1 Math for Evolution: Holy Grail or Poisoned Chalice?

Like any other advanced science, contemporary evolutionary theory is highly mathematized. The history and dynamics of evolutionary processes are described and explained in the language of probability, differential equations, and linear algebra, as can be easily confirmed by a look at major journals like *Evolution, Genetics*, or *The American Naturalist* or standard textbooks on evolutionary genetics. This is in stark contrast with Darwin's *Origin of Species*, which established the fact and principle of evolution with an overwhelming mass of empirical examples but not a single equation. Evolutionary theory, therefore, was mathematized at some point after its birth – but when, and why?

Although mathematics surely did not give birth to Darwin's theory, it *saved* its life, or at least the life of one of its halves – halves, because Darwin submitted two logically independent theses in his *Origin*. One is the historical hypothesis that diverse forms of life on earth have emerged by the branching of a few or possibly just one primitive kind. This is called *the principle of common descent*, the one that tells you that humans are distant relatives of bacteria. Darwin's second thesis, which was also independently proposed by Alfred Wallace, is the famous *principle of natural selection*, which claims that evolutionary changes and speciation occur because individuals in a population differ in their ability to survive and reproduce, and these abilities tend to be inherited by their offspring.

Of these two theses, the principle of common descent was soon accepted with little antagonism, at least in the scholarly circle of the late nineteenth century. Many biologists, however, resisted the idea of natural selection as a major cause of such historical changes for three reasons (Provine, 2001). The first source of disagreement was insufficient knowledge about the mechanism of inheritance. Darwin presupposed a sort of "blending" inheritance, whereby parents' characteristics mix in their offspring's phenotype so that if a new mutant with an advantageous characteristic mates with an average individual in the population, their offspring will show an intermediate character. But this entails that any advantageous trait that arises with a single mutant in a population will be diluted away after a few rounds of sexual reproduction, well before it could be spread throughout the population or species by selection (Fig. 1.1). Selection would then require a large number of mutational inputs to change the population structure, making it no more than a negligible factor. The second issue came from failures of contemporary experiments that tried to create a new species or a significant variant with visible morphological differences by repeated artificial selection in the laboratory. The negative results of these experiments suggested the existence of a deep gap between species that natural selection cannot overcome.
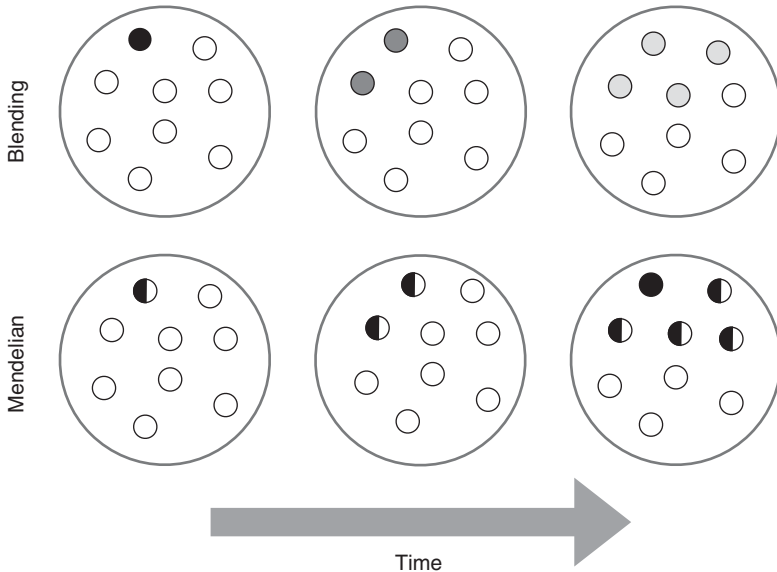
Figure 1.1 If parents traits "blended" in offspring's phenotype, a rare beneficial characteristic would be diluted away before selection can act on it. In Mendelian inheritance, a parent's allele is passed on to offspring as it is.

