Preface

Statistical genetics has played a pivotal role for more than a century in the discovery of genes that cause disease in humans. Driven by advances in molecular genetics and medicine and the continuing improvements in genotyping technology, statistical models and methods have adapted over time to the challenges presented by new study designs.

In this book we discuss the statistical models and methods that are used to understand human genetics from an historical perspective. Starting with Mendel's first experiments to more recent genome-wide association studies, we describe how genetic information can be incorporated into statistical models to discover disease genes. While we cover most of the commonly used approaches in statistical genetics (e.g., aggregation analysis, segregation, linkage analysis, etc.), the focus of the book is on modern approaches to association analysis. Our treatment of earlier topics is mainly to help the reader see the larger picture and understand the historical development of methods. We provide numerous examples to illustrate key points throughout the text, both of Mendelian and complex genetic disorders.

Most statisticians, biostatisticians and data analysts are aware of the key role that their disciplines have played in finding disease genes, but have little direct knowledge of how gene discovery via gene mapping works. This book arises from teaching courses to graduate students, with varying levels of statistical preparation, at the Harvard School of Public Health. Our intended audience for this book is largely quantitatively oriented health scientists, including biostatisticians, statisticians, epidemiologists, physicians and molecular geneticists, who want to learn about statistical methods for genetic analysis, whether to better analyze genetic data, or to pursue research in methodology. We assume familiarity with elementary probability, statistical inference and methods, specifically distributions for two or more variables, conditional, marginal and joint distributions, Bayes rule, likelihood methods, hypothesis testing, estimation, correlation and the essential ideas of regression, including linear, log-linear and logistic. However, the book emphasizes concepts and examples, and the exercises include problems for students with a broad range of skill levels. We assume no formal training in genetics, but familiarity with basic concepts in molecular genetics is necessary and will be reviewed in the first chapter.

There are many excellent texts in statistical methods currently available to students and we have used many of them in our teaching. This book shares much with

the classic texts of Sham (1998) and Lange (2002), both of which were written with a similar audience in mind. Our book is less focused on linkage and more focused on association analysis than the text by Sham, and provides easier reading for students with less mathematical training than the book by Lange. We also share much with the newer texts by Thomas (2004) and Yang (2000), being less epidemiologically oriented than Thomas, with more emphasis on human disease than Yang. The book by Foulkes (2009) has a stronger emphasis on software implementation while our focus is on statistical theory and methods.

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