hereditary diseases was weak. But what about the evolutionary logic behind compulsory sterilization? If the genetic assumptions had been correct, would sterilization have been an effective means of reducing the incidence of undesirable traits?

Before we try to answer this question, it will be helpful to address a more general one. How well does the theory of population genetics actually work? We developed this theory in Sections 6.1 and 6.2. The final product is a model of how allele frequencies change in response to natural selection (Figures 6.12 and 6.13, Computing Consequences 6.3 and 6.5). If our model is a good one, it should accurately predict the direction and rate of allele frequency change under a variety of selection schemes. It should work, for example, whether the allele favored by selection is dominant or recessive, common or rare. It should work whether selection favors heterozygotes or homozygotes. It should even predict what will happen when a particular allele is favored by selection under some circumstances and disfavored in others.

In this section, we will find out how well our model works. Using the theory we have developed to predict the course of evolution under different patterns of selection, we compare our predictions to empirical data from experimental populations. We then return to our question about the effectiveness of eugenic sterilization in changing the composition of populations.

Selection on Recessive and Dominant Alleles

For our first test, we focus on whether our theory accurately predicts changes in the frequencies of recessive and dominant alleles. Our example comes from the work of Peter Dawson (1970). Dawson had been studying a laboratory colony of flour beetles **(Figure 6.18)** and had identified a gene we will call the l locus. This locus has two alleles: + and *l*. Individuals with genotype +/+ or +/*l* are phenotypically normal, whereas individuals with genotype *l*/*l* do not survive. In other words, *l* is a recessive lethal allele.

Figure 6.18 Flour beetles, *Tribolium castaneum* Courtesy of Susan J. Brown, Professor/Kansas State University, Kansas.

Dawson collected heterozygotes from his beetle colony and used them to establish two new experimental populations. Because all the founders were heterozygotes, the initial frequencies of the two alleles were 0.5 in both populations. Because *l*/*l* individuals have zero fitness, Dawson expected his populations to evolve toward ever lower frequencies of the *l* allele and ever higher frequencies of the + allele. He let his two populations evolve for a dozen generations, each generation measuring the frequencies of the two alleles.

Dawson used the equations derived in Computing Consequences 6.3 and the method described in Computing Consequences 6.5 to make a quantitative prediction of the course of evolution in his populations. We can reproduce this prediction with a straightforward numerical calculation like the ones we performed in Figures 6.12 and 6.13. Imagine a gene pool in which alleles + and *l* are both at a frequency of 0.5. If we combine gametes at random to make 100 zygotes, we get the three genotypes in the following numbers:

+/+	+/*l*	*l*/*l*
25	50	25

Now we imagine that all the *l*/*l* individuals die and that everyone else survives to breed. Finally, imagine that each of the survivors donates 10 gametes to the new gene pool:

The 25 +/+ survivors together make 250 gametes: 250 carry +; none carry *l*.

The 50 +/*l* survivors together make 500 gametes: 250 carry +; 250 carry *l*.

This gives us 500 copies of the + allele and 250 copies of the *l* allele for a total of 750. In this new gene pool, the frequency of the + allele is 0.67, and the frequency of the *l* allele is 0.33. We have gone from the gene pool in generation zero to the gene pool in generation one. The frequency of the + allele has risen, and the frequency of the *l* allele has fallen.

To get from generation one's gene pool to generation two's gene pool, we just repeat the exercise. We combine the gametes in generation one's gene pool at random to make 100 zygotes—45 +/+, 44 +/*l*, and 11 *l*/*l*—and so on. The only problem with using pencil-and-paper numerical calculations to predict evolution is that chasing the alleles around and around the life cycle all the way to generation 12 is a tedious job.

With a computer, however, predicting how Dawson's population will evolve is quick and easy. We can use a spreadsheet application to set up the required calculations ourselves (see Computing Consequences 6.3 and 6.5), or we can use any of a variety of population genetics programs that are already set up to do the calculations for us. Such programs take starting allele frequencies and genotype fitnesses as input and use the model we have developed in this chapter to produce predicted allele frequencies in future generations as output. We encourage the reader to get one of these programs and experiment with it.

