 in the fall?
4. In pines, mussels, and other organisms, investigators have often found that components of fitness such as growth rate and survival are positively correlated with the number of allozyme loci at which individuals are heterozygous rather than homozygous (Mitton and Grant 1984; Zouros 1987). The interpretation of such data has been controversial (see references in Avise 2004). Provide two hypotheses to explain the data, and discuss how they might be distinguished.
5. Considering the principles of mutation, genetic drift, and natural selection discussed in this and previous chapters, do you expect *adaptive* evolution to occur more rapidly in small or in large populations? Why? Answer the same question with respect to nonadaptive (*neutral*) evolution.

6. Discuss whether or not natural selection would be expected to (*a*) increase the abundance (population size) of populations or species; (*b*) increase the rate at which new species evolve from ancestral species, thus increasing the number of species.
7. Both creationists (e.g., Wells 2000) and a science writer (Hooper 2002) have charged that H. B. D. Kettlewell's famous evidence that predatory birds exert natural selection on the color forms of the peppered moth was deeply flawed and possibly deceitful. Grant (2002), Cook (2003), and others have rebutted this claim, and provide an entrée into the extensive research literature on this topic. Discuss whether or not this charge, if true, would weaken the case for evolution by natural selection. Read some of the relevant literature and write an essay on whether or not there is evidence for Kettlewell's claim.