

## The Inductive Theory of Natural Selection

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Darwin (1859) got essentially everything right about natural selection, adaptation, and biological design. But he was wrong about the processes that determine inheritance (Smocovitis, chap. 2). How could Darwin be wrong about heredity and genetics, but be right about everything else? Because the essence of natural selection is trial and error learning. Try some different approaches for a problem. Dump the ones that fail and favor the ones that work best. Add some new approaches. Run another test. Keep doing that. The solutions will improve over time. Almost everything that Darwin wanted to know about adaptation and biological design depended only on understanding, in a general way, how the traits of individuals evolve by trial and error to fit more closely to the physical and social challenges of reproduction.

Certainly, understanding the basis of heredity is important. Darwin missed key problems, such as genomic conflict. And he was not right about every detail of adaptation. But he did go from the absence of understanding to a nearly complete explanation for biological design. What he missed or got wrong requires only minor adjustments to his framework. That is a lot to accomplish in one step.

How could Darwin achieve so much? His single greatest insight was that a simple explanation could tie everything together. His explanation was natural selection in the context of descent with modification. Of course, not every detail of life can be explained by those simple principles. But Darwin took the stance that when major patterns of nature could not be explained by selection and descent with modification, it was a failure on his part to see clearly, and he had to work harder. No one else in Darwin's time dared to think that all of the great complexity of life could arise from such simple natural processes. Not even Wallace.

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Now, more than a hundred fifty years after *The Origin of Species*, we still struggle to understand the varied complexity of natural selection. What is the best way to study natural selection: detailed genetic models or simple phenotypic models? Are there general truths about natural selection that apply universally? What is the role of natural selection relative to other evolutionary processes?

Despite the apparent simplicity of natural selection, controversy remains intense. Controversy almost always reflects the different kinds of questions that various people ask and the different kinds of answers that various people accept as explanations. Natural selection itself remains as simple as Darwin understood it to be.

### *Deductive and Inductive Theory*

There are two different ways we can think about natural selection. In the deductive way, we use our understanding of natural selection to make predictions about what we expect to find when we observe nature. For example, we might be interested in how a mother's resources influence her tendency to make daughters versus sons. A female wasp that lays her eggs on a caterpillar will sometimes have a large host and sometimes a small host.

We can make a model to predict what sex offspring the wasp will produce when faced with a large versus a small host. We make that deductive prediction by calculating the number of grandchildren that we think the mother can expect based on the size of the host and the sex of the offspring. A simple interpretation of natural selection is that the process favors a mother that behaves a way that gives her the highest number of grandchildren—the highest fitness—within the limits of what she can reasonably do given the biology of the situation.

Perhaps the simplest deductive theory of natural selection concerns the change in gene frequency. A gene associated with a higher fitness than average tends to increase in frequency, a simple mathematical deduction. We can deduce exactly how fast a gene will increase in frequency given its fitness relative to the average. Although the mathematical deduction is very simple, in practice it is difficult to know in advance what fitness is associated with a particular gene. That fitness will depend on the gene itself and what it does inside cells, and also on the interaction of that gene with other genes and with the environment (Scheiner, chap. 13).

The value of deductive theory is, of course, that we can compare our predictions to what we actually observe. When reality differs from what we observe, then we know that some aspect of our initial understanding

is incomplete or wrong. Much of the theory of natural selection develops deductive predictions, which can then be tested against observation.

Inductive analysis turns things around and begins with observations of what actually happened in nature. Suppose, for example, that we know the frequency of a gene at two points in time. From the observed change in frequency, we can infer the fitness of the gene by inductive reasoning: the strength of natural selection that would be required to cause the observed change. Although we can induce the power of the unseen cause of natural selection, we cannot rule out other processes that might have caused the change in frequency. For example, it might be that the frequency changed by random sampling of alternative genes rather than by differences in fitness caused by effects of those genes. Inductive studies often seek to determine which of the various possible causes is most likely given the observations.

In our wasp example, we might have begun with the observation that mothers gain greater fitness when laying daughters rather than sons on large hosts. We could inductively estimate the strength of natural selection when comparing the production of daughters versus sons on a given host size. To the extent that we identify natural selection as a primary causal force, we would be estimating the strength of that cause in shaping the decision behavior of mothers faced with hosts of different sizes.

Natural selection itself may be thought of as an inductive process. With each step in time, gene frequencies change. Characters become more prevalent when they are correlated with genes that increase in frequency. Roughly speaking, natural selection inductively assigns the likely causes of improved fitness to those characters that are correlated with reproductive success.

When thinking about natural selection, we must always be clear about which of the different points of view we wish to emphasize. We may have a deductive prediction to test against observation. Or we may have observed data that we can use to induce the likelihood of alternative underlying causes. Or we may think about how natural selection itself works as an inductive process that associates actual changes in gene frequencies, or other informational units, with underlying factors that can potentially act as causes.

In this chapter, we focus on inductive perspectives of natural selection in relation to underlying causes of fitness. The notion of cause here is subtle. The population geneticist C. C. Li observed that there are many formal definitions of causation, but it is often not necessary to adopt any one of them. "We shall simply use the words 'cause' and 'effect' as statistical terms similar to independent and dependent variables, or [predictor variables and response variables]" (Li 1975, 3).

*Partitioning Causes of Change*

We follow Li's suggestion to learn what we can about causation by studying the possible relations between potential causal factors. The structure of those relations expresses hypotheses about cause. Alternative structural relations may fit the data more or less well. Those alternatives may also suggest testable predictions that can differentiate between the relative likelihood of the different causal hypotheses (Crespi 1990; Frank 1997, 1998; Scheiner et al. 2000).

In evolutionary studies, one typically tries to explain how environmental and biological factors influence characters (Mindell and Scheiner, chap. 1). Causal analysis separates into two steps. How do alternative character values influence fitness? What fraction of the character values is transmitted to following generations? These two steps are roughly the causes of selection and the causes of transmission.

