4

Natural Selection

Charles Darwin had an incomplete understanding of natural selection in the wild. He never found any good examples of the process. His touchstone was instead artificial selection—the type of selection practiced on farms and ranches.

Today we understand the machinery of natural selection quite well, and we have found excellent examples of natural selection in the wild environment. We return to Darwin's original theory of natural selection at the beginning of this chapter. In Darwin's time, the best examples of selection were those of animal and plant breeders, though the type of selection that they practiced was contrived. Much the same is true today, so we will use artificial selection to make the process of selection absolutely transparent. You can think of natural selection as the unforced version of the general process of selection.

Natural selection has two faces, one pointed toward the phenotypes of organisms, one facing their genes. We will consider various types of natural selection, divided according to their effect on the phenotype or their effect on the genetic locus.

Observers of natural selection have studied it in two settings: the laboratory and the wild. Some scientists have strong preferences for one or the other. But it is probably more reasonable to admit that the study of natural selection under both controlled laboratory conditions and actual conditions in nature have jointly helped us to understand natural selection. Indeed, we have too few well-understood examples to neglect either arena of study, the laboratory or the wild. We will look at both. ❖

Darwin and Natural Selection

4.1 Darwin did not expect to observe natural selection

Charles Darwin's *Origin of Species* uses **natural selection** to explain many of the features of organisms. These features are now called adaptations. Adaptations were well known before Darwin ever wrote. Indeed, he learned a great about them from William Paley's theological works. For theologians and many biologists before Darwin, adaptations were instances of God's beneficence, demonstrating a provident creation. Darwin explained adaptation using natural selection, a material process. In Chapter 1 we consider the cultural impact of this change in explanations. Here we consider the scientific issues that arise from Darwin's innovation.

For theologians and many biologists before Darwin, adaptations were instances of God's beneficence, demonstrating a provident creation.

The problem Darwin faced was that he had no direct examples of natural selection. Indeed, he did not expect to have such examples, because he assumed that natural selection would take many generations to act noticeably, with each generation's selection causing undetectable amounts of change. Darwin expected such gradual change because his notion of causation was gradualist, deriving from the geological doctrines of the geologist **Charles Lyell**, as expounded in Lyell's treatise *Principles of Geology.*

Lyell had argued that large-scale geological change was produced by the slow cumulative action of everyday geological processes such as subsidence, erosion, and sedimentation. These processes are hard to detect over a short period of time, but they could nonetheless eventually produce mountains, valleys, and other major geological formations. Likewise, Darwin expected that very small changes in the composition of populations would be wrought by natural selection in each generation. But these changes could nevertheless finally produce animals and plants with very different morphologies and physiological functions.

Thus, Darwin did not expect to "see" natural selection himself. Nor did he expect any other biologist to be able to detect natural selection directly. Therefore, he had an enormous problem in arguing for the importance of natural selection. He could argue that a great many facts of biology could be explained using the two principles of evolution and natural selection. These principles were plausible because of their great explanatory value. But such *explanatory plausibility* is rarely enough to establish a scientific theory.

A major requirement that is usually added to explanatory appeal is *mechanistic plausibility:* Were there demonstrable processes that could generate the process assumed by the theory? In geology, for example, the plausibility of processes like sedimentation and erosion can be established by setting up a laboratory apparatus in which such processes are measurable under controlled conditions. Likewise, experimental science was begun by Galileo using simple experiments with rolling balls on inclines, among his other ingeniously simple demonstrations. Such demonstrations of mechanism are indispensable for experimental science. For Darwin to successfully convince other scientists of evolution by natural selection, he had to produce a similar demonstration of mechanism.

FIGURE 4.1A **The Irish Potato Famine**

The concrete demonstration of natural selection that Darwin used was artificial selection. In **artificial selection**, the breeder plays the role of nature, choosing the attributes that will determine the survival or reproductive success of the stock being bred. Most artificial selection is performed with agricultural species, such as grains, potatoes, tomatoes, chickens, cattle, and pigs. But it is also important in the breeding of less obviously useful domesticated species, such as dogs, pigeons, and sometimes even cats.

No one could dispute that breeders practiced selection. And none could dispute that it was often very successful. The increases in value in breeds of livestock were well established in the nineteenth century, and Darwin pointed them out in Chapter I of the *Origin of Species*. It seems that artificial selection readily supplied the support that Darwin needed for the mechanistic cogency of this theory of natural selection.

However, Darwin encountered some problems with using artificial selection to support his theory of evolution. First, much of the selection that breeders had been practicing was not intentional. For example, breeders often selected for increased docility in their handling of domesticated animals, even when they did not intend to do so. Overly violent livestock, particularly some males, would be destroyed or castrated because they were too much of a nuisance. By eliminating these animals, breeders unconsciously selected for docility, a well-known hallmark of domesticated breeds compared with their wild cousins.

Another problem with breeding by humans is that it has often involved inbreeding of the domesticated species. The negative effect of inbreeding is well known in dog breeds, as we noted in the preceding chapter. But it is also common in varieties of cultivated plants, such as roses. Inbreeding makes plant varieties highly susceptible to infection and other problems. The Irish potato famine was caused by the susceptibility to blight of the variety of potato that was ubiquitous in Ireland (Figure 4.1A). Thus breeding does not necessarily guarantee the best qualities. This fact undermines the analogy to natural selection, which is supposed to improve each species, according to Darwin.

These problems, although of great scientific interest, did not negate the basic point that Darwin wished to draw from the practice of artificial selection. This point was that the directly observable action of selection, as practiced by breeders, could produce material improvement in their stocks and varieties. Darwin's natural selection could then be reduced to the mechanistic processes of artificial selection, except that nature was to supply the careful scrutiny that the human breeder supplied in artificial selection. ❖

4.2 Darwin's original theory of natural selection made nature, through the struggle for existence, the breeder or selector

Reduced to its essence, Darwin's natural selection is just artificial selection, with Nature—almost as a personified agent—replacing the human breeder. Darwin clearly saw artificial and natural selection as two forms of the same thing, as revealed by the second quotation in Figure 4.2A. Notice the phrase "variations useful to man" before the suggestion that there might be "variations useful in some way to each being in the great and complex battle of life."

But the important thing is Darwin's argument, in the first quotation, concerning why nature would act as a selector. The first point is that "more individuals are produced than can possibly survive." In other words, there is a potential reproductive excess. Hence, point two—there must be ecological factors that hold the size of populations in check. These factors define a "struggle for existence," involving competition, predation, and an inimical environment. Life in a state of nature is nasty, brutish, and short, making ecology a stern breeder.

The raw material that natural selection acts on is not, however, always ideal. In the quotation given in Figure 4.2B, Darwin uses a metaphor of stones falling from the side of a cliff to characterize what we would today call hereditary variations. These stones—from which natural selection must build—are not hewn to any functional purpose. They arise by accidents of physical, especially geological, processes. Likewise, the materials that breeders or nature use in the course of selection arise accidentally. Yet the power of natural and artificial selection is such that they can nonetheless use accidental genetic variation to mold attributes that are beneficial, either for the fitness of the organism or for human purposes, respectively. ❖

Darwin begins with the "struggle for existence," which we would now call ecology:

"as more individuals are produced than can possibly survive, there must in every case be a struggle for existence, either one individual with another of the same species, or with the individuals of distinct species, or with the physical conditions of life. It is the doctrine of Malthus applied with manifold force to the whole animal and vegetable kingdoms."

(Origin of Species, Chapter III)

This struggle for existence sets the stage for the action of natural selection:

"Can it, then, be thought improbable, seeing that variations useful to man have undoubtedly occurred that other variation useful in some way to each being in the great and complex battle of life, should occur in the course of many successive generations. If such do occur, can we doubt (remembering that many more individuals are born than can possibly survive) that individuals having any advantage, however slight, over others, would have the best chance of surviving and of procreating their kind? On the other hand, we may feel sure that any variation in the least degree injurious would be rigidly destroyed. This preservation of favorable individual differences and variations, and the destruction of those which are injurious, I have called Natural Selection."

(Origin of Species, Chapter IV)

FIGURE 4.2A Darwin's Version of Natural Selection

Darwin never knew about genetics. He usually referred to hereditary variants as "variations" or "variability." But he had a good intuition for the way natural selection uses hereditary variation during evolution:

"I have spoken of selection as the paramount power, yet its action absolutely depends on what we in our ignorance call spontaneous or accidental variability. Let an architect be compelled to build an edifice with uncut stones, fallen from a precipice. The shape of each fragment may be called accidental; yet the shape of each has been determined by the force of gravity, the nature of the rock, and the slope of the precipice—events and circumstances, all of which depend on natural laws; but there is no relation between these laws and the purpose for which each fragment is used by the builder. In the same manner the variations of each creature are determined by fixed and immutable laws; but these bear no relation to the living structure which is slowly built up through the power of selection, whether this be natural or artificial selection."

(The Variation of Animals and Plants Under Domestication, p. 236 of the 1896 edition)

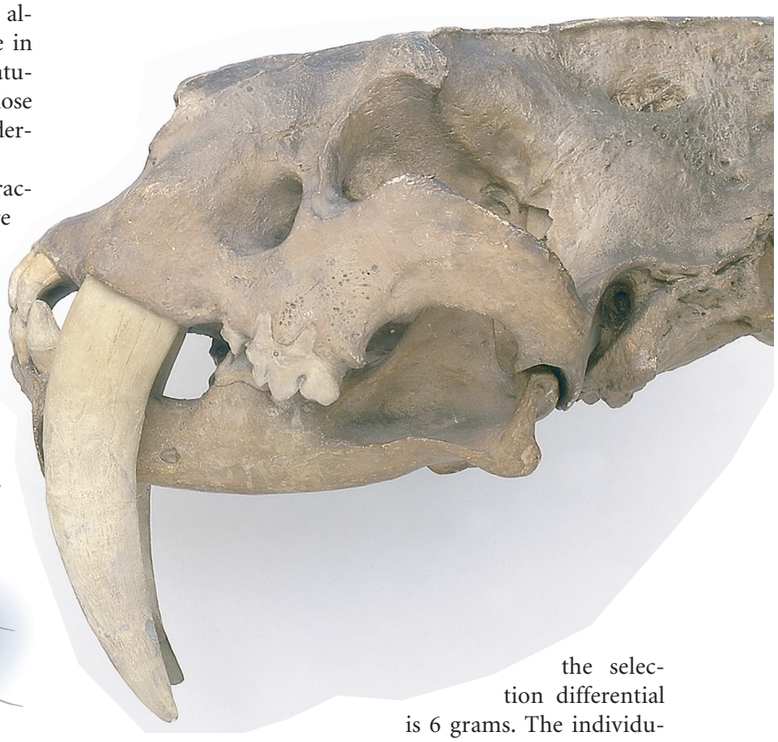
FIGURE 4.2B How Darwin's Natural Selection Uses Variation

4.3 The workings of selection are evident in the procedures of artificial selection

Natural selection is often difficult to detect in nature, although we will examine examples where it is detectable in Modules 4.22–25. It is even difficult to understand how natural selection might be working in nature. Therefore, a close look at artificial selection is a better starting place for understanding selection.

With artificial selection, we know explicitly the character(s) that are undergoing selection. For example, in Figure 4.3A we are selecting for body weight in mice. Once we identify the selected group (individuals that display the character being selected, in this case greater body weight), the rest of the population can be used for some other purpose.

With artificial selection, we can determine the quantitative magnitude of selection: It is the deviation of the selected group from the population as a whole, known as the **selection differential *(S)*.** In Figure 4.3A, the selection differential is 6 grams. The individuals in the selected group are mated to each other, and their offspring are reared. The average difference between the offspring of the selected group and the rest of the breeding population is the **response to selection *(R)*.** In Figure 4.3A, the response to selection is 2 grams.



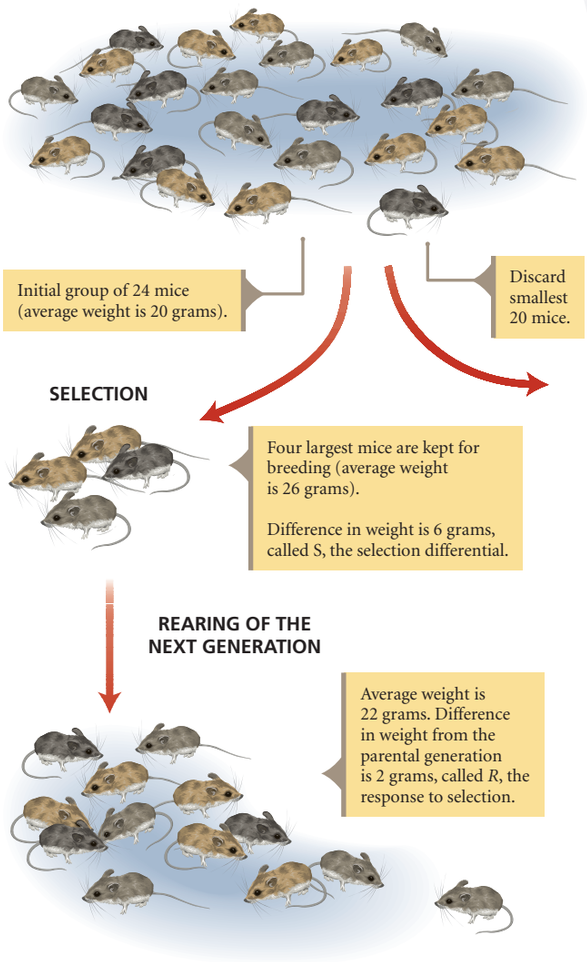


FIGURE 4.3A Artificial Selection on Mouse Body Weight

The only feature of this process that is not mere bookkeeping is that the offspring resemble the selected parents. This, of course, depends on heredity. To predict the response to artificial selection in quantitative terms, the only genetic parameter that we need is the **heritability** (h^2), defined in Chapter 3. The product of heritability and the selection differential gives the predicted response to selection. This formula is displayed in the accompanying box. Because heritability gives the predicted resemblance of offspring as a function of the average character value of the parents, this formula makes intuitive sense. ❖

Quantitative Genetics Predicts the Response to Artificial Selection

The response to artificial selection can be predicted from the heritability of a character (h^2):

$$R = h^2S$$

In words, this equation says

(response to selection) is equal to
(heritability) times (selection differential).

4.4 Multiple generations of artificial selection can change a character substantially

As Darwin suspected would be true of natural selection, artificial selection over multiple generations leads to progressively greater deviation of selected characters. The gains from selection in just one generation of artificial selection are usually measurable, but they are not often very great. When artificial selection is applied generation after generation, we gain a quantitative picture of the power of selection in general—including natural selection, when it is strong and sustained.

There are two basic ways to keep track of the response to artificial selection. First, in Figure 4.4A, we see a common type of graphical plotting of selection data. The average phenotype of the selected line is shown for each generation. The qualitative expectation is that more generations of selection will give a greater response to selection. However, there is no simple way to predict what the selection response will be, generation by generation.

To make a quantitative prediction over multiple generations of selection, we must plot (on the y-axis) the **cumulative selection response** (ΣR), measured as deviations of the offspring of selected organisms from the average of the total population in each generation, summed over the generations of selection that have occurred. The x-axis must show the **cumulative selection differential** (ΣS), measured as the sum of the deviations of the selected parents from the average of the total population in each generation. The cumulative selection differential accumulates over all generations, just as the mileage of your car accumulates over all the days you drive it. Figure 4.4B shows this kind of plot for selection on mouse body weight.

The predicted response to selection is then given by the sum of selection differentials times the heritability, a quantity that is the analog of the one-generation calculation. This is shown in the accompanying box, "Estimating Heritability from the Response to Artificial Selection."

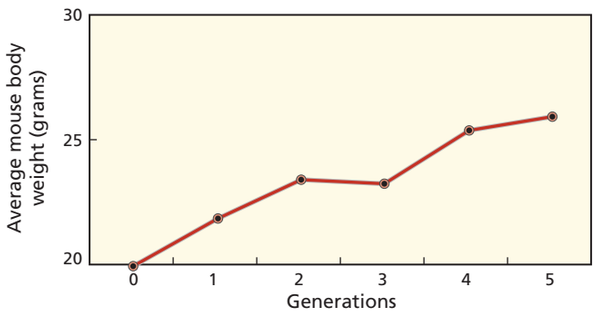


FIGURE 4.4A Response to Selection on Mouse Body Weight Response to selection per generation.

