A View of Population Genetics

Mathematical Population Genetics. WARREN J. EWENS. Springer-Verlag, New York, 1979. xii, 328 pp. $32. Biomathematics, vol. 9.

Population genetics is surely a strange field. It contains the most developed body of theory in biology, with an 80-year history of mathematical treatment. But experimental population genetics has remained poorly developed and in only fragmentary contact with the theory. Experimentalists have remained second-class citizens within the field. This situation has not been improved by the entrance into population genetics of applied mathematicians, bringing with them notation, terminology, and concerns distant from the experience of experimentalists.

Ten years ago, a sudden flood of electrophoretic data on protein polymorphisms promised to bring theoretician and experimentalist into fruitful contact at last. The neutralist-selectionist controversy focused attention on population genetics, and the resolution of the controversy was regularly promised and occasionally announced. After a decade of frustrated hopes, it seems likely that our observations have insufficient power to discriminate between many hypotheses, particularly ones involving weak selection or neutrality. It is a tribute to the immaturity of the theory that it has taken us so long to suspect this and that we still cannot prove it formally.

We need both more data and more theory. More data are coming, in the form of population samples of DNA sequences and samples from an increasing range of species. It is fairly clear that the theory is not up to the challenge.

At this uncomfortable juncture, Warren Ewens has produced an advanced-level treatise on theoretical population genetics. Ewens intends his book as a graduate-level account of the mathematical theory, with no pretense of covering the results of experimental population genetics, or even of treating theoretical topics that have been dealt with by highly approximate and nonrigorous arguments.

Those familiar with Ewens's 1969 book *Population Genetics*, to which this is a successor, will expect a simple, clear, graceful style and will not be disappointed. Ewens seems incapable of writing badly. Clarity is admirable in any other author, given its rarity in this field. In Ewens it is to be expected.

The opening chapter, "The golden age," gives a quick summary of the basic work of Wright, Haldane, and Fisher. Ewens's respectful treatment will be a useful antidote to the view held in some quarters that theoretical population genetics was invented in California about 1970 and that the preceding half-century of work was done by sloppy thinkers who could not get their mathematical notation right.

The titles of the chapters will convey the flavor of the rest of the book: "Technicalities and generalizations," "Discrete stochastic models," "Diffusion theory," "Applications of diffusion theory," "Two loci," "Many loci," "Molecular population genetics," "The neutral theory," and "Generalizations and conclusions."

The two topics covered most completely are the neutral mutation theory, with the diffusion methods used to analyze it, and the theory of natural selection in infinite populations with two loci. In the former, Ewens is much concerned with developing the machinery for formal statistical testing of the neutrality hypothesis. Ewens has himself been the major pioneer in bringing formal statistical testing to bear on the neutral hypothesis. His treatment is fully up to date, certainly the best available summary of this highly complicated area. We are nowhere near a satisfactory test of neutrality versus selection, particularly since the behavior of various test statistics is known under some variants of the neutrality hypothesis, but only under a few rather implausible kinds of balancing selection.

With respect to two-locus theory, Ewens places some emphasis on Fisher's "fundamental theorem" and its failure to be true in virtually all interesting cases. Ewens correctly emphasizes that even though the mean fitness of a population may either decline or increase as a result of natural selection, in model systems it seems to increase a great deal more often than it declines. If this were not true in nature, evolution would never have allowed population geneticists the opportunity to write papers implying that fitness usually decreases as a result of natural selection.

It is well to keep in mind that Ewens is not attempting a survey of theoretical population genetics but intends to concentrate on those areas that have been invaded most successfully by sophisticated mathematical theory. Even within these areas, the treatment tends to concentrate on matters in which he is interested, and though he has broad interests some bodies of successful theory are slighted. Noticeably absent is treatment of the rapidly expanding application of quantitative genetic models to ecological and evolutionary questions, in particular the work of Lande, Slatkin, Bulmer, and Roughgarden.

To his credit, Ewens does make an effort to point out some areas of future expansion of mathematical theory in population genetics. He is ahead of most of his colleagues in appreciating the importance of work on methods of estimating evolutionary trees and testing hypotheses using them. As DNA sequence data become available over a range of related species, these kinds of macroevolutionary applications of population genetics will grow in importance. Other macroevolutionary concerns such as models of speciation are the focus of much current work, but Ewens provides little coverage of them, either from lack of interest or because their theory is so complex that it does not lend itself to exact mathematical methods.

This is an idiosyncratic work, but a very good one. It comes at a time when theory and data are too immature to attempt a post-neo-Darwinian synthesis, so that we can benefit from idiosyncrasy, particularly when it is elegantly, concisely, and knowledgeably presented.

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A Medical System Examined

Health, Medicine and Mortality in the Sixteenth Century. CHARLES WEBSTER, Ed. Cambridge University Press, New York, 1979. xiv, 394 pp., illus. $39.95.

This collection of interdisciplinary essays on Tudor times is dedicated to the memory of Sanford V. Larkey (1898–1969), a Johns Hopkins researcher who pioneered the historical analysis of medical systems. A medical system includes a natural environment, diseases and crop failures, the economy, institutions, competing medical theories, various types of medical practitioners, and, of course, the patients who provide the prerequisite for the existence of medicine. The essays

provide fascinating glimpses of facets of the system they deal with but too few insights into its overall functioning; the fundamental question suggested by the title, that of the impact of medicine on health and mortality, is not touched. The reader must decide whether the system fulfilled its assumed purpose (to save lives and relieve suffering) and is led to conflicting answers. From the perspectives of the various authors, this was a time of great medical sophistication, terrible famines and epidemics, drastically deteriorating economic conditions, and remarkably low mortality. Because of their contradictory nature, these conclusions inspire caution, and it is possible that they are a better index of the character of our knowledge than of the state of health and welfare in the 16th century.

