——— (1978), *The Methodology of Scientific Research Programmes*. Edited by J. Worrall and G. Currie. Cambridge: Cambridge University Press.
Magee, B. (1977), *Popper*. London: Fontana.
Miller, D. (1974a), "On the Comparison of False Theories by Their Bases," *British Journal for the Philosophy of Science* 25: 178–188.
——— (1974b), "Popper's Qualitative Theory of Verisimilitude," *British Journal for the Philosophy of Science* 25: 166–177.
Munz, P. (1985), *Our Knowledge of the Growth of Knowledge: Popper or Wittgenstein?* London: Routledge.
O'Hear, A. (1980), *Karl Popper*. London: Routledge.
Poincaré, H. (1902), *La science et l'hypothèse*. Paris: Flammarion.
——— (1905), *La valeur de la science*. Paris: Flammarion.
Popper, K. R. ([1935] 1959), *The Logic of Scientific Discovery*. London: Hutchinson. Originally published as *Logik der Forschung*. Vienna: Julius Springer Verlag.
——— (1945), *The Open Society and Its Enemies* (2 vols.). London: Routledge.
——— ([1957] 1961), *The Poverty of Historicism* (2nd ed). London: Routledge.
——— ([1963, 1965] 1969), *Conjectures and Refutations: The Growth of Scientific Knowledge*. London: Routledge.
——— (1972), *Objective Knowledge: An Evolutionary Approach*. Oxford: Clarendon Press.
——— (1976), *Unended Quest: An Intellectual Autobiography*. London: Fontana.
——— (1992), *In Search of a Better World: Lectures and Essays from Thirty Years*. Translated from German by Laura J. Bennett, with additional material by Melitta Mew. London: Routledge.
——— (1994), *The Myth of the Framework: In Defence of Science and Rationality*. Edited by M. A. Notturno. London: Routledge.
——— (1997), *The Lesson of This Century: With Two Talks on Freedom and the Democratic State*. Interviewed by Giancarlo Bosetti. Translated from Italian by Patrick Camiller. London: Routledge.
——— (1998), *The World of Parmenides: Essays on the Presocratic Enlightenment*. Edited by A. Petersen and J. Majer. London: Routledge.
——— (1999), *All Life Is Problem Solving*. Translated from German by Patrick Camiller. London: Routledge.
Popper, Karl, and John C. Eccles (1977), *The Self and Its Brain: An Argument for Interactionism*. Berlin: Springer Verlag.
Quine, Willard Van (1963), *From a Logical Point of View* (2nd ed., rev). New York: Harper and Row.
Schilpp, P. A. (ed.) (1974), *The Philosophy of Karl Popper* (2 vols.). LaSalle, IL: Open Court.
Simkin, C. (1993), *Popper's Views on Natural and Social Science*. Leiden, Netherlands: Brill.
Stokes, G. (1998), *Popper: Philosophy, Politics, and Scientific Method*. Cambridge, UK: Polity.
Tichý, P. (1974), "On Popper's Definitions of Verisimilitude," *British Journal for the Philosophy of Science* 25: 155–160.

See also **Cognitive Significance; Corroboration; Demarcation, Problem of; Duhem Thesis; Evolutionary Epistemology; Induction, Problem of; Logical Empiricism; Lakatos, Imre; Quine, Willard Van; Verisimilitude**

POPULATION GENETICS

Evolutionary population genetics is the study of the dynamics of change in the genetic constitution of populations. The discipline grew out of the need to establish the Darwinian theory of evolution by natural selection on Mendelian hereditary principles. Prior to 1900, the view that the diversity of life arose from common ancestry was widely accepted in the scientific community, but Darwin's hypothesis that natural selection was the main mechanism of descent with modification was controversial (see Bowler 1983). This was due in part to Darwin's confused views about heredity. If, as Darwin thought, any character in the offspring was a blend of the corresponding characters in the parents, then in every generation, the character would regress toward the mean. This would make natural selection ineffective at generating change beyond the "sphere of variation" of the species (Jenkin 1867). So, for Darwin's hypothesis to be vindicated, it was necessary to establish a theory of heredity according to which variation was not lost in every generation. Mendelism, rediscovered in 1900, met this need. Unfortunately, Mendelism was not immediately accepted. There was a disagreement between two competing schools of thought in the early 1900s on the nature of heredity and of evolutionary change. Two critics in particular, the biometricians Pearson and Weldon, accepted Darwin's claim that changes due to selection were gradual and that selection acted on variations in quantitative characters, or characters like height or weight (Provine 2001). In contrast, Mendelians by and large rejected