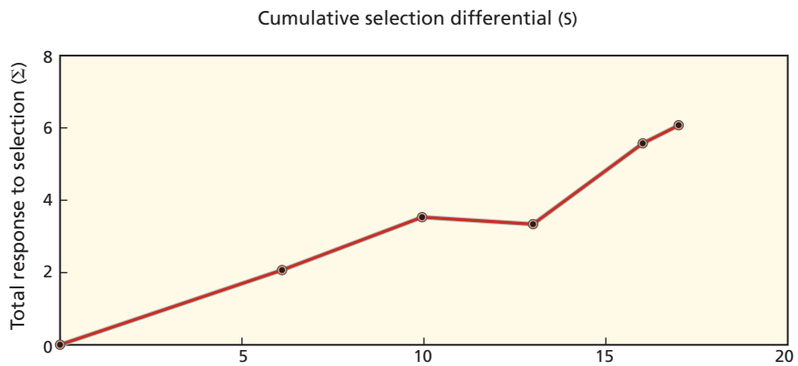


FIGURE 4.4B Response to Selection on Mouse Body Weight Cumulative response to selection versus cumulative selection differential. (Both variables are plotted in grams of increased weight relative to the weight of the initial population of mice before selection.)

Estimating Heritability from the Response to Artificial Selection

We can reverse the equation for the heritability of a quantitative character. If ΣR is the total cumulative response to artificial selection and ΣS is the total of the selection differentials added together

$$h^2 = \Sigma R / \Sigma S$$

The Cycle of Natural Selection

4.5 Natural selection will sometimes have more impact than artificial selection, sometimes less

With the example of artificial selection to guide us, we can think about natural selection with greater focus. Think of the life cycle of a mouse population as if all the young mice grow up together, become older mice, undergo selection together, reproduce, and then die. This is not usually true of the mice of North America, but it is true of the "marsupial mice" of Australia discussed further in Chapter 7. In any event, the simpler pattern is easier to visualize.

Natural selection within the life cycle is like artificial selection in many respects. As in the artificial selection example, the mice will be selected for particular attributes, possibly size. Larger mice might survive cold temperatures better, for example. Larger mice would then be more likely to survive to reproduce, and the offspring of the next generation should grow up to be larger, following the cycle shown in Figure 4.5A.

But there are also differences between natural and artificial selection. The most important of these is that natural selection normally acts on many organisms, perhaps millions or billions in a particular locale. Populations of insects and grasses and bacteria, among other organisms, can reach very high numbers—well into the trillions. In contrast, breeders practicing artificial selection rarely work with more than thousands of organisms. Often they are limited to a few hundred organisms, especially a small number of males.

Because breeders work with small populations, artificial selection is often slowed down, or stopped, by worsening inbreeding depression. Especially with large mammals, such as cattle and sheep, inbreeding is likely to be a problem. Dogs, as we have seen in Chapter 3, are highly inbred, causing numerous veterinary problems.

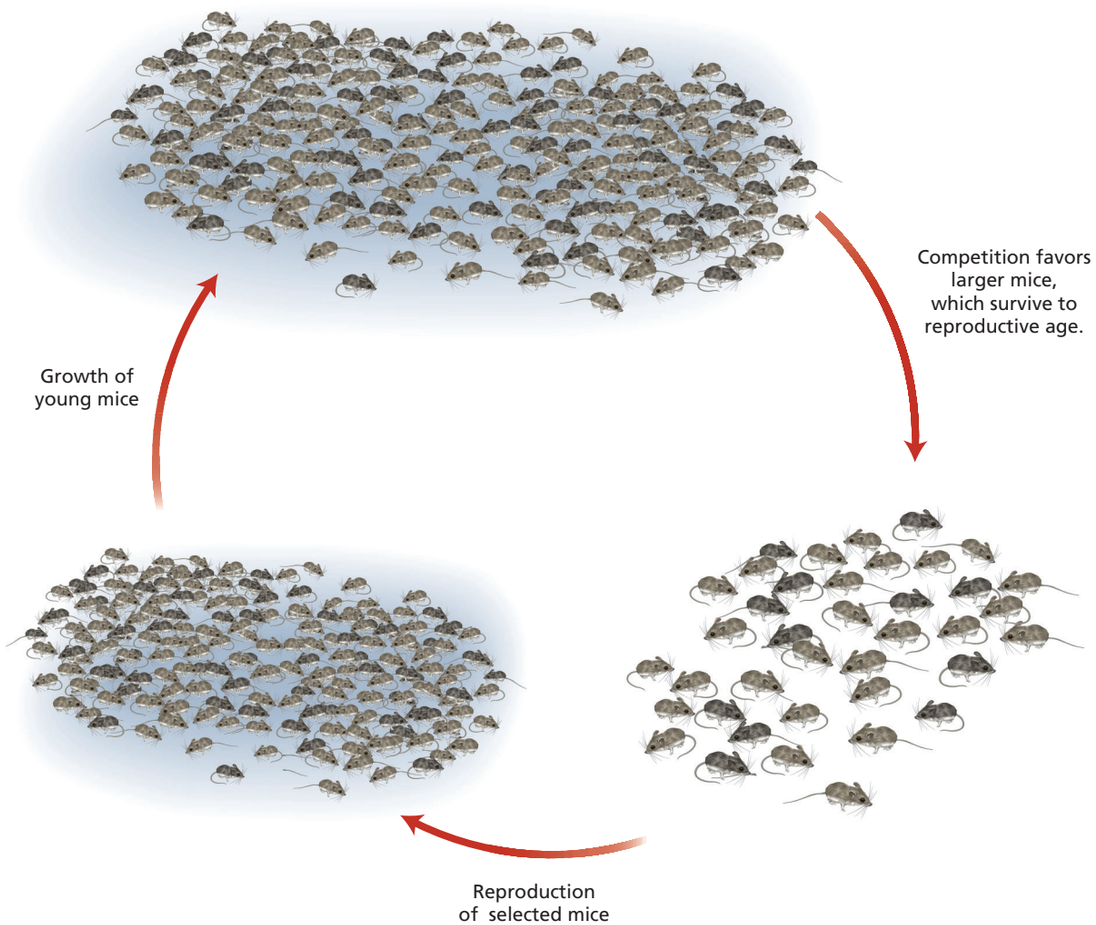


FIGURE 4.5A The Cycle of Natural Selection

Related to the problem of inbreeding depression, but distinct from it, is the problem of exhaustion of genetic variation. When artificial selection is sustained for a long period of time, heritability may fall due to a loss of genetic variation. Under these conditions, the progress of selection stops. There will not be enough heritability for the population to respond to selection.

Because natural selection is often free of problems of small population size, it sometimes continues to act over thousands or millions of years. In this respect, natural selection should ultimately prove more powerful than artificial selection.

A problem impeding the action of natural selection is that it is unlikely to be consistent in its action. For example, suppose that Australian mice are selected for larger body size because of intermittent frosts. But Australia is generally a fairly warm place, so some years may be largely free of frost. In such years, there will be no selection for increased size resulting from frost. Natural selection for larger body size will be on vacation in those years. In these circumstances, environmental fluctuation dilutes natural selection.

An additional complication arises from the multitudinous sources of mortality that organisms face in nature. It may happen that a large mouse made it through the winter frosts because of its large size, but it was eaten by a snake in the spring. Or perhaps it was picked off by a hawk. Or it could have succumbed to a gastrointestinal infection. Even in an environment that is constant on the whole, many factors are contributing to variation in survival or fertility. The action of this range of factors in the "struggle for existence" will dilute selection arising from any one of them. We consider this issue further in Module 4.9.

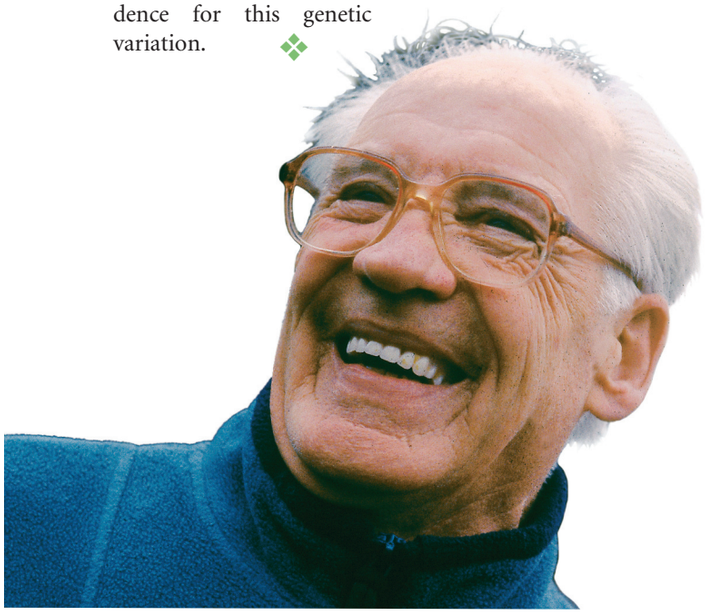
For all these reasons, natural selection is usually not as focused as artificial selection; and this relative lack of focus will leave it weaker. The rate of progress in response to natural selection should therefore be considerably slower than that normally achieved by artificial selection. However, as we will show in Module 4.22–25, even natural selection can sometimes act with great speed and power.

In the meantime, we will break down some of the elements in the cycle of natural selection, particularly with a view to defining the factors that establish natural selection and delineating the consequences of natural selection at different points in its cycle. ❖

4.6 Natural selection requires genetic variation for characters related to fitness

For the cycle of natural selection to start, a basic requirement is genetic variation that affects characters related to fitness. It is not enough just to have genetic variation. DNA sequences can differ in their sequence of nucleotides, but this difference may have no effect on the phenotype of the organism. Even a genetic difference in phenotype may have no selective importance. The specific patterns of human fingerprints, for example, probably have no importance for natural selection. Finally, **phenotypic variation** for fitness-related characters will not necessarily have any importance for natural selection if that variation is due to the environment rather than genes; in other words, if $V_P = V_E$.

For example, Figure 4.6A contrasts the consequences for selection on body weight of the presence or absence of genetic variation for the character. In part (i), the variability for body weight in mice is entirely environmental. Different levels of nutrition might have produced this variation in body size, for example. There is no genetic variation, and there is no genetic difference in the mice before and after selection. In part (ii), there is genetic variation for body weight. In this case, the selected mice are genetically different from the original group of mice. One of the big questions about natural selection is how often fitness-related characters have significant amounts of genetic variation (V_G), particularly selectable genetic variation (V_A). It turns out that it is surprisingly common for components of fitness—such as female fertility, male mating success, development time, and longevity—to have significant amounts of selectable genetic variation. Characters that are related to fitness but are not components of it—such as stress resistance and endurance—show even more selectable genetic variation. The box, "Is there Genetic Variation for Characters Related to Fitness?" discusses the evidence for this genetic variation. ❖



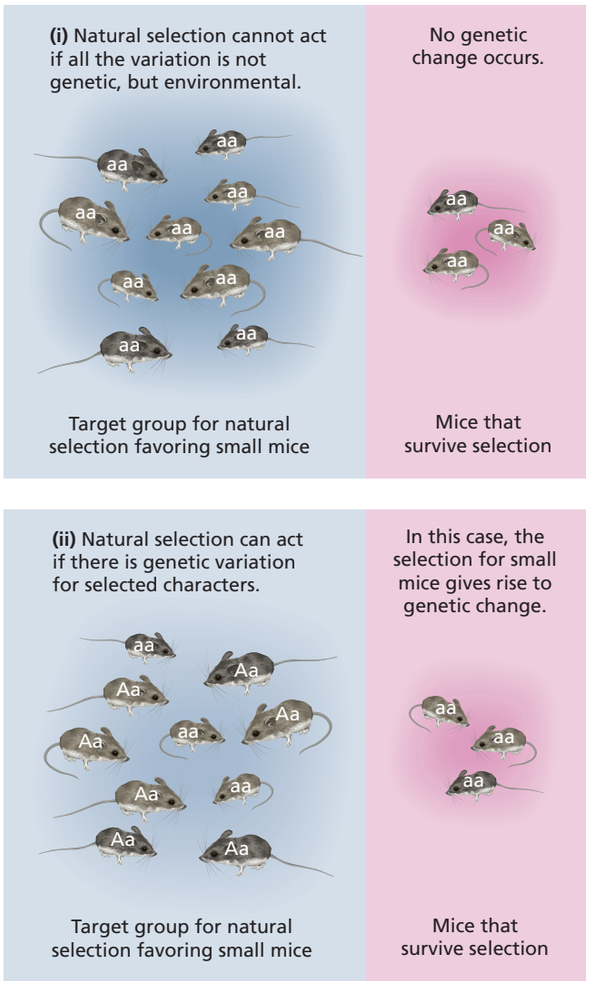


FIGURE 4.6A Natural selection requires genetic variation.

Is There Genetic Variation for Characters Related to Fitness?

Recall our discussion of the inheritance of quantitative characters in Chapter 3. We pointed out that there was more genetic variation for morphological characters than there was for fitness-related characters.

But is there enough genetic variation for selection to act on characters related to fitness?

The answer is yes. There are two lines of evidence. The first is that studies of genetic variation themselves reveal significant heritabilities for such characters as viability and fertility. The second line of evidence is that it is possible to apply artificial selection on fitness-related characters, like fecundity or longevity, and obtain a detectable response.

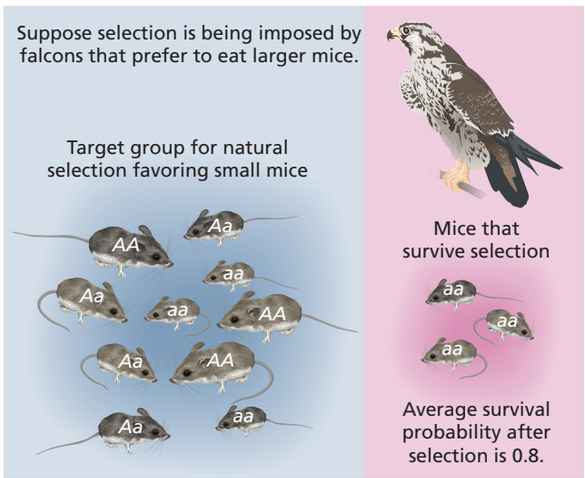
Natural selection changes the patterns of survival and reproduction of organisms undergoing selection 4.7

If there is selectable genetic variation on which natural selection can act, it will act to change the components of fitness. Figure 4.7A presents an example involving survival probabilities related to different sizes of mice.

In the absence of genetic variation, differential mortalities and fitnesses may also produce a temporary change in fitness characters. But note that the assertion here is that *if* there is selectable variation, there will be change in fitness (not *only if* there is such selectable variation). Naturally selected organisms will have detectable superiority in their fitness, and these organisms can be discriminated *if* there is selectable genetic variation (but not *only if*).

An intriguing question about natural selection is how precisely it discriminates between individuals of different phenotypes. When Darwin wrote about natural selection, he used phrases like "careful scrutiny" and "rigidly destroyed" to convey his sense of Nature as a personified breeder of infinite power and patience. There is now some controversy about this idea among biologists, as highlighted in the box, "How Powerful Is Natural Selection?"

Some biologists tend to follow Darwin, assuming that natural selection is sensitive to very slight differences between phenotypes. Others emphasize the chanciness of natural selection. In particular, a common theme in modern evolutionary biology involves the limitations to the power of natural selection. We will take up this theme repeatedly. ❖



This group of mice of different sizes has a range of survival probabilities that go with their different sizes as follows:

AA — average size 30 grams; average survival probability is 0.0 due to falcons and other risks

Aa — average size 24 grams; average survival probability is 0.1 due to falcons and other risks

aa — average size 18 grams; average survival probability is 0.8 due to falcons and other risks

Average survival probability of this group is 0.25.

