6

Phenotypic Evolution

What was the most important advance in human history? Fire? The wheel? The computer? A strong case can be made for the harnessing of evolution by our ancestors some 11,000 years ago. They bred wheat that provided more grain and cows that produced more milk. Selective breeding produced domesticated plants and animals that gave the first farmers vastly more food than their ancestors could have imagined (**FIGURE 6.1**). For the first time in history, humans had abundant resources. They abandoned a nomadic lifestyle and settled in communities that became the earliest villages, towns, and then cities. Much of civilization—buildings, writing, commerce—only then became possible. In short, the genetic modification of plants and animals by selective breeding is the foundation of human civilization. The discovery of the power of selective breeding is simply the discovery that selection and inheritance together can produce large evolutionary changes. And, as Darwin pointed out, evolutionary changes caused by artificial selection of domesticated animals and plants illustrate what natural selection can do in the wild.

Traits such as crop yield in corn, milk production in cows, and body height in humans are examples of **quantitative traits**. These are traits that vary continuously and that are affected by several, sometimes thousands, of loci (and for that reason they are also called **polygenic traits**). **Quantitative genetics** is the study of how quantitative traits are inherited and how they evolve.

This chapter begins by looking at how genes and the environment affect quantitative traits, how selection acts on them, and how fast they evolve in response. The next topic is artificial selection, in which people selectively breed

The common sunflower (*Helianthus annuus*) has been selectively bred for its showy flowers, and to increase its production of oil and seeds. Hundreds of domesticated animal and plant species have been vastly modified by artificial selection.

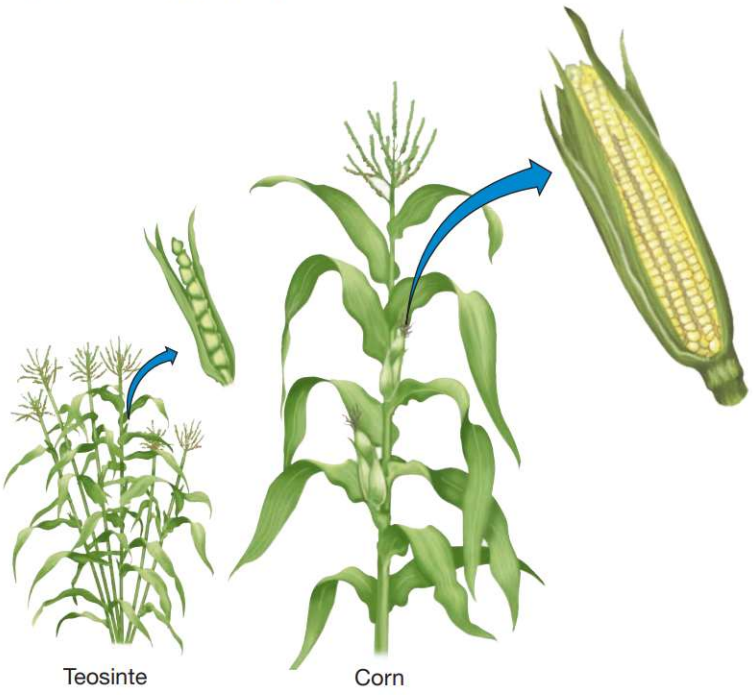

FIGURE 6.1 Modern corn and its wild ancestor, teosinte, differ in many ways. The striking differences in the pattern of branching result from a small number of genetic changes. Other differences, for example in the size of the cob, involve changes at many loci.

animals and plants to improve them for food production and other purposes. The chapter then describes how correlations between traits alter evolutionary trajectories. The final topic is the genetic basis of quantitative traits. Quantitative genetics is largely based on statistics, and the Appendix provides a quick introduction to the key concepts.

Genotypes and Phenotypes

Variation in DNA is discrete. At any particular site on a chromosome, the DNA can be one of four possible bases (A, C, G, or T). But a quantitative trait like height in humans varies in a continuous way (**FIGURE 6.2**). What is the connection between discrete variation in the DNA and continuous variation in height? Height is affected by thousands of loci [53]. It is also affected by environmental (nongenetic) influences, such as nutrition during early development. Identical twins have slightly different heights for that reason. The distinction between phenotypes and genotypes made in Chapter 5 is particularly important for quantitative traits: the phenotype can be directly seen, but the genotype cannot.

The variation in quantitative traits like height that is visible is measured by the **phenotypic variance**. This is simply the variance in the measurements of the trait in the population. (Variance is a key concept in this chapter, and is explained in the Appendix.) The phenotypic variance results from both genetic and environmental (nongenetic) causes. **FIGURE 6.3** shows how these factors combine to determine

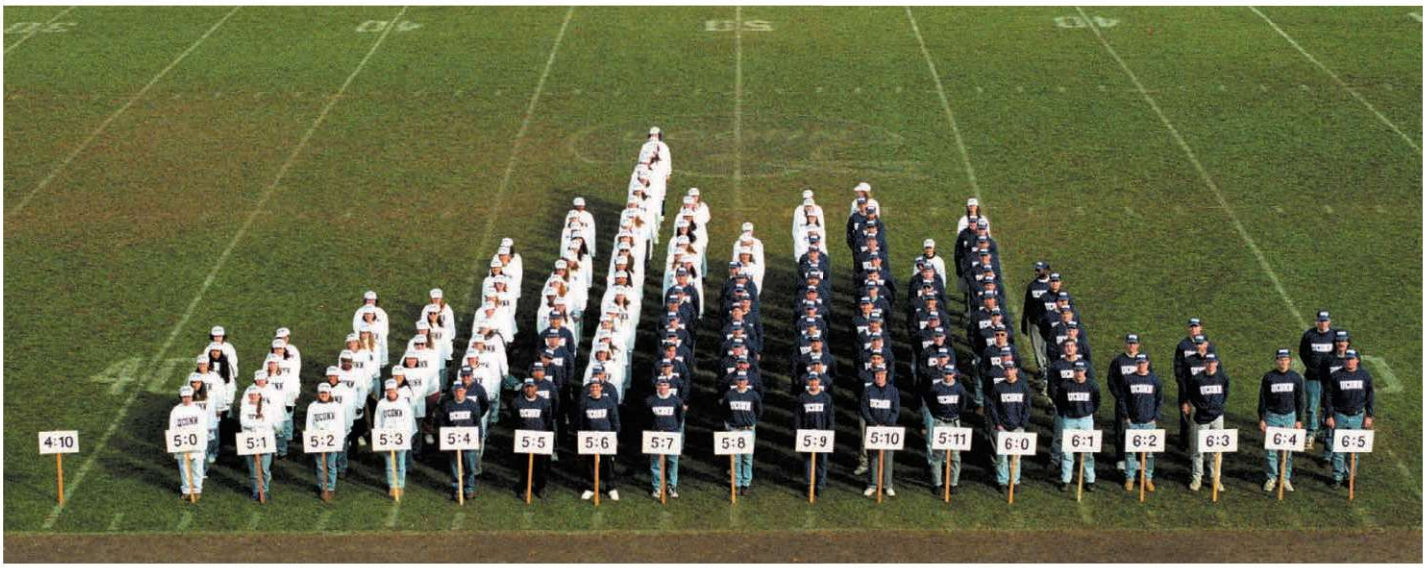

FIGURE 6.2 Height in humans is a classic example of a quantitative trait that varies continuously. These college students are lined up behind signs that show their heights, varying from short on the left to tall on the right. Women are dressed in white and men in blue. This is an example of a normal (or bell-shaped) distribution. Other continuous distributions have different shapes.

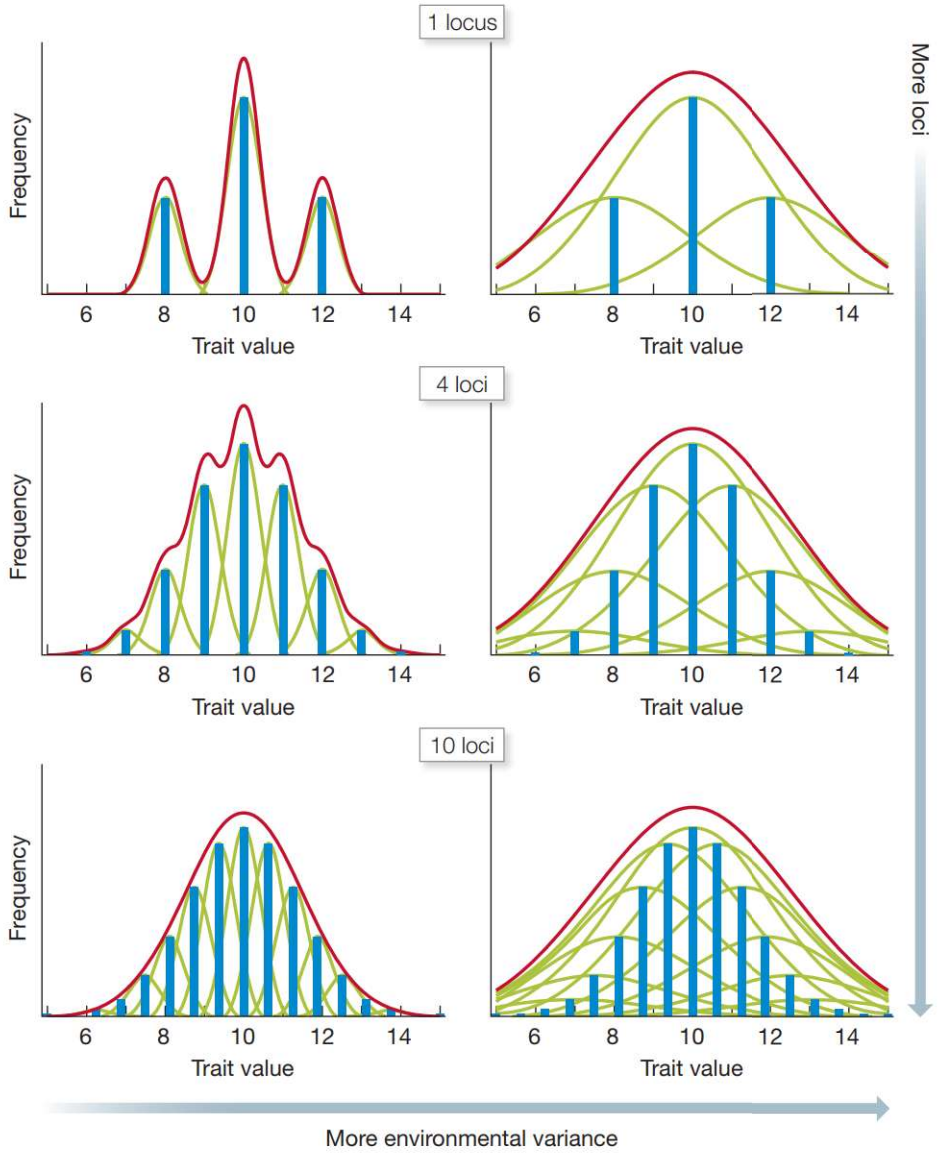

FIGURE 6.3 A phenotypic distribution is determined by genetic and environmental factors. The vertical blue bars show the phenotypes that would be produced without any environmental influence. The green curves show the phenotypic distributions for each of the genotypes that result with the addition of environmental variance. The red curve shows the phenotypic distribution for the entire population. Each locus has two alleles with frequencies 1/2. The loci are in linkage equilibrium, and alleles have equal and additive effects on the trait (there is no dominance or epistasis). The phenotypic distributions become smoother with larger numbers of loci. Left panels: Small environmental variance. Right panels: Large environmental variance.

the distribution of phenotypes in a population. The three rows show the situation when different numbers of loci contribute variation to the trait. The left-hand panels show traits that have small amounts of environmental variation, while the right-hand panels show traits for which the genetic and environmental sources of variance are about equally large (a situation typical of many traits). When just a single locus affects the trait, the phenotypic distribution shows distinct categories if environmental variation is small, but the distribution is smooth if there is more environmental variation. When ten loci contribute variation to the trait, the distribution is very smooth even when there is little environmental variation. The combination of a moderate number of loci with some environmental variation explains why so many familiar traits such as body height vary in a smooth, continuous way. Figure 6.3 shows another feature common to quantitative traits: phenotypes often follow a **normal distribution**, which is also known as a Gaussian or bell-shaped distribution.

The mean value of the trait in the population evolves when allele frequencies at the loci change. The change in the mean can be so large that the range of trait values in the population falls entirely outside the range that was present in the

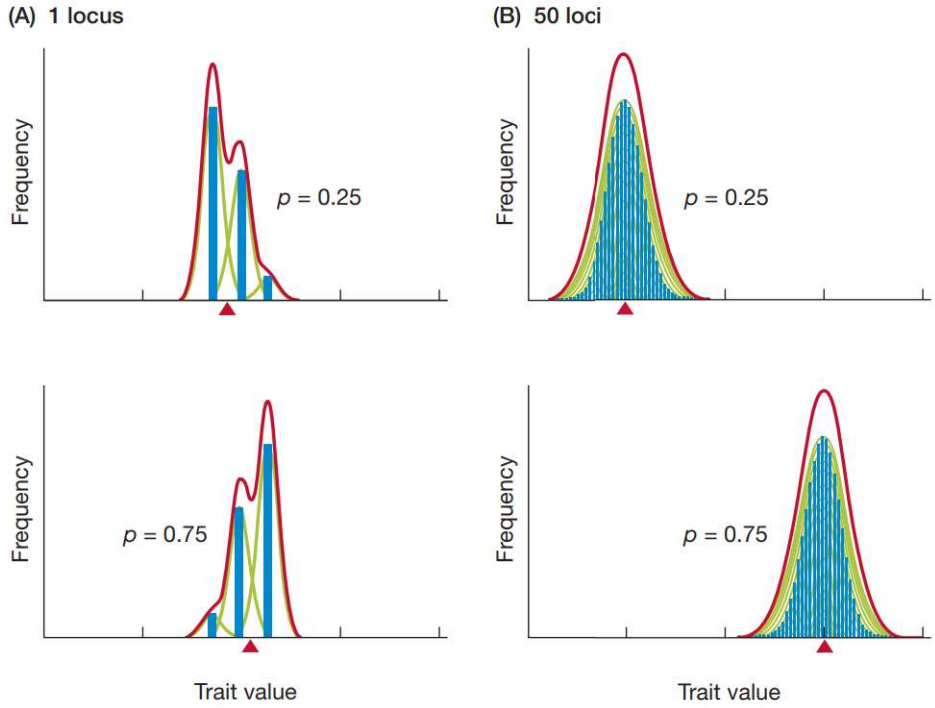

FIGURE 6.4 Large changes in quantitative traits can occur by the evolution of allele frequencies without the addition of new mutations. Colors of bars and lines are as in Figure 6.3. (A) The trait is affected by one locus with two alleles. Each copy of the A_2 allele increases the trait by 3 units, so A_2A_2 individuals are 3 units larger than A_1A_2 individuals, which are 3 units larger than A_1A_1 individuals. In the top graph, the frequency of the A_2 allele is $p = 0.25$, while in the bottom it is $p = 0.75$. The change in the allele frequency causes the mean of the trait to increase by 3 units (red triangles). The two phenotypic distributions overlap substantially. (B) The trait is now affected by 50 loci. One of the alleles at each locus increases the trait value by 0.4 units. For simplicity, we assume the frequency of the allele that increases the trait is the same at all 50 loci. The top and bottom graphs again compare the trait distributions when the allele frequency is $p = 0.25$ and $p = 0.75$. The mean of the trait now increases by 20 units. That change is larger than in (A), even though the effect of each allele is smaller. A key point is that the distributions for $p = 0.25$ and $p = 0.75$ do not overlap.

original population. This is because the new allele frequencies produce significant numbers of some genotypes that previously were rare or absent. **FIGURE 6.4A** shows how the phenotypic distributions change for a trait affected by one locus. There are two alleles, A_1 and A_2. Each copy of the A_2 allele that an individual carries increases the value of the trait by 3 units. With the frequency of allele A_2 at $p = 0.25$, the Hardy-Weinberg ratio tells us that the frequency of the rarest genotype (the $A_2\,A_2$ homozygote) is $(0.25)^2$, or 6.25 percent. Thus even the rarest genotype is common enough to be seen. When the allele frequency increases to $p = 0.75$, the frequencies of the genotypes shift and the mean of the trait increases by 3 units, but the distribution of the trait still overlaps substantially with the original distribution.