*Domain of the Theory*

In a broad sense, the domain of the theory is evolutionary change in response to natural selection. This domain of natural selection is not the whole of evolution. For example, smoky pollution might darken the color of trees in a nearby forest, causing a change over time in the average coloration of the population. In this case, tree color did not change by selection. Instead, the change was simply a consequence of a changed environment. However, natural selection remains the only force that could potentially explain a consistent tendency toward adaptation—the match between an organism's characters and the environmental and social challenges faced by that organism.

Following our distinction between deductive and inductive perspectives, the theory of natural selection has two complementary subdomains. Deductively, we may begin with known or assumed characters and with known or assumed fitnesses, and then work out how selection will change the characters over time. Although that sounds simple, it can be challenging to work out how various characters and various selection processes interact over time to cause evolutionary change. In this case, it is often useful to partition selection into different causes (e.g., how a character changes the fitness of a neighboring sibling, and how the same character changes the fitness of the individual bearing the character).

Inductively, we may begin with observed characters and observed fitnesses, and then work out how the various characters and their interac-

tions caused the values of fitness that we observed. Again, this is not easy to do in practice. For example, we might see that bacteria secrete a digestive enzyme that causes some external food source to break down into components that are more easily taken up by cells. We might have measurements on how much enzyme is secreted by different kinds of cells and on the fitnesses of the various cell types. For a given fitness, can we infer how much of that fitness value is caused by the amount of enzyme secreted and how much of that fitness is caused by the amount of digested food taken up? The amount secreted is a direct cause of the fitness of the associated cell type, but the amount of food taken up depends on the amount of enzyme secreted by all neighbors—a partition of causes between direct and social aspects of selection.

## Basic Models

### *Prelude*

Improvement by trial and error is a very simple concept. But applying that simple concept to real problems can be surprisingly difficult. Mathematics can help but can also hinder. One must be clear about what one wants from the mathematics and the limitations of what mathematics can do. Useful mathematical modeling involves some subtlety. The output of mathematics reflects only what one puts in. If different mathematical approaches lead to different conclusions, the approaches have made different assumptions. There is a natural tendency to develop complicated models, because we know that nature is complicated. However, false or apparently meaningless assumptions often provide a better description of the empirical structure of the world than precise and apparently true assumptions.

The immense power of mathematical insight from false or apparently meaningless assumptions shapes nearly every aspect of our modern lives. The problem with the intuitively attractive precise and realistic assumptions is that they typically provide exactness about a reality that does not exist. One never has a full set of true assumptions, and we generally cannot estimate large numbers of parameters accurately. Worse yet, model error may grow multiplicatively with many parameters, so that even if we can estimate the parameters, the resulting predictions are often so broad as to be useless (Walters 1986; Hilborn and Mangel 1997). By contrast, false or apparently meaningless assumptions, properly chosen, can provide profound insight into the logical structure of nature. Experience has supported this truth over and over again.

**Table 9.1. The Theory of Evolution by Natural Selection**


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*Domain: Evolutionary change in response to natural selection.*

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Propositions:

1. Evolutionary change can be partitioned into natural selection and transmission.
  2. Fitness describes the evolutionary change caused by natural selection.
  3. Information can be lost during transmission of characters from ancestors to descendants.
  4. The balance between information gain by selection and information loss by transmission can be used to explain the relative roles of different evolutionary forces.
  5. Fitness can be partitioned into distinct causes, such as the amount of change caused by different characters.
  6. Characters can be partitioned into distinct causes, such as different genetic, social, or environmental components.
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Six propositions, shown in table 9.1, provide the logical structure of the theory of evolution by natural selection. Proposition 1 says that we can account for evolutionary change in populations by ascribing it to two basic causes: selection and transmission of information between generations. This first proposition requires a definition of fitness, such as the evolutionary change caused by natural selection (proposition 2). We now consider how these concepts are used in models of fitness and frequency change in populations, which include both deductive and inductive approaches.

### *Frequency Change and Selection*

In a basic model of fitness and frequency change, there are  $n$  different types of individuals. The frequency of each type is  $q_i$ . Each type has  $R_i$  offspring. The average reproductive success is  $\bar{R} = \sum q_i R_i$ , summing over all of the different types indexed by  $i$ . Fitness is  $w_i = R_i / \bar{R}$ , used here as a measure of relative success. The frequency of each type after selection is:

$$(9.1) \quad q'_i = q_i w_i$$

To obtain useful equations of selection, we must consider change. Subtracting  $q_i$  from both sides of eq. 9.1 yields:

$$(9.2) \quad \Delta q_i = q_i (w_i - 1),$$

in which  $\Delta q_i = q'_i - q_i$  is the change in the frequency of each type. Rearranging shows that  $q'_i / q_i = w_i$ , a mathematical expression of proposition 2.

We often want to know about the change caused by selection in the value of a character. Suppose that each type,  $i$ , has an associated character value,  $z_i$ . The character  $z$  can be a quantitative trait or an allele frequency

from the classical equations of population genetics. The average character value in the initial population is  $\bar{z} = \sum q_i z_i$ . The average character value in the descendant population is  $\bar{z}' = \sum q'_i z'_i$ . For now, assume that descendants have the same average character value as their ancestors,  $\bar{z}' = \bar{z}$ . Then  $\bar{z}' = \sum q'_i z_i$ , and the change in the average value of the character caused by selection is:

$$\bar{z}' - \bar{z} = \Delta_s \bar{z} = \sum q'_i z_i - \sum q_i z_i = \sum (q'_i - q_i) z_i,$$

where  $\Delta_s$  means the change caused by selection when ignoring all other evolutionary forces (G. R. Price 1972b; Ewens 1989; Frank and Slatkin 1992). Using  $\Delta q_i = q'_i - q_i$  for frequency changes yields:

$$(9.3) \quad \Delta_s \bar{z} = \sum \Delta q_i z_i.$$

This equation expresses the fundamental concept of selection (Frank 2012a). As defined in proposition 2, frequencies change according to differences in fitness (eq. 9.2). Thus, selection is the change in character value caused by differences in fitness, holding constant other evolutionary forces that may alter the character values,  $z_i$ .