Darwin's claim of gradual change. Their theory of heredity focused primarily on qualitatively varying characters, or characters like color or shape. On the whole, Mendelians held that evolution was the result of selection acting on major mutations, and not gradual selection on slightly varying traits. Gradually, however, biologists came to accept that Darwinian gradual selection was compatible with a Mendelian theory of inheritance. The development of a quantitative theory of evolution relying upon Mendelian principles of inheritance (population genetics) was crucial to the acceptance of Darwin's hypothesis that natural selection played a significant role in evolution and thus in generating the diversity of life.

The early population geneticists, R. A. Fisher, J. B. S. Haldane, and Sewall Wright, used primarily single-locus algebraic models to describe changes at the population level (see Evolution for an example). These were *prospective* models—given a set of values for selective parameters, migration rates and mutation rates, equations could be solved indicating, for instance, the rate at which evolutionary change would occur, or predicting genotype frequencies from one generation to the next. The above parameters describe deterministic factors effecting change in allelic frequencies. However, allelic frequencies change because of purely random factors as well. Fisher (1918) was the first to use diffusion methods to consider the stochastic changes in gene frequencies arising in finite populations, and Wright (1931) made "drift" a factor in his overall evolutionary theory. *Drift* refers to the random changes in gene frequency brought about by the random sampling of genes from one generation to the next, that is, the chance survivorship and reproduction of individuals irrespective of their fitness relative to their cohort. Any population that is sampled from one generation to the next will show some shift in distribution of characters due to chance alone. The effects of drift are accelerated in smaller populations; that is, the smaller the population, the more quickly will random sampling tend to make a population homogeneous, or uniformly of one or another genotype. In sum, prospective models describe how allele frequencies may change as a result of five different factors: mutation, migration, assortative mating, drift, and selection (cf. Haldane 1924). (Genotypic frequencies can change with or without changes in allelic frequency; for instance, as a result of assortative mating, inbreeding, and [in multilocus systems] recombination between gene loci.) Since the 1950s, multilocus models have been developed, which represent the change from one generation to the next at two or more loci. For the most part, however, many evolutionary questions can be answered using simple one-locus models. In the past twenty-five years, *retrospective* or "coalescent" models have been developed to assist in drawing inferences about the history of some lineage. Given some DNA sequence data, one can use retrospective models to answer questions like: "Given this information, when did the most recent common female ancestor of all humans alive today live?"

Evolutionary population genetics is but one part of population genetics generally. The mathematical component of population genetics is used not only in the evolutionary context but also in plant and animal breeding theory and in theoretical aspects of human genetics, especially in the search for the chromosomal location of disease genes. This article will focus on evolutionary questions and their mathematical analysis. First, there will be a summary of several of the major results of early population genetics theory and some of its more controversial aspects. Second, there will be an overview of some recent developments in population genetics—in particular, the influence of developments in molecular biology on theoretical population genetics. In conclusion, there will be a brief discussion of the scope and limitations of modeling in evolutionary genetics more generally.

The History of Population Genetics

The Hardy-Weinberg Law and the Maintenance of Variation

As mentioned above, the Darwinian theory of evolution by natural selection requires genetic variation. Variation is ultimately caused by mutation and subsequently also by chromosomal rearrangements, but it must be preserved for long periods for natural selection to act. The hereditary theory assumed by Darwin, that the characteristic of any child is in some sense a blend of that characteristic in the two parents, leads to rapid dissipation of variation. Thus, the very variation needed by the Darwinian theory is not supplied by the hereditary mechanism that he assumed. The Mendelian hereditary mechanism was rediscovered some forty years after the publication of *On the Origin of Species* and seventeen years after Darwin's death. Not only did this prove to be the correct hereditary model: It was one of the early triumphs of the mathematical theory to show that the Mendelian hereditary system is a variation-preserving one. Indeed, Mendelism supplies possibly the only hereditary mechanism maintaining the variation that is necessary for the Darwinian theory to work.