Tudor medicine was eclectic. Medical theory and the teaching by medical faculties in England as well as on the Continent were still dominated by the Galenic tradition. Astrological physics was compatible with the classical explanations of health and disease because it resorted to humors, elements, and affinities as the receptors of astral influence. For example, the moon was thought to control the amount of blood in the veins, and phlebotomy (bloodletting) was a favorite recommendation of the astrologers. But empirical investigations, among them the dissection of cadavers, which constituted a growing part of the curriculum in medical schools, were yielding results that clearly contradicted Greek textbooks and scholastic logic. At the same time, explanation of human afflictions in terms of celestial influences was taken less and less seriously. On the other hand, the alchemical tradition was revitalized. It attracted the intelligentsia with the promises of chemical therapy, the virtues of distillations from plants, and the beneficial properties of nature's substances.

Historians of population debate the impact of medicine on mortality before the 19th century. It would have been interesting to know how our authors evaluate the efficacy of treatment. But this may be a crass and irrelevant question to the intellectual historians. Charles Webster, who contributes an essay on alchemical and Paracelsian medicine, and Allan Chapman, who discusses astrological medicine, do not even mention what ailments these forms of treatment were designed to cure. The text of one of the plates, misplaced in a chapter on diet (p. 111), suggests that not every medical discovery of the age was useless. The plate reproduces a 1607 broadsheet by Sir Hugh Plat entitled "Certaine Philosophical Preparations of Foode and Beuerage for Sea-men in their long voyages" that is of alchemical inspiration. To this reviewer, it appears to propose, among other recipes, the sterilization of water "by a philosophical fire" so that it "will bee warranted to last sweete, good and without any intention to putrefaction, for 2, 3, or 4 yeeres together." And Plat goes on: "Here I may not omit the preparation of the iuce of Limons with this fire: because it hath of late been found by that worthy Knight Sir Iames Lancaster to be an assured remedy in the scurby." The philosophical fire apparently kept lemon juice from fermenting.

In his inventory of vernacular medical literature, Paul Slack comes closest to discussing the usefulness of medical science at the time. Diagnosis ordered the disease in a logical theory of the universe, and the rituals involved in administering medication gave the suffering patient his or her proper place in a complicated social hierarchy. Even if remedies were of no instrumental help, medicine had important social and psychological functions, and the customers were generally satisfied. Medical texts shared many characteristics with religious writings and had a similar appeal; if nothing else, they prepared for death. Whether life was prolonged in the process is moot. There was demand for a diversified gallery of medical practitioners ranging from quacks and matrons to highly trained physicians. The undoubted prestige of the last was due in part to the formidable length of medical studies, much of it spent abroad in an international network of universities. "The training of the sixteenth-century physician was often so involved and prolonged that by comparison moderns seem distinctly underqualified" (Pelling and Webster, p. 189).

Our knowledge of medical lore and literature is more developed than our knowledge of Tudor England as a disease environment. Plague was visiting regularly, and periodic mortality crises resulted from famine or epidemics. Little is known about particular diseases: it is an indication of the haziness surrounding causes of deaths that lunacy receives nine quotations in the book's index and smallpox only four. The evidence in Thomas Forbes's chapter on the "changing face of death" in London is fragile. Tuberculosis may well have been the most important cause of death, but in the registers of one parish, at least, "con" was the abbreviation for either "convulsions" or "consumption" or both.

Similarly, we know little about diet in the 16th century, and Andrew Appleby's inferences from price data seem questionable. The conclusion that real wages fell by half during the century is predicated on the representativeness of the last decade, dominated by the famine of 1596–97; and, furthermore, what was the relation between prices, wages, and the standard of living in a subsistence economy? Even in the cities, poor relief was reducing the impact of crisis prices. More evidence will be required before we can accept the Malthusian interpretation that "there were too many people in rural England at the end of the sixteenth century to be fed given the inequitable distribution of land and the existing agricultural technology" (p. 107).

Although other statistical sources seem unreliable, Roger Schofield and E. A. Wrigley claim that parish registers, which provide the raw material of family reconstitution, attained their best quality in the 100 years before 1650, prior to the loss of coverage due to nonconformism. They use groups of parishes to compute infant and child mortality and get results that are suprisingly low by premodern European standards. If we trust their data—and they are very careful in their presentation and testing of the evidence—then infant mortality was only 139 (deaths under one year per 1000 births) in their group of eight parishes. Rates for rural France, Sweden, or England prior to 1800 were above 200 and for England at mid-19th century they were close to 150. It is disturbing that the main source of variability in the rates for the English parishes is at the beginning of life, when birth trauma and congenital defects predominate, rather than later, when mortality results from infectious diseases and childrearing customs. The underregistration of deaths soon after birth is also most likely, and cannot be excluded here. But a fact remains: a claim has been staked, on solid evidence, for low mortality figures in provincial Tudor England. Changes in the structure of mortality visible after 1600 suggest the appearance of new infectious diseases and, perhaps, a deterioration of expectation of life; and Forbes reports much higher mortality for London.

The high standards of scholarship maintained throughout the book augur well for the new series of Cambridge monographs on the history of medicine, of which this is the first volume.

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