### *Frequency Change during Transmission*

We may consider the other forces that alter characters as the change during transmission. Define  $\Delta z_i = z'_i - z_i$  as the difference between the average value among descendants derived from ancestral type  $i$  and the average value of ancestors of type  $i$  (proposition 3). Then  $\sum q'_i \Delta z_i$  is the change during transmission when measured in the context of the descendant population. Here,  $q'_i$  is the fraction of the descendant population derived from ancestors of type  $i$ .

Thus, the total change,  $\Delta \bar{z} = \bar{z}' - \bar{z}$ , is exactly the sum of the change caused by selection (proposition 2) and the change during transmission (propositions 3 and 4):

$$(9.4) \quad \Delta \bar{z} = \sum \Delta q_i z_i + \sum q'_i \Delta z_i,$$

a form of the Price equation (G. R. Price 1972a; Frank 2012a). We abbreviate the two components of total change as:

$$(9.5) \quad \Delta \bar{z} = \Delta_s \bar{z} - \Delta_c \bar{z},$$

which partitions total change into a part ascribed to natural selection,  $\Delta_s$ , and a part ascribed to changes in characters during transmission,  $\Delta_c$  (prop-

osition 4). The change in transmission subsumes all evolutionary forces beyond selection.

### *Characters and Covariance*

We can express the fundamental equation of selection in terms of the covariance between fitness and character value. Combining eqs. 9.2 and 9.3 leads to:

$$(9.6) \quad \Delta_s \bar{z} = \sum \Delta q_i z_i = \sum q_i (w_i - 1) z_i.$$

The right-hand side matches the definition for the covariance between fitness,  $w$ , and character value,  $z$ , so we can write:

$$(9.7) \quad \Delta_s \bar{z} = \text{Cov}(w, z),$$

which we can rewrite as a product of a regression coefficient and a variance term:

$$(9.8) \quad \Delta_s \bar{z} = \text{Cov}(w, z) = \beta_{zw} V_w,$$

in which  $V_w$  is the variance in fitness and

$$\beta_{zw} = \frac{\text{Cov}(w, z)}{V_w}$$

is the classic statistical definition of the regression of phenotype,  $z$ , on fitness,  $w$ . The statistical covariance, regression, and variance functions commonly arise in the literature on selection (Robertson 1966; G. R. Price 1970; Lande and Arnold 1983; Falconer and Mackay 1996).

### *Gene Frequencies*

Treating the character  $z$  as an allele frequency, we can relate the above equations with the classical equations of population genetics. Assume that each individual carries one allele. For the  $i$ th individual,  $z_i = 0$  when the individual carries the normal allelic type, and  $z_i = 1$  when the individual carries a variant allele. Then the frequency of the variant allele in the  $i$ th individual is  $p_i = z_i$ , the allele frequency in the population is  $\bar{p} = \bar{z}$ , and the initial frequency of each of the  $N$  individuals is  $q_i = 1/N$ . From eq. 9.6, the change in the allele frequency is

$$(9.9) \quad \Delta_s \bar{p} = \frac{1}{N} \sum (w_i - 1) p_i.$$

From the prior section, we can write the population genetics form in terms of statistical functions:



$$(9.10) \quad \Delta_s \bar{p} = \text{Cov}(w, p) = \beta_{pw} V_w.$$

For analyzing allele frequency change, the population genetics form in eq. 9.9 is often easier to understand than eq. 9.10, which is given in terms of statistical functions. This advantage for the population genetics expression in the study of allele frequencies emphasizes the value of using specialized tools to fit particular problems.

By contrast, the more abstract statistical form in eq. 9.10 has advantages when studying the conceptual structure of natural selection and when trying to partition the causes of selection into components (proposition 5). Suppose, for example, that one wishes to know only whether the allele frequency is increasing or decreasing. Then eq. 9.10 shows that it is sufficient to know whether  $\beta_{pw}$  is positive or negative, because  $V_w$  is always positive. That sufficient condition is difficult to see in eq. 9.9, but is immediately obvious in eq. 9.10. One use of the kind of theory discussed in this volume is to understand the fundamental relationships between models that appear initially to be quite different from one another (see also Phillips, chap. 4).

### **Generalizing from the Basic Models: Scale, Distance, and Invariance**

This volume focuses on the structure of evolutionary theory. To consider the fundamental role of natural selection within that broad theory, this section discusses a few key conceptual issues. In the first subsection below, we show that selection can be described in several equivalent forms: as a variance, as a distance, or as a gain of statistical information. Each of those descriptions is especially useful in a different context. The second subsection considers the common alternatives for analysis of evolutionary change: the change in phenotypic characters or the change in fitness. We show that these two alternatives for the analysis of evolutionary change are just alternative coordinate systems (like Cartesian and polar coordinates) that can readily be related to one another. Each alternative is especially useful under particular circumstances. These first two subsections provide three different ways to describe selection and two different coordinate systems for evolutionary change. Those combinations show the connections between various approaches and give us some freedom in developing evolutionary models.

The third subsection examines what we need to know in order to address particular questions about natural selection. For example, if we want to study questions about the detailed dynamics of evolutionary change for

a particular trait, we typically need to know a lot about the trait's genetic architecture. On the other hand, if we want to ask whether selection is likely to account for some part of the difference between two populations, the answer will not generally depend on such details. Understanding what information is sufficient to answer a question provides crucial guidelines for the development of useful models.