Weinberg and Hardy independently established the "law of panmictic equilibrium," today known as the Hardy-Weinberg law or principle. The law might be better described as a neutral or equilibrium model—a mathematical derivation starting from assumptions (some known to be false) for the purposes of evaluating the baseline state of a Mendelian system absent perturbing forces. Interestingly, the consequences of the segregation law were issues that Mendel himself explored but did not follow through to the case of random mixing—he was working with self-pollinating plants, and his "law of disjunction" treated only the case of reversion to type. In 1902, and later in 1903, Yule and Pearson independently examined the consequences of Mendel's law of segregation for a randomly mating population. However, their examinations of the question were yet again specific to a case in which the two factors were at the same initial frequency.

In 1908, Punnett, then a geneticist at Cambridge, asked Hardy, a mathematician, to derive the consequences of Mendel's laws for a randomly breeding population. Hardy demonstrated that *whatever the genotype frequencies* might be in a population, stable frequencies will result after one generation of random mating. The significance of this result is that given a particulate, or Mendelian, system of heredity, variation will be maintained in a population. The initial genotype frequencies in a population will remain unchanged from one generation to the next. This simple consequence of Mendel's law had been discovered a few months earlier by Weinberg. The derivation is as follows.

First, assume a diploid organism, sexual (or hermaphrodite) reproduction, nonoverlapping generations, perfectly random mating (no assortative mating), infinite population, and no migration, mutation, or selection. Let the two alleles at a locus be A and a. Suppose that in any generation the proportions of the three genotypes AA, Aa, and aa are P, Q, and R, where $P + Q + R = 1$. Correspondingly, let the frequencies of the A allele equal p, where $p = (2P + Q)/2 = P + Q/2$, and, for the a allele, the frequency $q = (2R + Q)/2 = R + Q/2$. The frequency of matings of $AA \times AA$, given random pairing of individuals, will be P^2. Likewise, the probability of an $AA \times Aa$ mating is $2PQ$, and the probability of an $Aa \times Aa$ mating is Q^2. Only these three matings can produce AA offspring, and they do so with respective probabilities 1, $\frac{1}{2}$, and $\frac{1}{4}$. Table 1 lists the genotypic frequencies resulting from each mating.

It follows that the frequency of AA offspring after one generation will be:

Table 1. Frequencies of offspring genotypes in a randomly mating population

Mating	Frequencies of mating	Offspring genotype frequencies		
		AA	Aa	aa
$AA \times AA$	P^2	1	0	0
$AA \times Aa$	$2PQ$	$\frac{1}{2}$	$\frac{1}{2}$	0
$AA \times aa$	$2PR$	0	1	0
$Aa \times Aa$	Q^2	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{1}{4}$
$Aa \times aa$	$2QR$	0	$\frac{1}{2}$	$\frac{1}{2}$
$aa \times aa$	R^2	0	0	1

$$P' = P^2 + \frac{1}{2}(2PQ) + \frac{1}{4}(Q^2)$$
$$= (P + Q/2)^2 = p^2.$$

Similarly, the frequency of Aa and aa after one generation will be:

$$Q' = \frac{1}{2}(2PQ) + 2PR + Q^2/2 + 2QR/2$$
$$= 2(P + Q/2)(R + Q/2) = 2pq$$
$$R' = Q/4 + 2QR/2 + R^2 = (R + Q/2)^2 = q^2.$$

Thus, the frequency of each genotype after one generation of random mating will be p^2, $2pq$, and q^2. Replacing the values P', Q', and R', in the above equations, in order to determine the values for P'', Q'', and R'' in the subsequent generation, the same frequencies result. In other words, the genotype frequencies obtained after one generation of random mating are maintained in all subsequent generations. Thus, Hardy and Weinberg demonstrated that given the assumptions above, after one generation of random mating, stable genotype frequencies will result and be maintained. The key point here is that if there is no action by external forces (selection, mutation, migration, or random drift), then variation will be preserved in a population. This simple mathematical demonstration of the consequences of Mendel's law on the assumption of random mating thus answers one of the long-standing objections to Darwinism, *viz.*, that given a blending theory of inheritance, the variation needed for evolution through natural selection would rapidly be dissipated (Jenkin 1867). In contrast, under a Mendelian or particulate scheme of inheritance, variation will be preserved, *ceteris paribus*.