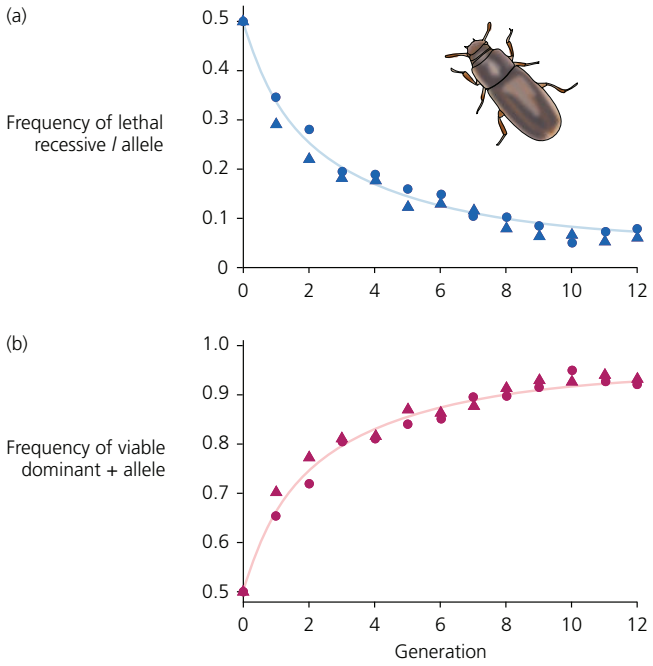

Figure 6.19 Evolution in laboratory populations of flour beetles (a) The decline in frequency of a lethal recessive allele (blue symbols) matches the theoretical prediction (blue curve) almost exactly. As the allele becomes rare, the rate of evolution slows dramatically. (b) This graph plots the increase in frequency of the corresponding dominant allele. Redrawn from Dawson (1970).

The prediction for Dawson's experiment appears as a curve in each of the graphs in Figure 6.19. The curve in the top graph predicts the falling frequency of the *l* allele; equivalently, the curve in the bottom graph predicts the rising frequency of the + allele. Our theory predicts that evolution will be rapid at first but will slow as the experiment proceeds.

Dawson's data appear in the graphs as colored circles and triangles. They match our theoretical predictions closely. This tight fit between prediction and data may seem unsurprising, even mundane. It should not. It should be astonishing. We

Empirical research on flour beetles shows that predictions made with population genetics models are accurate, at least under laboratory conditions.

COMPUTING CONSEQUENCES 6.6

An algebraic treatment of selection on recessive and dominant alleles

Here we develop equations that illuminate the differences between selection on recessive versus dominant alleles. Imagine a single locus with two alleles. Let p be the frequency of the dominant allele A, and let q be the frequency of the recessive allele a.

Selection on the recessive allele

Let the fitnesses of the genotypes be given by

w_{AA}	w_{Aa}	w_{aa}
1	1	$1 - s$

where s, called the **selection coefficient**, represents the strength of selection against homozygous recessives relative to the other genotypes. (Selection in favor of homozygous recessives can be accommodated by choosing a negative value for s.)

Based on Computing Consequences 6.3, the following equation gives the frequency of allele a in the next generation, q', given the frequency of a in this generation and the fitnesses of the three genotypes:

$$q' = \frac{pqw_{Aa} + q^2w_{aa}}{\overline{w}} = \frac{pqw_{Aa} + q^2w_{aa}}{p^2w_{AA} + 2pqw_{Aa} + q^2w_{aa}}$$

Substituting the fitness values from the table above, and $(1 - q)$ for p, then simplifying, gives

$$q' = \frac{q(1 - sq)}{1 - sq^2}$$

If a is a lethal recessive, then s is equal to 1. Substituting this value into the preceding equation gives

$$q' = \frac{q(1 - q)}{1 - q^2} = \frac{q(1 - q)}{(1 - q)(1 + q)} = \frac{q}{(1 + q)}$$

A little experimentation shows that once a recessive lethal allele becomes rare, further declines in frequency are slow. For example, if the frequency of allele a in this generation is 0.01, then in the next generation its frequency will be approximately 0.0099.

Selection on the dominant allele

Let the fitnesses of the genotypes be given by

w_{AA}	w_{Aa}	w_{aa}
$1 - s$	$1 - s$	1

where s, the selection coefficient, represents the strength of selection against genotypes containing the dominant allele relative to homozygous recessives. (Selection in favor of genotypes containing the dominant allele can be accommodated by choosing a negative value of s.)