FIGURE 4.7A Natural selection changes probabilities of survival or reproduction.

How Powerful Is Natural Selection?

This question can be rephrased as, "How much of a difference in probabilities of survival or their reproductive output is there likely to be between individuals having different phenotypic characteristics?"

The best answers to this question come from studies of natural selection in the wild, which we will discuss later in this chapter. But recent research with birds and with human medical disorders does indicate large differences in survival rates between birds with different beak sizes and between humans with genetically different enzymes.

4.8 With selectable genetic variation, natural selection changes the gene frequencies and phenotypes of the next generation

To complete a cycle of natural selection, the offspring of the selected parents must be changed, as shown in Figure 4.8A. This will not happen if the selected parents are not genetically different from the rest of the population. But there is still the question of whether or not genetically different parents will have genetically, and thus phenotypically, different offspring.

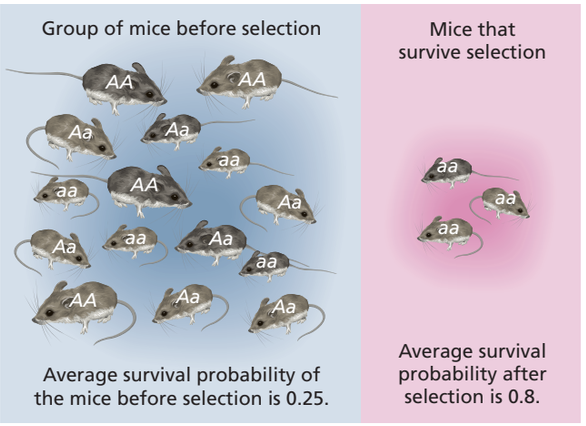
The question is essentially answered by quantitative genetics, as described in Chapter 3. The key concept is the heritability (h^2). Given a distinct group of selected individuals, with artificial or natural selection, the offspring will be different according to the equation for the response to selection: $R = h^2S$. (Recall what this equation says, in words: The response to selection is equal to the heritability times the selection differential.) In this respect, there is no difference between artificial and natural selection. In both cases, quantitative genetics predicts a response to selection under the same conditions of (1) a significant selection differential (S) and (2) significant heritability (h^2).

Once again, the quantitative values of selection differential and heritability are the key issues for natural selection. If natural selection can carve out a selection differential for a character, and there is heritability for that character, then there will be a response to natural selection. The accompanying box summarizes this idea. ❖

How Much Will the Offspring of Selected Parents Resemble the Parents?

One of the most common points of confusion about natural selection is the extent to which the selected offspring will resemble their parents.

It turns out that we have already solved this problem. The heritability of the selected character(s) tells us the extent to which the offspring will deviate from the mean. Using the heritability concept explained in Chapter 3 and the artificial selection arithmetic of Module 4.3, we can expect the response to natural selection to approximate the heritability times the difference between the selected group and the entire population, before selection.



The frequency of *A* and *a* alleles is 0.5, which will not change much in the absence of selection. So their offspring would have had average survival probabilities of 0.25 as well.

Selection has fixed the little *a* allele, so all the offspring of the selected parents will have an average survival probability of 0.8, much greater than 0.25.

FIGURE 4.8A Selected parents have offspring that are different from the offspring that the population would have had without selection.

Phenotypic Patterns of Natural Selection

4.9 Natural selection acts powerfully on just a few characters at a time

Although the cycle of natural selection is an integrated process, it has two very different faces. One is pointed at the gene, and the ways in which different patterns of inheritance determine the outcome of selection. We will take up this topic later in this chapter. The other face is pointed at the phenotype of the organism—its external characteristics (Figure 4.9A). This phenotypic selection is the focus of the present portion of Chapter 4.

It is a common error to suppose that natural selection precisely targets the ideal phenotype for each species, and then "rigidly destroys" any deviations from this ideal. This strict discrimination among organisms is not usually the case. In reality, there is a great deal of sheer chance in life and death. Organisms that natural selection favors might die for completely accidental reasons. They might be trampled by large animals. They might die of desiccation in a freak drought. For these reasons, it is important to understand that natural selection is *not* some kind of perfect winnowing process in which only the best-adapted reproduce and all others are eliminated.

When natural selection acts effectively, it is likely to do only a few things with any intensity. Only strong selection can dominate over accidents in shaping a population. When selection is weak or variable in direction, it cannot act effectively. An additional factor limits the capacity of natural selection to reshape a population—the number of reproductive deaths the population can sustain and still maintain itself. If multiple selection processes act on several characters at the same time, then too few organisms may survive to reproduce. For example, as Figure 4.9B shows, a shrub might be selected for (1) resistance to drought, (2) growth under conditions of poor nutrients, and (3) mechanical damage from large animals trampling the plant. Suppose that the first factor kills 80 percent of the shrubs, the second kills 70 percent of the re-

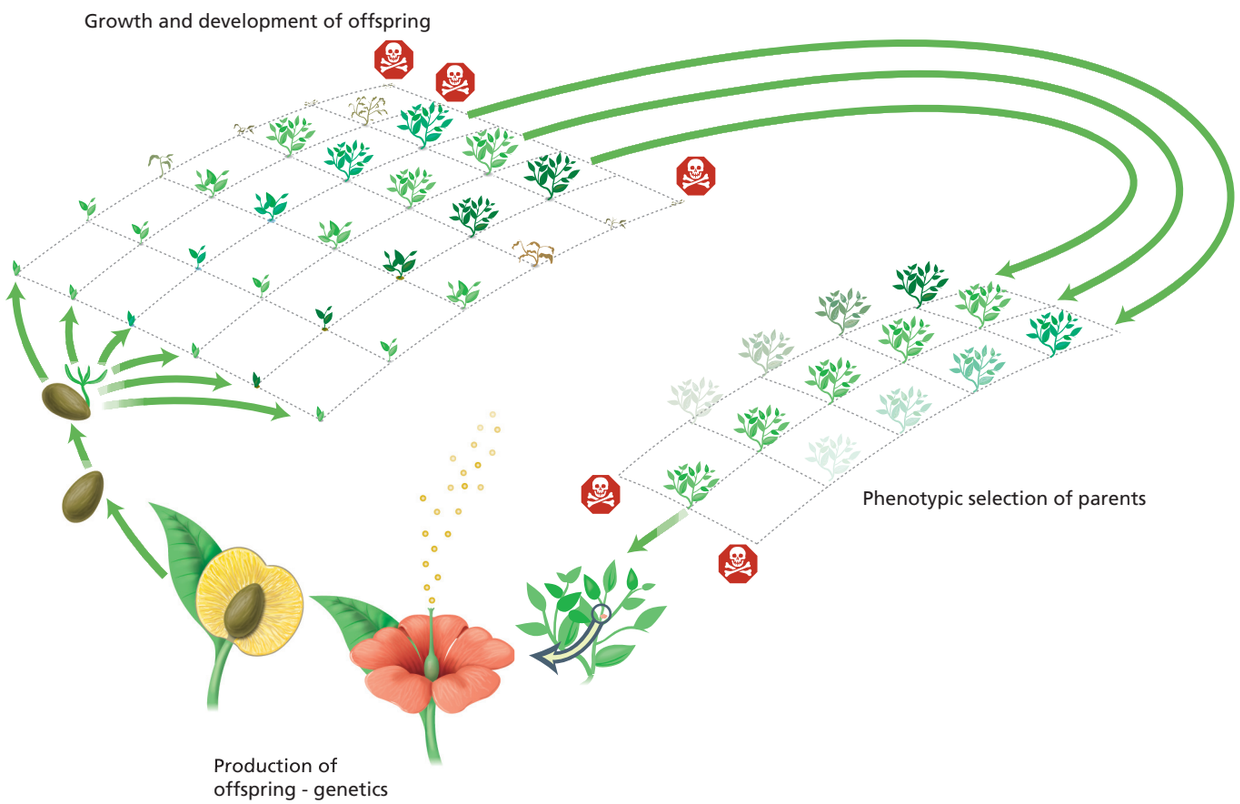


FIGURE 4.9A Phenotypic and Genotypic Facets of Natural Selection

mainder, and the third kills 40 percent of the shrubs surviving the first two selective factors. With these assumptions, only 3.6 percent of the population survives selection. For the population to maintain itself, each shrub would have to produce almost 30 offspring that survive to adulthood. If these plants reproduce less than that, the population will die out.

On the other hand, the population might be able to maintain itself if it is subject to just one of these selective pressures. Then the population size would be reduced to 20–60 percent of its level without selection. Darwin's "reproductive excess," a concept he took over from Malthus, might be enough to sustain the population during selection.

A further limitation on natural selection, as opposed to artificial selection, is that the focus of selection is likely to change from time to time, as shown in Figure 4.9C. Some of this change will occur within the life of a single organism; some of it will change only from generation to generation. In the latter case, the entire direction of natural selection may change from generation to generation. Both of these possibilities will weaken the power of selective mechanisms.

In the following modules, we consider three different phenotypic patterns of natural selection: directional selection, stabilizing selection, and disruptive selection. ❖

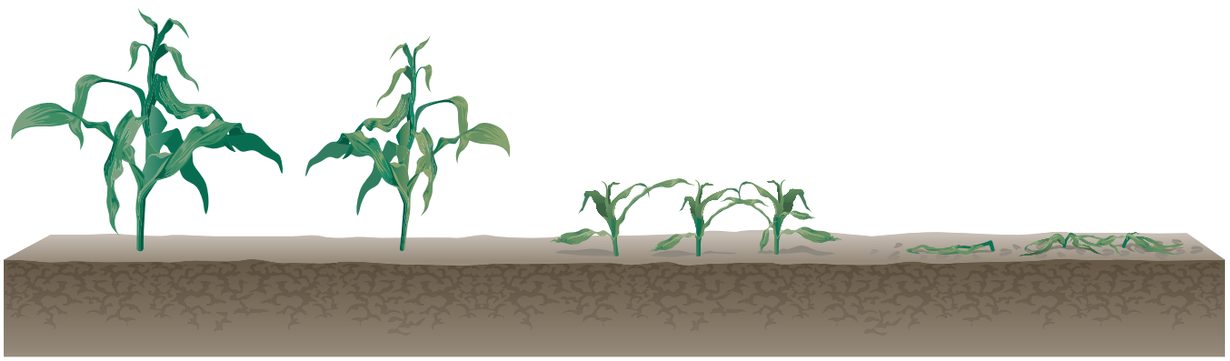


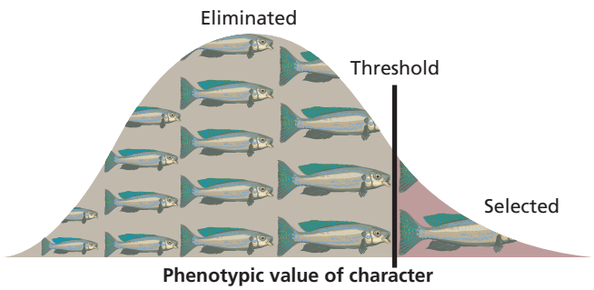
FIGURE 4.9B **Multiple Processes of Natural Selection**

FIGURE 4.9C **Variable Natural Selection**

4.10 Directional selection favors organisms with phenotypes that are at one extreme relative to the average phenotype

Directional selection is the type of selection that the phrase "natural selection" calls to mind. In directional selection, only the biggest, the fastest, or the smallest are able to survive and reproduce. **Directional selection** favors a particular phenotypic extreme, which most of the population does not attain. Selection for the phenotypic extreme results in strong selection against most members of the population. The result is the progressive movement of the population toward the extreme favored by natural selection.

Figure 4.10A diagrams a simple form of directional selection—the distribution of a particular character, represented by values on the horizontal axis. The peak shows the most common character values. The mean of the population will be near this peak. In this case, selection strongly favors individuals that have a high value of the character. Indeed, there is an absolute threshold, indicated by the vertical bar, for successful reproduction. Individuals with phenotypic values below this bar do not reproduce at all. This type of stringent selection is expected to increase the average value of the character, assuming that the character has significant heritability.



- With directional selection, the individuals with the most extreme phenotypes survive the selection process.
- The selected phenotypes do not necessarily belong to those individuals that will have correspondingly extreme offspring.
- Phenotypic selection is only about phenotypes, not underlying genotypes, or anything else.

FIGURE 4.10A Directional Selection

How often does natural selection take the form of directional selection? This is an open question for most phenotypic characters. Will natural selection always favor the larger organisms, the organisms that best resist cold, and so on? Isn't natural selection more likely to favor a compromise between high and low values for most characters? (This possibility is considered next.)

But there is one character for which natural selection will be consistently directional. That character is **fitness**. Natural selection always favors phenotypes that have higher Darwinian fitness. Therefore, there is at least one character for which directional selection will always be the pattern of selection. (Later in the chapter, we give additional examples of directional selection in the wild.) ❖

4.11 Stabilizing selection favors organisms that have intermediate characteristics

If directional selection is the type of selection that we can readily associate with Darwin's concept of progressive natural selection, then *stabilizing selection* can be associated with **Aristotle's** original model of selection. Aristotle was interested in the stability of species, in why they retained their typical anatomy and physiology. His explanation, more than two thousand years ago, was that deviant individuals would be less successful in life. They would be less likely to survive or to reproduce. Thus selection would act to stabilize the species, eliminating "monsters." In modern quantitative terms, this sort of stabilizing selection can be represented as in Figure 4.11A. **Stabilizing selection** eliminates individuals at the extremes of the distribution of a quantitative character, favoring those with intermediate phenotypes.

Aristotle was interested in the stability of species, in why they retained their typical anatomy and physiology.

Note that stabilizing selection is unlikely to change the average value of a character much. Instead, its main effect is on the variance of the population. In each generation, the reproducing parents will have a *lower* variance for the selected phenotype, compared to the variance that might have existed in the absence of stabilizing selection. This type of **phenotypic selection** can be thought of as conservative. As Aristotle supposed, it is likely to help conserve species attributes.

Several examples of stabilizing selection are known to biologists. One for which we have excellent data is stabilizing selection on the weight of human newborns, shown in Figure 4.11B. However, there is evidence of stabilizing selection for many other characters—particularly morphological characters, such as total body weight and the size of body parts in both animals and plants—from bone lengths to gall size. ❖

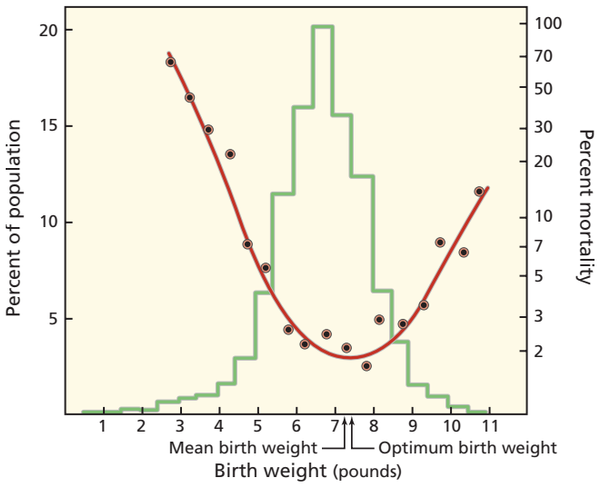
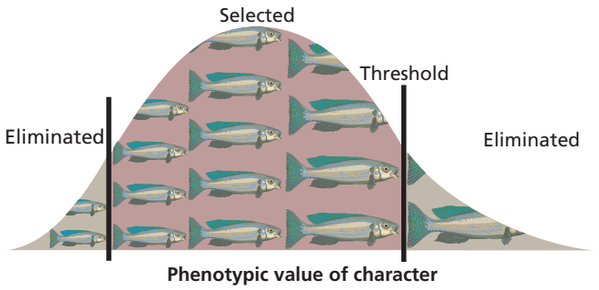


FIGURE 4.11B Mortality and Birth Weight The average human birth weight is about 7 pounds. The mortality rate is much higher among very small and very large babies than among babies of average size. The best birth weight is close to the population average. Data from Cavalli-Sforza and Bodmer (1971) and reference therein.