### *Variance, Distance, or Information*

The variance in fitness,  $V_w$ , arises in one form or another in every expression of selection. Why is the variance a universal metric of selection? Clearly, variation matters because selection favors some types over others only when the alternatives differ. But why does selection depend exactly on the variance rather than on some other measure of variation? We will show (proposition 2) that natural selection moves the population a certain distance. That distance is equivalent to the variance in fitness. Thus, we may think about the change caused by selection equivalently in terms of variance or distance.

We begin by noting from eq. 9.2 that  $\Delta q_i/q_i = w_i - 1$ . Then, the variance in fitness is:

$$(9.11) \quad V_w = \sum q_i (w_i - 1)^2 = \sum q_i \left( \frac{\Delta q_i}{q_i} \right)^2 = \sum \frac{(\Delta q_i)^2}{q_i}.$$

The squared distance in Euclidean geometry is the sum of the squared changes in each dimension. On the right is the sum of the squares for the change in frequency. Each dimension of squared distance is divided by the original frequency. That normalization makes sense, because a small change relative to a large initial frequency means less than a small change relative to a small initial frequency. The variance in fitness measures the squared distance between the ancestral and descendant population in terms of the frequencies of the types, as proposition 2 and eq. 9.2 imply (Ewens 1992; Frank 2012b, a).

When the frequency changes are small, the expression on the right equals the Fisher information measure (Frank 2009). A slightly different measure of information arises in selection equations when the frequency changes are not small (Frank 2012b), but the idea is the same. Selection acquires information about environmental challenges through changes in frequency. Although this point may seem abstract, it may be a more accurate description of the process of adaptation than to say that phenotypes

have fitnesses and populations climb fitness peaks, because individuals and populations respond to the environment rather than possess fitnesses.

Thus, we may think of selection in terms of variance, distance, or information. Selection moves the population frequencies a distance that equals the variance in fitness. That distance is equivalent to the gain in information by the population caused by selection.

### *Characters and Coordinates*

We can think of fitness and characters as alternative coordinates in which to measure the changes caused by natural selection in frequency, distance, and information. Using eq. 9.2, we can rewrite the variance in fitness from eq. 9.11 as:

$$V_w = \sum q_i (w_i - 1)^2 = \sum \Delta q_i w_i.$$

Compare that expression with eq. 9.3 for the change in the character value caused by selection. If we start with the right side of the expression for the variance in fitness and then replace  $w_i$  by  $z_i$ , we obtain the change in character value caused by selection. We can think of that replacement as altering the coordinates on which we measure change, from the frequency changes described by fitness,  $w_i = q_i'/q_i$ , to the character values described by  $z_i$ .

Although this description in terms of coordinates may seem a bit abstract, it is essential for thinking about evolutionary change in relation to selection. Selection changes frequencies. The consequences of frequency for the change in characters depend on the coordinates that describe the translation between frequency change and characters (Frank 2012b, 2013a).

Eq. 9.4 provides an exact expression that includes four aspects of evolutionary change. First, the change in frequencies,  $\Delta q_i$ , causes evolutionary change. Second, the amount of change depends on the coordinates of characters,  $z_i$ . Third, the change in the coordinates of characters during transmission,  $\Delta z_i$ , causes evolutionary change (proposition 3). Fourth, the changed coordinates have their consequences in the context of the frequencies in the descendant population,  $q_i'$  (proposition 4).

In models of selection, one often encounters the variance in characters,  $V_z$ , rather than the variance in fitness,  $V_w$ . The variance in characters is simply a change in scale with respect to the variance in fitness—another way in which to describe the translation between the coordinates for frequency change and the coordinates for characters. In particular,


$$(9.12) \quad \Delta_s \bar{z} = \text{Cov}(w, z) = \beta_{zw} v_w = \beta_w \text{ (with icon)}$$

thus

$$V_z = \begin{pmatrix} \beta_{zw} \\ \beta_{wz} \end{pmatrix} V_w = \gamma V_w.$$

Here,  $\gamma$  is based on the regression coefficients. The value of  $\gamma$  describes the rescaling between the variance in characters and the variance in fitness. Thus, when  $V_z$  arises in selection equations, it can be thought of as the rescaling of  $V_w$  in a given context (Frank 2013a).

### Sufficiency and Invariance

Having seen that there are alternative ways to model evolution and adaptation (Phillips, chap. 4), and that they are all related to one another, it seems appropriate to ask: What do we need to know to analyze natural selection? The notion of *sufficiency* is useful here. Informally, a statistic is sufficient for estimating a quantity if no other statistic can be calculated from a sample that provides more information. A familiar example is that of the normal distribution. If we know the variance, , then the mean in a sample,  $x$ , is a sufficient statistic for the true mean,  $\mu$ , because we cannot calculate any other statistic that provides more information about the true mean.

We compare two alternative modeling approaches. One provides full information about how the population evolves over time. The other considers only how natural selection alters average character values at any instant in time.

A full analysis begins with the change in frequency given in eq. 9.2. For each type in the population, we must know the initial frequency,  $q_i$ , and the fitness,  $w_i$ . From those values, each new frequency can be calculated. Then new values of fitnesses would be needed to calculate the next round of updated frequencies. Fitnesses can change with frequencies and with extrinsic conditions. That calculation provides a full description of the evolutionary dynamics over time. The detailed output concerning dynamics reflects the detailed input about all of the initial frequencies and all of the fitnesses over time.

A more limited analysis arises from the part of total evolutionary change caused by selection. If we focus on the change by selection in the average value of a character at any point in time, we have

$$\Delta_s \bar{z} = \sum \Delta q_i z_i = \text{Cov}(w, z) = \beta_{zw} \text{ (with icon)}$$

from eqs. 9.6 and 9.8.