The Correlation Between Relatives

The Mendelian theory did not win immediate acceptance upon its rediscovery in 1900. One reason why it was not accepted quickly was that it was

widely felt that biometrical data, including in particular the correlation between parent and offspring for characters such as height and weight, could not be explained on Mendelian grounds. Fisher (1918) showed not only that the broad pattern of these correlations could be explained assuming a Mendelian hereditary system, but that the numerical values for the correlations could also be explained. A Mendelian system of inheritance had to account for the observations of the normal distribution of most quantitative characters (e.g., height, weight) and the measurements of correlations between relatives with respect to these same characters. Fisher's (1918) paper showed that Mendelism did just that. First, by assuming that the character value for the heterozygote could be halfway between those of the two homozygotes, that the relevant Mendelian factors were entirely independent in their effects, and that the number and effects of such factors affecting any particular trait were quite large, Fisher showed how a normal distribution of measurements of some trait followed from a particulate scheme of inheritance. Second, and more significantly, Fisher demonstrated the consistency of the biometricians' observation of correlations between continuously varying traits and the Mendelian theory. There is no doubt that Fisher's specific genetical models were simplified. However, by showing that a reasonable fit to the observed correlations could be obtained under the Mendelian scheme, Fisher's work was a major force in leading to the acceptance of that hereditary scheme. A model does not have to be too precise to be useful.

The Fundamental Theorem

Having fused the biometrical and Mendelian viewpoints, Fisher then tried to establish general principles of evolution as a Mendelian process. Perhaps the best-known of these is his *fundamental theorem of natural selection:*

> The rate of increase in fitness of any organism at any time is equal to its genetic variance in fitness at that time. (Fisher 1930, 37)

Careful attention to Fisher's intended meaning shows that although this is a true theorem, its significance is perhaps more circumscribed than Fisher claims. With the fundamental theorem, Fisher believed that he had discovered a universal generalization akin to the second law of thermodynamics. He believed the theorem to be a law of nature. Fisher (1930) describes his object in the opening pages of his chapter on the fundamental theorem:

> [t]o combine certain ideas derivable from a consideration of the rates of death and reproduction in a population of organisms with the concepts of a factorial scheme of inheritance, so as to state the principle of natural selection in the form of a rigorous mathematical theorem, by which the rate of improvement of any species of organisms in relation to its environment is determined by its present condition. (22)

Despite the appearance of progressivist language here, the fundamental theorem is not a statement about the unending or necessary adaptation of the species to its environment, but an expression of a fundamental relationship between the reservoir of genetic variation available and accessible to selection and the rate of increase in fitness in a population. Fisher was well aware that genetic interactions, rapid changes in or deterioration of the environment, overpopulation, and many other factors could affect whether or not a population of organisms would increase in numbers or continue to adapt over time. The fundamental theorem is thus a statement not of the necessary improvement of the species, but about the relation between genetic variance in some trait and increase in numbers of individuals possessing such a trait.

What Fisher's demonstration actually shows is simply that the additive variance in fitness (or that portion of the genetic variance that contributed to the correlation of relatives) is equal to that component of the increase in mean fitness in the population brought about by changes in gene frequencies only. This change was called the "partial change" by Ewens (1989), following a clarification of the meaning of the theorem by Price (1972). However, almost all commentators, starting with Wright (1930), have misunderstood the meaning of the theorem. Wright, for example, "corrected" the theorem as follows: "The total variance in fitness of a population is ascribable to the variance in fitness due to natural selection, which excludes the effects of dominance, epistasis, mutation, migration, change in environment, and drift." Subsequent commentators, and indeed the majority of textbooks in population genetics through the 1970s (Li 1955; Moran 1962; Crow and Kimura 1970; Jacquard 1974), misinterpreted Fisher's theorem along the same lines. The "received" interpretation thus came to be that "the increase in mean fitness of a population is approximately the current additive genetic variance in fitness, and this is non-negative"(Edwards 1994). This takes the theorem to refer to the mean fitness of the population and to be an approximate result. However, Price (1972), Ewens (1989), and Lessard (1997) have shown that the theorem, as correctly interpreted, is exact, not approximate.