- With stabilizing selection, the individuals that have the most extreme phenotypes are eliminated by natural selection.
- The immediate phenotypic effect of stabilizing selection is to reduce the ***variance*** of the selected group compated to the population's distribution before selection.
- This type of selection may not change the mean of the phenotypic distribution very much.

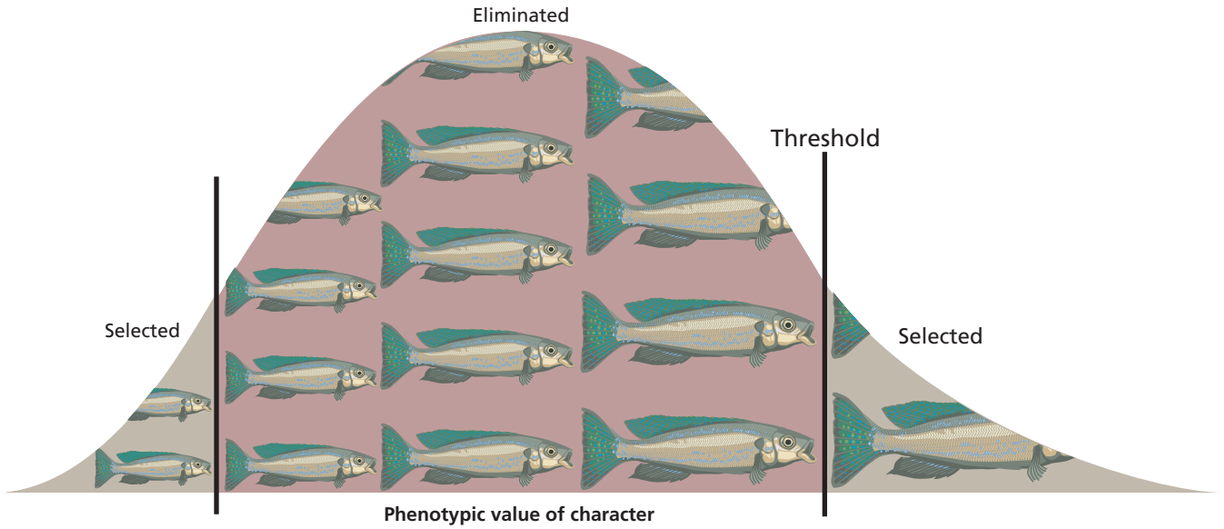
FIGURE 4.11A Stabilizing Selection

4.12 Disruptive selection favors organisms that have character values at both extremes of the phenotypic distribution

Natural selection can do things that are very difficult to conceive intuitively, at least at first. Logically, if natural selection can select *against* organisms at either end of a distribution of phenotypes, then it is conceivable that natural selection might select *for* organisms at the extremes of the distribution. This pattern would be the opposite of stabilizing selection, with its conservative pattern. For this reason, selection against the middle of a distribution is called **disruptive selection**. Figure 4.12A shows this pattern.

How could disruptive selection ever arise? One general context in which it might arise would be if a predator or a herbivore preferentially fed on the most common type of food. Consider plant evolution. Assume that the plants that produce medium-sized seeds are the most abundant, and therefore their seed is preferred by seed-eating birds. Under these conditions, plants that gave smaller or larger seeds might have a selective advantage. Figure 4.12B gives an actual example of disruptive selection involving bill size in a seed-eating bird. However, examples of disruptive selection are not common.

Like stabilizing selection, disruptive selection changes the variance of the population. The difference is that disruptive selection is likely to *increase* the variance. In addition, disruptive selection can change the phenotypic distribution, favoring two-peaked, or **bimodal**, phenotypic distributions. The example in Figure 4.12B is a case in which such bimodality has evolved.



- Disruptive selection is the precise opposite of stabilizing selection: Selection eliminates the individuals from the middle of the phenotypic distribution, keeping only the individuals from the extremes.
- A key feature of this type of selection is that it produces a bimodal distribution of selected individuals, unlike the unimodal distributions produced by directional and stabilizing selection.

FIGURE 4.12A Disruptive Selection

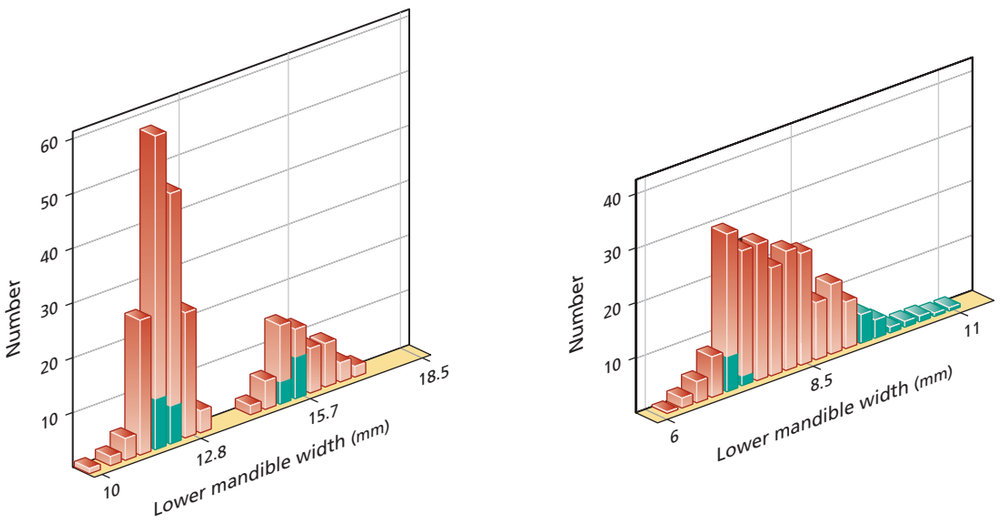


FIGURE 4.12B Disruptive Selection on Bill Size in the Black-Bellied Seedcracker (*Pyrenestes o. ostrinus*) The red portion of each bar represents juveniles that did not survive to adulthood; the green portion represents juveniles that did survive. The survivors were those individuals with bills that were either relatively large or relatively small. Data from Bates Smith (1993).

Genetic Mechanisms of Natural Selection

4.13 Genetics complicates the action of natural selection

The basic principles of selection are the same in all living things. But the specific effects of selection are much more complicated in organisms that have sex, because the genetic engine that sex introduces into the evolutionary machinery makes inheritance tricky. For this reason, let's first look at organisms that do without the complications of sex.

Without sex, mothers have daughters that are genetically identical to themselves. The daughters are **clones** of the mother. The main complication to this *clonal* pattern of reproduction is **mutation**, which occurs when specific DNA sequences that determine the phenotype are chemically changed or miscopied, producing a daughter with a different gene, or genes. For most genes, mutation occurs at a rate of once every 10^5 to 10^8 acts of reproduction. On the other hand, there are at least a thousand genes in even the simplest organisms, so that the rate of mutation over all the genes of an organism might be 10 to 10^{-4} mutations for each act of reproduction. This can create many mutations in microbial populations that might contain billions or trillions of individuals, which is good from an evolutionary point of view because natural selection needs varied genotypes that confer varied biological abilities to survive and reproduce.

Put another way, natural selection exploits genetic variance to increase fitness. (More on this later.) In **clonal selection**, mutation supplies that genetic variance. The mutations that are big genetic improvements will be found and fixed by natural selection.

Purifying selection may be the easiest form of natural selection to understand, perhaps because it is like correcting bad grammar, discarding defective products, or choosing a date. We sort, evaluate, and eliminate. The idea that a similar process goes on in nature appeals to the human mind.

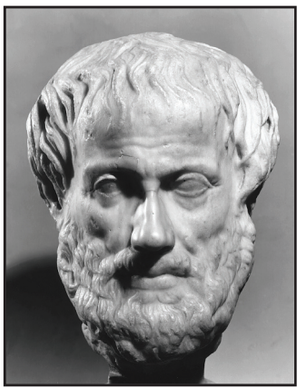


FIGURE 4.13A Aristotle, the Founder of Biology

The idea of natural selection is much older than Darwin. Aristotle (Figure 4.13A) used the idea of selection to explain the preservation of the typical form of each species. He argued that when highly deviant offspring are born, they will be defective in survival and reproduction. Such deficiencies will then prevent the appearance of monstrosities in subsequent generations. (Some fanciful monsters are shown in Figure 4.13B.) In this way, Aristotle proposed, species are kept separate. Notably, this *purifying* type of selection will also keep the members of the species functional, adapted to their particular way of life.

The main target of purifying selection is mutations, especially mutations that decrease fitness. Many mutations generate such deleterious effects. Some of these may be small or specific, such as losses of metabolic pathways that break down toxins or that extract energy from specific sugars. Other mutations may have pervasive and disastrous effects, creating anatomical monsters, sterilizing, or killing. Large or small in their effects, all these mutations are targets of purifying selection. And indeed, as Aristotle originally realized, without purifying selection our lives would be disastrous.

Natural selection may not consistently favor a single allele. This occurs, for example, in cases of **heterozygote superiority**, when heterozygotes, which have two different alleles, have the highest fitnesses in diploid sexual populations. Because of the sexual process, a population that starts out consisting entirely of heterozygotes will generate 50 percent homozygotes in the next generation. Selection will not be able to eliminate this half of the population immediately, unless all the homozygotes have zero fitness. Even when this unusual situation applies, the population will keep both alleles at frequencies of 0.5. Selection cannot eliminate genetic variation with heterozygote superiority, because the genotype with the greatest fitness itself is a repository of genetic variation. (Less extreme cases of heterozygote superiority are discussed later in the chapter.) But natural selection still acts to maintain genetic variation, by a pattern called **balancing selection**.

Balancing selection is important because there is abundant genetic variation for virtually every character that is related to fitness in outbred sexual populations: viability, fertility, running speed, seed production, height, weight, and so on. Why is there so much genetic variation for fitness-related characters? Purifying selection is expected to purge populations of genetic variation; but balancing selection is not. Balancing selection has therefore been proposed as a possible explanation for genetic variation in important characters. We give an important example of balancing selection later in this chapter. ❖

FIGURE 4.13B **A Gallery of Humanoid Monsters**

4.14 Selection in asexual populations increases mean fitness until the variance in fitness is used up

If every organism is the same, selection cannot work. Instead, when there is variation between organisms, selection takes the different groups in a population and makes them compete with each other. The key to this competition is differences in *net reproduction*, or **fitness**. **Net reproduction** is the product of total reproduction times the viability (survival probability) of offspring. For example, if a flatworm produces 12 offspring, but only 1/6 of these survive to become adult flatworms, then net reproduction is 2. Most microbes reproduce by splitting in two, so their total reproduction is always 2. In this case, net reproduction then varies only because viability varies.

Figure 4.14A illustrates an asexual population of microbes in which different groups of organisms have different viabilites, or survival probabilities. In this example, all reproduction is by splitting in two, or **fission**. Therefore, total reproduction is always two. In the illustration, the pink cells have a survival probability of about $^1/_4$; that is, one in four of these cells will survive to reproduce. The green cells have a survival probability of $^1/_2$, and the blue cells have a survival probability of 1. Their corresponding fitnesses can then be obtained by multiplying these survival probabilities by the total reproductive output of two. This gives fitnesses of $^1/_2$ for pink cells, 1 for green cells, and 2 for blue cells.

What happens in this population over time? From the fitness numbers just given, we intuitively expect the pink cells to be eliminated from the population. Indeed, by generation 10, all the pink cells are gone (see Figure 4.14A). During these 10 generations, the average fitness of the population steadily increases. After 100 generations, the mean fitness becomes very close to 2.00, the same as the fitness of the blue cells. This is natural because, by generation 100, the population is made up almost entirely of blue cells.

What about variance? The variance for fitness is high in the population for the first few generations. But by generation 10, it has already fallen a lot. And by generation 100, there is hardly any variance left. Again, this is natural, because by generation 100 almost the entire population is blue cells, which all have the same fitness. Selection has fed on the variance for fitness, and the consequence is a high mean fitness.

Notice that the mean fitness and the variance of the population changed, but *not* because of any change in the fitnesses of pink, blue, and green cells. Those stayed the same. The population changed in *composition*, but the different types of cells did not change. Selection works with what it is given. It is an editor, not a writer. ❖

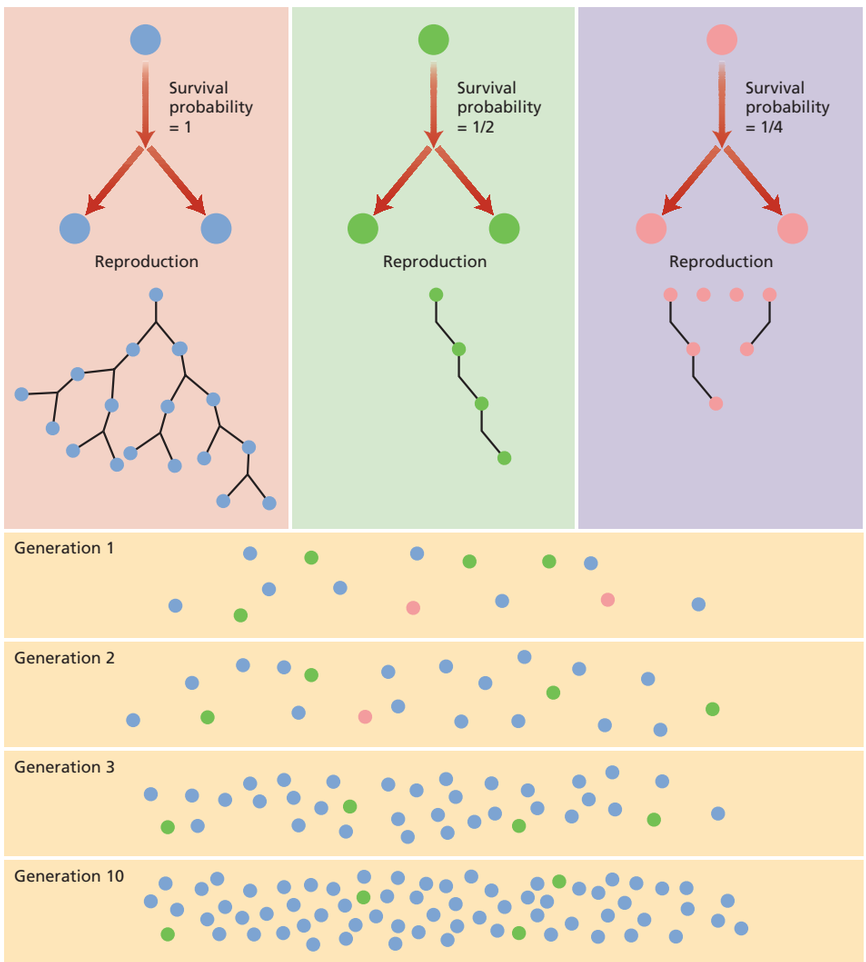


FIGURE 4.14A **Selection without Sex**

4.15 When heterozygotes are intermediate, selection with sex is similar to selection without sex

The role of selection is that of a filter or sieve. Some genotypes don't make it through the filter as often; they are selected against. These differences are summarized by numbers giving the chance that different genotypes will make it to adulthood; that is, fitnesses. In normal notation, we write that W_{ij} is the fitness of genotype *ij*, where *i* and *j* are the two alleles at the diploid locus of interest. Typical values for fitnesses (*W*'s) range from 0 for lethal genetic diseases, to values over 1.0 for genotypes of superior fitness.

In Figure 4.15A, the bookkeeping of genetics and fitness is laid out for cases where there is a consistent relationship between genotype and fitness. Fitness (*W*) is graphed for three cases: where allele *a* is dominant (part i); where the heterozygote *Aa* produces characteristics that are intermediate between those produced by *aa* and *AA* (part ii); and where the allele *A* is dominant (part iii). Note that in all three cases, the *A* allele is favored by natural selection, making the *AA* genotype as good as any other genotype, or better.

