The Molecular Approach to Evolution

Molecular Evolutionary Genetics. MASATOSHI NEI. Columbia University Press, New York, 1987. x, 512 pp., illus. $50.

Although the decks of modern genetics may seem to be awash in DNA sequences, for some purposes there are not nearly sequences enough. Granted that the sequences of many individual genes have been determined, most of the genes are derived from a small group of organisms, and for only a few genes are there even enough interspecific data to allow the construction of evolutionary trees. The greatest gap is that we know very little about DNA sequence polymorphisms within populations and how to use this information to make inferences about population structure and evolutionary mechanisms. By happy fortuity, DNA sequences contain many noncoding regions and nucleotide sites in which alternative nucleotides are synonymous. The nucleotide sequences of allelic genes at these and other telltale sites contain critical information that differentiates identity by descent from identity in kind, and intrapopulational variation in DNA sequences, if you know how to interpret it, can reveal the evolutionary history of the gene and the forces that shaped it. Although the statistical methods for making such inferences are still being developed, they have a solid foundation based in the theory of population genetics. The little experimental and theoretical work that has been done demonstrates the power of the approach and encourages still more sequencing and refined methods of analysis.

The current status of the molecularization of population genetics is summarized in *Molecular Evolutionary Genetics*. It is the first book emphasizing statistical methods for analyzing molecular data, and its novelty is apparent in the unusual feature that the basic deterministic and stochastic theory of population genetics is relegated to the back of the book. Up front are discussions of the estimation of amino acid and nucleotide substitutions; processes in genome evolution; use of population data to estimate allele frequencies, fixation indexes, and linkage disequilibrium; and measures of genetic polymorphism and heterozygosity. There are chapters on measures of genetic distance, DNA polymorphisms within and between populations, and the use of sequence data in the construction of phylogenetic trees. Throughout the book, Nei demonstrates the sure grasp of one who has made numerous important contributions to the field. The methods are explained in detail, and their use is illustrated through frequent numerical examples. All those foundering in a sea of sequences who need to learn how to analyze molecular variation within and among species will welcome this book as an important reference.

Casual readers may find the last chapter the most interesting because it is nonmathematical and summarizes Nei's views of how studies of molecular evolution bear on evolutionary theory. One of its themes is that mutation plays a prominent role in evolution at both the molecular and the phenotypic level. The emphasis on mutation at the molecular level comes largely from the paradoxes and seeming contradictions that arise from a strictly selectionist interpretation of molecular evolution. For example, nucleotide positions that are less functionally constrained, such as those in introns or in the third positions in codons, evolve faster than positions that are more functionally constrained, and pseudogenes evolve at the fastest rates known. Likewise, functionally less important parts of genes are generally more polymorphic than functionally more important parts, and genetic variation within species is generally greater in large populations than in small ones. These observations and others are well in line with Kimura's theory of molecular evolution by neutral mutations and random genetic drift, but they are unaccountable for in theories in which all changes, no matter how small, are significant in adaptation.

In going from evolution at the molecular level to evolution at the phenotypic level, the data become sparser and the arguments fuzzier. Nei emphasizes the role of mutation in phenotypic evolution over that of selection. In strict neo-Darwinism, mutations are mainly simple nucleotide substitutions. Most mutations that can occur in a population have already occurred, and those that are favorable have long since been incorporated into the genome either as fixed alleles or as balanced polymorphisms. Extant populations contain genetic variability accumulated from mutations in past generations, and this variation provides the genetic basis for adaptive evolution in response to changing environments. In this theory, mutations, though essential to evolution, are a shadow in the background. Evolutionary advance is driven by environmental change and the natural selection of existing variability.

Nei puts mutation squarely in the foreground of adaptive evolution. In his opinion, the long-term ability of populations to respond to natural selection or to undergo adaptive advance is determined by the occurrence of novel favorable mutations. The role of natural selection is to incorporate favorable mutations as they occur and to eliminate harmful mutations, and the fate of the large number of neutral or nearly neutral mutations is left to chance.

Nei's view has the attraction that it reflects the complexity of the molecular mechanisms of mutation. The existence of transposable elements and other phenomena affecting genetic stability means that many theoretically possible insertions, duplications, deletions, gene fusions, exon shuffles, and other mutational events may occur uniquely, if they occur at all. Mutations that are favorable to survival and reproduction may therefore be nonrecurrent, and evolutionary advance beyond point mutations may in many cases be limited by the occurrence of the favorable mutations.

On the other hand, Nei too easily discounts the role of genetic variability in populations. Most natural populations contain genetic variation affecting virtually all morphological traits, and the genetic variation is usable (additive genetic variance) in that artificial selection changes the population mean. Nei dismisses this argument because "artificial selection is quite different from natural selection," it being the case that the heritability of typical quantitative traits is greater than that of traits closely related to fitness. But I fail to see how a difference in heritability negates the fundamental Darwinian analogy between the morphological diversity produced by natural selection among species and that produced by artificial selection among breeds of pigeons and dogs. Far from discounting the usefulness of artificial selection as a model of natural selection, Nei might have strengthened his argument by citing some examples in which new mutations are demonstrably important in the response to artificial selection: R. Frankham, in *Selection Experiments in Laboratory and Domestic Animals*, A. Robertson, Ed. (Commonwealth Agricultural Bureaux, Slough, U.K., 1980), pp. 56–68; and T. MacKay, *Genet. Res.* **44**, 231 (1984).

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