Sympathizers of Darwin could and did respond that adaptive processes take a much longer time than the duration of these experiments; but having no means to confirm consequences of such lengthy processes, their rebuttal remained speculative and held no water against most contemporary critics with a positivist slant who, in the wake of experimental biology, put much emphasis on well-controlled and reproducible experiments. The third obstacle for the Darwinian theory concerned its compatibility with Mendelian genetics, which was rediscovered around the beginning of the twentieth century and soon became accepted as a correct description of the mechanism of inheritance. Mendel's pea experiment showed that organismal characteristics "jump" from one type to another (yellow or green, smooth or wrinkled) by the transmission of discrete factors we now call genes or alleles. This result, however, seemed to contradict Darwin's claim that evolution by natural selection is a gradual process that acts on subtle, and mostly continuous, variations. Moreover, such a gradual evolution appeared to be far less effective. Upon the observation that significant morphological changes are often triggered by single genetic replacements, Mendelian geneticists concluded that the creation of new variants or "sports" by such mutations plays a far more important role in major evolutionary changes and speciation than does selection. Faced with these criticisms and difficulties, the Darwinian theory of

natural selection around the turn of the twentieth century was almost abandoned, even to the extent that American biologist Vernon Kellogg worried that Darwinism was on its "death-bed" (Bowler, 1983).

As seen from the discussion above, the skepticism against natural selection was targeted at its *efficacy*. The suspicion was not that natural selection is impossible, but that it plays only a minor and secondary role compared to other evolutionary forces such as mutation. To this question of degree, Darwin's qualitative and schematic arguments in his *Origin* had no substantive answer. The resolution of these issues had to wait for the integration of Darwin's theory with the Mendelian theory of genetics, in which mathematical formulations of selection and reproduction played an essential role in showing how and to what extent selection can alter biological populations (Provine, 2001, ch. 5). On the first problem of blending inheritance, G. H. Hardy and W. Weinberg independently found in 1908 that in the absence of other evolutionary forces (such as selection or migration) the genotype frequency of a Mendelian population stabilizes at a fixed ratio we now call the Hardy–Weinberg equilibrium. If, for instance, there are two alleles *A,a* in the population with the frequencies $Pr(A) = p$ and $Pr(a) = q = 1 - p$, the relative frequencies of the three genotypes *AA:Aa:aa* stay $p^2 : 2pq : q^2$. This implies that a variation introduced into a population as a few mutant alleles will not get diluted away but will remain as it is, giving room and opportunity for selection to increase its frequency. But how long does this process take? To examine the second skeptical argument that selection alone cannot achieve much evolutionary change, R. C. Punnett and his fellow mathematician H. T. J. Norton calculated the number of generations required for selection to change gene frequency in a population (Punnett, 1915). The result of their numerical calculation showed that even a trait with the slightest selective advantage can sweep through a population in a relatively short period, vindicating the efficacy of gradual selection. These mathematical developments culminated in Ronald Fisher's (1918) formal integration of the Darwinian theory of selection with Mendelian genetics, which reduced gradual evolution of continuous traits (such as height) to frequency changes of a large array of underlying genes, each having a small phenotypic effect. This result allowed Fisher to calculate and predict the evolutionary response of a continuous phenotype to a given selective pressure (see Section 5) and to reformulate the Darwinian gradual evolution within the Mendelian framework, showing their logical consistency. These theoretical developments dispelled the skepticism against the Darwinian theory, and in the early 1920s natural selection came to be acknowledged as one of the most important forces to produce evolutionary change.

The formal integration with Mendelian genetics not only helped Darwin's theory of natural selection, but also put mathematics at the center of evolutionary studies. Fisher's work, along with other seminal contributions by S. Wright and J. B. S. Haldane, gave birth to the new field of *population genetics* and formed the theoretical core of the "Modern Synthesis," the standard paradigm of evolutionary studies in the twentieth century. The canonical evolutionary theory characterizes organisms by two aspects, *genotype* (a set of genes organisms possess) and *phenotype* (any other physiological, morphological, or behavioral features such as height or metabolic rate), and accordingly a population of organisms by its genetic and phenotypic distributions. Population distributions can be formally represented as points in *genetic or phenotypic spaces*, in which evolutionary processes are conceptualized as trajectories or movements of these points (Lloyd, 1988). Since genotypic and phenotypic characterizations are two sides of the same coin, evolution in each space does not proceed independently but rather runs side-by-side. Lewontin (1974, see also Fig. 1.2) illustrates this tandem evolution as consisting of four transitional steps, namely: (T_1) development from fertilized eggs/genotype into adult form/phenotype; (T_2) change in phenotypic distributions due to selection,
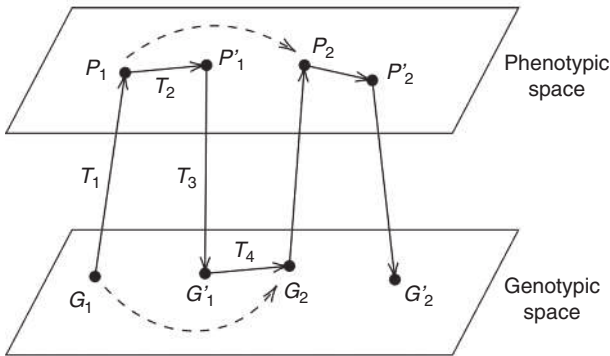