What if now there are two loci? Imagine that the alleles A_2 and B_2 increase the trait's value by the same amount, so that the genotypes $A_1A_2B_1B_2$, $A_2A_2B_1B_1$, and $A_1A_1B_2B_2$ all have the same phenotype on average. When alleles A_2 and B_2 are both at a frequency of $p = 0.25$, the rarest genotype ($A_2A_2B_2B_2$, which is also the biggest) is present at a frequency of $(0.25)^4$, which is less than 0.4 percent. But when the allele frequency shifts to $p = 0.75$, the frequency of that genotype rises to $(0.75)^4 \approx 32$ percent, which is more than 80 times its initial frequency. When multiple loci affect a single trait, changes in their allele frequencies can drastically change genotype frequencies and so change the distribution of the trait they affect.

The situation is even more extreme with 50 loci (**FIGURE 6.4B**). When the frequency of the allele that increases the trait is $p = 0.25$ at all loci, the frequency of

the genotype that is homozygous for the "big" allele at all 50 loci is expected to be $(0.25)^{100} \approx 10^{-60}$. That number is so small that this genotype—the one with the largest size—will never exist, let alone ever be seen. If the allele frequency at all loci increases to $p = 0.75$, the mean increases so much that the new distribution of the trait does not overlap at all with the original distribution. Quantitative traits can therefore evolve to produce entirely new phenotypes, using only alleles that are already in the population, without the introduction of new mutations.

Fitness Functions Describe Selection on Quantitative Traits

The horned lizards of the American Southwest would fit in well at Jurassic Park (**FIGURE 6.5**). Some species have dramatic horns projecting from the back and sides of their heads. The horns help deter predators, such as the fearsome loggerhead shrike. This bird has a remarkable and rather macabre behavior. After catching a horned lizard, the shrike often impales it on a branch (or in a pinch, on barbed wire), where it can eat it later.

Researchers have exploited that behavior to learn how natural selection acts on the size of the lizard's horns [56]. They compared the horn lengths of living lizards with those they found impaled by shrikes. From these data, the researchers were able to estimate how relative survival varies with horn length. A plot of survival against horn length shows that lizards with longer horns survive best (see Figure 6.5C). We don't know exactly how the horns protect the lizard. Perhaps shrikes have difficulty picking up a lizard with large horns, or perhaps the lizard stabs the shrike with its horns if it is caught.

The plot of survival against horn length is an example of a **fitness function**. This quantifies how selection acts on a quantitative trait. The horizontal axis is the value of the trait, and the vertical axis gives the expected fitness for individuals with that phenotype.

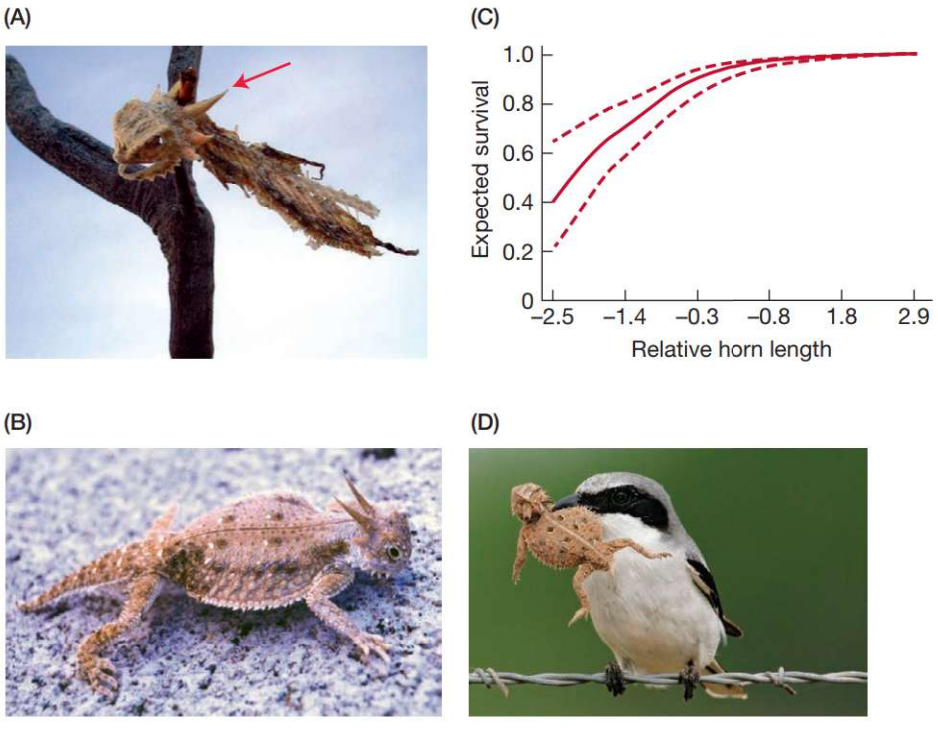

FIGURE 6.5 The fitness function for horn length in the horned lizard (*Phrynosoma mcalli*) has been estimated by comparing horn size in living and dead individuals. (A) A lizard that was caught and impaled on a thorn by a loggerhead shrike (*Lanius ludovicianus*). The arrow indicates one of the rear-most horns on the lizard's head. (B) A lizard that has avoided predation. (C) The fitness function showing how survival varies with the length of the horns. The function was estimated using the frequencies of live and shrike-killed lizards with a given horn length. (D) The loggerhead shrike is a major predator of horned lizards. The lizard shown here apparently did not successfully defend itself. (A courtesy of E. D. Brodie, Jr.; B courtesy of Kevin Young; C after [56].)

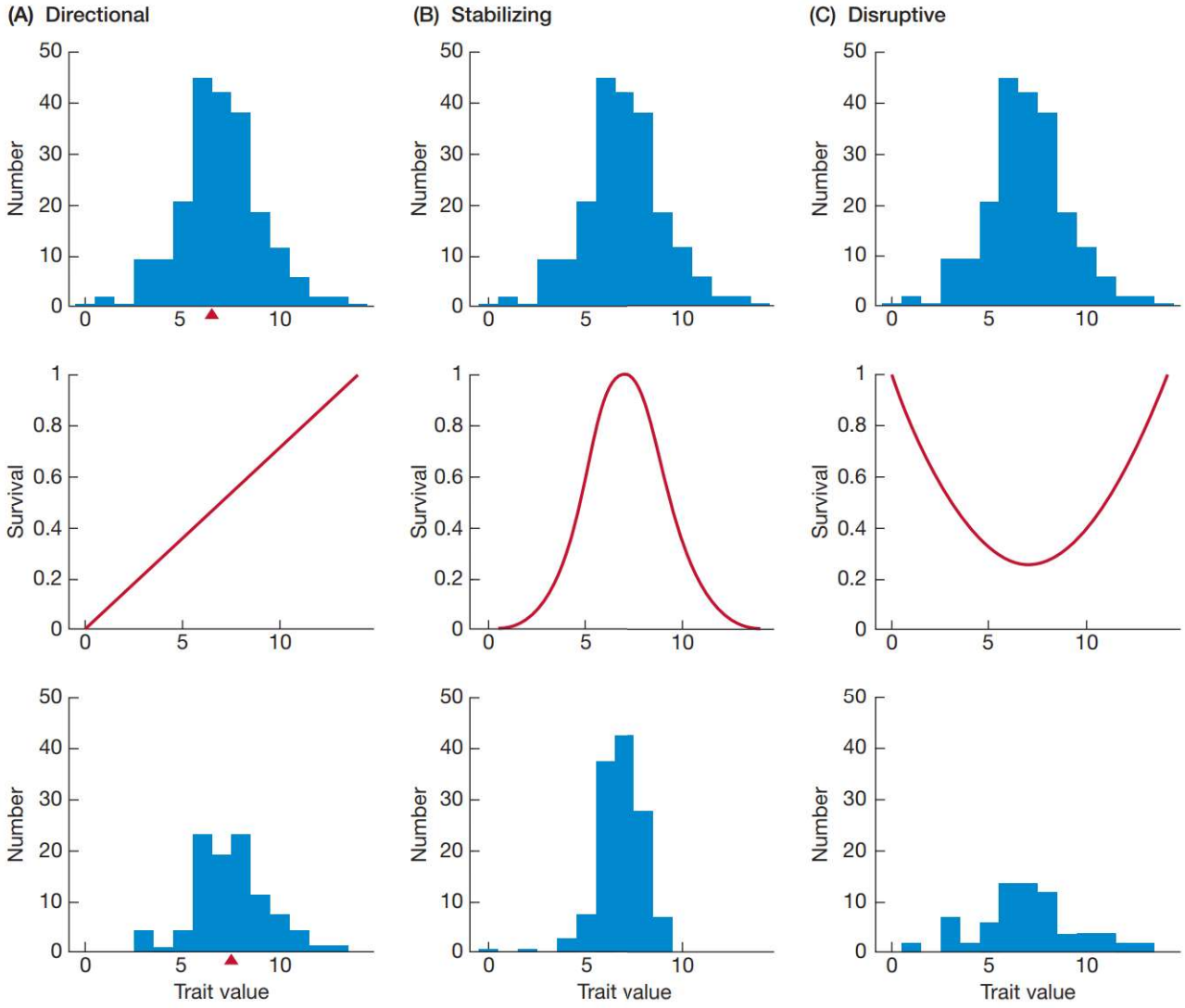

FIGURE 6.6 There are three basic modes of selection on a quantitative trait. (A) Directional selection favors a change in the trait mean, in this case toward a greater value. The top panel shows the distribution of the trait before selection acts, the middle panel shows the survival rate, and the bottom panel shows the distribution of the trait after selection. Triangles show the trait means before and after selection. (B) Stabilizing selection favors individuals near the population mean, which reduces the trait's phenotypic variance. (C) Disruptive selection favors the largest and smallest individuals, which increases the variance. (After [12].)

The horned lizards give an example of **directional selection**, which favors either an increase or a decrease in a trait's mean (**FIGURE 6.6A**). Many of the phenotypic differences we see among species are the result of directional selection. The ancestors of today's horned lizards had smaller horns that were enlarged by directional selection. In other cases, directional selection favors a decrease in a trait mean.

Earlier we emphasized that selection and evolution are two very different things. Selection happens *within* a generation, and may or may not lead to evolution. In 1977 a severe drought hit the Galápagos Islands, and many plants there failed to set seed. One of the seed-eating Galápagos finches (*Geospiza fortis*) was forced to eat new kinds of seeds, and birds with larger bills had higher survival rates (**FIGURE 6.7**). The mean size of survivors' bills was about 0.5 mm larger than the mean size in the population before the drought. The difference, which is highly

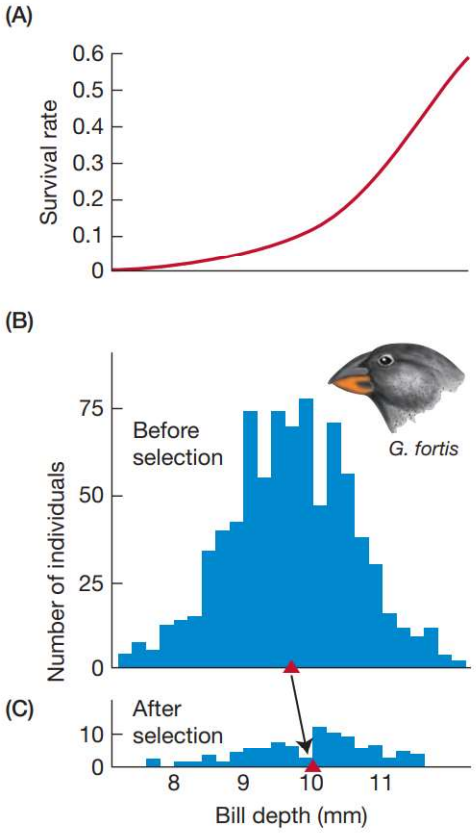

FIGURE 6.7 A severe drought in the Galápagos Islands in 1977 produced very strong directonal selection on bills of the Galápagos finch *Geospiza fortis*. Bill depth, which is the distance from the top to the bottom of the bill at its base, has a strong effect on the size of seed the finches are able to eat. (A) The fitness function of survival as a function of bill depth shows there was strong directional selection for deeper bills. The fitness function was estimated from the data in (B) and (C). (B) Distribution in bill depth of 751 *G. fortis* before the drought. (C) Distribution in bill depth of the 90 individuals that survived the drought. The selection differential *S*, which is the change in mean beak size (red triangles) from before to after selection (shown by the arrow), is highly statistically significant. (A after [42]; B and C after [8].)

statistically significant, shows there was directional selection. Note that this comparison is between individuals of the same generation, before and after the drought. At this point, no evolution has yet occurred.

A fitness function can also act on the variance of a trait (**FIGURES 6.6B and C**). **Stabilizing selection** favors individuals whose trait values are near the population's mean. After stabilizing selection acts, the phenotypic variance is reduced. This is a common form of selection because the means of many traits are near the values that have the highest fitness (often referred to as the **optimum phenotype**). In that situation, individuals that are much smaller or much larger than the mean have lower fitness. The result is that the tails of the phenotypic distribution are trimmed so the variance is smaller. Birth weight in humans is a classic example. Babies that weight much less or much more than the average at birth have a lower chance of surviving (**FIGURE 6.8A**).