Let us start with the basic genetic model of Chapter 3: one diploid locus with two alleles. We suppose a very large population, discrete generations, and random mating. These are the model assumptions of the Hardy-Weinberg Law, so we can assume that gene frequencies do not change unless there is selection. The consequences of directional selection are shown in Figure 4.15B, which graphs the change in the frequency of a favored allele *A* in a population over many generations. In overview, selection makes the favored *A* allele sweep through a population, eliminating the *a* allele—which has less fitness. In the example shown, the more copies of the *A* allele, the more fit the genotype. In other words, *AA* is more fit than the heterozygote *Aa*, which is more fit than *aa*. And with greater fitness comes the attainment of *A* allele frequencies near 1.0, a state called **fixation**.

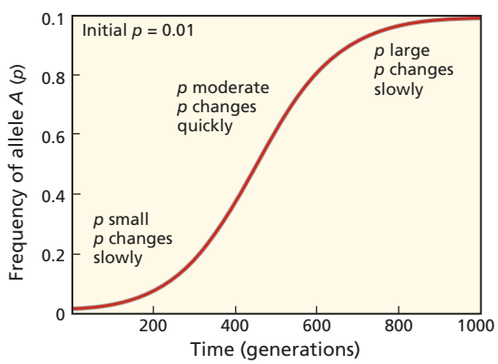


FIGURE 4.15B **The Dynamics of Directional Selection: $W_{AA} > W_{Aa}$ and $W_{Aa} > W_{aa}$.**

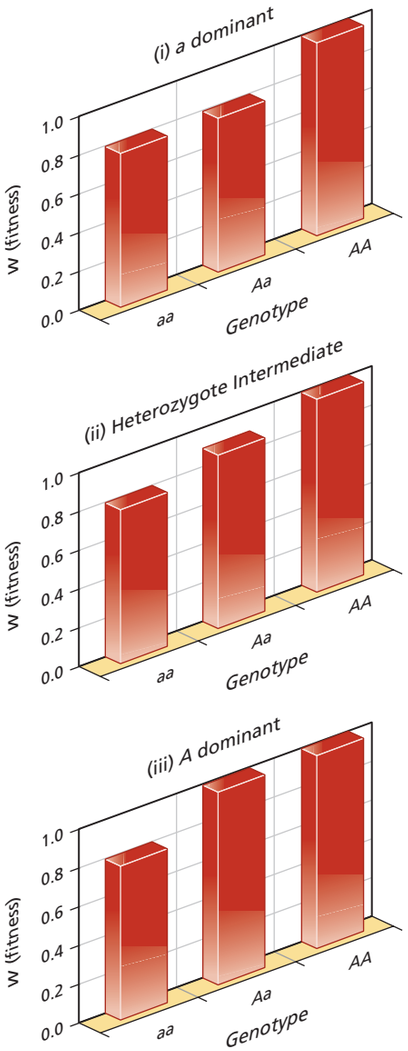


FIGURE 4.15A **Directional Selection with Sex**

4.16 Selection with recurring mutation prevents the achievement of maximum fitness

Because selection is an editor and not a writer, it works with what it is given—with the types of organisms that make up each population. Mutation is the initial creator in the evolutionary process. It produces all the "first drafts" of life. The only problem is that mutation occurs at random with respect to the direction of selection, so mutations often reduce fitness. This is a pattern called **deleterious mutation**. It is like noise introduced into the evolutionary process. Natural selection then makes messages from this noise by editing out deleterious mutations.

Mutation is like the "king of the hill," always preventing natural selection from making it all the way to the top.

But deleterious mutations keep on occurring. So, to change metaphors, natural selection is always pushing the boulder of mean fitness toward the top of an evolutionary hill, but never quite getting there. Mutation is like the "king of the hill," always preventing natural selection

Natural selection tends to increase the frequency of this type toward 100 percent, or fixation—as we just saw. Recurring deleterious mutation frustrates that tendency.

In sexual populations, individuals with the best alleles across all loci are produced only transiently, and then rarely, as the sexual process shuffles the best alleles among individual genotypes. In this sense, it is unlikely that natural selection will fix the best possible genotype in a sexual population. With sex, deleterious mutations further degrade the fitnesses of members of the population.

We will look at the effects of mutations in sexually reproducing populations in the next modules. For now, note that many mutations are highly deleterious. They are the source of some common human genetic diseases, as described in the box, "A Catalog of Misery."

eases. But Aristotle's cool reasoning has to be faced. In every reproductive act, there is the chance that our offspring are going to be targets of purifying selection.

Pulling back from the clinical horror of some genetic afflictions, we can see certain patterns from these examples of human genetic diseases. The first is that, even if the predisposing gene is not very rare, the syndromes themselves are rare. Cystic fibrosis is the most common lethal genetic disease in the United States, where it occurs in fewer than one in every 2000 live births. Even in modern medical surroundings, this is a small part of the full spectrum of disease. Perhaps part of our unease with genetic diseases is the sense of inevitability about them—making them unlike contagious diseases. Another part may be that they primarily afflict, and kill, children.

But our small list of genetic diseases is large enough to reveal the error in both of these conclusions. PKU is a genetic disease that is almost entirely treatable. There is nothing inevitable about the pathologies of genetic diseases. Huntington's disease makes a different point: Genetic diseases may strike older individuals exclusively. Genetic diseases do not stalk the sleeping babe alone. Indeed, many of the disorders of the elderly may be genetic in origin.

But the unavoidable conclusion about genetic diseases is that they can indeed turn life monstrous, frustrated, and barely—if at all—sustainable. And with survival, fertility may go, too. For some disorders, like Tay-Sachs disease, impaired fertility is medically irrelevant because victims usually die so young. But in the case of cystic fibrosis, fertility is now an overt concern of patients who survive into adulthood. On the other hand, there is the societal question regarding the fertility of individuals with some disorders, like Huntington's disease, who appear to be able to produce many offspring like themselves. Their afflicted offspring may impose huge medical costs on posterity. For all these reasons, and more besides, the problems of deleterious mutations are of great concern. ❖

A Catalog of Misery: Some Common Human Genetic Diseases

Dwarfism can be caused by a genetic disease called achondroplasia. **Achondroplasia** arises from a dominant mutation at the *FGFR3* gene. A single copy of this mutation causes short stature and distinctive proportions, large head, short limbs, and so forth. Intelligence is not affected. Two copies of the mutation usually cause death within the first year of life. The frequency of the mutant gene is about 0.002 percent. No medical cure is available for either the heterozygous or homozygous condition.

AT syndrome, or ataxia-telangiectasia syndrome, causes progressive loss of coordination, decreased resistance to infection, increased risk of cancer, and what is called the acceleration of aging, among other pathologies. Intelligence is normal. The full syndrome is caused by two defective mutations at the *ATM* gene, though a single copy may increase the risk of cancer. The frequency of the mutation is estimated as 1–3 percent. There is no specific medical treatment that relieves those afflicted with AT syndrome.

Cystic fibrosis is the single most common lethal genetic disease in the United States. Cystic fibrosis causes the secretion of thick mucus, disrupting the functions of pancreas, liver, intestine, and especially lung. Life expectancy without modern medical care is less than 10 years. With modern medical care, life expectancy is now about 30 years. Only 2 percent of males are fertile, while females have a less severe reduction in fertility. Intelligence is normal.

Cystic fibrosis is caused by two copies of a mutation of the *CFTR* gene. A single copy has no bad effects. Cystic fibrosis mutations are carried harmlessly in single copies by about 12 million Americans; one in 2300 children is born with the condition, having received copies of the mutation from both parents. The frequency of the gene in the U.S. population as a whole is about 2 percent. There is no known cure, though much research has been targeted at curing this particular genetic syndrome.

Huntington's disease, also known as Huntington's chorea, results in progressive deterioration of the central nervous system. This deterioration usually begins at from 30 to 50 years of age. From the first symptoms of neurological impairment, Huntington's disease takes 15–20 years, or longer, to kill its victims. During this period, the loss of coordination, mental function, and self-control become catastrophic.

The disease is caused by a single faulty copy of the *HD* gene. Because disease onset occurs later in life and progresses fairly slowly, fertility is roughly equal to that of normal individuals; life span is not dramatically curtailed. The frequency of the *HD* mutation varies considerably between populations, over the range of 0.0001– 0.01 percent. There is no medical treatment to prevent the start of the disease or to halt the progression of the disease; there is only treatment of the symptoms.

Phenylketonuria (PKU) results from the lack of the enzyme phenylalanine hydroxylase, which is responsible for the conversion of the amino acid phenylalanine to another amino acid, tyrosine. Interruption of this biochemical conversion results in the accumulation of phenylalanine to toxic levels, in turn causing neurotoxicity and eventually severe mental retardation.

PKU is caused by possession of two mutant copies of the gene coding for the phenylalanine hydroxylase enzyme. Carriers of single copies do not get the disease. The frequency of the PKU gene is about 1 percent in the United States. PKU can be treated very successfully by eliminating phenylalanine from the diet, starting with newborn infants. Screening of newborns for PKU is routine in the United States and other countries.

Tay-Sachs disease causes the accumulation in the brain of a fatty substance known as ganglioside GM2. This accumulation results in juvenile blindness, deafness, paralysis, and severe mental retardation. Death usually occurs before the age of 5. Tay-Sachs disease is caused by the lack of the enzyme hexosaminidase A, which helps degrade gangliosides.

Having two copies of mutations deficient in the production of this enzyme result in the disease. In Ashkenazi Jews and some French Canadians, the frequency of these mutations reaches 3 – 4 percent. In other groups, the frequency of Tay-Sachs disease mutations is much lower. There is no treatment available for infants suffering from Tay-Sachs disease.

4.17 When heterozygotes are superior, selection maintains genetic variation

Selection and genetics are both blind mechanisms, without foresight. These mechanisms reveal their blindness clearly when there is heterozygote superiority in sexual populations. In such cases, the homozygotes are inferior; this is shown in Figure 4.17A. It would be best if selection and genetics could work together to guarantee the fixation of the heterozygote. But this does not happen. Mendelian genetics ensure that heterozygotes produce abundant homozygotes, all with lower fitness. Yet the superiority of the heterozygote ensures that these homozygotes will be selected against. In short, selection pushes for the fixation of the heterozygote, while genetics regenerates the disfavored homozygotes every generation. Selection strives for what can never be, while genetics heedlessly produces the homozygotes that selection will penalize. Out of this stalemate, genetic variation is maintained.

The eventual outcome is stable, an equilibrium with one redeeming feature. At the equilibrium, when selection does not change gene frequencies any more, the average fitness is at its maximum value relative to the value of average fitness at all other gene frequencies, assuming Hardy-Weinberg proportions among the genotypes. In other words, even though superior heterozygotes frustrate the best possible outcome, selection still works to produce the highest average fitness, among the genetic states that the sexual population can attain, as shown in Figure 4.17B.

For the evolutionary biologist, heterozygote superiority provides one possible explanation for the abundant genetic variation for characters that are closely related to fitness. These characters include size, athletic performance, survival, and fertility, among others. This status as a possible explanation does not, however, mean that this explanation *has* to be true. (A very important feature of theoretical science is that it offers varied possibilities for the explaining the real world. But there is no certainty that such a possibility is actually true in a particular case.) Heterozygote superiority is an interesting possibility for the maintenance of genetic variation by natural selection. But it may be rare or common in evolution, nonetheless. ❖

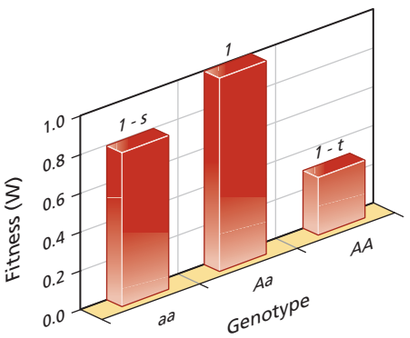
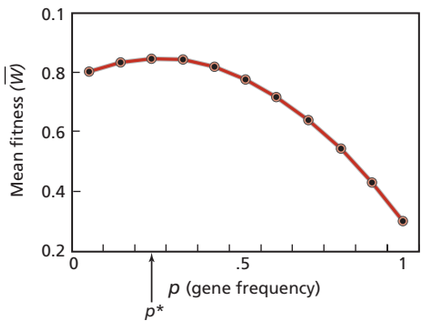


FIGURE 4.17A Fitnesses with Heterozygote Superiority



The evolutionary equilibrium is at p^*. At this gene frequency, mean fitness is at a maximum.

FIGURE 4.17B The Evolution of Mean Fitness with Heterosis

4.18 Selection in favor of rare genotypes can also maintain genetic variability

Another way to maintain genetic variability is when selection favors rare genotypes. This is a form of **frequency-dependent selection**. Selection gives the rare a "boost up" in a kind of Darwinian affirmative action. But how might selection do this?

Perhaps the most easily understood kind of favoritism of the rare occurs when predators learn to seek a particular type of prey because it is common. In the example shown in Figure 4.18A, the bird is seeking caterpillars crawling on the forest floor. The bird faces a problem: There are two kinds of caterpillars, green and brown. Both are equally camouflaged, because there are leaves on the ground, which are green, and the ground is otherwise brown dirt. But when there are many green caterpillars, it is easier for the bird to look at moving green objects and find food, compared to looking for the rare brown caterpillars. Eating the green caterpillars rewards the bird, and it associates the green color with the pleasure of feeding. So the bird develops a search image for green caterpillars, and eats a great many of them. But with time there are fewer and fewer green caterpillars. The brown caterpillars have been left alone, and they are now common. Birds will then be better off searching for brown caterpillars. So they switch to the brown caterpillars as prey, causing the numbers of the brown to drop. The caterpillar color variants are being selected for when they are rare, and selected against when they are common. This pattern of selection should maintain genetic variability for coloration.

Figure 4.18B shows a well-studied example of frequency-dependent selection—right- and left-handed scale-eating fish. The data show that the population tends to return to balanced frequencies of the two types of fish whenever the population deviates too far from equal proportions of the two types.

This idea can be extended to other types of selection. Common vertebrate pathogens face defeat by the responsive vertebrate immune system, which develops host defenses specific to common pathogens. New mutant forms of the pathogen then have an advantage because they do not have the same molecular cues for the vertebrate immune system. Several pathogens evolve this way, including HIV, the cause of AIDS. HIV continually generates new genetic variants that elude the human immune system.

Together with heterozygote superiority, frequency-dependent selection can explain the maintenance of genetic variation. But like heterozygote superiority, it is not known how common frequency-dependent selection is in nature. For now, these two genetic mechanisms of natural selection remain of interest as possibilities for evolution. ❖

FIGURE 4.18A Most predators seek new prey like the prey they have already eaten, which leads to frequency-dependent selection.

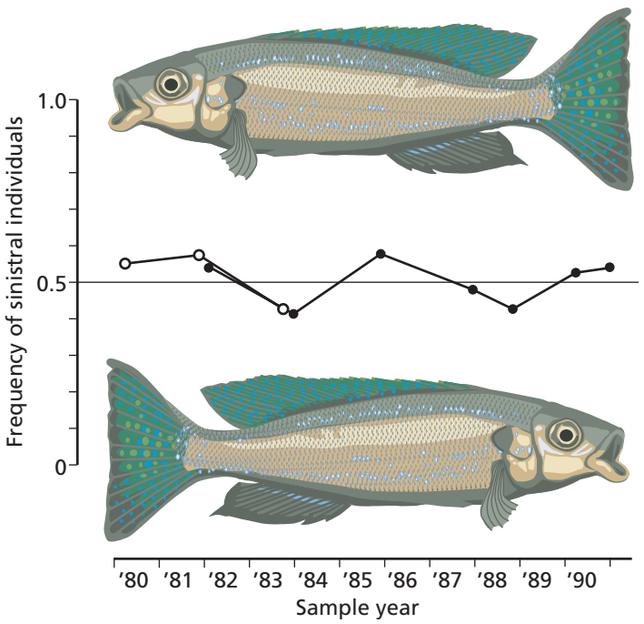


FIGURE 4.18B Frequency-Dependent Selection in Scale-Eating Fish That Scrape the Sides of Other Fish

Natural Selection in the Laboratory

4.19 Natural selection in the laboratory offers a view of what is possible in evolution

Earlier in this chapter, we discussed the use of artificial selection in breeding and in scientific experiments. In artificial selection, the experimenter or breeder chooses the target of selection. The entire breeding process is controlled, so that the main determinant of the outcome of the selection procedure is the amount and nature of the genetic variability present in the selected population.