Figure 1.2 Schematic representation of evolutionary processes adopted from Lewontin (1974). G and P are respectively genotypic and phenotypic descriptions of an evolving population, with $T_1 \sim T_4$ denoting steps in the life cycle. (T_1) A population of fertilized eggs (zygotes) G_1 develops into a population of adult individuals P_1. (T_2) Selection and other evolutionary forces act to alter the population composition. (T_3) Surviving individuals P_1' create eggs and sperm (gametes) G_1'. (T_4) Gametes combine and form the zygotes G_2 of the next generation, and the process continues. Although phenotypic and genotypic evolution thus proceed in tandem, most models focus on tracking changes in one dimension, as indicated by the dashed arrows.

migration, etc.; (T_3) gamete (eggs and sperm) production by surviving individuals; and (T_4) fertilization and formation of new genotypes. The "horizontal" transitions T_2 and T_4 represent shifts in phenotypic or genotypic distribution of a population by various evolutionary factors, while the "vertical" transitions T_1 and T_3 transcribe back and forth between the phenotypic and genotypic aspects of the population. The goal of population genetics is to build a mathematical model that takes into account all these transitional steps so that it accurately tracks the entire evolutionary trajectory.

In reality, however, most mathematical models focus on evolutionary dynamics in just one layer. Genetic models aim to directly calculate the change in genetic frequencies from G_i to G_{i+1}, while phenotypic models are concerned exclusively with the shift in phenotypic features from P_i to P_{i+1} (Fig. 1.2, dashed arrow). Such calculations are achieved by building a proper *transition function*. Let X denote either phenotypic or genotypic profile of a population, and $\Delta X := X_{i+1} - X_i$ the change of the population profile between two generations. A transition function has the form

$$\Delta X = f(X;\ \alpha, \beta, \ldots)$$

where $\alpha, \beta, \ldots$ are *parameters* of the function that summarize the developmental or evolutionary factors at work in the steps $T_1 \sim T_4$ above. If the function and parameters well capture these processes, one can successfully derive the evolutionary change based on the present state X of the population. The task of population genetics thus boils down to identifying the form of the transition function and determining its parameters for the evolutionary process under study.

As a concrete example, consider the following one-locus population genetics model that describes the change in the population frequencies p,q of alleles A,a in response to selection:[1]

$$\Delta p = f(p,q; \mathbf{w})$$

$$= \frac{pq[p(w_{AA} - w_{Aa}) + q(w_{Aa} - w_{aa})]}{p^2 w_{AA} + 2pq w_{Aa} + q^2 w_{aa}} \tag{1.1}$$

(Note that the lowercase p here denotes a *genetic* frequency and not a phenotypic one as denoted by the capital P above.) Here, the frequency change Δp is determined from the current allele frequencies (p and q) and three *fitness parameters* $\mathbf{w} = (w_{AA}, w_{Aa}, w_{aa})$, which represent the chance of survival from

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[1] This Element considers only infinite-population models, where population dynamics is deterministic with no drift.