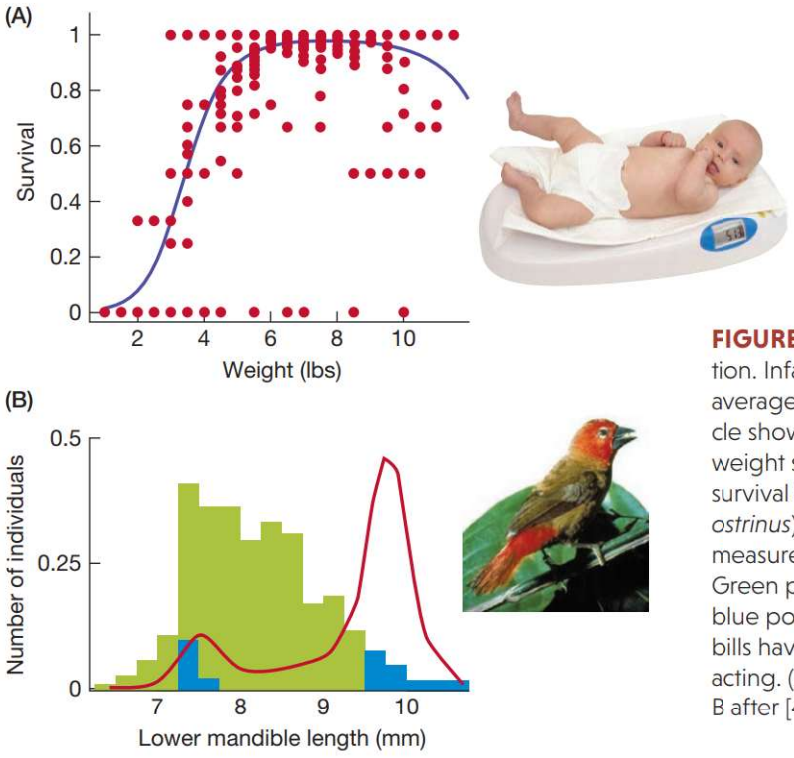

FIGURE 6.8 (A) Birth weight in humans is under stabilizing selection. Infants with birth weights much smaller or much larger than average have a lower probability of surviving to 28 days. Each circle shows the survival rate for a group of infants that had the birth weight shown and the same gestation time. (B) The probability of survival to adulthood in the black-bellied seedcracker (*Pyrenestes ostrinus*) depends on an individual's lower mandible length, a measure of bill size. The fitness function is shown by the curve. Green portions of the histogram show birds that did not survive; blue portions show birds that did. Birds with intermediate-sized bills have the lowest survival, showing that disruptive selection is acting. (A courtesy of Dolph Schluter after data from [42]; B after [47], with photo courtesy of Thomas B. Smith.)

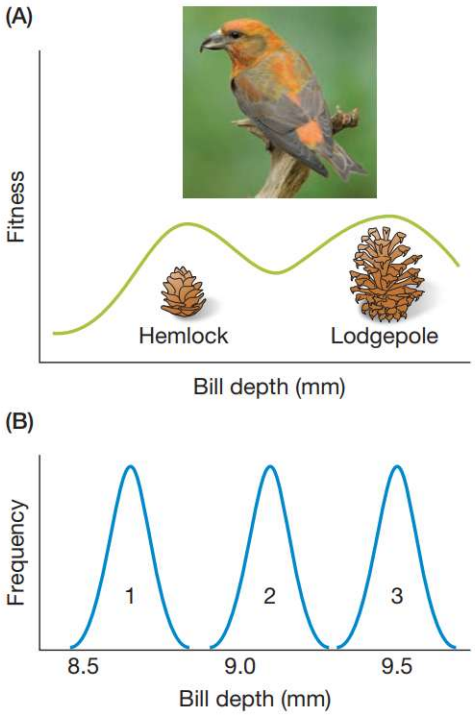

FIGURE 6.9 The type of selection acting on red crossbills (*Loxia curvirostra*) depends on both the phenotypic distribution in the birds and the cones on which they feed. (A) The fitness function for bill depth was estimated by the rate at which birds can feed. Small bills are efficient at opening the cones of western hemlocks, while large bills are efficient at opening cones of lodgepole pine. Intermediate-sized bills have low fitness. (B) The distributions of bill depth in three hypothetical populations of crossbills. Population 1 experiences directional selection to increase its mean bill size. Population 2 experiences disruptive selection. Population 3 experiences stabilizing selection. (A based on data from [6].)

The opposite situation is called **disruptive selection**. Here the smallest and largest individuals have higher fitness than individuals near the mean. After selection, the phenotypic variance is greater than it was before. Disruptive selection rarely splits a population into two separate groups, but rather makes intermediate individuals less common (**FIGURE 6.8B**).

Selection can alter both the mean and the variance of a trait at the same time. For example, if a trait's distribution after selection has a larger mean and a smaller variance than it did before, then both directional selection and stabilizing selection have acted.

The fitness function and the trait's distribution together determine whether selection is directional, stabilizing, or disruptive. **FIGURE 6.9** shows the fitness function for bill depth in the red crossbill, a bird that specializes in extracting seeds from the cones of pine trees and other conifers. The cones of different conifers vary in size and shape. This generates several peaks in the fitness function for the crossbill, with each peak representing the bill depth that is best for feeding on a particular type of cone. Is selection on bills directional, stabilizing, or disruptive? The answer depends on the distribution of bill depth relative to the fitness function. If most individuals in the population fall in a region where the fitness function is increasing or decreasing, then directional selection acts. If the population lies near a peak in the fitness function, then stabilizing selection acts. Last, if the population lies near a low point, then disruptive selection acts.

Fitness functions are also used to visualize selection acting on more than one trait. In these cases, the fitness function tells us which *combinations* of traits give high or low fitness. An example is shown in **FIGURE 6.10**. The northwestern

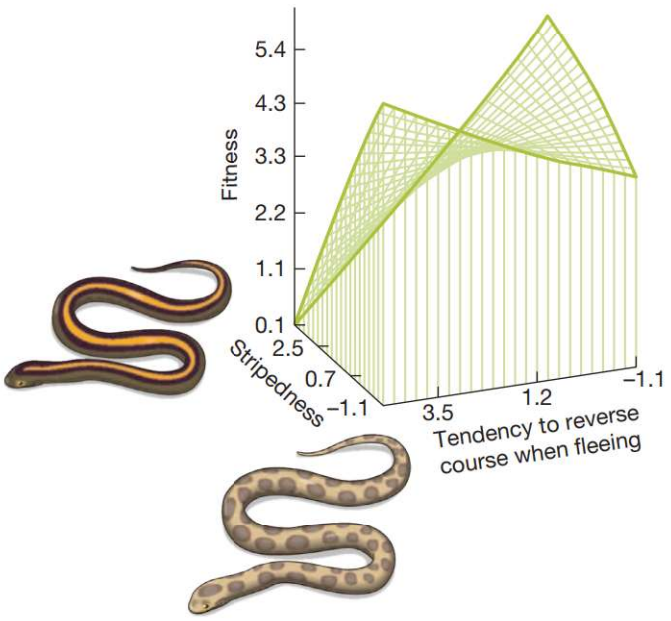

FIGURE 6.10 The fitness function for combinations of two traits in the northwestern garter snake (*Thamnophis ordinoides*), based on survival in the field. Snakes vary in their coloration and in their escape behavior. The height of a point on the surface represents the relative survival of individuals with a given combination of values for stripedness and the tendency to reverse course when escaping. Snakes with stripes that escape in a straight line have high fitness, as do snakes without stripes that reverse course. The fitness function shows that correlational selection is acting. (After [10].)

garter snake (*Thamnophis ordinoides*) varies in its color pattern: some individuals are striped, others are not. The snakes also vary in how they react to a predator. Some individuals escape in a straight line, while others often reverse their course. Survival of snakes with different combinations of these traits has been estimated by marking individuals, releasing them, and then recapturing the survivors at a later date [10]. Snakes that are striped and that escape in a straight line have high survival, probably because visual predators (such as birds) have difficulty judging the speed and location of a moving stripe. Snakes that are unstriped and reverse course also survive well, likely because reversals of unstriped snakes confuse the predator. Snakes with the two other combinations of coloration and behavior have lower fitness. Selection that favors particular combinations of traits, as in the garter snake, is called **correlational selection**.

Measuring the Strength of Directional Selection

Many of the questions that evolutionary biologists ask are about how and why the mean values of traits evolve. (Why did whales become so large?) Evolutionary changes in means are often caused by directional selection, and so it is important to be able to quantify its strength.

The **selection gradient** measures the strength of directional selection acting on a quantitative trait. It plays a role analogous to that of the selection coefficient for the alleles at a single locus. The basic recipe for estimating a selection gradient is simple. The data needed are measurements of the trait and of fitness on a set of individuals. Ideally, we would like to use the lifetime fitness. Often that is not possible to measure, so instead we use an important fitness component, such as survival or mating success. Relative fitnesses are calculated by dividing each individual fitness by the mean fitness of all the individuals, and these relative fitness values are plotted against the trait value. Finally, the selection gradient is the slope of the regression line fit through those points. (The Appendix gives a brief introduction to regression.) The selection gradient is symbolized by β, and its units are 1/[units of measurement]. If the trait is measured in millimeters, for example, then β is expressed as per millimeter. If the gradient is positive, then directional selection favors the mean to increase. A negative β implies that selection favors smaller values of the trait. Last, a value of $\beta = 0$ means that there is no directional selection acting.

The guppy (*Poecilia reticulata*) is a tropical freshwater fish that is popular among aquarium enthusiasts because males are colorful. Females prefer to mate with males that have more orange on their body (**FIGURE 6.11**). The estimate of the selection gradient from the data shown in the figure is $\beta = 3.8$. (In this case β has no units because the trait is measured as a proportion of the body surface.) If they existed, completely orange males would on average have 3.8 times more matings than males with no orange at all.

Evolutionary biologists have estimated the selection gradients acting on many natural populations of animals and plants. **FIGURE 6.12** shows the

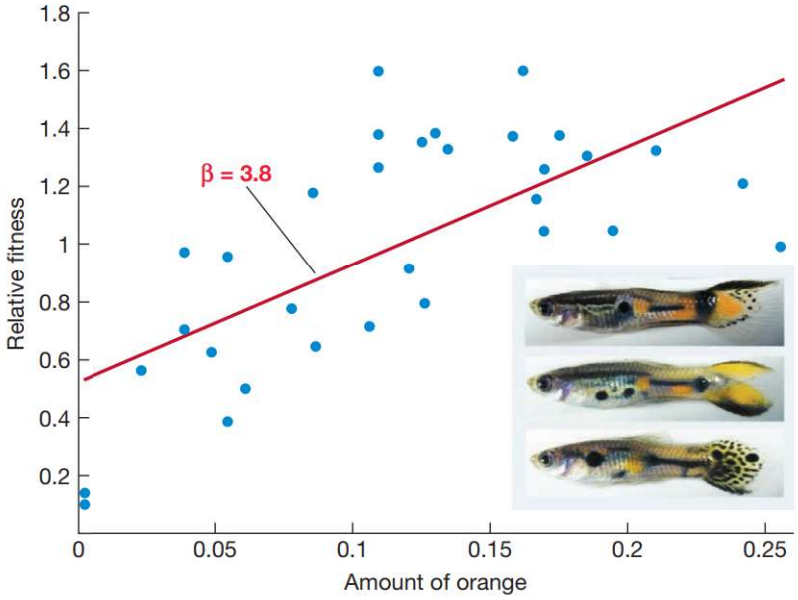

FIGURE 6.11 Selection gradient on orange coloration in male guppies. The horizontal axis shows the proportion of the body that is orange, and the vertical axis shows relative fitness, as measured by attractiveness to females in the lab. The slope of the regression line gives an estimate of the selection gradient: $\beta = 3.8$. (After [24]; photos from [26].)

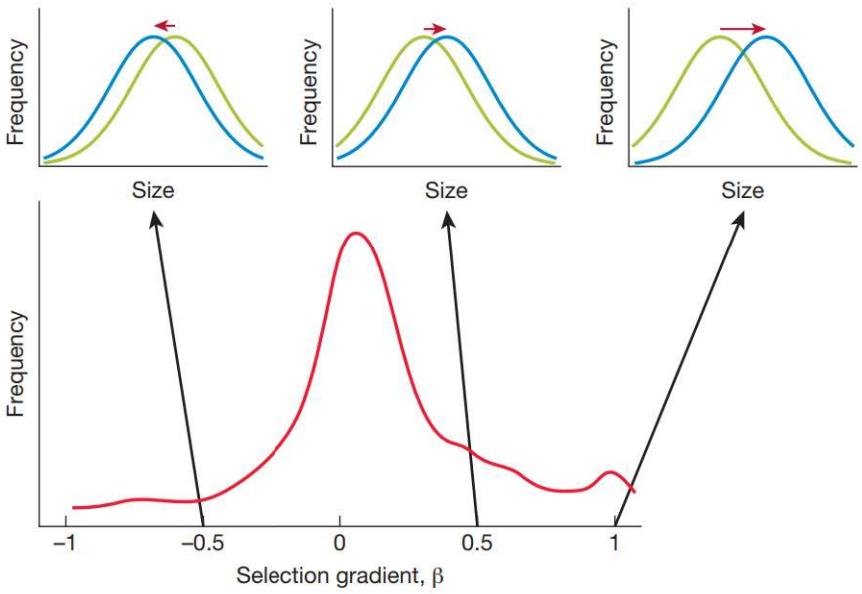

FIGURE 6.12 The distribution of selection gradients acting on size in natural populations of animals and plants show that directional selection is common and at times very strong. The distribution is based on 2819 estimates of β from 143 studies. Negative values of β reflect selection favoring smaller size, and positive values denote selection for larger size. To help visualize what different values of β represent, the insets show how much the phenotypic distribution of a trait is changed by moderately strong (β = 0.5 or −0.5) and very strong (β = 1) directional selection. Green curves show the distributions before selection, and the blue curves show the distributions after. The gradients shown here have been normalized by multiplying each β by the trait's phenotypic standard deviation. This makes β unit-free, which allows comparison of different kinds of traits. (Main panel after [32].)

frequency distribution of these gradients. Directional selection is common. In some cases, it is very strong: directional selection can cause the mean of the population to shift by more than one phenotypic standard deviation.

In Chapter 5 we saw that natural selection drives populations uphill on Wright's **adaptive landscape**. This landscape is a plot of the population's mean fitness against the frequency of an allele. The concept of an adaptive landscape also applies to quantitative traits [34]. Here the landscape plots the population's mean fitness against the mean value of the trait, rather than the allele frequency. (It is important to distinguish between the fitness function and the adaptive landscape. The first shows how the phenotype of an *individual* affects its fitness. The second shows how the *mean trait value in a population* affects the population's mean fitness.) When relative fitnesses are constant in time, natural selection causes populations to evolve uphill on this landscape. The mean will stop evolving when either it reaches a peak or the population runs out of genetic variation.