To calculate the change in average value caused by selection, it is sufficient to know the covariance between the fitnesses and character values over the population. We do not need to know the individual frequencies or the individual fitnesses. It is sufficient to know a single summary statistic over the population, the covariance. Put another way, a single assumed input (the covariance) corresponds to a single output (the change in average value caused by selection). We could, of course, make more complicated assumptions about inputs and get more complicated outputs.

Invariance provides another way to describe sufficiency and the causal effect of selection in populations. The mean change in the character value caused by selection does not depend on (is invariant to) any aspect of variability except the covariance. Many alternative populations with different character values and fitnesses have the same covariance and thus the same change in the character value caused by selection. The reason is that the variance in fitness,  $V_w$ , describes the distance the population moves with regard to frequencies, and the regression  $\beta_{zw}$  rescales the distance along coordinates of frequency into distance along coordinates of the character. Thus, simple invariances sometimes can provide great insight into otherwise complex problems (Frank 2013b).

For example, Fisher's fundamental theorem of natural selection is a simple invariance (Frank 2012c). The theorem states that at any instant in time, the change in average fitness caused by selection is equal to the genetic variance in fitness (discussed below). Fisher's theorem shows that the change in mean fitness by selection is invariant to all details of variability in the population except the genetic variance.

### Causal Models

We now turn to emphasize inductive approaches. Eq. 9.12 describes associations between characters and fitness. In that equation, we know only that a character,  $z$ , and fitness,  $w$ , are correlated, as expressed by  $\text{Cov}(w,z)$ . We do not know anything about the causes of correlation and variance. But we may have a model about how variation in characters causes variation in fitness. To study that causal model, we must analyze how the hypothesized causal structure predicts correlations between characters, fitness, and evolutionary change. Alternative causal models provide alternative hypotheses and predictions that can be compared with observation (Crespi 1990; Frank 1997, 1998; Scheiner et al. 2000).

Regression equations provide a simple way in which to express hypothesized causes (Li 1975). For example, we may have a hypothesis that the

character  $z$  is a primary cause of fitness,  $w$ , expressed as a directional path diagram  $z \rightarrow w$ . That path diagram, in which  $z$  is a cause of  $w$ , is mathematically equivalent to the regression equation

$$(9.13) \quad w_i = \varphi + \beta_{wz} z_i + \varepsilon_i,$$

in which  $\varphi$  is a constant and  $\varepsilon_i$  is the difference between the actual value of  $z_i$  and the value predicted by the model:  $\varphi + \beta_{wz} z_i$ .

### *Multiple Characters*

Proposition 5 asserts that we can partition fitness into the amounts of change caused by different characters. Here we show how this can be done. To analyze causal models, we focus on the general relations between variables rather than on the values of particular individuals or genotypes. Thus, we can drop the  $i$  subscripts in eq. 9.13 to simplify the expression, as in the following expanded regression equation

$$(9.14) \quad w = \varphi + \beta_{wz \cdot y} z + \beta_{wy \cdot z} y + \varepsilon.$$

Here, fitness  $w$  depends on the two characters  $z$  and  $y$  (Lande and Arnold 1983). The partial regression coefficient  $\beta_{wz \cdot y}$  is the average effect of  $z$  on  $w$  holding  $y$  constant, and  $\beta_{wy \cdot z}$  is the average effect of  $y$  on  $w$  holding  $z$  constant. Regression coefficients minimize the total distance (sum of squares) between the actual and predicted values. Minimizing the residual distance maximizes the use of the information contained in the predictors about the actual values.

This regression equation is exact, in the sense that it is an equality under all circumstances. No assumptions are needed about additivity or linearity of  $z$  and  $y$  or about normal distributions for variation. Those assumptions arise in statistical tests of significance when comparing the regression coefficients with hypothesized values or when predicting how the values of the regression coefficients change with context.

Note that the regression coefficients ( $\beta$ ) often change as the values of  $w$  or  $z$  or  $y$  change, or if we add another predictor variable. The exact equation is a description of the relations between the variables as they are given. The structure of the relations between the variables forms a causal hypothesis that leads to predictions (Li 1975).

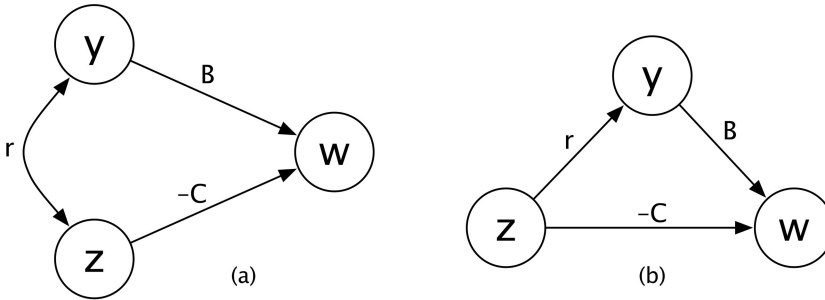


Figure 9.1. Path diagrams for the effects of phenotype  $z$  and secondary predictor  $y$  on fitness  $w$ . (a) An unknown cause associates  $y$  and  $z$ . The arrow connecting those factors points both ways, indicating no particular directionality in the hypothesized causal scheme. (b) The phenotype,  $z$ , directly affects the other predictor,  $y$ , which in turn affects fitness. The arrow pointing from  $z$  to  $y$  indicates the hypothesized direction of causality. The choice of notation matches kin selection theory, in which  $z$  is an altruistic behavior that reduces the fitness of an actor by the cost  $C$  and aids the fitness of a recipient by the benefit  $B$ , and  $r$  measures the association between the behaviors of the actor and recipient. Although that notation comes from kin selection theory, the general causal scheme applies to any pair of correlated characters that influences fitness (Lande and Arnold 1983; Queller 1992). From Frank (2013a).