Natural selection in the laboratory is a different kind of procedure. Instead of carefully controlling all aspects of selection, the experimenter sets up a particular kind of environment that may force the evolution of the experimental population. For example, a microbial population may be placed in a hot incubator for 1000 generations, to see if the microbe will evolve in response to this selection regime. In an experiment like this, the experimenter does not control anything more than a general feature of the environment. But this environment then makes natural selection act, picking among the cells with greater fitness under hot conditions. Any genetic tendency to such greater fitness leads to an increase in the frequency of cells that are better adapted to heat.

Natural selection observed in the wild clearly reveals how natural selection actually works. Artificial selection observed in the laboratory gives biologists a close look at how selection can operate, even though it provides no guarantee that natural selection will ever act in exactly this manner. So why perform natural selection in the lab?

This question is a particular example of a very general question in science. Why do scientists generally perform experiments under carefully controlled conditions, with good instruments, stable laboratory conditions, and repeated observations? They do so because it is very difficult to gather accurate data in natural environments. Should chemists do their experiments in rainstorms, outdoors? (See Figure 4.19A.) Should molecular biologists do biochemical experiments on banana splits in restaurants? Perhaps, if those particular circumstances are interesting to them, they should. But if scientists aren't interested in such scenarios, then it seems counterproductive to insist on their performing experiments under those conditions. Laboratories provide better conditions. Temperature, sunlight, and other environmental factors can be controlled.

Likewise, evolutionary biologists will normally be able to do natural selection experiments better in the laboratory. More data will be gathered under conditions that are better controlled and better known. But what can we learn from natural selection in the laboratory?

Biologists have many questions about evolution. How fast can natural selection change characters? Can it be reversed easily? If the question relates to what natural selection or evolution actually does in real populations, then natural selection in the lab is not useful. The lab will not tell us what actually happens in nature.

But observing selection in nature is often difficult, because so much environmental change is going on at the same time as selection is working. Usually the best way to see the *potential* power of selection is to study it in the laboratory, where its effects can be seen clearly against a background of environmental stability. In addition, biologists can replicate the same evolutionary process over and over. This helps us to answer major questions of principle about evolution.

We often want to know whether or not some selective process can occur at all. Can natural selection ever change X? Or our hypotheses may concern the consequences of a particular type of selection. If we impose environment Y on population Z, will that population evolve in response? Sometimes an evolutionary theory might even make a specific prediction about the response to a particular type of selection. For example, we might predict that bacteria kept in hot conditions would evolve greater Darwinian fitness at high temperatures after some hundreds of generations in the

FIGURE 4.19A A Chemist in a Rainstorm

heat. One way to think of this situation is that the laboratory can be used to discover what is *possible* for evolution by natural selection. What is *actually* occurring is better studied under natural conditions.

Of course these stipulations and limitations are quite general to the study of evolution, ecology, and organismal biology. All these fields have problems with interpreting experiments in the laboratory. However, these problems are sometimes little more than confusion about the difference between the possible and the actual. In the laboratory, we never learn anything beyond the merely possible, whether we are biologists, chemists, or physicists. ❖

4.20 Bacterial evolution in the laboratory shows that the response to selection is very powerful at first, but tends to slow down

The power of selection in the absence of sex has been studied systematically in the laboratory of **Richard E. Lenski,** a leading evolutionary microbiologist. The classic bacterial evolution experiment from this group is still one of the best examples of the action of selection without the complications of Mendelian genetics. Perhaps the single most important reason this experiment is a classic is that it used massive replication and numerous generations. The basic data involve 12 independent populations, evolving for 10,000 generations under identical conditions. (In human terms, that many generations would be about 250,000 years—a very long time indeed.) Not only were there many populations and many, many generations, but the size of each population was also large—fluctuating between 500,000 and 50 million cells. If we assume that the average population size per generation was 7–10 million, then the 10,000 generations of evolution involved about 1 trillion cells.

Figure 4.20A shows Lenski's experimental procedure, including the system of replication, the method of population cultivation, and the way that fitness was estimated. The basic point, however, is that these bacteria were given a novel environment to adapt to in the laboratory: growth medium with basic nutrients and a small amount of glucose for metabolic fuel. Over 10,000 generations, the descendants of the original bacteria became much better at competing with their ancestors under these conditions, as shown in Figure 4.20B. This result could be summarized as "fitness increased," or "the bacteria adapted to the laboratory conditions imposed." Either way, a lot of genetic change took place, especially in the first 2000 generations. But the rate of improvement fell, becoming much slower in later generations, as the graph of Lenski's results shows. Note how the curve is steep at first, as the populations adapt relatively quickly to the novel environment, but then flattens out after the first 2000 generations. This slowing is also expected: Initial adaptation should be faster, because the populations begin some distance from efficient exploitation of their environment, making selection stronger.

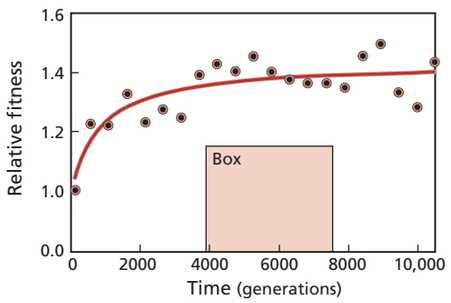
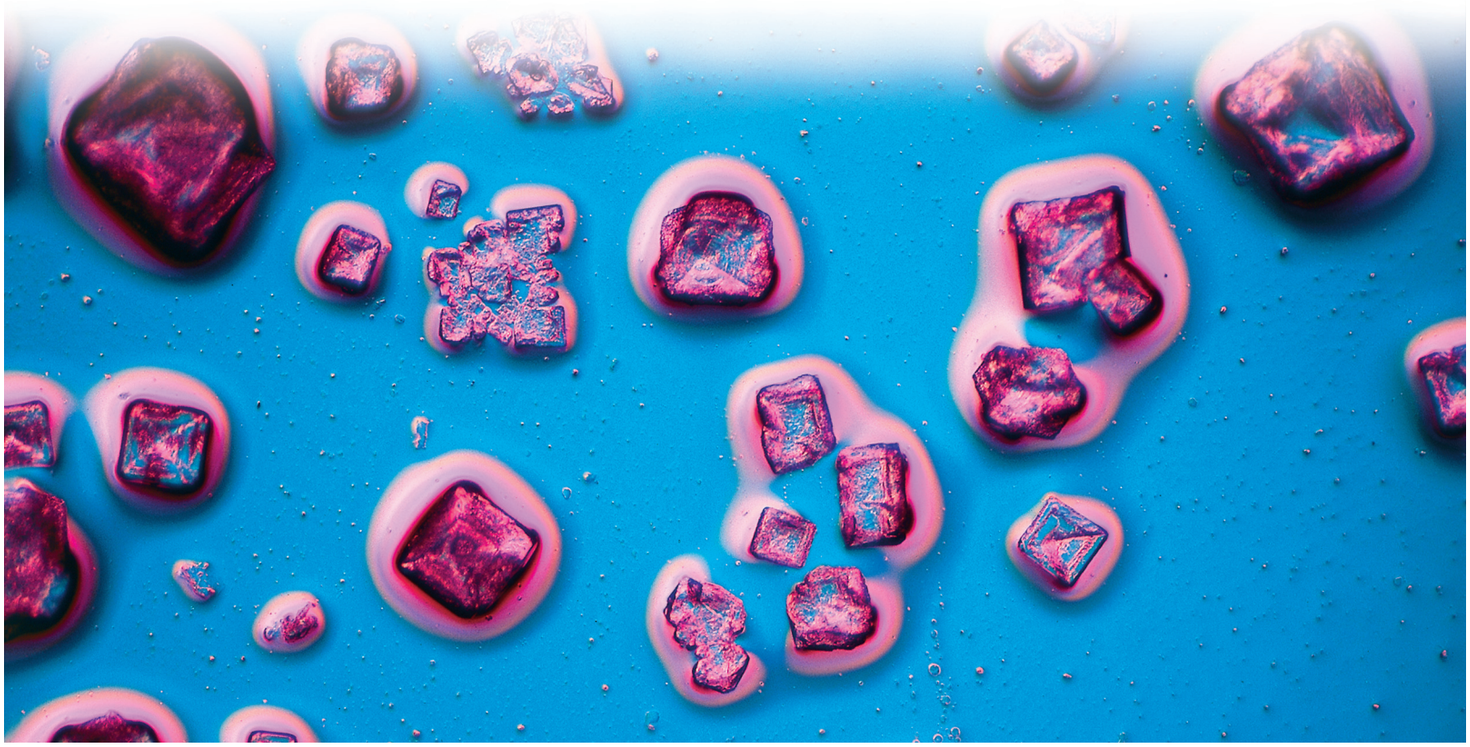


FIGURE 4.20B The Data for Fitness over 10,000 Generations of Microbial Laboratory Evolution



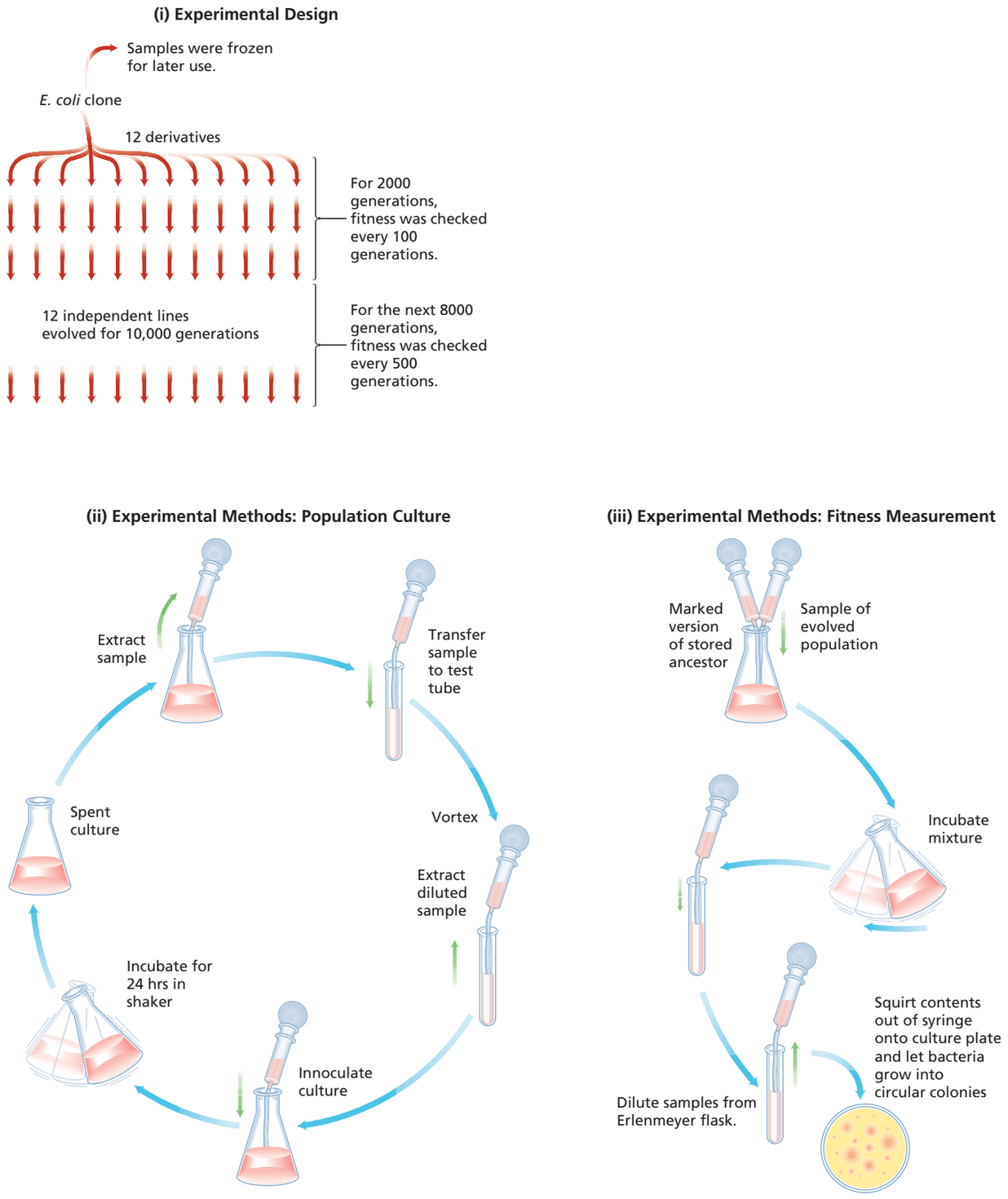


FIGURE 4.20A **The Laboratory Evolution of Fitness in a Microorganism**

4.21 Laboratory experiments show that sexual populations can respond quickly to intense directional selection

It is easy to show that sexual populations can respond quickly to directional selection. As in experiments with asexual bacteria, it is usually most convenient to use laboratory organisms. Like Mendelian geneticists, evolutionary geneticists like to work with the fruit fly *Drosophila melanogaster*. Many experiments have shown that directional selection on fruit flies can produce dramatic and sustainable genetic change. Here we give just one example.

The focus of selection in our example is speed of development in the fly. The term *development* refers to the complete progression, from development in the insect's egg, to larval growth and development, to the pupal transition from larva to adult, to the initial maturation and copulation of the adult. In human terms, this is the progression from fetus to wedding night. This developmental process takes the fly through a complete life cycle. Normally, the entire process takes 11–12 days in fruit flies, with standard temperatures of about 25°C and lots of good fly food. The question was, could development be speeded up using selection?

The flies used for selection came from a group of five populations that normally develop at a leisurely pace, labeled the CB flies. These flies usually take at least four weeks to complete an entire generation. B flies were the ancestors to the CBs and were used as controls for environmental fluctuations. Such controls are very important with small invertebrate animals, which can be affected by subtle features of the lab environment. The ACB flies were derived from the CB flies, and then subjected to selection for faster development, as shown in part (i) of Figure 4.21A.

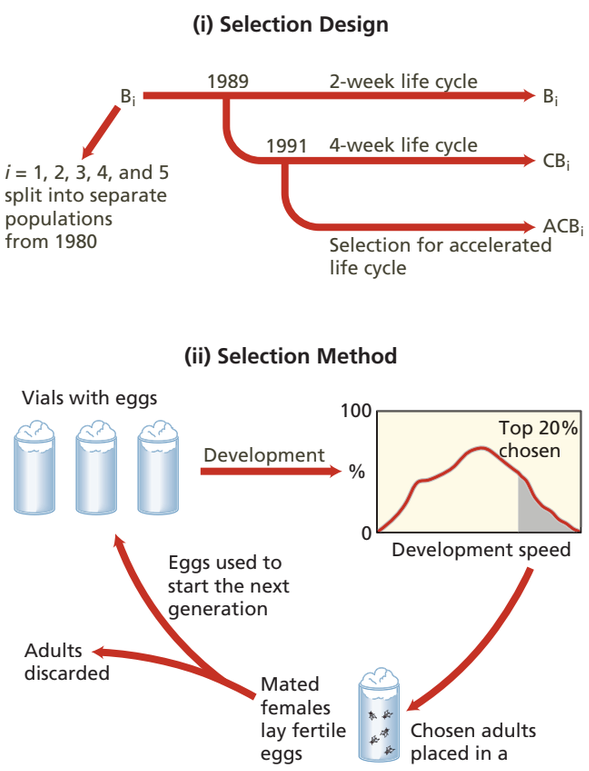


FIGURE 4.21A Selection for Rapid Development in *Drosophila*

There were five distinct sets of matched B, CB, and ACB populations, for a total of 15 populations. This quantity was important, because each population is a distinct, unique entity in evolution, like a corporation in a modern economy or a football team. To study evolution scientifically, we have to study multiple populations, not just one population. Only populations evolve, not individuals.