Wright Versus Fisher

A continuing point of controversy in population genetics theory is the relative significance of two different models of the evolution of adaptation: Wright's and Fisher's. According to Fisher, evolution takes place for the most part in large, panmictic populations, and the factor of greatest significance in shaping adaptation is selection acting on alleles, even those with small selective effects. According to Wright, the landscape of gene combination consists of multiple adaptive peaks, separated by maladaptive valleys, or gene combinations that are less fit. The most effective means of traversing such peaks is via a three-phase process of isolation of small subpopulations and intrademic and interdemic selection. Wright called this process the "shifting balance model" of evolution.

The diagnosis and resolution of this controversy is contentious. Some argue that at the core are differing views about the nature and extent of genetic interaction, tied to the presuppositions behind Wright's model of the adaptive landscape (Whitlock et al. 1995). If indeed genetic variation is held tightly in "balance," or if there are many epistatic interactions for fitness, then it would seem that a mechanism like shifting balance is necessary for populations to move from suboptimal, or lower, to higher peaks in the adaptive landscape. On the other hand, it may be the case that whatever the extent of epistatic interactions for fitness, populations may always find "ridges" to traverse adaptive valleys via selection. For instance, assortative mating may permit the traversion of valleys (Williams and Sarkar 1994).

Others argue that the core of the divide between Wright and Fisher has to do with the rather delicately timed balance of isolation, selection, and migration Wright requires for shifting balance to go forward. In particular, it seems unduly restrictive to expect no migration between demes for the time necessary for them to diverge significantly for there to be a difference in fitness between them, followed suddenly by migration. The controversy over the shifting balance model continues today. Coyne, Barton, and Turelli (1997), neo-Fisherians, and Wade and Goodnight (1998), neo-Wrightians, continue to debate the extent of empirical support and the interpretation of mathematical and metaphorical models such as Wright's adaptive landscape.

The Introduction of Molecular Biology and the Neutral Theory

In the mid-1960s, molecular methods were introduced into the study of evolution. Protein sequencing revealed that the number of amino acid substitutions among species increases approximately linearly with time since divergence (Zuckerkandl and Pauling, 1962). Electrophoretic studies by Lewontin and Hubby (1966) demonstrated that there was a great deal of genetic variation at the protein level within natural populations. These observations eventually led to Kimura's (1968) proposal of the neutral theory of molecular evolution, which says that most changes detected at the molecular level were not acted upon by natural selection, but were neutral with respect to selection (that is, did not affect fitness). Kimura's reasoning was as follows. First, he examined molecular data on the variation among hemoglobins and cytochromes *c* in a wide range of species. Second, he calculated the rates of change of these proteins. Third, he extrapolated these rates to the entire genome. When he saw the rapidity of change that this implied, Kimura concluded that there simply could not be strong enough selection pressures to drive such rapid evolution. He therefore hypothesized that most evolution at the molecular level was the result of random processes like mutation and drift. Kimura called this hypothesis the *neutral theory of molecular evolution.*

Kimura's theory met with a great deal of controversy, as many interpreted it to run counter to the neo-Darwinian view that selection was the main agent of evolutionary change. This false impression was exacerbated by a paper published immediately after Kimura's by King and Jukes (1969), defending roughly the same thesis. Many were led to the mistaken view that the neutral theory denies the fact of adaptive evolution. However, it simply states that a large quantity of the turnover of molecular variation within populations has nothing to do with adaptation—it is simply neutral with respect to selection; that is, it has no effect on an organism's survival.

Today, most biologists accept that there is a great deal of molecular variation that is neutral with respect to selection. However, the rate of sequence change in evolution varies considerably with the DNA region examined. The more important the function of the region, the lower the rate of sequence change, as would be expected (Nei 1987). Much of systematics today uses the rapid turnover of some relatively neutral regions, such as the region that controls cytochrome *c*, to reconstruct phylogenetic relationships.