The selection gradient and adaptive landscape are useful tools for visualizing how selection is acting. A second use for them is to test hypotheses about adaptation. If a trait has reached an optimum favored by natural selection, then the population should be at a peak on the adaptive landscape and there should be no directional selection. That idea has been used to study the evolution of clutch size (the number of eggs laid) in birds. Many birds are physiologically able to lay more eggs than they actually do. This seems like an evolutionary paradox: why doesn't natural selection favor them to lay more? In fact, the selection gradient on clutch size is close to zero [46]. Females that lay more eggs than average hatch more chicks, but many of the chicks starve because their parents are unable to feed so many mouths. Females that lay the average number of eggs leave the largest number of surviving offspring to the next generation. We'll look more closely at the evolution of clutch size in Chapter 11.

Evolution by Directional Selection

We saw in Chapter 5 that if selection acts on a trait and if that trait is inherited, then evolution will result. This is a condensed version of the most important point made by Darwin in *The Origin of Species*. We can now go further than what Darwin was able to do: we can predict how *much* evolution will result.

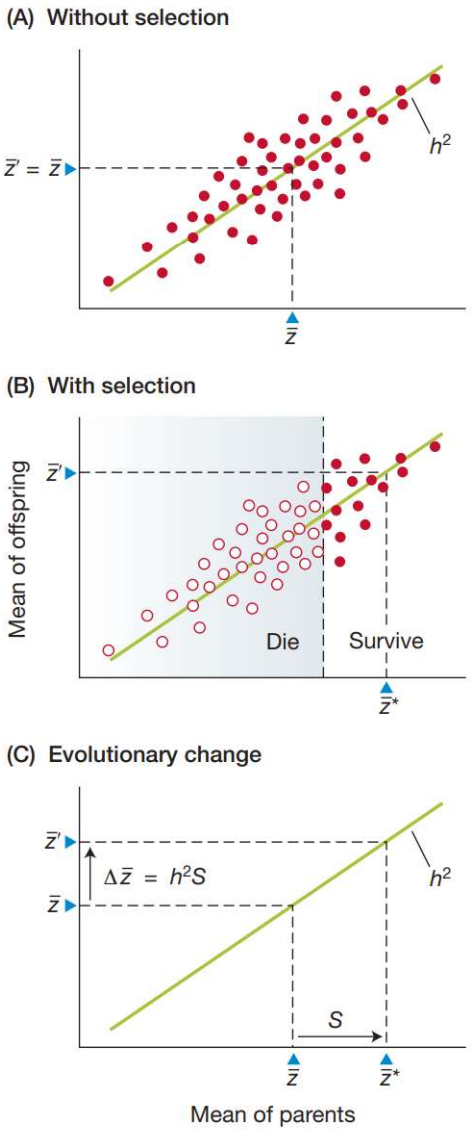

FIGURE 6.13 Schematic of the breeder's equation. Each dot represents a family. The mean size of the two parents is plotted on the *x*-axis, and the mean size of their offspring on the *y*-axis. The regression line shows the mean size of offspring that are expected from parents of a given size. The slope of this line is equal to the heritability, h^2. (A) With no selection, there is no evolutionary change, so the mean size of all offspring in the next generation, $\bar{z}'$, is equal to the mean size of all parents in the previous generation, $\bar{z}$. (B) Directional selection occurs. In this example, only parents whose size is larger than a threshold survive. The mean size of the surviving parents is $\bar{z}^*$. Now the mean size of their offspring ($\bar{z}'$) is larger than if selection had not acted: the mean of the population has evolved. (C) The selection differential, *S*, is the difference in the mean size of individuals before and after selection. The evolutionary change in the mean from one generation to the next is $\Delta\bar{z} = h^2 S$.

Both evolutionary biologists and breeders need to know how much the mean of a trait will evolve if there is directional selection (caused either by nature or by breeders). Happily, the answer is the simplest mathematical relationship that makes sense, and it can be understood with a diagram (**FIGURE 6.13**). The evolutionary change in the mean of a trait from a single generation of selection equals the product of two quantities: the strength of directional selection, and the amount of genetic variation. This is an exact parallel to the discussion in Chapter 5 of selection acting on a single locus (see Equation 5.3).

To make this point more quantitative, let $\bar{z}$ represent the mean of a trait at the start of a generation. Selection acts on the trait, and the survivors breed to produce the next generation. Using $\bar{z}'$ to represent the mean at the start of that new generation, the amount of evolutionary change is just the difference between $\bar{z}'$ and $\bar{z}$, which we symbolize by $\Delta\bar{z}$. As shown in Figure 6.13, that change is predicted to be:

$$\Delta\bar{z} = \bar{z}' - \bar{z} = h^2 S \qquad (6.1)$$

This is the famous **breeder's equation**, which is used to predict how much evolutionary change will result from selective breeding.

On the right side of Equation 6.1 is h^2, which represents the trait's **heritability**. The heritability is equal to the slope of the regression line that relates the value of a trait in two parents to its value in their offspring (**FIGURE 6.14**). The heritability therefore measures the strength of inheritance. If h^2 is 0, then there is no resemblance between offspring and their parents. At the other extreme, if h^2 is 1, then offspring look exactly like the average of their parents. (In this discussion, we assume that resemblance between parents and offspring is caused only by shared genes. Nongenetic factors can also contribute to that resemblance, as when some families live in good environments and others in poor environments. In those situations, a correction is made to remove the environmental effects from the estimate of heritability.)

The second quantity on the right of Equation 6.1 is *S*, which is the amount of change in the mean of the trait caused by selection within a generation. That is, *S* equals the difference between the mean of the population after selection, which is written $\bar{z}^*$, and the mean before selection, $\bar{z}$ (see Figure 6.7). If smaller individuals are more likely to survive and reproduce than larger individuals, for example, then *S* will be negative. A key point is that this difference is the change caused by selection *within* a generation, while $\Delta\bar{z}$ is the evolutionary change *between* one generation and the next. The selection differential is related to the selection gradient by the equation $S = P\beta$, where *P* is the phenotypic variance.

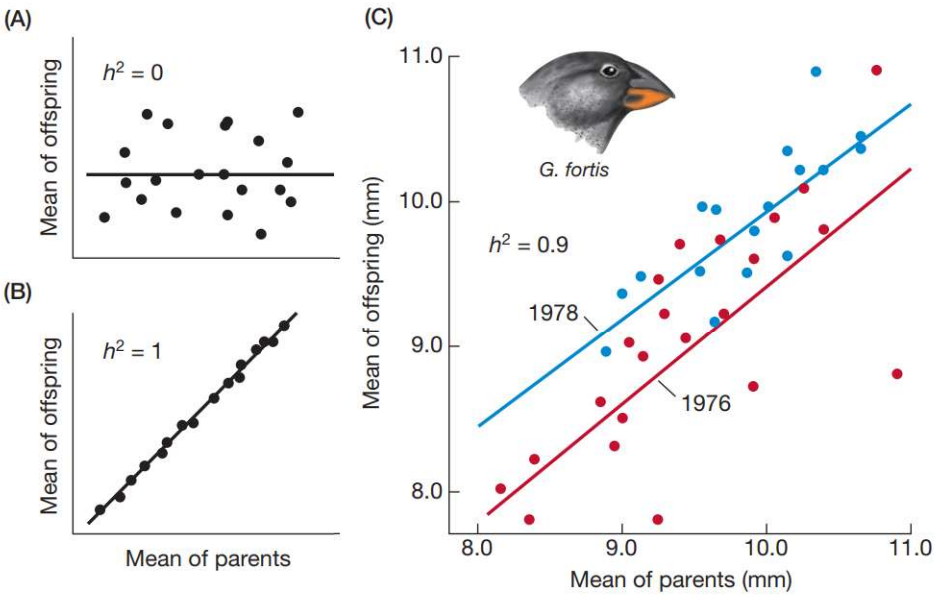

FIGURE 6.14 The plot of the phenotypes in parents and offspring is used to measure heritability. Each point represents the mean of all the offspring in a single family, plotted against the mean of their two parents. At left are two hypothetical cases showing what the plot looks like when (A) the heritability is $h^2 = 0$ and (B) when it is $h^2 = 1$. (C) The plot of parents and offspring for bill depth in the Galápagos finch *Geospiza fortis* in 1976 and 1978. Although offspring were larger in 1978, the slope of the regression between offspring and parents was nearly the same in both years. The heritability, estimated from the slope of the regression, is $h^2 = 0.9$ in both years. (C after [7].)

The essential message from Equation 6.1 is that the rate of evolution depends both on the strength of inheritance, measured by h^2, and the strength of directional selection, measured by S. The trait will not evolve if it is heritable ($h^2 > 0$) but there is no selection acting on it ($S = 0$). Likewise, a trait will not evolve if there is selection ($S \neq 0$) but no heritability ($h^2 = 0$).

A second version of the breeder's equation is mathematically equivalent but often more useful in evolutionary biology:

$$\Delta\bar{z} = G\beta \tag{6.2}$$

Here G is an important quantity called the **additive genetic variance**. It is the part of the phenotypic variation that is caused by genetic variation and that contributes to the resemblance between parents and offspring. In symbolic form, the additive genetic variance is defined as

$$G = h^2 P \tag{6.3}$$

where again P is the phenotypic variance of the trait. Equation 6.3 can be rearranged to give

$$h^2 = G/P \tag{6.4}$$

This shows that the heritability equals the fraction of the phenotypic variance that is due to heritable genetic variation. The rest of the phenotypic variance is contributed by two other sources. The first (and most important) source is nongenetic factors, such as nutrition. These contribute **environmental variance** to the trait, causing individuals with the same genotype to have different phenotypes (see Figure 6.3). The other source is genetic variation that is not additive, caused by dominance and epistasis, which we will discuss shortly.

Genetic analysis of hundreds of species has shown that most quantitative traits are heritable and evolve if selection acts on them [22, 35]. Heritabilities vary among traits and species. The values for morphological traits in vertebrates typically fall in a range between 0.2 and 0.6. That means that much (and sometime most) of the phenotypic variation we see for quantitative traits is genetic in origin and can respond to selection. Traits that are more closely connected to fitness (such as fecundity and longevity) tend to have lower heritabilities than morphological traits because they often have more environmental variance [25].

We now have everything needed to predict the direction and distance that the mean of a trait will evolve in one generation. The heritability h^2 is estimated from the regression of the trait measured in offspring plotted against the trait in their

parents (see Figure 6.14). We can also use those measurements to find P, the phenotypic variance of the trait. With those values in hand, Equation 6.3 gives us the additive genetic variance G. The strength of directional selection, measured by the selection gradient β, is estimated by the regression of relative fitness onto the trait value (see Figure 6.11). Finally, the evolutionary change in the mean of the trait, $\Delta\bar{z}$, is simply the product of G and β (see Equation 6.2).

Consider this implication: we can predict the outcome of genetic evolution without knowing anything about the genes that affect the trait! This means that the rate of evolution is not determined by the number of genes that affect the trait (at least in the short term). A second insight is that the rate of evolution is not determined by the population size (again, in the short term). A small population does not evolve more quickly than a large one if the two have the same additive genetic variance G.

When genes interact: Dominance and epistasis

You may be wondering why G is called the "additive" genetic variance. The answer is that there are also other types of genetic variation. It is important to distinguish between them because only the additive genetic variance contributes directly to evolutionary change.

Imagine that the height of a plant is completely determined by variation at a single locus, with no environmental variance. This locus is overdominant (see Chapter 5): both A_1A_1 homozygotes and A_2A_2 homozygotes are 20 cm tall, while A_1A_2 heterozygotes are 25 cm tall. If both the A_1 and A_2 alleles have a frequency of 1/2 and the population is at Hardy-Weinberg equilibrium, then half the plants will be 20 cm tall and half will be 25 cm tall. There is lots of variation in this population, and all of it is caused by genetic differences. Now imagine that all the short plants die, and only the tall plants (the heterozygotes) reproduce. In the next generation, the population looks exactly like it did before selection acted, with equal numbers of short and tall plants.

Why didn't selection cause an evolutionary change? Certainly not because of a lack of genetic variation. Rather, it is because none of it is additive genetic variance. In this example, the genetic variation is of a form called *dominance variance*, which results when the phenotype of heterozygotes is not intermediate between the phenotypes of the homozygotes. Here the two alleles interact: the effect of an allele on an individual's phenotype depends on the other allele that is carried at the same locus. Alleles at different loci can also interact, a situation called epistasis (see Chapter 4), which generates *epistatic variance*. Like dominance variance, epistatic variance does not contribute to evolutionary change.

For the great majority of traits, the additive genetic variance is much larger than the dominance variance and the epistatic variance. (The example of the plants was made extreme to make the concepts clear, and is not typical.) In short, most but not all genetic variation contributes to how fast a population evolves in response to directional selection. The additive genetic variance (as well as the dominance and epistatic variance) can evolve as allele frequencies change. For some traits, the additive variance stays relatively stable, and the trait can evolve at a constant rate for many generations. In other cases, selection fixes alleles at the loci that contribute genetic variation. This causes the additive genetic variance and heritability to decline, slowing and even halting the trait's evolutionary response to selection.

Adaptation from standing genetic variation versus new mutations

As our atmosphere becomes enriched in CO_2, many of Earth's organisms are experiencing directional selection caused by changed temperatures, acidified oceans, and other new conditions. Will they be able to adapt? Many traits will evolve rapidly

using genetic variation that already exists, what is called **standing genetic variation** (see Chapter 5). Other traits do not have genetic variation now and cannot evolve until new mutations favored by the new environmental conditions appear. In some cases this happens quickly, but in other cases the critical mutations may not appear for long periods of time. This kind of speed limit to adaptation is particularly common to small populations because fewer new mutations enter a population when there are fewer copies of the genes to mutate. We currently have a poor understanding of how often adaptation is based on standing genetic variation and how often on new mutations [1]. This is a topic of active research.

Can adaptation rescue species from extinction?

Although all species now alive owe their existence to adaptation in the past, the fact that well over 99 percent of species that ever lived are now extinct tells us that evolution does not guarantee survival. When conditions change, what determines whether a species can adapt fast enough to avoid extinction?

We can use mathematical models to explore when an abrupt change in the environment will cause extinction [21]. Imagine that a species is initially at a fitness peak for a quantitative trait. The environment then changes, favoring a new value for the trait and causing the mortality rate to exceed the birth rate. Then the population will decline to extinction unless the trait is heritable and so can evolve towards the new optimum value that maximizes survival. Thus, there is a race between adaptation and extinction. If the species can adapt quickly enough, survival rates will rebound and the species will be rescued. If it cannot, however, the population can fall below a critical threshold size where extinction will occur.