### Partitions of Fitness

We can interpret eq. 9.14 as a hypothesis that partitions fitness into two causes (proposition 5). Suppose, for example, that we are interested in the direct effect of the character  $z$  on fitness. To isolate the direct effect of  $z$ , it is useful to consider how a second character,  $y$ , also influences fitness (fig. 9.1).

The condition for  $z$  to increase by selection can be evaluated with eq. 9.12. That equation simply states that  $z$  increases when it is positively associated with fitness. However, we now have the complication shown in eq. 9.14 that fitness also depends on another character,  $y$ . If we expand  $\text{Cov}(w, z)$  in eq. 9.12 with the full expression for fitness in eq. 9.14, we obtain

$$(9.15) \quad \Delta_s \bar{z} = \beta_{wz} V_z = (\beta_{wz \cdot y} + \beta_{wy \cdot z} \beta_{yz}) V_z.$$

Following Queller (1992), we abbreviate the three regression terms. The term  $\beta_{wz \cdot y}$  describes the association between the phenotype,  $z$ , and the other predictor of fitness,  $y$ . An increase in  $z$  by the amount  $\Delta z$  corresponds to an average increase of  $y$  by the amount  $\Delta y = r \Delta z$ . The term  $\beta_{wy \cdot z} = B$  describes the direct effect of the other predictor,  $y$ , on fitness, holding constant the focal phenotype,  $z$ . The term  $\beta_{wz \cdot y} = -C$  describes the direct effect of the phenotype,  $z$ , on fitness,  $w$ , holding constant the effect of the other predictor,  $y$ .

The condition for the increase of  $z$  by selection is  $\Delta_s \bar{z} > 0$ . The same condition using the terms on the right side of eq. 9.15 and the abbreviated notation of the previous paragraph is:

$$(9.16) \quad rB - C > 0$$

This is Hamilton's famous equation for kin selection (Hamilton 1964a, 1970). We use this equation here to emphasize the fact that Hamilton's model is a particular case of a much more general relationship. The condition in eq. 9.16 applies whether the association between  $z$  and  $y$  arises from some unknown extrinsic cause (fig. 9.1a) or by the direct relation of  $z$  to  $y$  (fig. 9.1b).

This expression describes the condition for selection to increase character  $z$  when ignoring any changes in the character that arise during transmission. Thus, when one wants to know whether selection acting by this particular causal scheme would increase a character, it is sufficient to know if this simple condition holds.

### *Testing Causal Hypotheses*

If selection favors an increase in character  $z$ , then the condition in eq. 9.16 will always be true. That condition simply expresses the fact that the slope of fitness on character value,  $\beta_{wz}$ , must be positive when selection favors an increase in  $z$ . The expression  $\beta_{wz} = rB - C$  is one way in which to partition  $\beta_{wz}$  into components. However, the fact that  $rB - C > 0$  does not mean that the decomposition into those three components always provides a good causal explanation for how selection acts on the character  $z$ .

There are many alternative ways in which to partition the total effect of selection into components. Other characters may be important. Environmental or other extrinsic factors may dominate. How can we tell if a particular causal scheme is a good explanation?

If we can manipulate the effects  $r$ ,  $B$ , or  $C$  directly, we can run an experiment. If we can find natural comparisons in which those terms vary, we can test comparative hypotheses. If we add other potential causes to our model, and the original terms hold their values in the context of the changed model, that stability of effects under different conditions increases the likelihood that the effects are true.

Three points emerge. First, a partition such as  $rB-C$  is sufficient to describe the direction of change, because a partition simply splits the total change into parts. Second, a partition does not necessarily describe causal



relations in an accurate or useful way. Third, various methods can be used to test whether a causal hypothesis is a good explanation.

### Partitions of Characters

We have been studying the partition of fitness into separate causes, including the role of individual characters. It is sometimes useful to partition individual characters into separate causes as well, such as contributions of different alleles, or of other factors (proposition 5). Each character may itself be influenced by various causes. We can describe the cause of a character by a regression equation:

$$z = \varphi + \beta_{zg}g + \delta,$$

in which  $\varphi$  is a constant traditionally set to zero,  $g$  is a predictor of phenotype, the regression coefficient  $\beta_{zg}$  is the average effect of  $g$  on phenotype  $z$ , and  $\delta = z - \beta_{zg}g$  is the residual between the actual and predicted values. For predictors  $g$ , we could use temperature, neighbors' behavior, another phenotype, epistatic interactions given as the product of allelic values, symbiont characters, or an individual's own genes.

Fisher (1918) first presented this regression for phenotype in terms of alleles as the predictors. Suppose

$$(9.17) \quad g = \sum_j b_j x_j,$$

in which  $x_j$  is the presence or absence of an allelic type. Then each  $b_j$  is the partial regression of an allele on phenotype, which describes the average contribution to phenotype for adding or subtracting the associated allele. The coefficient  $b_j$  is called the average allelic effect, and  $g$  is called the breeding value (Fisher 1930; Crow and Kimura 1970; Falconer and Mackay 1996). When  $g$  is defined as the sum of the average effects of the underlying predictors, then  $\beta_{zg} = 1$ , and

$$(9.18) \quad z = g + \delta$$

where  $\delta = z - g$  is the difference between the actual value and the predicted value.

### Transmission

Now we turn to include transmission in our models. To do so it is useful to note some facts. If we take the average of both sides of eq. 9.18, we get  $\bar{z} = \bar{g}$ ,

because  $\bar{\delta} = 0$  by the theory of regression. If we take the variance of both sides, we obtain  $V_z = V_g + V_\delta$ , noting that, by the theory of regression,  $g$  and  $\delta$  are uncorrelated.