Kimura was in part inspired by the work of Sewall Wright, and in particular by Wright's emphasis on drift as a significant factor in evolutionary change. It should be noted, however, that it is a confusion to equate the neutral theory with Sewall

Wright's view on adaptive evolution in populations, the shifting balance theory. In other words, there may well be a great deal of turnover in a population at the molecular level, whether or not selection or drift is the main force changing the genotypic constitution of such a population over the long term. "Random drift" in the classical sense refers to chance fluctuations in the genetic constitution of a population, or sampling error. By chance alone, some individuals, irrespective of their selective advantages, may not survive to reproduction. In this way, one or another allele may become fixed in a population, irrespective of its selective advantage (or disadvantage). Reduction in population size accelerates the effects of drift in the sense that the average time to fixation of an allele is shorter, the smaller the population. So, over the short term, and in smaller populations, drift will be of greater significance in any population relative to selection. The neutral theory simply describes the turnover of sequence at the molecular level. Changes in some loci are effectively neutral with respect to selection, so there is significant turnover at the molecular level in such loci. This does not preclude that over the longer term, the effect of selection may significantly change the constitution of populations.

Retrospective Models, Molecular Genetics, and Coalescence Theory

Much of the early modeling in population genetics theory was prospective: Given certain fitness values, mutation rates, etc., equations could be solved indicating the rate at which evolution could occur. In the early years of this century such an analysis was needed, largely to support the Darwinian theory. But the Darwinian theory is now in effect accepted, and with the information provided by DNA sequence data, theory and modeling have branched into a retrospective analysis, as noted above.

Coalescent theory uses mathematical models and molecular data to determine times since most recent common ancestor of different lineages, or time to *coalescence*. While the mathematical demonstration of coalescence theory is beyond the scope of this article, the following are some basic premises of coalescence theory. All genes in a population ultimately trace their way back to a single ancestor gene, so that their ancestry coalesces at that gene. However, the allelic types of the genes in the population might differ from that of this common ancestor, because of mutation. These mutational differences help answer questions about the size, structure, and history of populations.

Coalescence theory assumes, in part for reasons of simplifying the mathematics, that most changes in the genome are neutral, so that most of the changes seen are a result of drift. This is in fact a very reasonable assumption when the scope of investigation is shorter time frames, or changes in populations over thousands, as opposed to tens of thousands, of years. For shorter time frames, the effects of drift will predominate. With the development of molecular methods, and of coalescence theory, there has thus been a shift in focus of the models of evolutionary genetics from longer to shorter time frames, and in these models, the significance of selection relative to drift will be negligible. For longer-term evolutionary questions of the sort that interested Wright and Fisher, selection will, relatively speaking, be a more significant factor, changing the genetic constitution of populations.

Conclusion

Theoretical population geneticists use mathematical models to investigate the dynamics of evolutionary change in populations. Essentially, they describe and explain the conditions on the possibility of evolution. Thus, population genetics constitutes that theoretical core of evolutionary biology. While the mathematical models of theoretical population genetics are necessarily idealized, they nonetheless constitute a useful tool for describing the main mechanisms of evolutionary change and answering questions about the relative significance of this or that factor in evolution, under some description of initial conditions. Rather than attempt to capture all the subtleties of inheritance (cytoplasmic as well as nuclear), development, and gene expression, classical population genetics treats evolution as simply change in allele frequency. In the context of investigating loci that contribute to disease, classical Mendelian models represent the disease of interest as a product of a single allele that is either dominant or recessive. Of course, many loci contribute in the expression of most diseases (and most traits), and the same allele may be expressed differently in different genetic contexts. Given what is known now about the nature and extent of genetic interaction, one may think that Mendelian "beanbag" genetics is obsolete (Provine 2001).

To the contrary, simplified treatment is necessary—first, because the complexity of the genetics of evolving populations ensures that a completely accurate description of reality is impossible; and second, were such descriptions possible, they would be mathematically intractable (see Crow 2001 for further discussion). Theoretical population

genetics gives mathematically tractable ways to begin to describe the evolutionary process. Such models are in some sense idealizations, but they are useful tools to answer many simple questions, providing a framework for looking at phenomena that often take place over the lifetimes of many individual scientists.