The selection method imposed on the ACB flies involved choosing the fastest 20 percent of flies completing maturation to the adult stage, as shown in part (ii) of Figure 4.21A. These flies then had to get mated quickly, so that the fast-developing females could lay fertilized eggs. This selection procedure was followed for 125 generations, about three years. As shown in Figure 4.21B, development time was reduced by 15 percent in the selected ACB lines. Directional selection led to the evolution of "faster" flies—flies that got to their nuptials sooner. ❖

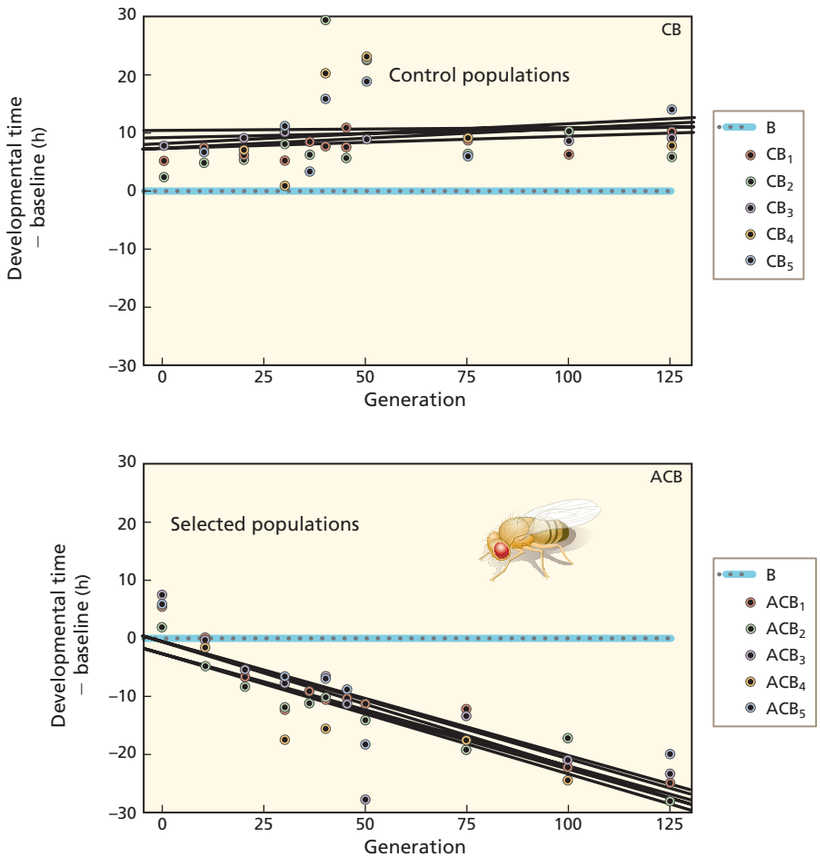
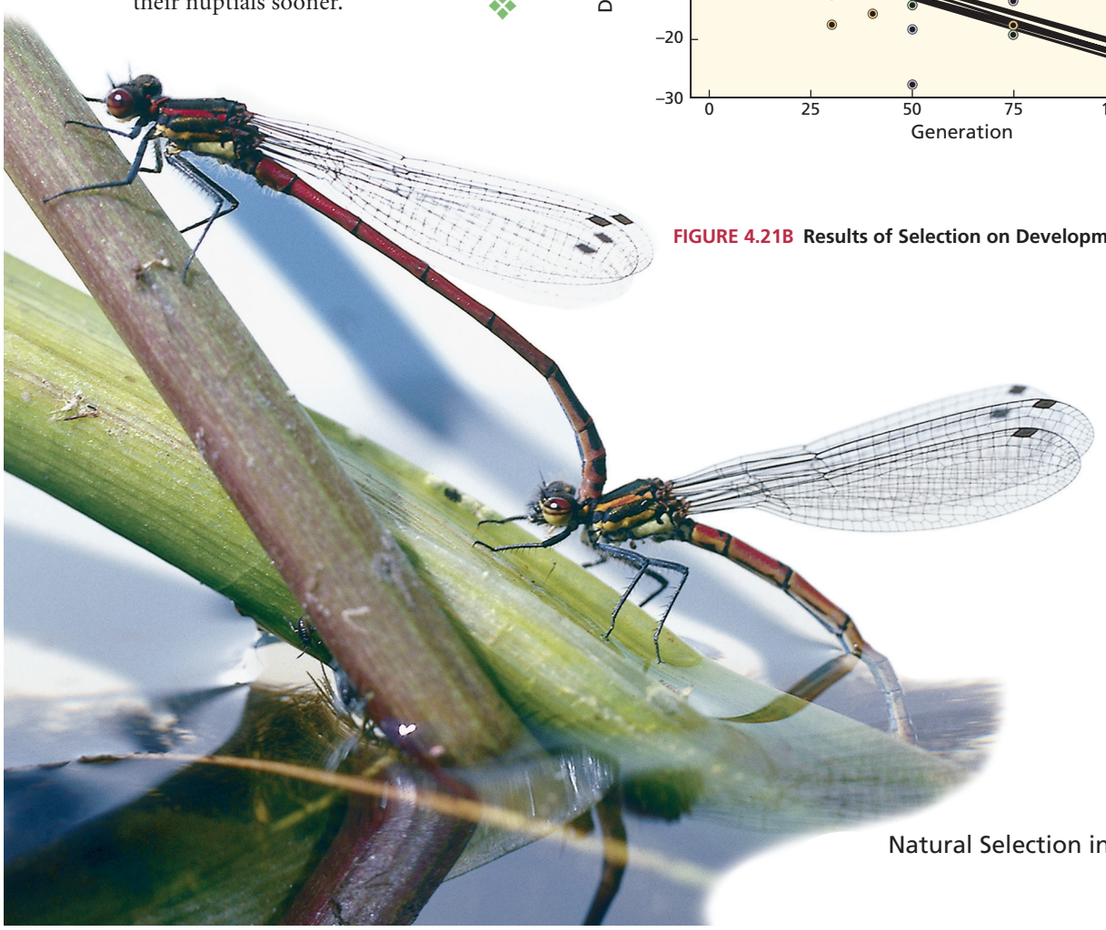


FIGURE 4.21B **Results of Selection on Development in *Drosophila***



Natural Selection in the Wild

4.22 The evolution of antibiotics illustrates the basic principles of natural selection in the wild

To study what natural selection actually does, scientists must examine how populations evolve in nature. We will be considering several laudable studies that demonstrate how much can be learned by studying how natural selection operates in the wild. But many of the basic ideas about how natural selection works are illustrated by the evolution of **antibiotic resistance**. When antibiotics were first used medically, at the time of World War II, they were very successful in clearing up bacterial infections. Very few bacteria were able to resist being killed by antibiotics. And there was not enough genetic variation in bacterial populations to mount a successful evolutionary defense against the antibiotics.

But within a few years, antibiotic resistance started to appear. The use of antibiotics had imposed selection for genetic variants of normal bacteria, variants that had the capacity to resist being killed by the antibiotics. For this reason, in the treatment of some infections, a particular antibiotic might fail. And over the decades since World War II, resistance to antibiotics such as penicillin (obtained from the mold *Penicillium,* Figure 4.22A), one of the first introduced, became common. Medicine had created a new selective environment against which bacteria were at first helpless. But with time, natural selection exploited initially rare genetic variants to produce increasingly resistant strains of bacteria. Today these bacteria pose a considerable threat to the medical battle against bacterial diseases, from gonorrhea to staphylococcus infections.

But this tale gets more complicated with respect to the bacteria as organisms evolving in "nature." (Their habitat is of course our bodies.) The pattern of medical use of antibiotics is one of the basic selective factors for the bacteria. Sensitive bacteria undergoing antibiotic attack die off in large numbers, at first. However, some may survive the first 24 hours of treatment, perhaps because the tissues in which they are located receive less of the antibiotic. These bacteria may be partially resistant, as well. If antibiotics were then withdrawn from the patient, relatively more bacteria that were partly resistant would have survived. If their descendants remain within the body, they could produce a later bout of infection; but these descendants might be resistant to further antibiotic treatment.

For this reason, doctors tell their patients to finish the complete course of antibiotic treatment—for 7, 10, or 14 days. This type of prescription is very different from symptomatic medication, from aspirin to Demerol, for which doctors often specifically warn against continued medication because of potential side effects or addiction. The medical doctors are trying not only to kill off their targeted pathogen but also to reduce the chance that some bacteria will evolve increased resistance because of the antibiotic medication.

Despite the great care that Western doctors have taken to prevent the spread of antibiotic resistance among bacteria, it has in fact spread—and spread widely. Doctors try to prescribe different antibiotics when their first prescriptions do not work, but bacteria are now often resistant to multiple antibiotics. Bacterial evolution by natural selection has modern medicine on the run. We discuss this problem in more detail in Chapter 22.

But this fight has not been entirely fair. We have learned that bacteria are not as asexual as we had supposed. It turns out that bacteria exchange DNA with each other, particularly using plasmids. **Plasmids** are large circles of DNA, somewhat like the large circle of DNA that is each bacterium's genome. Most bacteria can live without their plasmids. In fact, plasmids may

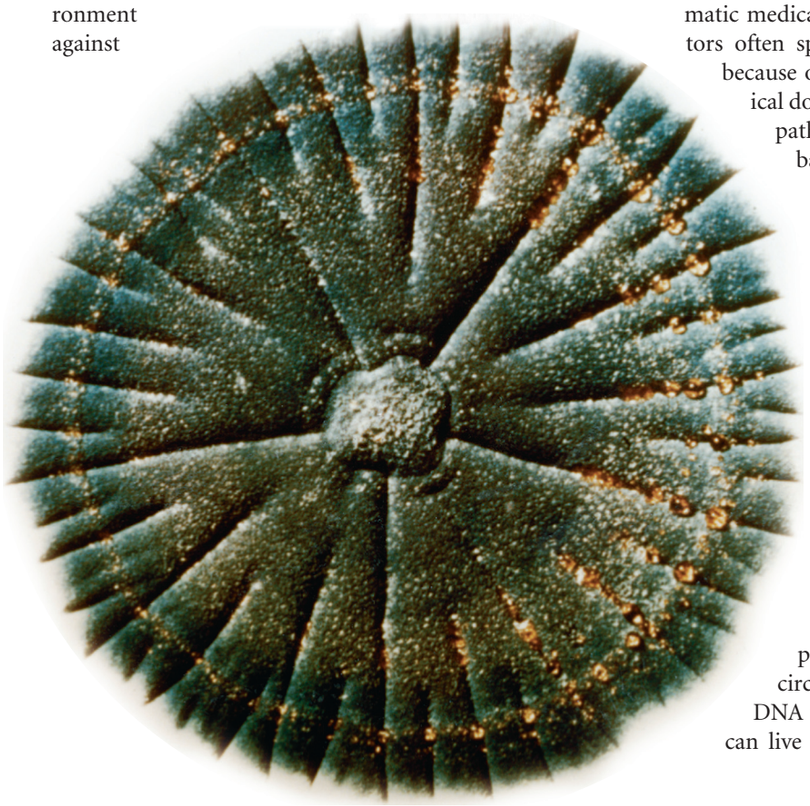


FIGURE 4.22A ***Penicillium notatum*, a Source of Antibiotics**

often be parasites within the bacterial cell. Plasmids are transmitted from one bacterium to another by a bridge called the *pilus*, a microscopic analog of a penis. The pilus injects copies of plasmids from one cell into another, by a process called *conjugation* (Figure 4.22B; see also Chapter 18). The donating bacterium usually keeps copies of the plasmid, so plasmids can rapidly accumulate in bacterial populations. We now know that some plasmids carry genes for resisting antibiotics, so that the use of antibiotics must have selected for bacteria carrying such plasmids. This is a more complicated story than that of simple selection on bacteria, but it reveals a profound truth about organisms without genetic organization of reproduction: They may be somewhat sexy anyway. A clone may not be a clone, after all. This is taken up further in Chapter 18.

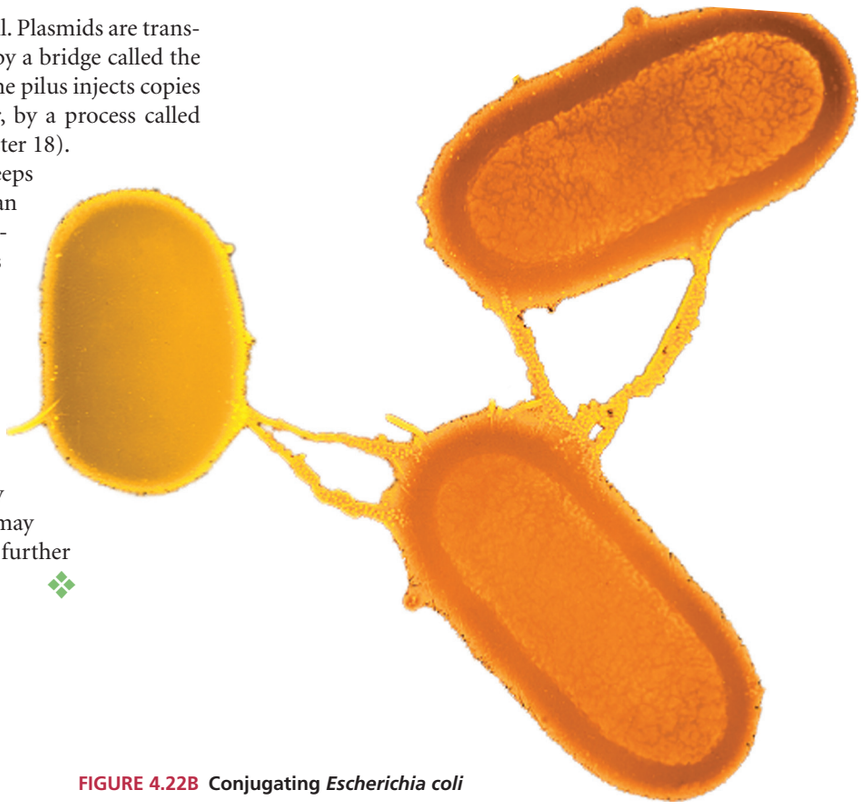


FIGURE 4.22B Conjugating *Escherichia coli*

4.23 The best example of long-term natural selection in the wild is industrial melanism

In the nineteenth century, while Charles Darwin lived in the leafy surroundings of southeast England, the "satanic mills" of northern England's Industrial Revolution were creating one of the most important examples of directional selection in the history of evolutionary biology. This example was **industrial melanism**. The term refers to the darkening of butterflies and moths in the industrial regions of Western Europe during the period when coal was the main fuel. *Melanin* is a darkening pigment. This phenomenon of industrial melanism was discovered in the collections of English amateur lepidopterists (those who study the butterflies and moths of the insect order Lepidoptera). These were mostly middle-class naturalists with the time and athletic ability to collect flying insects using nets. Sometimes their collections were immense, including numerous species gathered over several decades.

In several of the affected moth and butterfly species, the melanism pattern was striking. Beginning sometime after the introduction of extensive coal burning in the mid-nineteenth century, butterflies and moths of these species started to exhibit more and more dark *morphs*, or forms, with a lot of pigment. Over the course of the late nineteenth century, these morphs became more common, until they were in the majority of some species in the period from 1920 to 1950. This change is illustrated in Figure 4.23A. Much later, with the introduction of environmental laws and reduced production of coal soot, the frequency of dark morphs declined.

How can these evolutionary changes be explained? The record of butterfly and moth collections in England is good enough that it is unlikely to be a product of accident or fashions in butterfly collecting. In some species, dark morphs were not in any of the collections from early in nineteenth century. It was proposed that coal soot might have changed the physiology of some butterflies and moths, making them darker. But laboratory rearing of the offspring of dark morphs under controlled conditions still gave dark morph progeny.