birth to the adult stage; so if eight out of ten *AA* individuals survive to reproduce, $w_{AA} = 0.8$. Since the survival rate reflects the strength of selection, Eqn. 1.1 can be thought of as describing how the population frequencies change – that is, evolve – in response to selection. Just to give an idea, suppose further $w_{Aa} = w_{aa} = 0.5$, that is, half of *Aa* and *aa* individuals die before reproduction. We also assume the initial population contains the same amount of *A* and *a* alleles, so that $p = q = 0.5$. When we plug these figures into Eqn. 1.1, the change in the frequency is calculated as follows:

$$\Delta p = \frac{(0.25)[(0.5)(0.8 - 0.5) + (0.5)(0.5 - 0.5)]}{(0.25)(0.8) + 2(0.25)(0.5) + (0.25)(0.5)} \approx 0.065 \tag{1.2}$$

Thus, the frequency of *A* allele will increase to about 56.5%, in response to selection favorable for *AA* individuals. This process can be reiterated to yield the population frequencies of arbitrary generation (Fig. 1.3).

Although this model only deals with selection, other evolutionary factors such as mutation, migration, randomness (drift), population structure, and so
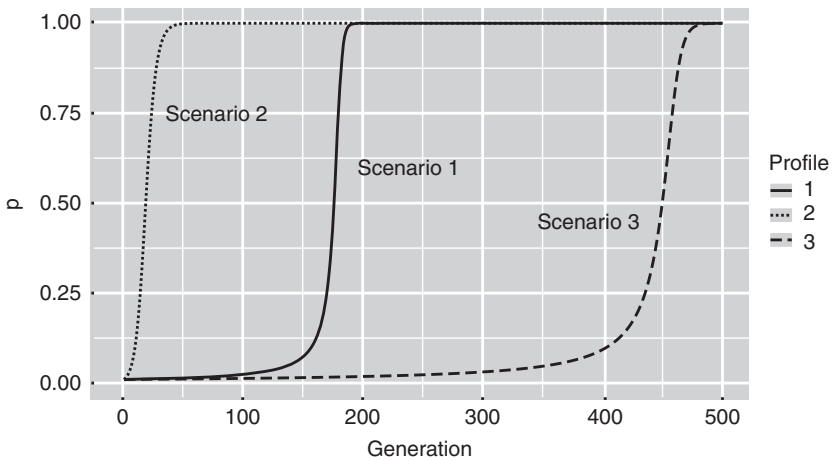

Figure 1.3 Simulation of evolutionary trajectories generated from repeated applications of Eqn. 1.1 with three different fitness parameters, all starting from the initial frequency $p = 0.01$. **Scenario 1** ($w_{AA} : w_{Aa} : w_{aa} = 0.8 : 0.5 : 0.5$) is the example in the main text, and in this case *A* almost reaches fixation in less than 200 generations. *A* evolves even faster in **Scenario 2** ($w_{AA} : w_{Aa} : w_{aa} = 0.8 : 0.65 : 0.5$) where the heterozygote fitness is intermediate (i.e., no dominance). The adaptive evolution slows down in **Scenario 3** ($w_{AA} : w_{Aa} : w_{aa} = 0.8 : 0.65 : 0.65$) where the fitness difference is less significant.

forth can be incorporated into the model, and their relative importance in evolutionary processes can be assessed by comparing the model's prediction and actual observations. If, for example, a target population did not respond as predicted by Eqn. 1.2, we may infer either that our fitness estimate was incorrect (i.e., wrong parameters) or that other evolutionary forces not included in the model were at work (wrong functional form).

Models can also be used the other way around to estimate parameters. From the early nineteenth to the mid-twentieth centuries in a forest near Manchester, a dark (melanic) form of peppered moth, *Biston betularia*, increased its frequency at the expense of the original light-colored form. When a model like the one above was fitted to the actual records of frequency change, it was estimated that the light-colored moths had two-thirds the survival rate of melanic moths, so that $w_{light} : w_{dark} = 2 : 3$. In these ways, population genetics models have enabled prediction, estimation, and testing of evolutionary dynamics and factors in a quantitative, hypothetico-deductive fashion.