### *Heritability and the Response to Selection*

To study selection, we first need an explicit form for the relation between character value and fitness, which we write here as

$$w = \varphi + \beta_{wz}z + \varepsilon.$$

Substituting that expression into the covariance expression of selection in eq. 9.12 yields:

$$(9.19) \quad \Delta_s \bar{z} = \text{Cov}(w, z) = \beta_{wz} V_z = sV_z,$$

because  $\varphi$  is a constant and  $\varepsilon$  is uncorrelated with  $z$ , causing those terms to drop out of the covariance. Here, the coefficient  $s = \beta_{wz}$  is the effect of the character on fitness. Expanding  $sV_z$  by the partition of the character variance (proposition 5) given in the previous section leads to:

$$(9.20) \quad \Delta_s \bar{z} = sV_z = sV_g + sV_\delta = \Delta_g \bar{z} + \Delta_n \bar{z}.$$

We can think of  $g$  as the average effect of the predictors of phenotype that we have included in our causal model of character values. Then  $sV_g = \Delta_g \bar{z}$  is the component of total selective change associated with our predictors, and

$$(9.21) \quad \Delta_g \bar{z} = \Delta_s \bar{z} - \Delta_n \bar{z}$$

shows that the component of selection transmitted to descendants through the predictors included in our model,  $\Delta_g$ , is the change caused by selection,  $\Delta_s$  (proposition 1), minus the part of the selective change that is not transmitted through the predictors,  $\Delta_n$  (proposition 4). Although it is traditional to use alleles as predictors, we can use any hypothesized causal scheme. For example, one of the predictors could be the presence or absence of a particular bacterial species in the gut. When one adds gut bacteria as predictors, or new alleles not previously accounted for, the expanded causal model typically assigns greater cause to the totality of predictors,  $\Delta_g$ , and less cause to the remaining component of change,  $\Delta_n$ . Thus, the separation between transmitted and nontransmitted components of selection depends on the hypothesis for the causes of the phenotype.

If we choose the predictors for  $g$  to be the individual alleles that influence the phenotype, then  $V_g$  is the traditional measure of genetic vari-


ance, and  $sV_g$  is that component of selective change that is transmitted from parent to offspring through the effects of the individual alleles. The fraction of the total change that is transmitted,  $V_g/V_{z'}$ , is a common measure of heritability.

### *Changes in Transmission and Total Change*

We now have the tools needed to find the total evolutionary change when considered in terms of the parts of phenotype that are transmitted to descendants. Here, the transmitted part arises from the predictors in an explicit causal hypothesis about phenotype.

From eq. 9.18,  $\bar{z} = \bar{g}$ , because the average residuals of a regression,  $\bar{\delta}$ , are zero. Thus, when studying the change in a character, we have  $\Delta\bar{z} = \Delta\bar{g}$ , which means that we can analyze the change in a character by studying the change in the average effects of the predictors of a character. From eq. 9.4, we can write the total change in terms of the coordinates of the average effects of the predictors,  $g$ , yielding:

$$(9.22) \quad \Delta\bar{z} = \sum \Delta q_i g_i + \sum q'_i \Delta g_i = \Delta_g \bar{z} + \Delta_t \bar{z},$$

in which  is the change in the average effects of the predictors during transmission (Frank 1997, 1998). The total change divides into two components (proposition 4): the change caused by the part of selection that is transmitted to descendants plus the change in the transmitted part of the phenotype between ancestors and descendants. Alternatively, we may write  $\Delta_g \bar{z} = \Delta_s \bar{g}$ , the total selective component expressed in the coordinates of the average effects of the predictors, and  $\Delta_t \bar{z} = \Delta_c \bar{g}$ , the total change in coordinates with respect to the average effects of the predictors.

### *Choice of Predictors*

If natural selection dominates other evolutionary forces, then we can use the theory of natural selection to analyze evolutionary change. When does selection dominate? From eq. 9.22, the change in phenotype caused by selection is  $\Delta_g$ . If the second term  $\Delta_t$  is relatively small, then we can understand evolutionary change primarily through models of selection.

A small value of the transmission term,  $\Delta_t$ , arises if the effects of the predictors in our causal model of phenotype remain relatively stable between ancestors and descendants. Many factors may influence the phenotype, including alleles and their interactions, maternal effects, various epigenetic processes, changing environment (Scheiner, chap. 13), and so on. Finding

a good causal model of the phenotype in terms of predictors is an empirical problem that can be studied by testing alternative causal schemes against observation.

Note that the equations of evolutionary change do not distinguish between different kinds of predictors. For example, one can use both alleles and weather as predictors. If weather varies among types and its average effect on phenotype transmits stably between ancestors and descendants, then weather provides a useful predictor. Variance in stably transmitted weather attributes can lead to changes in characters by selection. Calling the association between weather and fitness an aspect of selection may seem strange or misleading. One can certainly choose to use a different description. But the equations themselves do not distinguish between different causes.

## Discussion

### *The Uses of Inductive versus Deductive Approaches*

Sometimes it makes sense to think in terms of deductive predictions. What do particular assumptions about initial conditions, genetic interactions, and the fitnesses predict about evolutionary dynamics? For example, if we know the current frequency of genotypes, the fitnesses of those genotypes, and the pattern of mating between genotypes, then we can deductively predict the dynamics of change in genotype frequencies between the original population and their descendants.

Sometimes it makes sense to think in terms of inductive analysis. Given the observed changes between ancestor and descendant populations, how much do different causes explain of that total distance? For example, if we know the current phenotypes of individuals, and we observe the phenotypes of offspring, then we can inductively estimate the causes of the observed changes in terms of the partitioning of fitness into different estimated strengths of selection acting on the individual phenotypes.

### *Accomplishments of Inductive Theory*

We illustrate the value of inductive theory with three examples. First, inductive approaches provide empirical methods for the study of natural selection in populations. Typically, one begins with data about the reproductive success of individuals and about measurements of various characters of those individuals. One then asks questions such as: How much does

an increase in body weight enhance reproductive fitness? How much does stress measured by cortisol level reduce reproductive fitness?