As Wimsatt (1987) has pointed out, null (or false) models can be enormously useful tools for arriving at true theories. For instance, oversimplified models may serve as the starting point in a series of models of greater complexity and realism and may provide a simpler arena for answering questions that would be impossible to answer in more complex models. Or false models may describe extremes of a continuum in which the real case is presumed to lie (Wimsatt 1987, 30–31). For example, the neutral theory claims that all change at the molecular level is neutral, but using the neutral theory as a null model, biologists have now found that different regions of the genome turn over at different rates, indicating that the truth lies somewhere in between the continuum of complete neutrality and selection at every locus. Coalescent theory assumes that all change is neutral, but this strictly false assumption allows biologists to determine times since divergence of modern taxa.

Population genetics models, despite their many simplifications of genetic systems, provide real insight not otherwise obtainable into the evolutionary process. Such models may enable one to describe the common features of many systems that all differ in detail, determine how varying outcomes depend on the relative magnitude of one or another parameter, and decide which factors may legitimately be ignored, given the question or time frame under consideration. For example, population genetics theory shows that selection is more effective than drift in populations of large size (where $4Ns \gg 1$), whereas the effects of drift will overpower those of selection when the opposite is the case.

One may use such models to conclude which outcomes are very unlikely or impossible given some initial conditions. And mathematical analysis may serve to generate conclusions that could not be arrived at by empirical research at a given stage of inquiry. Lewontin (2000) describes the role of modeling in population genetics as delimiting what is possible and what is prohibited in microevolutionary change. And some biologists have extended the use of these models to answer questions about change above the species level, such as in speciation (e.g., Barton and Charlesworth 1984).

Exact prediction in population genetics is a near impossibility. While the models of Newtonian mechanics may be used to predict the motions of the planets or the trajectory of a projectile here on Earth with a high degree of accuracy, one ought not to expect this sort of predictive power from population genetics models. While one might hope that models of biological evolution will help with short-term predictions, one cannot hope that they will lead to explicit long-term predictions. In effect, the allele passed on by a parent to a child at any locus results from a random choice of one of the two alleles that the parent has at that locus, and one can never know which one this will be for each gene in each individual. At best, one may predict trends, given initial population sizes and rates of mutation and migration. Thus, theoretical population genetics is an irreducibly probabilistic theory. However, population genetics theory provides a rigorous way to determine the relative significance of different factors over long time frames in the changes of the genetic constitution of populations.

Which simplifications to employ in modeling a biological system will depend upon the context and the question at issue. For example, when considering the effects of geographical dispersal, it might be reasonable to assume only one sex; and when addressing questions asking why sexual dimorphism exists, it might be reasonable to ignore geographical distribution. In general, the problem of finding a balance between a model's being sufficiently complex to describe reality adequately and at the same time being sufficiently simple to allow a mathematical analysis is not only a question of philosophical interest, but also a serious one faced in the everyday practice of theoretical biology.

ANYA PLUTYNSKI
WARREN J. EWENS

References

Barton, N. H., and B. Charlesworth (1984), "Genetic Revolutions, Founder Effects, and Speciation," *Annual Review of Ecology and Systematics* 15: 133–165.

Bowler, P. (1983), *The Eclipse of Darwinism: Anti-Darwinian Evolution Theories in the Decades around 1900*. Baltimore, MD: Johns Hopkins University Press.

Coyne, J., C. Barton, and M. Turelli (1997), "Perspective: A Critique of Sewall Wright's Shifting Balance Model of Evolution," *Evolution* 51: 306–317.

Crow, J. (2001), "The Beanbag Lives On," *Nature* 409: 771.

Crow, J. F., and M. Kimura (1970), *An Introduction to Population Genetics Theory*. New York: Harper & Row.

Edwards, A. W. F. (1994), "The Fundamental Theorem of Natural Selection," *Biological Review* 69: 443–475.

Ewens, W. (1989), "An Interpretation and Proof of the Fundamental Theorem of Natural Selection," *Theoretical Population Biology* 36: 167–180.