Based on Computing Consequences 6.3, we can write an equation that predicts the frequency of allele A in the next generation, p', given the frequency of A in this generation and the fitness of the three genotypes:

$$p' = \frac{p^2w_{AA} + pqw_{Aa}}{\overline{w}} = \frac{p^2w_{AA} + pqw_{Aa}}{p^2w_{AA} + 2pqw_{Aa} + q^2w_{aa}}$$

Substituting the fitnesses from the table, and $(1 - p)$ for q, then simplifying, gives

$$p' = \frac{p(1 - s)}{1 - 2sp + sp^2}$$

If A is a lethal dominant, s is equal to 1. Substituting this value into the foregoing equation shows that a lethal dominant is eliminated from a population in a single generation.

Selection on recessive alleles versus selection on dominant alleles

Selection on recessive alleles and selection on dominant alleles are opposite sides of the same coin. Selection against a recessive allele is selection in favor of the dominant allele, and vice versa.

used a simple model of the mechanism of evolution combining the fundamental insights of Gregor Mendel with those of Charles Darwin to predict how a population would change over 12 generations. If the creatures in question had been humans instead of flour beetles, it would have meant forecasting events that will happen in 300 years. And Dawson's data show that our prediction was not just reasonably accurate, but spot on. If we had a theory that worked like that for picking stocks or racehorses—well, we could have retired years ago. Our model has passed its first test.

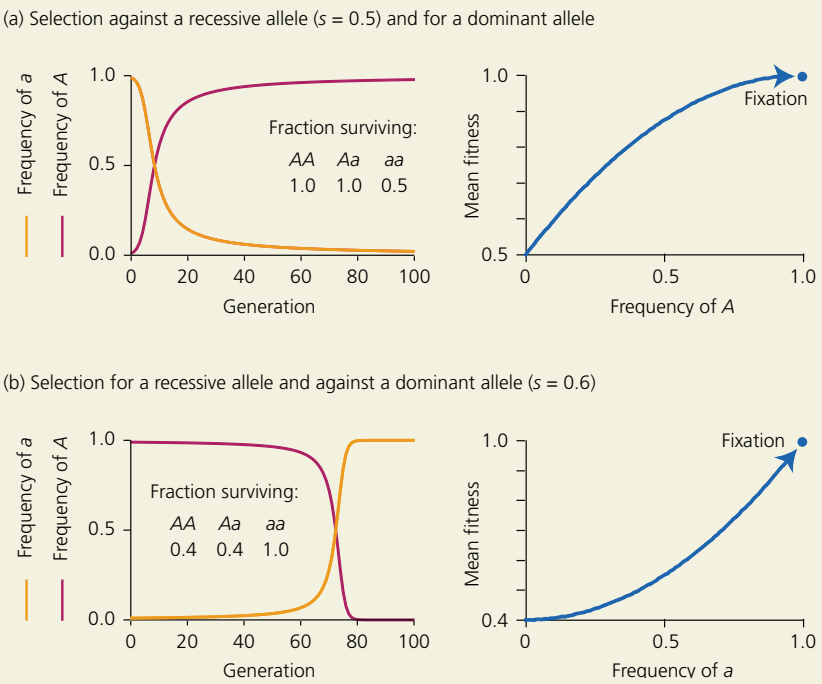

Figure 6.20 Evolution in model populations under selection on recessive and dominant alleles Graphs on the left show changes in allele frequencies over time. Graphs on the right show adaptive landscapes: Changes in population mean fitness as a function of allele frequencies.

Figure 6.20a (left) shows 100 generations of evolution in a model population with selection against a recessive allele and in favor of the dominant allele. At first, the allele frequencies change rapidly. As the recessive allele becomes rare, however, the rate of evolution slows dramatically. When the recessive allele is rare, most copies in the population are in heterozygous individuals, where they are effectively hidden from selection.

The figure also shows (right) the mean fitness of the population (see Computing Consequences 6.3) as a function of the frequency of the dominant allele. As the dominant allele goes from rare to common, the mean fitness of the population rises. Mean fitness is maximized when the favored allele reaches a frequency of 100%. Graphs of mean fitness as a function of allele frequency are often referred to as adaptive landscapes.