H.B.D. Kettlewell, a dedicated evolutionary lepidopterist working in the middle of the twentieth century, spent years lying in the grass of damp English meadows watching butterflies and moths. What he found was a beautiful example of natural selection at work. In regions with little coal burning, tree trunks were usually mottled with light-colored lichen. Moths and butterflies rested on these tree trunks, where the light-colored morphs would blend in with their surroundings (Figure 4.23B). The dark morphs were much more visible to Kettlewell. They were also more visible to birds, who picked them off the trees in greater numbers than the light morphs. But with coal burning, soot covered the tree trunks and most lichen died off. Under these conditions, the dark morphs were camouflaged, while the light morphs were picked off by birds in greater numbers. We have since learned that some of Kettlewell's experiments were artificially staged; moths were glued onto tree trunks, among other contrivances. But there is no evidence that his essential conclusions are not valid.

Natural selection was selecting moths and butterflies with appropriate protective coloration, and birds were playing the role of selective agent. The pigment change in moth and butterfly coloration is one of most straightforward examples of directional selection now known to evolutionary biologists. If Darwin had lived near Manchester, instead of south of London, he might have seen this vindication of natural selection with his own eyes.

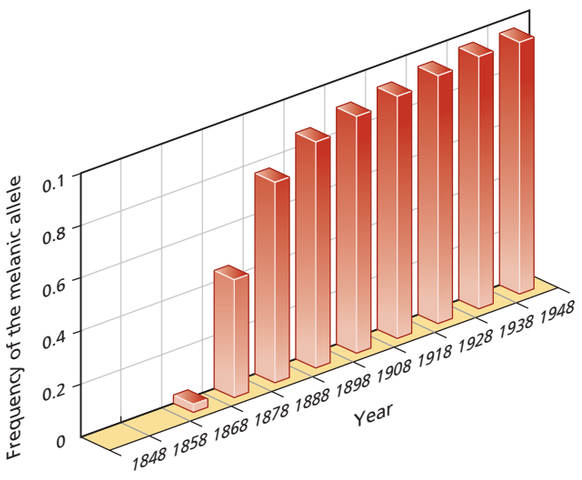


FIGURE 4.23A Estimated Pattern of Substitution of the Gene for Melanism in a Moth Data from Ridley (2004, p. 110).

FIGURE 4.23B Melanic and Speckled Moths on an Unpolluted Tree Trunk

Selection for increased beak size occurred in Darwin's finches on the Galápagos Islands 4.24

Darwin's visit to the Galápagos Islands in 1835 uncovered several interesting organisms for biological research, such as the very long-lived Galápagos tortoise. But the group that scientists have studied most is the group of finches named after Darwin—Darwin's finches, of the genus *Geospiza*. **Peter Grant** of Princeton University has for some time led a group of biologists who have studied these birds, banding each bird when young and carefully keeping track of deaths.

In the late 1970s a major drought struck the Daphne Major Island of the Galápagos archipelago. Rainfall levels fell very low. Many of the plants on the island produced few or no seeds. In the species *Geospiza fortis*, a ground finch that depends on seeds for food, the population size fell precipitately—from about 1400 to a few hundred—over just two years, as shown in Figure 4.24A. At the same time, the sex ratio shifted from 1 male:1 female to 6 males:1 female. Some details of this ecological disaster are shown in Figure 4.24B. This is the kind of large-scale misfortune that the demographer Malthus had foreseen, though its causes in this case were meteorological and not crowding. In a Darwinian view of life, we would expect intense natural selection to occur under these conditions.

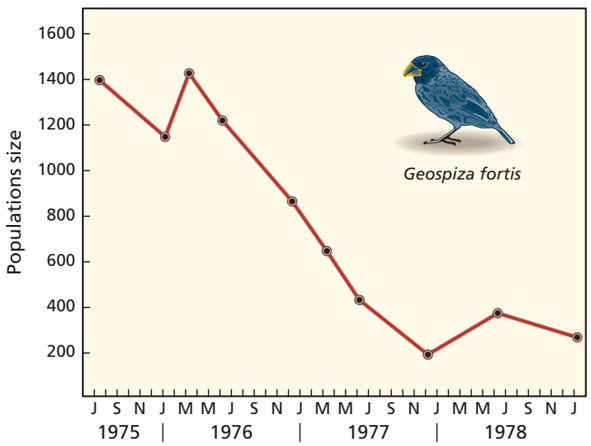


FIGURE 4.24A **A Darwin's Finch Species (*Geospiza fortis*) Dying off During a Drought**

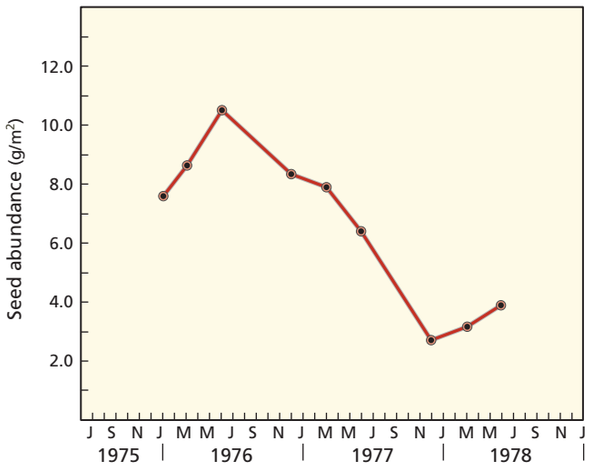


FIGURE 4.24B **Falling Seed Abundance during a Drought on the Galápagos Islands**

What Grant's group observed was a dramatic increase in the average body size and the average beak size of the ground finch population. This change occurred because small seeds were rare during the drought. However, even during the drought, large seeds with thick husks were still available. Only the large birds with large beaks could successfully crack open the large seeds and eat their contents. Because smaller birds with smaller beaks had few seeds that they could eat successfully, they either starved or died of exposure, from lack of the caloric reserves to survive lower nighttime temperatures. (See Figure 4.24C for photos of some of the finches.) From this differential pattern of death, the finch population rapidly changed in response, presenting a clear-cut case of natural selection. ❖

FIGURE 4.24C **Various Species of Darwin's Finches**

4.25 Human sickle-cell anemia is maintained by heterozygote superiority

The best-understood example of heterozygote superiority is the human medical problem of **sickle-cell anemia.** The medical importance of this problem is considerable, because thousands of people die of sickle-cell anemia every year. The immediate medical situation is that a change in the amino acid sequence of a subunit of the hemoglobin molecule causes the blood's erythrocytes (red blood cells, or RBCs) to bend out of shape, a change called sickling (Figure 4.25A). The erythrocytes get stuck in capillaries, causing circulatory blockage. These stuck cells are then degraded by other cells, reducing the patient's overall level of erythrocytes and causing anemia. The patient experiences chronic pain, anemia, and difficulty respiring, with death usually coming before reproduction.

This particular case handily, though tragically, illustrates the anomalies of balancing selection with heterozygote superiority. Unlike the genetic syndromes of purifying selection, in which natural selection acts to reduce the frequency of a harmful allele, natural selection actively maintains the allele that causes sickle-cell anemia. This occurs in regions where malaria is common, as shown in Figure 4.25B. The malarial parasite, *Plasmodium* (Figure 4.25C), is not as good at infecting genotypes that have erythrocyte sickling. Even the heterozygote for the sickle-cell allele is protected from malarial infection. Because **malaria** remains a major cause of death in Africa, Asia Minor, and southern Asia, these regions have high frequencies of the sickle-cell allele. As shown in Table 4.25A, the heterozygote (*AS*) has significantly greater fitness in malarial areas compared to the homozygote for the normal allele (*AA*). Unfortunately, there is also a spectacular loss of fitness in the homozygote for the sickle-cell allele (*SS*).

If we didn't know that the heterozygote is of higher fitness in malarial areas, we might think that sickle-cell anemia is a genetic disease that is similar to Tay-Sachs disease. But the tip-off is the greater frequency of the disorder. Sickle-cell anemia affects about 2 percent of the population in malarial regions. Cystic fibrosis, the most common genetic disease, attacks only about 0.04 percent of the U.S. population—a population that is relatively more afflicted with this disorder compared with other countries. So sickle-cell anemia is two orders of magnitude more common than the most common genetic disease. This tells us that selection must have played a role in establishing sickle-cell anemia in malarial populations. This is a case where selection actively fosters human misery. ❖

TABLE 4.25A Human Polymorphism for Hemoglobin

S—sickle-cell hemoglobin
A—normal hemoglobin

Genotypes	*AA*	*AS*	*SS*
Initial genotype frequencies	0.77	0.21	0.02
Death due to sickling	0	+	+++
Death due to malaria	+++	+	+
Fitness in malarial areas	0.88	1.0	0.14

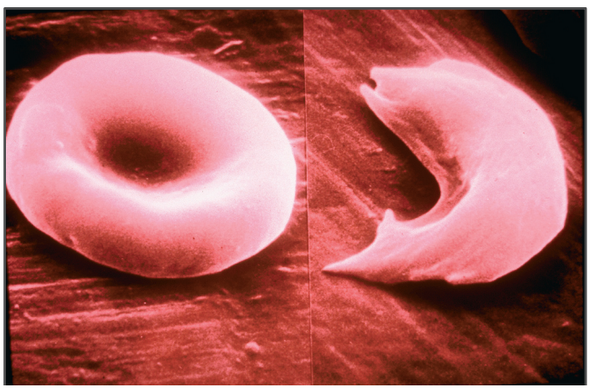
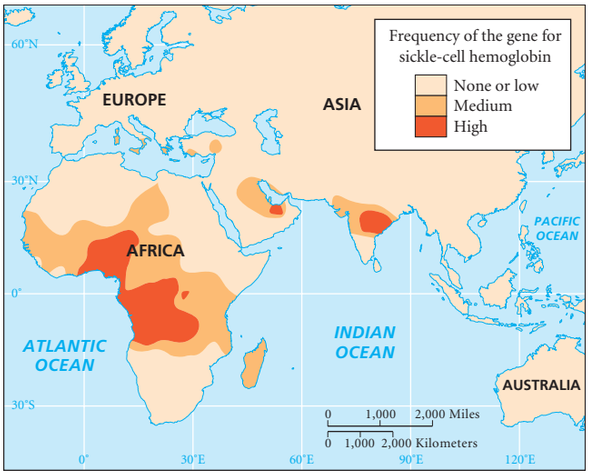


FIGURE 4.25A Sickled and Normal Red Blood Cells (RBCs)



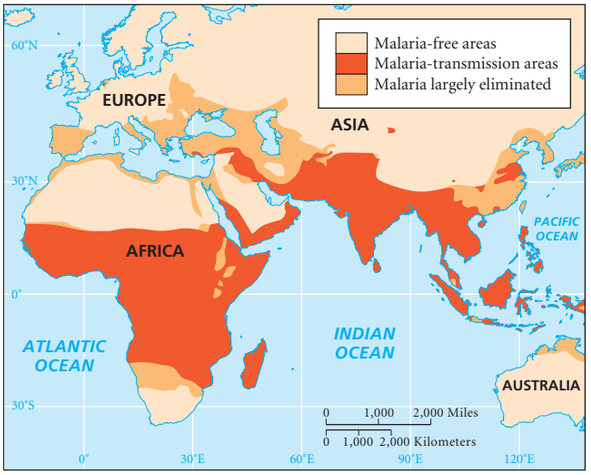


FIGURE 4.25B The Geography of Sickle-Cell Anemia and Malaria in Africa

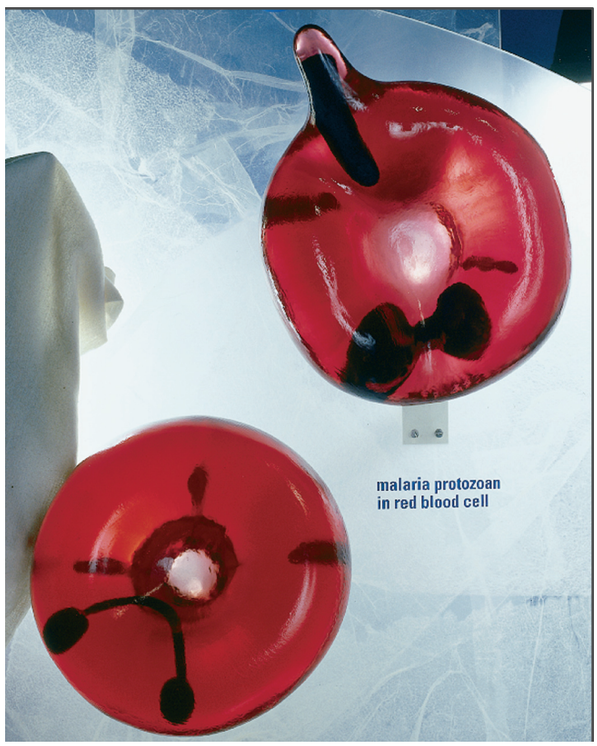


FIGURE 4.25C *Plasmodium*, the Pathogen that Causes Malaria

SUMMARY

1. Darwin's views concerning natural selection were thoughtful, though not always correct. Darwin did not expect to observe natural selection, because he thought that its action would be too protracted. Although this is often the case, we now know that it is not always true. But this lack of faith in the speed of natural selection left Darwin short of examples of the action of selection in nature. He compensated by heavily using the literature on artificial selection. Perhaps as a result, Darwin cast nature as a kind of breeder or selector. He emphasized that many generations of breeding can produce breeds of animal and varieties of plants that are strikingly different.
2. The way selection works is transparent in artificial selection. This helps us to understand natural selection, which parallels artificial selection. Both require the presence of genetic variation for the selected character. But there are some differences between artificial and natural selection. Natural selection can act on more organisms than artificial selection can. Natural selection usually fluctuates more in direction. Which type of selection will act with the greater power is uncertain.
3. Selection operates according to phenotype in different ways. Sometimes selection favors a directional change toward one extreme or another. At other times selection favors intermediate phenotypes, by a pattern called stabilizing selection. Selection can alternatively penalize intermediate phenotypes, by a pattern known as disruptive selection.
4. The genetics of natural selection are also varied. When there is no sexual reproduction in a population, natural selection efficiently increases the frequency of the clone with highest fitness, using up the genetic variance of fitness. Deleterious mutations lead to purifying selection and to reduction in genetic variation. Heterozygote superiority and frequency-dependent selection can maintain genetic variation.
5. Natural selection can be studied in the laboratory with good environmental control and replication. This research shows us what is possible in evolution, not what actually occurs. Bacterial evolution of fitness suggests that fitness evolution may decelerate through time. The life-history characters of fruit flies evolve readily in laboratory experiments.
6. Natural selection in the wild is illustrated by a few important examples: antibiotic resistance in bacteria, industrial melanism, the beaks of Darwin's finches, and sickle-cell anemia in humans.

REVIEW QUESTIONS

1. Why did Darwin discuss artificial selection in the *Origin*?
2. Does the speed of natural selection always fit Darwin's expectations?
3. What is a phenotype?
4. Why does heterozygote superiority lead to genetic variation?
5. Industrial melanism is a case where selection focused on what type of adaptation?
6. Why might natural selection favor an intermediate phenotype?
7. If natural selection is steady, always applying the same pressure, what would the pattern of evolution look like?
8. Are natural environments always moderate in their selection pressures?
9. The evolution of sickle-cell anemia in humans is an example of what kind of selection?

KEY TERMS

achondroplasia
adaptation
Aristotle
artificial selection
AT syndrome
balancing selection
bimodal
clonal selection
clone
cumulative selection differential
cumulative selection response
cystic fibrosis
deleterious mutation
directional selection
disruptive selection
dwarfism
fission
fitness
fixation
frequency-dependent selection
Grant, Peter
heritability
heterozygote superiority
Huntington's disease
industrial melanism
Kettlewell, H.B.D.
Lenski, Richard E.
Lyell, Charles
malaria
mutation
natural selection
net reproduction
phenotypic selection
phenotype variation
phenylketonuria (PKU)
plasmid
polymorphism
purifying selection
selection differential (S)
selection response (R)
sickle-cell anemia
stabilizing selection
Tay-Sachs disease

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