How this race ends depends on several key factors (**FIGURE 6.15A**) [11]. A population is more likely to survive if it has greater standing genetic variation, which will allow it to adapt more quickly. A large initial population size helps survival in several ways: the population size must decline a long way before it is at risk of extinction, and more new beneficial mutations enter the population in each generation. Some species can buffer themselves from the environmental change by adjusting to new conditions physiologically [13].

One approach used to study how these and other factors affect the risk of extinction is experimental evolution [4, 5]. **FIGURE 6.15B** shows results from a laboratory study with yeast. Populations were suddenly subjected to high concentrations of

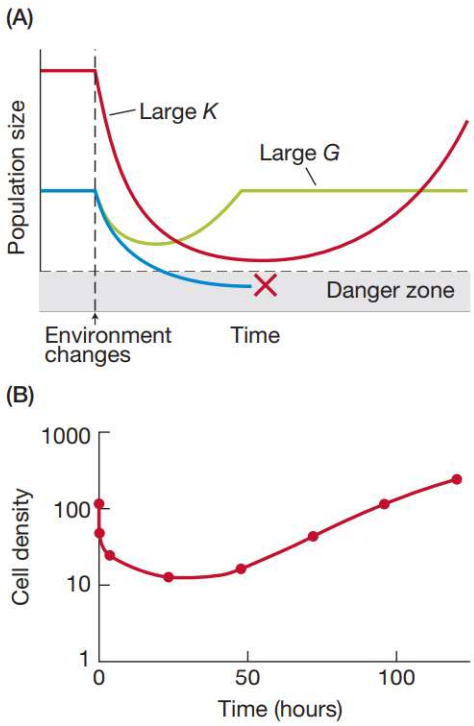

FIGURE 6.15 Adaptation can rescue some species but not others from extinction. (A) Simulations of how the size of a population changes in time following an environmental change that suddenly favors a different value of a quantitative trait. The environmental change (vertical dashed line) triggers declines in the population sizes of three species. The population size of the blue species falls below a critical threshold and into the "danger zone" (shaded area), leading to its extinction (marked by the X). The green species has larger genetic variance (*G*) for the trait, which allows it to adapt more rapidly to the new adaptive peak and avoid extinction. The red species has a larger carrying capacity (equilibrium population size, *K*). It avoids extinction because it has a longer time to adapt before reaching the danger zone. For simplicity, these simulations assume that the additive genetic variance is the same in all three cases and does not change in time. (B) Evolutionary rescue allows laboratory populations of yeast to avoid extinction following the sudden introduction of salt into their medium at time 0. The trajectory of population size during the decline and recovery is a good match for the "Large *K*" simulation shown in (A). Note that cell density (on the *y*-axis) is plotted logarithmically, so the changes in density are very large. (B after [4].)

salt. Initially, population sizes declined as the salt killed off yeast cells more rapidly than they were able to divide. As the populations adapted to the salt, population growth rates became positive. In this case, adaptation happened quickly enough to prevent extinction.

Studies of populations in nature also inform us about which species may or may not survive changing conditions [45]. Genetic variation for several traits was measured in three populations of the partridge-pea (*Chamaecrista fasciculata*) along a north-south transect, and seedlings were then transplanted among the three sites [15]. Plants that were moved farther south experienced warmer and drier environments, which are predicted to occur in their native population by 2050. These transplants showed reduced fitness. Only one of three transplanted populations showed sufficient genetic variation that it will likely be able to adapt to the new conditions. These results suggest that the partridge-pea may not be able to avoid extinction in the face of climate change that is currently happening.

While we expect that adaptation will allow some species to avert extinction as humans change the planet, many (perhaps most) will not be so lucky. The climate changed rapidly many times during the Pleistocene (see inside back cover), with warm periods interspersed by cold glacial periods. Many species survived by colonizing new areas where the altered climate matched the climate they were adapted to. But others did not adapt rapidly enough and became extinct. Currently, global change caused by the burning of fossil fuels is causing the climate to change at rates more than 100 times greater than during the Pleistocene, probably too fast for most species to shift their ranges to favorable regions [41]. It is likely that a large part of life on Earth is together with the partridge-pea on a path to extinction.

Artificial Selection

Humans have been selectively breeding animals and plants for millennia. Long before Equations 6.1 and 6.2 were known, people were genetically improving animals and plants by breeding together the best individuals in their fields and flocks. That process is called **artificial selection**, and it continues to this day as a critical part of modern agriculture.

The next time you walk into a supermarket, think about the animals and plants used to make the food you are about to buy. Virtually all of them have been radically changed by artificial selection, some so much that they only vaguely resemble the wild species that were domesticated by prehistoric farmers. The wheat for a pizza's crust, the tomatoes for its sauce, the cows whose milk makes the Parmesan cheese on top—all of these species have been changed dramatically by human-caused evolution (**FIGURE 6.16**).

Despite centuries of selective breeding, domesticated species continue to evolve in response to artificial selection. Milk production and poultry growth are increasing at 1 to 2 percent per year (see Figure 5.3). This is

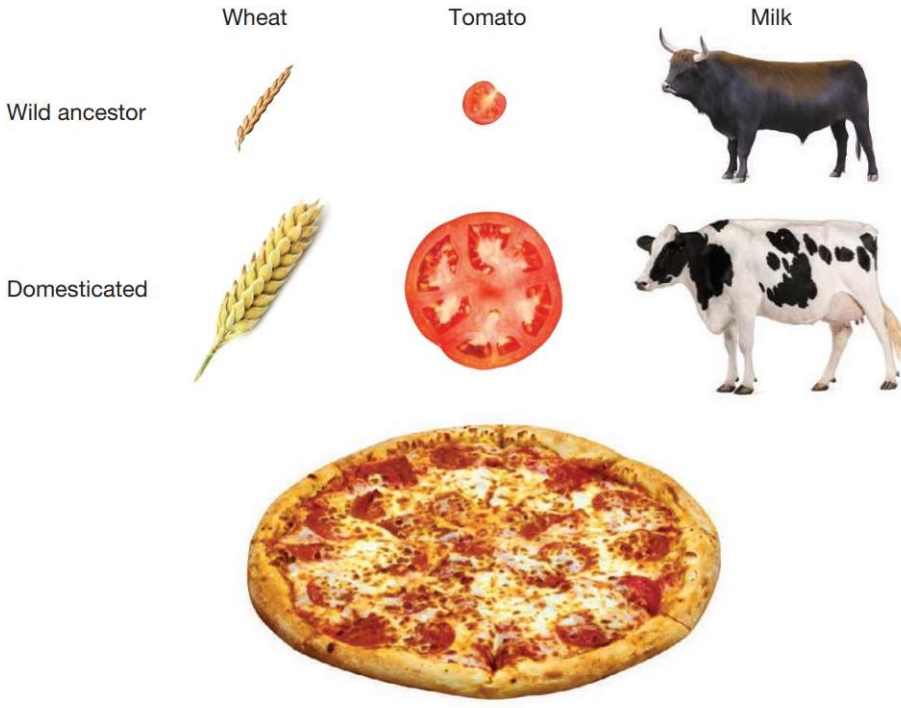

FIGURE 6.16 A familiar food item, showing the sources for three major ingredients as they looked in their wild ancestors before domestication and as they do today.

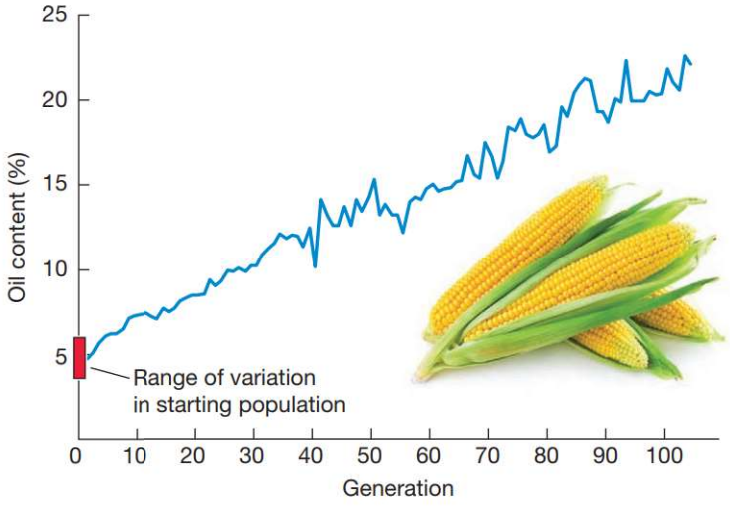

FIGURE 6.17 The oil content of corn kernels increased over 107 generations of artificial selection. In the initial population, the mean oil content was 4.7 percent, and the highest oil content measured on any corn ear was 6 percent. The average oil content in the most recent generation was 22 percent, more than 4.5 times higher than in the initial population. (Data from [14].)

a critical contribution to society since it allows us to produce more food with the same or even fewer resources. Artificial selection on many species is now done using sophisticated statistical methods that evaluate each individual's genetic potential.

In addition to improving domesticated species, artificial selection is used by biologists to study basic questions about evolution. This research often uses model organisms such as *Drosophila* and *E. coli* because they are convenient and well known genetically. Several general conclusions have emerged are likely to apply to all species:

Almost all traits evolve when selected. Results from hundreds of selection experiments show that most traits in diverse species immediately respond to selection based on standing genetic variation [23]. We will see shortly, however, that there are exceptions to this rule that have significance for our understanding of the limits to adaptation.

Selection can cause a trait to evolve far beyond its original range of variation. We saw early in this chapter that changes in allele frequencies can cause a quantitative trait to evolve far beyond the range of variation that was originally present in the population. An example in real organisms comes from a famous artificial selection experiment on corn that is still continuing after more than 100 years (**FIGURE 6.17**). Early in the experiment, evolutionary change was based on standing genetic variation, but new mutations contributed in later generations.

Large populations evolve faster and farther than small populations. Researchers have used artificial selection to learn what factors affect how populations adapt. One pattern that emerges is that large populations tend to evolve faster and farther (**FIGURE 6.18**). That finding is interesting because there is nothing in Equations 6.1 and 6.2 that suggests population size should have an effect. The explanation is that over the course of several generations, the additive genetic variance can decline, and it tends to do so more rapidly in smaller populations (see Chapter 7). An important conclusion is that species that are already rare are particularly vulnerable to environmental change because they may not adapt as quickly as abundant species.

Strong selection on one trait often has negative side effects on other traits. Over a span of 50 years, artificial selection on dairy cows increased milk production by 1 percent per year, but also caused fertility to decline at about the same rate [23]. This is an example of how selection on one trait often causes evolutionary side effects on other traits, which is our next topic.

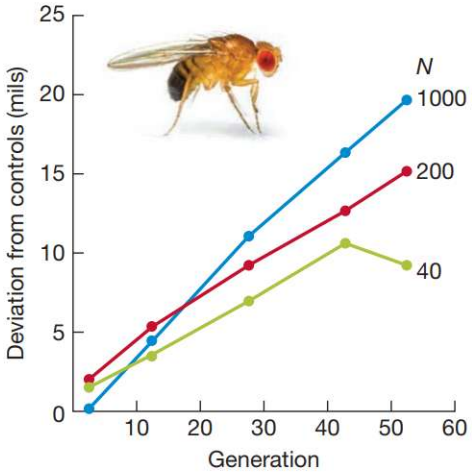

FIGURE 6.18 A selection experiment for increased wing-tip height in *Drosophila melanogaster* shows evolutionary change over 54 generations in populations of different sizes. Shown are the numbers of individuals that are selected to start each generation. (For example, with $N = 200$ flies, a total of 1000 flies were measured, and the 200 flies with the longest wings were bred to begin the next generation.) The largest population has evolved the fastest and farthest. (After [52].)

Correlated Traits

Traits are correlated: if you have long arms, you probably also have long legs. This kind of correlation is in part heritable and genetic, meaning that individuals with long arms tend to have offspring that have both long arms and long legs. **Genetic correlations** such as these cause evolutionary side effects. When selection acts to increase one trait, it will not only cause the mean of that trait to increase, it will also change the means of other traits that are genetically correlated with it.

These evolutionary side effects are described by an expanded version of Equation 6.2. Let's say that directional selection is acting on two traits. The evolutionary change in trait 1 caused by one generation of selection is

$$\Delta\bar{z}_1 = G_1\beta_1 + G_{1,2}\beta_2 \tag{6.5}$$

There are two terms on the right side. The first is just as we saw in Equation 6.2: it is the product of G_1, the additive genetic variance for trait 1, and β_1, the selection gradient acting on trait 1.

The second term in Equation 6.5, however, is new. It is the product of $G_{1,2}$, which is the **genetic covariance** between trait 1 and trait 2, and β_2, which is the selection gradient on trait 2. A genetic covariance measures how strongly two traits tend to be inherited together. (A covariance is closely related to a correlation, which is a covariance that has been rescaled so that it ranges from –1 to 1. Covariances and correlations are explained in the Appendix.) A genetic covariance of 0 means that the traits are inherited independently. A positive covariance means that individuals that are larger than average for one trait will tend to have offspring that are larger for both traits. That is typically the case for morphological traits, simply because big individuals tend to be big for all traits. A negative genetic covariance implies the opposite: individuals that are bigger than average for one trait will have offspring that are big for that trait but smaller than average for the second trait. An example is reproductive rate and longevity in fruit flies. Females that lay many eggs survive less well than females that lay few eggs.

The two terms on the right side of Equation 6.5 show that a trait can evolve in two ways. The first way is as a **direct response** to selection, meaning that the trait is evolving as the result of selection acting on it. The second way is as an **indirect response** to selection, meaning that the trait is evolving because of selection on another trait with which it is correlated.

One implication of Equation 6.5 is that a trait can evolve by natural selection even if selection does not act on that trait. If that statement sounds nonsensical at first, consider what happens to trait 1 when the selection gradient on that trait is zero. Its mean will nevertheless evolve if directional selection acts on trait 2 and there is genetic covariance between the traits (that is, neither β_2 nor $G_{1,2}$ are 0). This situation is sketched in **FIGURE 6.19**. Even more remarkable is that selection can cause a trait to evolve in the direction opposite to what selection on that trait favors. For example, if there is weak selection to increase leg length but very strong selection to decrease arm length, both traits can evolve smaller size.

Earlier we discussed selection on bill size in one of the Galápagos finches during an intense drought. Trevor Price and colleagues found that selection favored finches with narrower beaks, likely because they could better crack open new seed types [40]. Nevertheless, the average bill width among birds that survived the drought was larger than it was before the drought. The explanation for this counterintuitive result is that bill width has strong positive correlations with other traits, including body size. Those traits caused indirect selection on beak width that was stronger than the direct selection on beak width.