Although these are simple questions, one has data only about the correlations between various characters and fitness. Teasing out estimated causal relations from such correlational data can be difficult. In other words, it is not so easy to inductively arrive at the relative causal strengths for the various characters in the explanation of variation in observed values of fitness. For example, suppose that larger body size is correlated with both reduced cortisol level and increased fitness. How do we explain the causes of increased fitness? It could be that large body size directly increases fitness and that reduced stress is correlated with large body size. Or it could be that reduced stress reflects good physiological health and immune system status, which directly enhance both fitness and body size.

Distinguishing between these alternative hypotheses requires a careful approach to the inductive analysis of natural selection. Lande and Arnold (1983) initiated modern approaches to inductive methods. Many subsequent approaches to inductive analysis have been developed, including techniques such as path analysis (Crespi 1990; Frank 1997, 1998; Scheiner et al. 2000) and an analytical approach known as Aster (R. G. Shaw and Geyer 2010).

Second, the theory of kin selection has developed complementary deductive and inductive approaches. The original deductive theory by Hamilton (1964a, 1970) made assumptions about the frequencies and fitnesses of alternative genes. Those genes were associated with altruistic behaviors that benefit relatives at a cost to the actor that performs the behavior. For example, a bee in a social colony might help her mother to reproduce rather than reproduce herself. That altruistic behavior benefits her mother's reproduction and simultaneously imposes a cost on her own reproduction. When would natural selection favor such an altruistic behavior that reduces the actor's own direct fitness?

From assumptions about the direct cost of altruistic behavior and the benefit to the recipient of the altruism, Hamilton used population genetics to deduce the conditions under which increased altruism would evolve by natural selection. Put another way, he analyzed the conditions that favor an increase in the frequency of genes associated with altruism. He found the condition  $rB - C > 0$  for the increase in altruism, in which  $C$  is the direct cost in fitness of the altruistic behavior,  $B$  is the recipient's benefit from the altruistic behavior, and  $r$  is the relatedness between actor and recipient.

Hamilton's original theory assumed a given partition of the causes of fitness into a part attributed to the cost of the behavior and a part attrib-

uted to the benefit of the behavior. That deductive theory makes predictions about behavior. By contrast, actual studies of natural populations often obtain data about observed behaviors, relatedness, and reproductive fitness. From those data, one inductively estimates the partition of fitness into costs to the individual that expresses the character and benefits to the individuals that receive the consequences of the character.

Queller (1992) recognized the identical structure of Hamilton's original deductive theory and the inductive methods of Lande and Arnold (1983). Following Queller's insight, the modern theory of kin selection unified deductive and inductive theories into a single approach that focuses on the partitioning of fitness into causal components associated with various characters and their associated costs and benefits (Frank 1997, 1998). In this context, group selection is an alternative way to partition the causes of fitness into components (Goodnight, chap. 10; Hamilton 1975; Frank 1986, 1998).

Third, inductive approaches provide methods for the analysis of molecular genetic data. Before extensive molecular data were available, almost all population genetic theory was deductive. After molecular data became common, inductive theory dominated (Ewens 1990). Classically, one began with alleles and fitnesses, and then deduced gene frequency changes (Crow and Kimura 1970). Since the molecular revolution, one typically begins with current samples of alleles and then tries to induce the historical states and processes of the past (Graur 2016). For example, given an observed sample of DNA sequences in a population, one may compare a variety of alternative processes that might have generated the observed sample. One can ask which of the alternative processes is most likely to generate the observed pattern, an inductive perspective that begins with the observed data.

Suppose we have a sample of nucleotide sequences obtained from influenza viruses over a series of annual epidemics. We can reconstruct a phylogenetic history of the viruses from those nucleotide sequences. Within that history, we can estimate how particular nucleotides and associated amino acids changed over time. We can then ask: How has natural selection acted on particular amino acids that coat the surface of the virus? We may inductively conclude that certain amino acids changed in a manner correlated with the virus's escape from recognition by host immunity and subsequent spread in the next epidemic, suggesting that natural selection favors rapid evolution of those particular amino acids (R. M. Bush et al. 1999). Once again, we have inductively assigned a potential causal role of natural selection to explain the pattern of changes we observe in populations.

### *Status of the Theory*

The theory of natural selection provides many of the key insights for understanding how organisms evolve. Several chapters in this volume illustrate the primacy of selection, including chapter 11 on the evolution of life histories (Fox and Scheiner), chapter 12 on ecological specialization (Poisot), chapter 13 on phenotypic plasticity (Scheiner), and chapter 14 on recombination (Orive).

As the theory of natural selection matured in the 1970s and 1980s, empirical studies showed it to be one of the best-supported theories in science (Endler 1986). The advent of modern computers and modern statistical methods led to extensive reviews of this empirical support, including quantification of such things as the strength of selection (Hoekstra et al. 2001; Kingsolver et al. 2001; Nielsen 2005). Nevertheless, the subtlety of the concepts suggests a need for evolutionary biologists to pursue deeper understanding of the theory and its implications.

As an example of deeper conceptual issues, we have emphasized that Price's formulation provides a useful way to understand the relations between deductive and inductive approaches to selection. Both deductive and inductive approaches play key roles in efforts to understand the diverse evolutionary patterns discussed in chapters 11–14 below. The approach taken in this chapter helps to clarify the points of connection (and of contrast) between the inductive and deductive approaches. Because of the recent increase in scientists' interest in and capability of collecting large datasets, we expect that inductive approaches to understanding natural selection will become increasingly important.

There has also been a trend in many information sciences to develop new methods of learning and inference that can be applied to large datasets beyond biology. The conceptual challenges in those various subjects often hint at the need to understand more deeply how information accumulates by various trial and error algorithms. Our understanding of natural selection will likely contribute to and gain from those broader developments in modern science.

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