Book Review

Am. J. Hum. Genet. 68:548, 2001

Genetics and Analysis of Quantitative Traits, By Michael Lynch and Bruce Walsh. Sunderland, MA: Sinauer Associates, Inc., 1998. Pp. 980. $74.95 (hardcover).

Until the 1990s, the majority of work done in the field of quantitative genetics was limited to plants and animals. During this period, the majority of gene-mapping projects for humans involved Mendelian traits. Observations for these traits were dichotomous; that is, the study subjects were either affected or unaffected, sometimes with the features of reduced penetrance, age-related penetrance, and phenocopies. Even when quantitative measures were used to define a phenotype (e.g., blood glucose measures for non–insulin-dependent diabetes mellitus), these measures were often treated in analyses as qualitative traits, for which a cutoff value was used to determine which study subjects were affected and unaffected. A problem with this scheme is that the dichotomized phenotype can have lower heritability, as well as reduced power, when used in analyses to detect susceptibility loci.

The late 1980s and 1990s saw advances in the availability of dense maps of microsatellite markers and computational methods. Emphasis in the area of gene mapping shifted from Mendelian traits to "complex traits," which are responsible for the majority of genetic-disease morbidity. Complex traits often have underlying quantitative phenotypes that define disease etiology. Researchers use a variety of methods to analyze quantitative traits to map the underlying susceptibility loci, which are often referred to as quantitative trait loci (QTLs). A search of the literature reveals a long list of quantitative measures that are used to study complex traits: BMI in the study of obesity, bone mineral density to investigate osteoporosis, etc. Quantitative measures are also used for phenotypes that usually are not thought of as being quantitative in nature—for example, positive and negative symptom measures for schizophrenia. Given the shift in human genetics to the study of diseases with underlying quantitative phenotypes, researchers and students in the field of genetic epidemiology/statistical genetics must be well versed in the area of quantitative genetics. Lynch and Walsh's opus *Genetics and Analysis of Quantitative Traits* is a welcome addition to this area of scientific study.

Genetics and Analysis of Quantitative Traits deserves high marks. The authors, Michael Lynch and Bruce Walsh, have covered a wealth of material in this first volume of two. The book is written clearly and can be used as a reference book, a self-learning resource, or a textbook. Each section has applied examples that the reader can work through with the guidance of the authors. Answers are provided, enabling readers to check their work. Although the authors begin the book with some basic statistical concepts, I would not recommend this book to students of genetics before they have learned the fundamentals of statistics from other sources.

The book is divided into four sections: "The Foundations of Quantitative Genetics," "Quantitative Trait Loci," "Estimation Procedures," and "Appendices." A summary of the information covered in each chapter is presented below; however, for sake of brevity, some topics are omitted. A complete table of contents is available at http://nitro.biosci.arizona.edu/zbook/volume_1/vol1.html.

The first section of the volume, "The Foundations of Quantitative Genetics," opens with "An Overview of Quantitative Genetics" (chapter 1), which presents a historical background and states the major goals of the field. The authors then review some basic concepts, including properties of distributions (chapter 2) and covariance, regression, and correlation (chapter 3). "Properties of Single Loci" (chapter 4) presents a variety of topics, including the Hardy-Weinberg principle and the basis of dominance. "Sources of Genetic Variation for Multilocus Traits" (chapter 5) covers the concepts of epistasis, linkage, and linkage disequilibrium. "Components of Environmental Variation" (chapter 6) examines causes of within-individual variation, repeatability of measures, maternal environmental effects, and genotype/environment interactions. "Resemblance between Relatives" (chapter 7) presents the concepts of identity by state and by descent, coefficient of inbreeding, assortative mating, and heritability. In brief, the next three chapters present an overview of matrix and linear models (chapter 8), analysis of line crosses (chapter 9), and inbreeding depression (chapter 10). The last chapter (11) of this section, entitled "Matters of Scale," presents transformations to achieve normality, test for normality, and variance-stabilizing transformations.

The second section, "Quantitative Trait Loci," begins with a chapter (12) entitled "Polygenes and Polygenic Mutation," which touches on the molecular nature of QTL variation. Chapter 13, "Detecting Major Genes," delves into the area of segregation analysis covering mixed models, complex segregation analysis, ascertainment bias, and estimation of single-locus penetrance models. "Principles of Marker-Based Analysis" (chapter 14) covers a wide range of topics, including genetic maps, fine mapping of major genes using population-level linkage disequilibrium, the transmission/disequilibrium test, and estimation of the effects of candidate loci. The last two chapters of this section cover mapping and characterization of QTLs using inbred line crosses (chapter 15) and outbred populations (chapter 16). Chapter 15 examines experimental designs, QTL detection and estimation using linear models and maximum likelihood, maximum-likelihood inter-

val mapping, likelihood maps, calculation of support and confidence intervals for QTL position, sample-size requirements for detection of QTLs, and problems of multiple testing. Chapter 16 presents measures of marker informativeness, including mating types (fully informative, backcross, and intercross), heterozygosity, polymorphism content, and proportion of fully informative matings; sib-pair analysis (linear models and maximum likelihood estimation); Haseman-Elston regression; variance-components analysis; affected sib-pair tests; and affected pedigree-member tests.

The third section, "Estimation Procedures," revisits some of the topics previously covered, presenting them in detail: "Parent-Offspring Regression" (chapter 17), "Sib Analysis" (chapter 18), "Genotype × Environment Interaction" (chapter 22), "Maternal Effects" (chapter 23), "Estimation of Breeding Values" (chapter 26), and "Variance-Component Estimation with Complex Pedigrees" (chapter 27). This section also delves into new areas: "Twins and Clones" (chapter 19), "Cross-Classified Designs" (chapter 20), "Correlations between Characters" (chapter 21), "Sex Linkage and Sexual Dimorphism" (chapter 24), and "Threshold Characters" (chapter 25).

There are five appendices: "Expectations, Variances, and Covariances of Compound Variables," "Path Analysis," "Further Topics in Matrix Algebra and Linear Models," "Maximum Likelihood Estimation and Likelihood Ratio Tests," and "Computing the Power of Statistical Tests." The reference section provides a rich resource for the reader to tap for additional material.

Genetics and Analysis of Quantitative Traits is an excellent resource for both novice and experienced researchers. It is not surprising that the genetics community is eagerly awaiting the second volume of this series, entitled *Evolution and Selection of Quantitative Traits*. For a preview of the second volume, refer to the draft of the table of contents and selected book chapter excerpts at http://nitro.biosci.arizona.edu/zbook/volume_2/vol2.html.

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0002-9297/2001/6802-0033$02.00