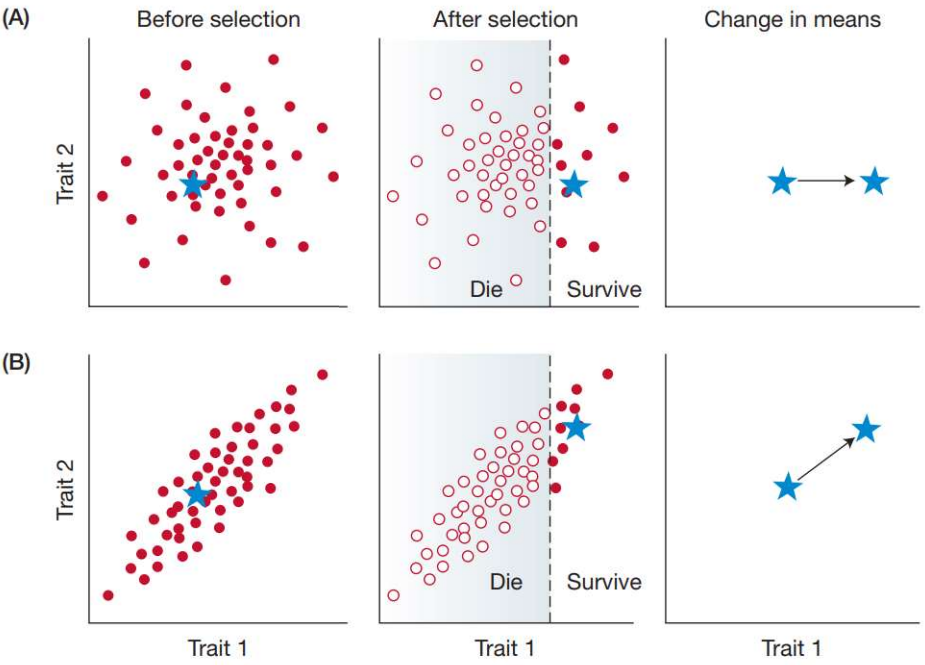

FIGURE 6.19 Directional selection on one trait can cause another trait to evolve as a correlated response. In these plots, each point represents the values for two traits in a single individual. (A) The two traits are not correlated. Selection acts only on trait 1, and only individuals larger than the threshold shown by the dotted line survive (red points in the middle panel). After selection, the mean of trait 1 has increased, but the mean of trait 2 is unchanged. (B) The two traits have a strong positive correlation. Selection again acts only on trait 1 (middle panel). After selection, the means of both trait 1 and trait 2 have increased. The change in trait 2 is a correlated response to selection.

Side effects like these may explain some evolutionary enigmas. The Mexican tetra (*Astyanax mexicanus*) is a fish that has both surface-dwelling and cave-dwelling populations. Fish from the surface have eyes and can see, but fish from caves have lost their eyes (**FIGURE 6.20**). Why does adaptation to the dark and nutrient-poor environment in caves favor mutations that eliminate sight? Cave fish find prey in the dark using sensory cells on their heads that respond to vibrations in the water. Genetic analysis shows that mutations that increase the responsiveness of this detection system also cause a reduction in the eyes as a correlated side effect [55]. The blind cave fish also illustrate one of the ways that natural selection can cause the loss of a complex structure such as the eye.

(A)

(B)

FIGURE 6.20 Populations of the Mexican tetra (*Astyanax mexicanus*) that live in streams on the surface have eyes (A), while populations that live in caves have lost their eyes (B).

Constraints and trade-offs

While the great majority of quantitative traits have standing genetic variation, not all do. Traits that lack variation cannot respond to directional selection, and so we say they have an **evolutionary constraint** that can prevent them from adapting. Species of *Drosophila* that live only in wet tropical habitats have little or no genetic variation that would allow them to adapt to cool and dry habitats. This may explain why their ranges do not expand outward into drier habitats [30, 31].

The cliché that there's no such thing as a free lunch applies to the evolution of many quantitative traits. Say that natural selection favors deer that can run faster. Increased speed puts more stress on the deer's leg bones, which selects for stronger bones. If there is genetic variation for growing thicker bones, that trait can increase. But there's a catch: bones that are thicker are also heavier, which decreases speed.

This is an example of an evolutionary **trade-off**, which occurs when increasing fitness in one way decreases it in another. Trade-offs can be understood at different levels. The trade-off between the strength and weight of a femur results from simple physics: more bone mass increases both strength and weight. A complementary perspective comes from genetic correlations. Bone strength and bone weight are highly correlated, so an evolutionary increase in one necessarily causes an increase in the other. Genetic correlations can therefore cause evolutionary constraints. Even though individual traits show genetic variation, there can be combinations of trait values for which there is little or no variation.

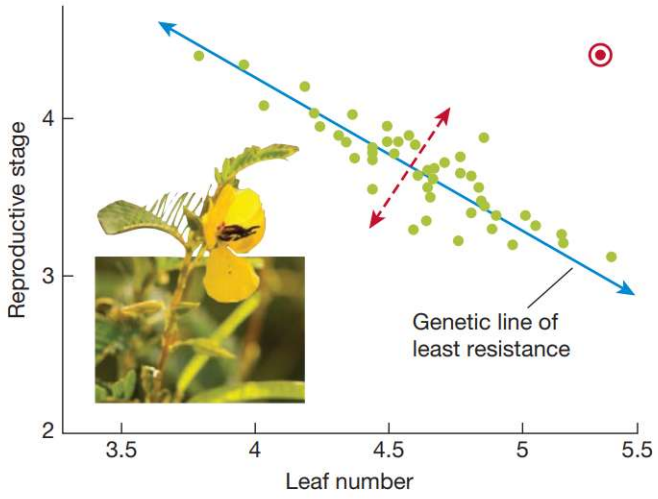

FIGURE 6.21 A negative genetic correlation in the partridge-pea (*Chamaecrista fasciculata*) results in an evolutionary trade-off. Plant size, measured by leaf number, is plotted on the x-axis. Plant growth rate, measured by the reproductive stage, is plotted on the y-axis. Each dot shows the values of those traits for a genotype in a population from the northern United States (Minnesota). The genetic line of least resistance (in blue) is the combination of traits that can evolve rapidly because there is abundant standing genetic variation. There is little variation to evolve in the directions indicated by the red dashed arrows. Climate change is selecting for the combination of traits indicated by the bull's-eye. This population is predicted to become extinct because there is little genetic variation to evolve in the direction favored by selection. (After [16].)

Earlier in the chapter we discussed the partridge-pea, which may not adapt quickly enough to avoid extinction. **FIGURE 6.21** develops that story further. It plots the growth rate against plant size for genotypes sampled from a northern population. The two traits show a strong negative genetic correlation. There is abundant genetic variation that will let the population evolve either more leaves and slower growth, or fewer leaves and faster growth. This is an example of a **genetic line of least resistance**, which is a combination of traits for which a population has abundant genetic variation [43]. In contrast, there is little variation that would allow the population to evolve toward either more leaves and faster growth, or fewer leaves and slower growth. The challenge faced by the partridge-pea is that adaptation to changing climates requires evolving both more leaves and faster growth.

Genetic correlations can evolve as gene frequencies change (just as genetic variances do), so correlations like those in the partridge-pea will only constrain adaptation in the medium to long term if they remain relatively constant. Many morphological traits are highly correlated with overall body size, and genetic correlations between them may be stable over thousands or even millions of years [34]. Other genetic correlations change over shorter time scales.

The hypothesis that genetic correlations can constrain evolutionary change in the short term has been tested in a selection experiment. A butterfly with the curious name of squinting bush brown (*Bicyclus anynana*) has spots on its wings (**FIGURE 6.22**). Artificial selection on the two large spots can change their sizes independently, so they are not constrained. Selection on the colors of two other eyespots was able to make both become more black or both become more golden, but it was unsuccessful in making one eyespot black and the other gold. The color of these two eyespots is constrained to be the same by a genetic correlation [3]. Genetic correlations between traits are a major cause of evolutionary constraints [22, 33, 43]. An important but unanswered question is how often the evolutionary limits seen in short-term experiments like that with the butterfly persist over longer evolutionary time scales.

The causes of genetic correlations

Genetic correlations have two sources. The first is **pleiotropy**, the situation in which a single locus affects more than one trait (see Chapter 4). Many loci affect body size in humans. These genes generate correlations among virtually all morphological traits, since individuals who are large for one body part tend to be large for others. They also generate correlations among other types of traits. For

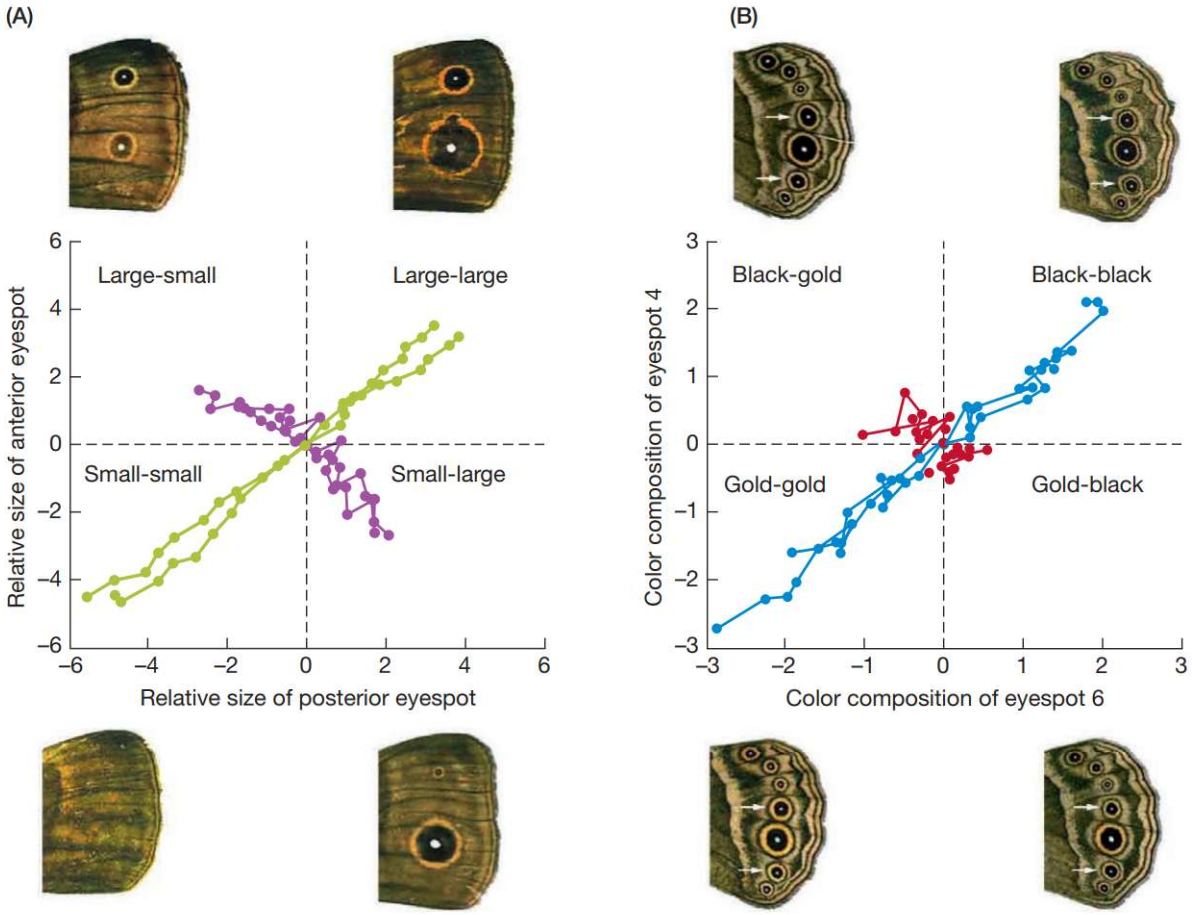

FIGURE 6.22 Artificial selection experiments showing different levels of constraint on the evolution of eyespots in wings of the butterfly *Bicyclus anynana*. (A) Evolutionary trajectories that result from selection on the sizes of the two eyespots on the dorsal side of the wing. The graph shows the results of selection for both eyespots to be large or small (Large-large and Small-small, green trajectories) and for one to be large and the other to be small (Large-small and Small-large, purple trajectories). Each point represents one generation. Rapid evolution occurred for all combinations of traits that were selected, showing there is no evolutionary constraint. (B) Trajectories resulting from selection on the colors of two other eyespots (shown by arrows) on the ventral hind wing. Selection to make both eyespots more black or more gold caused substantial evolutionary change (Black-black and Gold-gold, blue trajectories). In contrast, selection for different colors in the eyespots was largely ineffective (Black-gold and Gold-black, red trajectories). This is an example of an evolutionary constraint caused by a genetic correlation between two traits. (After [1a], courtesy of Cerisse Allen and Paul Brakefield.)

example, smaller individuals tend to have higher metabolic rates per body mass. A second source of genetic correlations is **linkage disequilibrium**, the nonrandom association between alleles at different loci (see Chapter 4).

In some cases, selection favors genetic correlations. We saw earlier that correlational selection on garter snakes favors certain combinations of coloration and predator escape behaviors. These traits are also genetically correlated, and the high fitness combinations of traits are more common than they would otherwise be [9]. While we do not know whether the genetic correlation in garter snakes results from pleiotropy or linkage disequilibrium, in other cases we do. The butterfly *Heliconius numata* has several wing-color morphs that mimic different species of model butterflies. (See Chapter 13 for more on mimicry.) Selection caused by predation favors certain combinations of color elements. Genetic analysis showed that the color morphs are controlled by a small segment of chromosome with 18 genes [29]. The high fitness combinations of alleles that control the colors have been locked

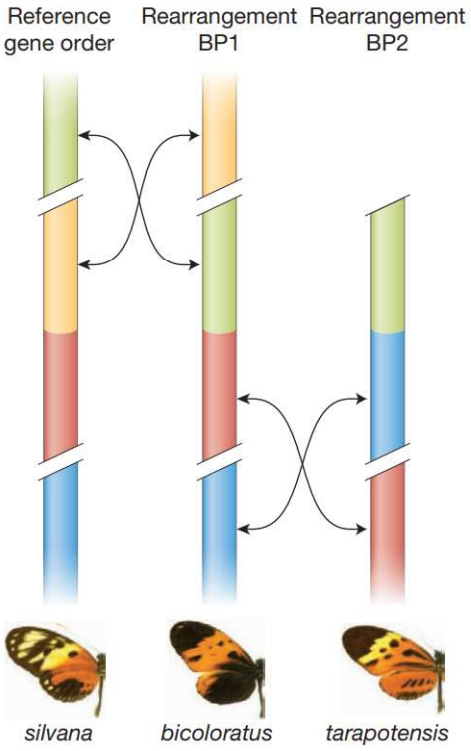

FIGURE 6.23 A wing-color polymorphism in the butterfly *Heliconius numata* is controlled by a small segment of chromosome. Genetic analysis shows that the segment consists of two overlapping inversions that do not recombine. These inversions carry loci with alleles that alter the pattern and coloration of the wings. The different color morphs are favored in different parts of the species' range because they mimic other species of toxic butterflies that are common in those regions. Top: Schematics of the chromosomes showing the changes in gene order produced by the inversions. Bottom: The wing-color patterns produced by the different chromosomes. (After [29].)

together by a series of chromosome inversions that prevent recombination from producing low fitness color patterns (**FIGURE 6.23**). Selection favored a genetic correlation between the colors controlled by several loci, and the inversions spread because they strengthened that correlation.