These rigorous and formal treatments of evolutionary dynamics took on great significance not only for their predictive value, but also for their metascientific implications for the status of evolutionary theory. Unsurprisingly, the rise of modern evolutionary theory has generated much philosophical reflection on its theoretical status, especially its integrity and relationship to the physical sciences (Smocovitis, 1996, ch. 5). One of the primary contributors to the Modern Synthesis, J. B. S. Haldane (1931, p. 150) stressed that "biology must be regarded as an independent science with its own guiding logical ideas, which are not those of physics." What concerned him was the reductionist atmosphere of the time engendered by adamant physicists like Lord Kelvin, who infamously proclaimed that every natural phenomenon eventually could be explained by combinations of physical laws, making the rest of the sciences just applied physics or even "stamp collecting." In order for evolutionary biology to be an autonomous and respectable science, thought Haldane, it must have its own set of laws or "guiding logical ideas" that are as rigorous as those of physics but not reducible to them. Population genetics, with its quantitative treatment of evolutionary change, was expected to provide just such laws of evolution. It is for this reason that Fisher (1930) called his formula on the rate of adaptive change the "fundamental theorem of natural selection" and likened it to the second law of thermodynamics. This basic formula, Fisher proclaimed, holds true "of any organism at any time," and the existence of such universal laws of evolution was taken to establish evolutionary biology as a rigorous scientific discipline with its own principles.

The search for universal laws has led to abstraction and distillation of the logical essence of the evolutionary process. Darwin formulated evolution by

natural selection as a necessary consequence of three conditions, namely (i) phenotypic variation (organisms in a population are not all the same but differ from each other), (ii) associated fitness variation (difference in phenotype results in a difference in organisms' chance of survival and reproduction), and (iii) heritability (offspring resemble their parents) (Darwin 2003, ch. 4; Lewontin 1970). Presented as such, the argument does not make any substantive assumption about the biology of an evolving population. Indeed, any collection of entities – even inanimate things – that make their "copies" at differential rates evolves through the process of natural selection according to this construal. For this reason some biologists have concluded that adaptive evolution in its purest form is a logical fact, holding true of any population in arbitrary environmental circumstances as long as it satisfies very general premises (e.g., Endler, 1986; Ridley, 2004)

The Darwinian syllogism derives adaptive evolution from the three conditions. But can we be more precise and calculate *how much* a particular population quantity, say its mean height or weight, changes due to selection and other evolutionary factors? The answer is yes. The so-called *Robertson-Price identity* or simply the *Price equation* (Robertson, 1966; Price, 1970) gives the change in the mean of any phenotypic character between two generations, expressed by $\Delta\overline{Z}$, as a statistical function:

$$\Delta\overline{Z} = \mathrm{Cov}(W,Z')/\overline{W} + \overline{\delta Z}. \tag{1.3}$$

The variables W, Z, Z' and δZ in the equation quantify properties of individuals in the population. The fitness W is simply the number of offspring, so if an individual has two offspring its W value is 2.[2] Z quantifies any phenotypic characteristic of an individual, while Z' is the average phenotypic value of its offspring; so if we are interested in weight, and the above individual weighed 9 grams while its two offspring weighed 8 and 12 grams, its values of Z and Z' are 9 and 10 respectively. Finally, δZ is defined as $Z' - Z$, that is, the difference between the phenotypic value of a parent and the average phenotypic value of its offspring, and is often interpreted as the *transmission bias*. For the above individual, this value is $10 - 9 = 1$. That is, the offspring produced from this individual were on average 1 gram heavier.

With this in mind, the Price equation can be explicated in two parts. The first term $\mathrm{Cov}(W,Z')/\overline{W}$ is the *covariance* of the fitness and the average offspring phenotype divided by the *mean* fitness. Since the mean fitness is never negative, the sign of this term is entirely determined by how the two variables

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[2] Here we assume asexual reproduction for expository convenience. In the case of sexual reproduction fitness must be divided by two to take into account the fact that each offspring has two parents.

W and $Z^{'}$ covary. If the covariance is positive and (as in the above case) individuals having heavier offspring tend to leave more offspring, this term tends to push up the mean population weight, but the reverse if those individuals tend to procreate less. This term thus captures Darwin's basic idea that a characteristic contributing to fitness (that is, number of offspring) will spread in a population. The second term $\overline{\delta Z}$, in contrast, is the mean transmission bias and measures whether and to what extent offspring on average differ from their parents, irrespective of selection (because this term does not contain fitness W as a factor). Combining these terms together, the Price equation calculates the mean phenotypic change $\Delta \overline{Z}$ of a population from the quantitative expressions of selection and the transmission bias.