Fisher, R. A. (1918), "The Correlation Between Relatives on the Supposition of Mendelian Inheritance," *Transactions of the Royal Society, Edinburgh* 52: 399–433.

——— (1930), *The Genetical Theory of Natural Selection*. Oxford: Clarendon Press.
Haldane, J. B. S. (1924), "The Mathematical Theory of Natural and Artificial Selection, Part I," *Transactions of the Cambridge Philosophical Society* 23: 19–41.
Jacquard, A. (1974), *The Genetic Structure of Populations*. Berlin and New York: Springer-Verlag.
Jenkin, F. ([1867] 1973), "*Review of On the Origin of Species,*" *in D. L. Hull (ed.), Darwin and His Critics. Cambridge, MA: Harvard University Press, 303–350. Originally published in North British Review 44: 277–318.*
Kimura, M. (1968), "Evolutionary Rate at the Molecular Level," *Nature* 217: 624–626.
King, J., and T. H. Jukes (1969), "Non-Darwinian Evolution," *Science* 164: 788–798.
Lessard, S. (1997), "Fisher's Fundamental Theorem of Natural Selection Revisited," *Theoretical Population Biology* 52: 119–136.
Lewontin, R. C. (2000), "*What Do Population Geneticists Know and How Do They Know It?*" in R. Creath and J. Maienschein (eds.), *Biology and Epistemology*. Cambridge: Cambridge University Press.
Lewontin, R. C., and J. L. Hubby (1966), "A Molecular Approach to the Study of Genetic Heterozygosity in Natural Populations II: Amount of Variation and Degree of Heterozygosity in Natural Populations of Drosophila pseudoobscura," *Genetics* 54: 595–609.
Li, C. C. (1955), *Population Genetics*. Chicago: Chicago University Press.
Moran, P. A. P. (1962), *The Statistical Processes of Evolutionary Theory*. Oxford: Clarendon Press.
Nei, M. (1987), *Molecular Evolutionary Genetics*. New York: Columbia University Press.
Pearson, K. R. (1898), "Mathematical Contributions to the Theory of Evolution: On the Law of Ancestral Heredity," *Proceedings of the Royal Society* 62: 386–412.
Price, G. R. (1972), "Fisher's 'Fundamental Theorem' Made Clear," *Annals of Human Genetics* 36: 129–140.
Provine, W. (2001), *The Origins of Theoretical Population Genetics*. Chicago: University of Chicago Press.
Wade, M., and C. J. Goodnight (1998), "Perspective: Theories of Fisher and Wright in the Context of Metapopulations: When Nature Does Many Small Experiments," *Evolution* 52: 1537–1553.
Whitlock, M., P. C. Phillips, F. B. C. Moore, and S. J. Tonsor (1995), "Multiple Fitness Peaks and Epistasis," *Annual Review of Ecology and Systematics* 26: 601–629.
Williams, S. M., and S. Sarkar (1994), "Assortative Mating and the Adaptive Landscape," *Evolution* 48: 868–875.
Wimsatt, W. (1987), "*False Models as Means to Truer Theories,*" in H. Nitecki and A. Hoffman, (eds.), *Neutral Models in Biology*. Oxford: Oxford University Press, 23–55.
Wright, S. (1931), "Evolution in Mendelian Populations," *Genetics* 16: 97–159.
Zuckerkandl, E., and L. Pauling (1966), "*Evolutionary Divergence and Convergence of Proteins,*" in V. Bryson and H. J. Vogel (eds.), *Horizons in Biochemistry*. New York: Academic Press, 189–225.

POSITIVISM

See **Logical Empiricism**

PREDICTION

Whether one predicts rainfall, recessions, or racetrack winners, predicting an event or state of affairs often, perhaps even typically, involves saying that it will happen before it occurs, and this common association is presumably responsible for the idea that predictions must be about the future. But in scientific contexts one often characterizes a theory's predictions as its implications or entailments without regard for temporal constraints, as when one says a successful theory of cosmology predicts the existence of cosmic background radiation at all times. The language of prediction is also used to describe declarative assertions about past and present events made in light of a theory, as when