Phenotypic Plasticity

Most tadpoles (the larval stage of frogs and toads) live on a diet of algae and detritus. Spadefoot toads (*Spea*), however, have a remarkable trick (**FIGURE 6.24**). When their eggs hatch in ponds where algae are the main food source, they develop into typical omnivorous tadpoles. But when they hatch in ponds with a high density of shrimp and other animal prey, they develop into carnivorous tadpoles with a greatly enlarged head and sharp horny beak [39]. The omnivorous tadpoles have large fat reserves that increase their survival as adults. The carnivorous tadpoles sacrifice these reserves but can develop more rapidly on their diet of animal protein, which allows them to metamorphose at an earlier age. That is adaptive because the conditions that trigger development of carnivores occur in ponds that dry up quickly, and tadpoles die if they have not yet metamorphosed when that happens.

This developmental shift is an example of **phenotypic plasticity**, which occurs when an individual's phenotype changes in response to the environment it experiences. In the case of spadefoot tadpoles, the change is developmental and irreversible. Plasticity can also be physiological and reversible, for example the tanning that light-skinned people show after exposure to ultraviolet (UV) light. Plasticity is seen in a wide range of traits that range from gene expression to morphology and physiology to behavior.

Phenotypic plasticity can be visualized with the **reaction norm**, which is a plot showing how environmental conditions affect how a phenotype is expressed. Reaction norms can differ among genotypes, which means that reaction norms themselves can evolve. Genetic variation in a reaction norm is referred to as **genotype-environment interaction** (or **G×E**, for short). **FIGURE 6.25** shows that reaction norms for increased pigmentation in response to UV light differ between populations of water fleas (*Daphnia*). These differences are adaptive because in some populations survival is increased by plasticity while in other populations it is not.

Not all phenotypic plasticity is adaptive [20]. When people who live at sea level ascend to high elevations, physiological changes are triggered by

FIGURE 6.24 A carnivorous tadpole cannibalizes a typical tadpole of the spadefoot toad *Spea bombifrons*. This is a dramatic example of phenotypic plasticity: tadpoles of this species develop into either typical or carnivorous morphs depending on environmental conditions.

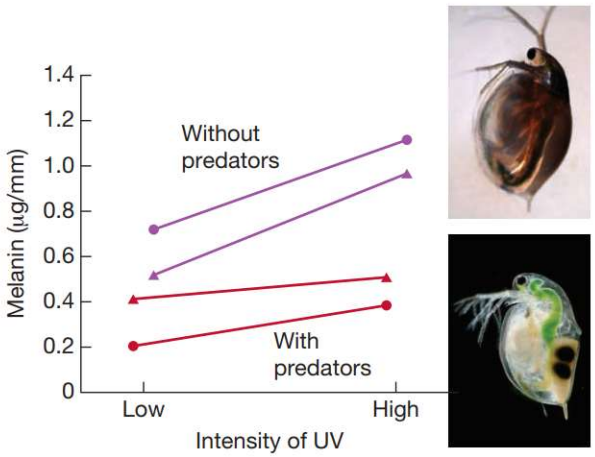

FIGURE 6.25 Reaction norms for pigmentation in the water flea *Daphnia melanica* differ between lakes with and without predators. When water fleas from lakes without predators are exposed to high levels of UV, they develop dark melanic pigmentation that protects their internal organs from the radiation (purple lines). In contrast, water fleas from lakes with predators do not become pigmented under high UV (red lines), which would make them conspicuous and increase the chance that they would be eaten. Phenotypic plasticity in pigmentation is therefore adaptive when predators are absent, while lack of plasticity is adaptive when predators are present. (After [44].)

the decrease in oxygen pressure. Among these changes is an increase in the concentration of red blood cells (RBCs) in the blood. Since RBCs transport oxygen, this change may sound adaptive, but in fact it is not. Increased concentrations of RBCs make the blood more viscous, which slows oxygen delivery and can even trigger medical emergencies. Populations of humans adapted to very high elevation in the Himalayas and Andes have RBC concentrations similar to those of lowland populations. They have adapted to low oxygen pressures by genetic changes to other traits. Increased RBC density is not favored by natural selection at high elevation. In summary, people adapted to living at low elevations show phenotypic plasticity in RBC concentrations when they move to high elevations, but that is a maladaptive response [49].

The Genetic Architecture of Quantitative Traits

We have seen that we can predict the outcome of evolution without knowing anything about the genes that underlie the traits. While that is a tremendous strength of quantitative genetics, there are times when it is important to understand the genetic basis of traits. Questions we would like to answer include: Are the differences among species caused by many or just a few genes? Does the variation in quantitative traits result mainly from genetic variation in the coding or the noncoding regions of the genome? When changing environments generate directional selection, do traits typically respond quickly by evolving with standing genetic variation, or is there a lag until new beneficial mutations occur? When the same phenotypic adaptation evolves independently in different species, are the same or different genes responsible?

Quantitative trait loci

The regions of the genome that affect a quantitative trait are called **quantitative trait loci**, abbreviated as **QTL**. They can range in size from a single nucleotide to a segment of chromosome that contains many genes. Several strategies are used to determine the number, genomic locations, and effects of QTL. Variation in melanism in the peppered moth and sickle cell anemia in humans are caused almost entirely by single loci with alleles that have large effects (see Chapter 4). The inheritance of these traits was discovered by controlled breeding experiments in the moth and by studying inheritance of sickle cell disease in human families. But those research strategies have limitations: without additional data, they do not tell us what the genes are, and they do not work when many genes contribute to the trait.

To make further progress, we use **QTL mapping**. This starts with a genetic map of the species that shows the location of genetically variable markers on chromosomes. Often these markers are single nucleotide polymorphisms, or SNPs. The next step is to genotype a large number of individuals at these markers and measure their values for the trait. Last, the variants that individuals carry at the markers are correlated with the trait phenotype (**FIGURE 6.26**). A significant correlation is evidence that a QTL affecting the trait lies on the chromosome near the genetic marker. (More specifically, a correlation means that the marker and the QTL are in linkage disequilibrium—see Chapter 4.)

The large juicy tomatoes you can see in your local supermarket are very different from their wild ancestors. QTL mapping revealed that alleles at a single QTL change the weight of a tomato by up to 30 percent [18]. To find this QTL, plant geneticists used a *mapping cross* (**FIGURE 6.27**). They hybridized a domesticated

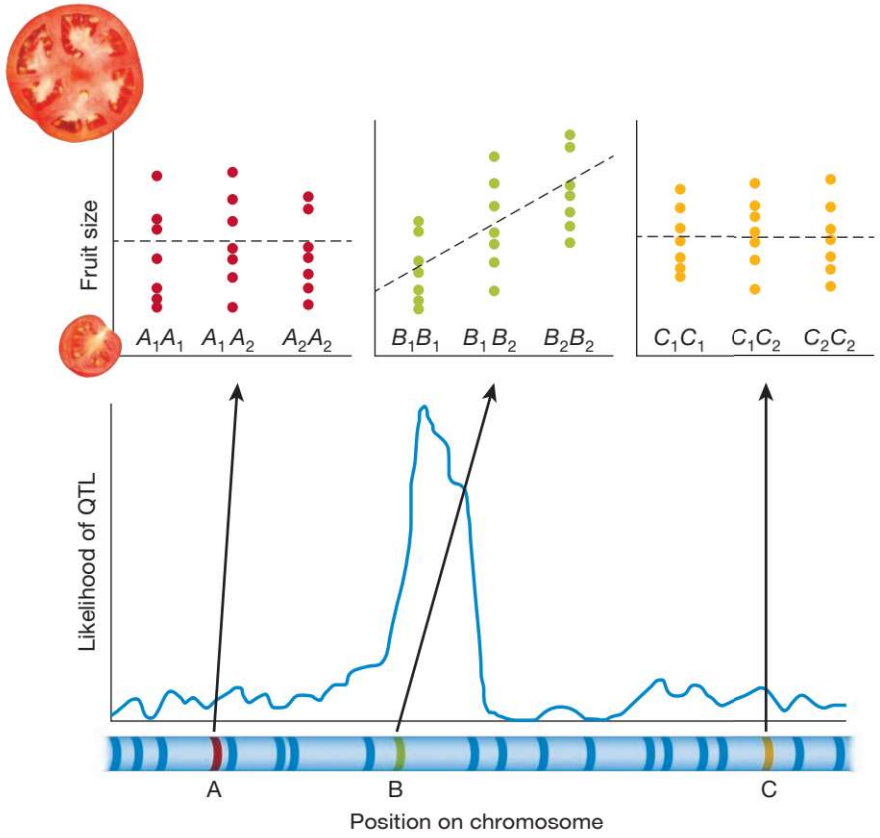

FIGURE 6.26 QTL can be mapped by associating phenotypic variation in a trait with DNA polymorphisms along a chromosome. The positions of genetic markers (for example, SNPs) on a chromosome are shown by the bands on the chromosome at bottom. Individuals are genotyped at each marker, and their phenotypic values are plotted against their genotypes. Examples are shown for three markers. At markers A and C, there is no relation between genotype and phenotype. At marker B, however, individuals with the B_2 allele have a larger phenotype. This suggests that a locus that affects the trait lies near marker B on the chromosome. By combining results across all of the markers, a plot is generated that shows the likelihood of a QTL at each point along the chromosome (blue curve).

tomato with a much smaller wild relative. Several more generations of breeding among the hybrids produced a population whose genomes were a mixture of pieces of chromosomes that came from the two parental species. Correlating marker genotypes with tomato size zeroed in on a region of chromosome 2 with a large effect. Further molecular studies revealed that the locus responsible is a gene called *ORFX* that is expressed early in tomato development. The tomato example shows a basic feature of mapping crosses: they are most powerful when used to find genes that contribute to large differences among populations or species.

There is tremendous interest in finding QTL in humans. Finding genes that affect disease resistance could lead to new therapies, while genes that differ among populations give us insight into how we have adapted to different environments around the planet. Mapping crosses in humans are generally frowned on, so other strategies must be used. One is called a *genome-wide association study*, or *GWAS*. Once again, we look for correlations between the genotypes at genetic markers and phenotypic traits of interest. There are, however, important differences between the GWAS and mapping cross approaches. With GWAS, we are looking for QTL that contribute to genetic variation within a population, while a mapping cross seeks the QTL responsible for differences between populations (or species). Furthermore, because the phenotypic differences are typically smaller

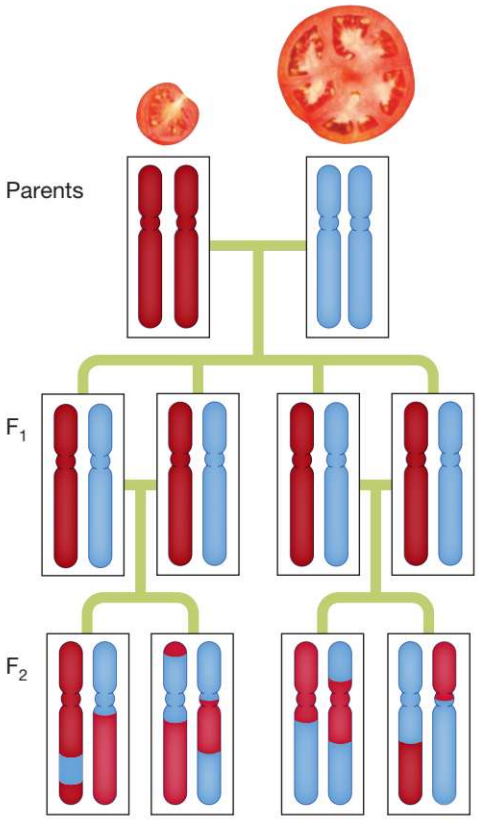

FIGURE 6.27 Mapping crosses are one strategy used to locate QTL. Two parents with very different phenotypes are genotyped at a large number of genetic markers throughout their genomes. The diagram shows a single pair of chromosomes, where red represents the chromosomes that come from the small individual and blue the chromosomes from the large individual. These individuals are crossed to produce an F_1 generation, which is again crossed for one or more additional generations. The offspring from one of these later generations are analyzed by the QTL mapping strategy shown in Figure 6.26.

FIGURE 6.28 QTL involved in adaptive evolution of several traits in humans have been identified by correlating large differences in allele frequencies among populations with distinct phenotypes. (After [51].)

and environmental effects on the phenotype are more difficult to control, much larger sample sizes are needed with GWAS.

Another approach that is used to find human QTL takes advantage of the distinctive traits seen in some populations. The strategy is to scan the genome for loci that have large allele frequency differences among populations with divergent phenotypes. This strategy has discovered QTL that underlie adaptive evolution of traits that include disease resistance, body height, and tolerance to high elevation and cold (**FIGURE 6.28**).

QTL mapping identifies regions of chromosomes that can range in size from a few hundred to many hundreds of thousands of DNA bases. A single QTL often spans several genetic loci. Other research strategies are needed to find which DNA base or bases within a QTL are responsible for the phenotypic variation. The cause is sometimes discovered to be just a single nucleotide. In other cases, several loci or a chromosomal rearrangement are responsible (see Figure 6.23).

The genetics of quantitative traits

One of the most basic questions we can ask about the genetics of quantitative traits is how many loci contribute to their phenotypic variation. The answer is important for several reasons. Population genetics theory tells us that if many loci

contribute, then the trait can evolve further before genetic variation is exhausted as alleles become fixed (see Figure 6.4). The dramatic responses to artificial selection in the growth rate in chickens (see Figure 5.3) and in the oil content of corn (see Figure 6.17) show how far and how fast traits can evolve when many loci are involved.

A second reason to ask about the number of loci is that the answer affects strategies for fighting certain diseases. When one or two genes contribute to a disease, it may be possible to exploit knowledge about what those genes are and how they work. Hemophilia is a hereditary disease in which blood clotting is impaired because of a mutation in one of the genes that produce clotting factors. It can now be treated by introducing a working copy of the defective gene [38]. This type of gene therapy may not be feasible for diseases that involve contributions from dozens or even hundreds of loci, such as diabetes [17], heart disease [37], and schizophrenia [19].