The striking fact about Eqn. 1.3 is that it is obtained through pure deduction as a mathematical theorem that follows from the basic axioms of probability theory and the definitions of mean and covariance (see, e.g., Okasha, 2006; Frank, 2012, for accessible expositions). Free from any biological or empirical assumption, the equation is thus applicable to any population change, just as $7 + 5 = 12$ holds true of any countable objects. Due to this logical austerity and universality, the Price equation has played essential roles in theoretical biology (Frank, 1995, 2012; Luque, 2017) and is often touted as "the most fundamental theorem of evolution" (Queller, 2017).

All the refinement and purification of evolutionary principles, however, has invoked a philosophical puzzle: why can such mathematical theorems tell anything at all about actual and concrete evolutionary processes? In part, this is an echo of an old philosophical conundrum dubbed by Eugene Wigner (1960) as "the unreasonable effectiveness of mathematics in the natural sciences." Ever since Galileo, scientists have made use of mathematics to study empirical and causal structures of the world, evidently with great success. But why do mathematical theories, which are seemingly constructed "in our head," describe the world, which is obviously "outside our head"? This question has been asked time and again by, to name just a few, Descartes, Kant, and the logical positivists, each in response to the contemporary developments of the natural sciences: Galilean physics (in the case of Descartes), Newtonian mechanics (Kant), relativity theory (logical positivists), and quantum mechanics (Wigner). Just as the successes of these physical theories have invited metaphysical reflections on the conditions that would sanction the use of mathematics in the physical sciences, the development of population genetics in the twentieth century naturally led philosophers to a similar inquiry regarding the role and nature of mathematical reasoning in evolutionary studies.

In effect, the unreasonableness of the effectiveness of mathematics is even more acute in the case of evolutionary biology due to the aforementioned

a priori character of its fundamental principles. Physics does extensively use abstract mathematical formulae, but the ultimate arbiter is Nature. The truth or falsity of Newton's or Einstein's laws is not guaranteed by mathematics alone. You need observations and experiments to decide which, if any, are true – otherwise, Eddington could have better sat in his armchair and calculated, rather than mounting his famous expedition to the island of Principe. In this sense, these equations are not themselves products of mathematics but rather mathematical expressions of empirical hypotheses. In contrast, we have just seen above that the fundamental principles of evolution are often considered to be mathematical theorems that hold without any empirical assumptions. We don't need any observation or experiment to bear out the Price equation, because its truth is entailed by probability theory alone. But if so, it is all the more puzzling why such a priori statements could sustain hypotheses about historical origins of species or predictions about future evolutionary trajectories. This puzzlement gave rise to a suspicion that evolutionary theory is in fact not an empirical theory with falsifiable hypotheses but rather an elaborated set of tautologies (Smart, 1959; Popper, 1974). The apparent a priori-ness of evolutionary principles also casts a shadow on Haldane's hope for the autonomy of biology, for if the putative laws of evolution turn out to be mathematical facts that would obtain regardless of any empirical conditions, it would be utterly unclear why they could serve as the basis for the autonomy and integrity of *biological* sciences.

At stake here is not just the empirical nature but also the predictive capability of evolutionary theory. Darwin's principle of natural selection arrives at adaptive change from the premise that individuals in a population differ in their capacity to survive and reproduce and that the capacity is heritable. This reasoning is apparently *ampliative*, that is, its conclusion seemingly delivers new information that was not included in the premises. In other words, evolutionary change is *predicted* from the heritable differences in fitness, and, as we have seen, this predictive ability of Darwin's principle, backed up with quantitative formulations of population genetics, played a central role in its acceptance among biologists in the early twentieth century. But how is such ampliative reasoning possible if the underlying principle was a logical or mathematical truth? Logical deductions may explicate the information contained in the premises, but never extend our knowledge beyond them. Hence, should Darwin's principle be a kind of logical deduction, it would never be able to predict an adaptive change before it actually happens – what it could do would be, at most, relating a past change to the selective and hereditary conditions. The deductive outlook of evolutionary principles thus casts a serious doubt on the ampliative nature and predictive ability of evolutionary theory.