Figure 6.20b (left) shows 100 generations of evolution in a model population with selection in favor of a recessive allele and against the dominant allele. At first, the allele frequencies change slowly. The recessive allele is rare, most copies present are in heterozygotes, and selection cannot see it. However, as the recessive allele becomes common enough that a substantial fraction of homozygotes appear, the rate of evolution increases dramatically. Once the pace of evolution accelerates, the favorable recessive allele quickly achieves a frequency of 100%. That is, the recessive allele becomes fixed in the population.

The figure also shows (right) the mean fitness of the population (see Computing Consequences 6.3) as a function of the frequency of the recessive allele. As the recessive allele goes from rare to common, the mean fitness of the population rises. Mean fitness is maximized when the favored allele reaches a frequency of 100%.

An algebraic treatment of selection on recessive and dominant alleles appears in **Computing Consequences 6.6.** Even without the algebra, we can draw some important conclusions by reflecting further on Dawson's experiment.

Dawson's experiment shows that dominance and allele frequency interact to determine the rate of evolution. When a recessive allele is common (and a dominant allele is rare), evolution by natural selection is rapid. In contrast, when a recessive allele is rare, and a dominant allele is common, evolution by natural selection is slow. The Hardy–Weinberg equilibrium principle explains why.

First imagine a recessive allele that is common: Its frequency is, say, 0.95. The dominant allele thus has a frequency of 0.05. By multiplying the allele frequencies, we can calculate the genotype frequencies:

AA	*Aa*	*aa*
$0.05^2 = 0.0025$	$2 \cdot 0.05 \cdot 0.95 = 0.095$	$0.95^2 = 0.9025$

Roughly 10% of the individuals in the population have the dominant phenotype, while 90% have the recessive phenotype. Both phenotypes are reasonably well represented, and if they differ in fitness, then the allele frequencies in the next generation may be substantially different.

Natural selection is most potent as a mechanism of evolution when it is acting on common recessive alleles (and rare dominant alleles). When a recessive allele is rare, most copies are hidden in heterozygotes and protected from selection.

Now imagine a recessive allele that is rare: Its frequency is 0.05. The dominant allele thus has a frequency of 0.95. The genotype frequencies are

AA	*Aa*	*aa*
$0.95^2 = 0.9025$	$2 \cdot 0.95 \cdot 0.05 = 0.095$	$0.05^2 = 0.0025$

Approximately 100% of the population has the dominant phenotype, while approximately 0% has the recessive phenotype. Even if the phenotypes differ greatly in fitness, there are so few of the minority phenotype that there will be little change in allele frequencies in the next generation. In a random mating population, most copies of a rare recessive allele are phenotypically hidden inside heterozygous individuals and thereby immune from selection.

As a final consideration in our discussion of dominant and recessive alleles, note that selection may favor or disfavor both kinds of variants. We emphasize this point because many people new to population genetics expect that dominant alleles are necessarily beneficial and thus tend to rise in frequency. While it is certainly true that some dominant alleles are beneficial, many others are deleterious. For example, Eileen Shore and colleagues (2006) identified a dominant mutation, located in a gene encoding a receptor for bone morphogenic protein, as the cause of fibrodysplasia ossificans progressiva, a rare and severely disabling condition in which skeletal muscle and connective tissue transform inexorably into bone. In all, some 30% of the alleles known to cause human diseases are autosomal dominants (López-Bigas et al. 2006). The terms *dominant* and *recessive* describe the relationship between genotype and phenotype, not the relationship between genotype and fitness.

Selection on Heterozygotes and Homozygotes

In our next two tests, we focus on whether our model can accurately predict what happens when selection favors heterozygotes or homozygotes. Both tests will use data on laboratory populations of fruit flies (*Drosophila melanogaster*).

Selection Favoring Heterozygotes

Our first example comes from research by Terumi Mukai and Allan Burdick (1959). Like Dawson, Mukai and Burdick studied evolution at a single locus with two alleles. We will call the alleles *V*, for viable, and *L* for lethal. This is because flies with genotype *VV* or *VL* are alive, whereas flies with genotype *LL* are dead. The researchers used heterozygotes as founders to establish two experimental populations with initial allele frequencies of 0.5. They let the populations evolve for 15 generations, each generation measuring the frequency of allele *V*.

So far, Mukai and Burdick's experiment sounds just like Dawson's. If it is, then our theory predicts that *V* will rise in frequency—rapidly at first, then more