We've seen that the vast majority of quantitative traits are heritable, meaning there is standing genetic variation that selection can act on. What maintains that variation? The answer is not entirely clear, but it must involve a combination of the factors that maintain polymorphism at individual loci. Mutation is likely the most important force. Mutation at QTL introduces alleles that are typically deleterious, leading to a mutation-selection balance (see Chapter 5). Although mutation rates at individual loci are usually very small, a considerable amount of additive genetic variance can be generated when there are many QTL. Experiments with *Drosophila* show that mutation typically increases the phenotypic variance of a trait by 0.1 to 1 percent per generation [35]. An equilibrium level of standing genetic variation is reached when selection removes the same amount of variance. In addition to standing variation, new mutations also contribute to the evolution of quantitative traits in the long term. The remote ancestor of the blue whale, the largest animal that has ever lived, was about the size of a cat. That enormous change in body size must have involved many new mutations that appeared as the whale's ancestor evolved to larger and larger sizes.

The QTL responsible for the standing genetic variation within species may be quite different than those responsible for differences among species [27, 50, 54]. A major reason for this discrepancy is that many mutations that contribute to genetic variation for quantitative traits have deleterious pleiotropic effects. When directional selection acts over long periods, for example to produce an animal the size of a blue whale, only those mutations that are largely free of these negative side effects will survive and become fixed. Thus while many alleles may contribute to standing genetic variation within species, a much smaller number may be important to adaptive evolution and contribute to differences among species.

The kinds of loci that contribute to the variation within species may also differ from those responsible for adaptation. A study of the genetics of flower color found that all of the molecular differences among species in color intensity that have been studied result from mutations in transcription factors, which are a type of regulatory locus. By contrast, transcription factors are in the minority of spontaneous mutations that occur within species [50]. In populations of stickleback fishes that have recently adapted to fresh water, some of the genetic changes are in coding regions, but the large majority (perhaps 80 percent) are regulatory [28].

A final question about the genetic basis of quantitative traits is how often convergent evolution of phenotypes, which occurs when two species independently evolve the same trait, involves changes at the same genes [48]. When very

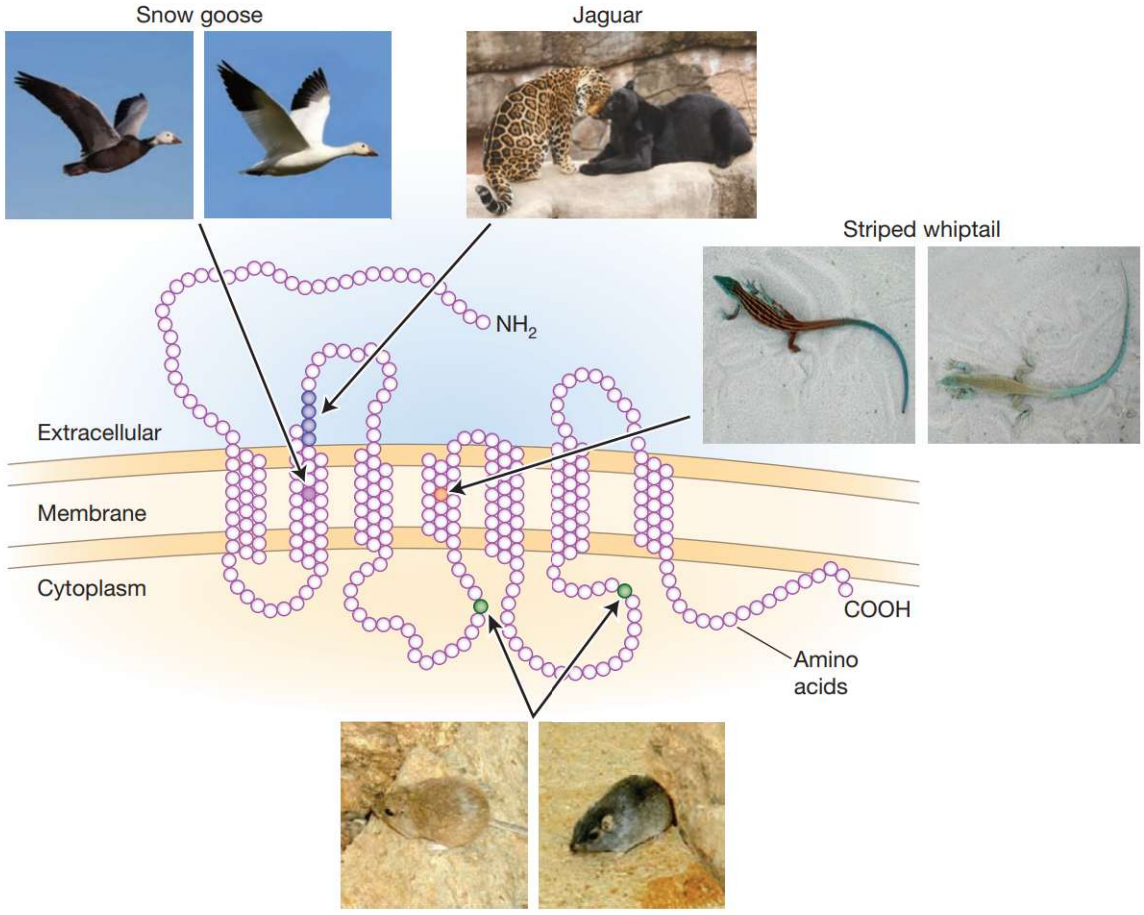

FIGURE 6.29 Diagram of the melanocortinin-1 receptor bound to the cell membrane. The arrows point to positions where selection has changed amino acids to produce new coloration in four species of animals. In these cases, the results are polymorphisms within species (shown in the photos). Many other polymorphisms within species and differences between species have also evolved by changes to the *Mc1r* gene. (After [36].)

different animals independently evolve similar coloration, is that the result of changes at the same or at different genes? Surprisingly, the evolution of darker and lighter colors in many species of mammals, birds, and reptiles is often due to changes at just a single locus, the *melanocortin-1 receptor,* or *Mc1r.* The protein produced by this gene regulates the production of pigments in hair, feathers, and scales. Mutations at several different nucleotides in the *Mc1r* gene have produced dark (melanic) coloration (**FIGURE 6.29**). Here parallel phenotypic evolution results from genetic changes that are parallel at the level of the gene but not at the level of the nucleotides.

SUMMARY

- An individual's phenotype—the set of its visible traits—is determined by a combination of its genotype and environmental factors.
- Variation in quantitative traits can be caused by just a few or by a very large number of loci. When variation results from many genes, the trait can evolve far past its original range of variation by changes in allele frequencies, without contributions from new mutations.
- A fitness function shows the relation between the value of a trait and the average fitness that individuals with that value have. A fitness function can result in selection that is directional (favoring an increase or decrease of a trait's mean), stabilizing (selection against extreme individuals, which decreases variation in the population), or disruptive (selection against intermediate individuals, which increases variation).
- The force of directional selection on a trait is measured by the selection gradient, which is slope of the regression line that relates relative fitness to the trait value. The selection gradient can be used to predict the rate at which a trait will evolve and to test hypotheses about adaptation.
- The rate at which the mean value of a trait will evolve is given by the breeder's equation, and it depends on the amount of genetic variation (measured either by the additive genetic variance or the heritability) and the strength of directional selection.
- Almost all quantitative traits have standing genetic variation and will evolve when selection acts on them. When selection acts on traits that do not have heritable variation, new mutations must arise before the trait will evolve.
- Artificial selection has been essential to civilization. Selective breeding has caused many species of domesticated animals and plants to evolve dramatically new forms, very different from those of their wild ancestors. The results of artificial selection demonstrate that selection can produce very large changes in relatively short periods of time. Natural selection can do the same in natural populations.
- Genetic covariance (or correlation) between traits causes evolutionary side effects: selection on one trait will cause others to evolve. This can result in trade-offs and constraints, in which adaptation in one trait has negative fitness effects on other traits. Genetic correlations result from pleiotropy and linkage disequilibrium.
- Some traits show phenotypic plasticity, the situation in which the phenotype produced by a genotype is altered by the environment that an individual experiences. Plasticity of some traits has evolved adaptively, but in other cases the response to the environment is not adaptive.
- Genetic variation in quantitative traits can be caused by a small or a large number of quantitative trait loci (QTL). These chromosome regions can be localized by QTL mapping, in which variation at genetic markers is correlated with a trait's phenotypic value.
- The number and types of loci that contribute to additive genetic variation within populations may often be quite different than those involved in adaptive differences among species.

TERMS AND CONCEPTS

adaptive landscape
additive genetic variance
artificial selection
breeder's equation
correlational selection
direct response to selection
directional selection
disruptive selection
environmental variance
evolutionary constraint
fitness function
genetic correlation
genetic covariance
genetic line of least resistance
genotype-environment interaction (G×E)
heritability
indirect response to selection
linkage disequilibrium
normal distribution
optimum phenotype
phenotypic plasticity
phenotypic variance
pleiotropy
polygenic trait
QTL (quantitative trait locus or loci)
QTL mapping
quantitative genetics
quantitative trait
reaction norm
selection gradient
stabilizing selection
standing genetic variation
trade-off

SUGGESTIONS FOR FURTHER READING

There are two classic texts on quantitative genetics. *Introduction to Quantitative Genetics* by D. S. Falconer and T. F. C. Mackay (Longman, Essex, 1996) is written from the perspective of animal breeding but gives a wonderfully clear overview of the basic concepts. *Genetic Analysis of Quantitative Traits* by M. Lynch and J. B. Walsh (Sinauer Associates, Sunderland, MA, 1998) is a comprehensive review of genetic and statistical quantitative genetics. Both books are quite technical and (sadly) now a bit dated, particularly regarding the many advances that have been made in identifying QTL. Quantitative genetic variances and covariances can be estimated in natural (as well as domestic) populations; see "Estimating genetic parameters in natural populations using the 'animal model'" by L. E. B. Kruuk (*Philos. Trans. Roy. Soc. Lond. B* 359: 873–890, 2004) for an overview.

A tremendous amount of effort is being devoted to finding QTL that affect a variety of traits in a variety of species. In "Commentary: When does understanding phenotypic evolution require identification of the underlying genes?", M. D. Rausher and L. F. Delph (*Evolution* 69: 1655–1664, 2015) discuss when this approach can give us valuable insights to evolutionary questions. G. A. Wray's "Genomics and the evolution of phenotypic traits" (*Annu. Rev. Ecol. Evol. Systemat.* 44: 51–72, 2013) gives an excellent overview of how rapid advances in genomics are opening new insights to the genetic basis of quantitative traits and how they evolve.

Much of the interest in quantitative genetics among evolutionary biologists was inspired by research done by R. Lande and colleagues beginning in the 1980s. In "Quantitative genetic analysis of multivariate evolution, applied to brain:body size allometry" (*Evolution* 33: 402–416, 1979), Lande developed the multivariate breeder's equation (Equation 6.1). Lande and S. J. Arnold pioneered methods for estimating selection gradients in "The measurement of selection on correlated characters" (*Evolution* 37: 1210–1226, 1983). J. G. Kingsolver and colleagues provide excellent reviews of selection gradients in natural populations in "The strength of phenotypic selection in natural populations" (*Am. Nat.*157: 245–261, 2001) and "Phenotypic selection in natural populations: What limits directional selection?" (*Am. Nat.* 177: 346–357, 2011).

Human height is widely used as a model system for methods used to detect QTL that underlie variation in quantitative traits. See P. M. Visscher's "Sizing up human height variation" (*Nat. Genet.* 40: 489–490, 2008) for a review of this topic.

Artificial selection experiments are used by evolutionary biologists to study the evolution of quantitative traits under controlled conditions. W. G. Hill and A. Caballero review this interesting field in "Artificial selection experiments" (*Annu. Rev. Ecol. Systemat.* 23: 287–310, 1992).

PROBLEMS AND DISCUSSION TOPICS

1. In a study of selection on the leg length of migratory locusts, the mean leg length is 18.6 mm, the selection gradient is $\beta = -0.13$/mm, the phenotypic variance is $P = 1.4$ mm2, and the heritability is $h^2 = 0.37$. What is the expected response to selection in the next generation? What do you predict the average leg length will be in the next generation?
2. In the same population of locusts, the mean wing length is 47 mm, the selection gradient on wing length is $\beta = 0.12$/mm, the phenotypic variance for wing length is $P = 3.6$ mm^2, and the heritability of wing length is $h^2 = 0.27$. In addition, we know that the additive genetic covariance between wing length and leg length is 0.6 mm^2. What is the expected evolutionary change in mean leg length due to selection on wings? What is the expected evolutionary change in mean leg length due to selection on both wings and legs? Repeat these calculations to predict what will happen to wing length as a result of the selection on both wings and legs. What do you predict the average wing and leg lengths will be in the next generation?
3. We told you that Figure 6.8A shows stabilizing selection, while Figure 6.8B shows disruptive selection. If the traits shown in this figure have heritabilities greater than 0, do you predict that the mean in the next generation will be equal to the mean of the data shown? Can selection simultaneously be directional and stabilizing? Directional and disruptive? Stabilizing and disruptive?

4. In some cases, inheritance of a single allele, such as the sex-determining factor, will cause phenotypes to be so different that we can see which individuals carry which allele. List the reasons why this is unusual. Why can't we usually tell at a glance who carries which allele?
5. In Equations 6.1 and 6.2 we wrote the equation for evolutionary change in the mean of a trait ($\Delta \bar{z}$) two different ways. Using the definitions of h^2 and β from the text, investigate the differences between these two equations. Can you write the equation in a form that involves just the quantities P, G, and β? Equations 6.1 and 6.2 seem to suggest that h^2 and G measure inheritance, while β and S measure selection. Given the ways you can rewrite these equations, which of these are the best measures of inheritance and selection?
6. There are many traits for which it seems natural selection should favor an increase every generation, such as survival from birth to reproduction. In most cases, when we look for such increases in natural populations we do not see the predicted change. Make a list of all the reasons we might not see a response to directional selection on such a trait. Include reasons suggested by the material in this chapter, as well as any other reasons you can think of.
7. When the technology for QTL mapping first became available, researchers studying human genetic diseases hoped to discover common alleles that cause increased risk for those diseases. What would be the advantages to studying the causes of diseases that are caused by common, as opposed to rare, alleles? What would be the advantages to treating diseases that are caused by common alleles?
8. The results of QTL mapping studies for human diseases tend to show that disease-causing alleles are either rare or have very small effects on risk. Knowing that this is true, discuss the evolutionary forces that are most likely to be responsible for this state of affairs. Does this observation suggest something about the evolutionary forces that maintain disease risk in human populations?