Preface

Human population genetics has grown tremendously in importance and in centrality to the broader field of human genetics, particularly since the era of genomics. The Human Genome Project began in 1990 and was declared essentially complete in 2003. However, having a genome sequence did not immediately yield the medical and research benefits that were used to justify the project. It quickly became apparent that these benefits required the study of variation: variation in the human genome, variation in health status, variation in demographic histories, etc. As a result, additional projects were spawned to create databases that focused on variation. Once the focus was on variation, human population genetics became central to the medical and research goals of these projects. The reason is simple: human population genetics is the science of human genetic variation: its past, its current significance, and its evolutionary fate. Population genetics provides the principles and tools used by many human geneticists in at least some aspects of their research programs. Many of these human geneticists do not consider themselves population geneticists, but an effective and appropriate use of these tools and principles requires some knowledge of population genetics. I have therefore written this book not only for human population geneticists and their students but also for the broader human genetics community. Moreover, because of the immense amount of knowledge and data about our own species, humans have become an ideal model organism for population genetic studies. Many of the techniques, both molecular and analytical, which were first developed for human studies are portable to other species. Moreover, most of the principles of human population genetics are applicable to all species and to a general understanding of evolution within a species. Hence, this book is relevant to all population geneticists and not just those who focus mainly on humans.

Besides the advances in genetics and genomics that have propelled population genetics to its increasingly central role in human genetics, there have also been tremendous analytical advances in statistics, bioinformatics, and computational biology. Advances in these areas have not only allowed us to handle large data sets, but also to make use of principles that have been central to population genetics since its inception as a field—often in ways unimaginable to the originators of these principles. For example, the population genetic principle of identity-by-descent has played in a critical role in much population genetic theory since the 1920s, but by coupling this old principle with modern genomic data we can apply it powerfully to identify and localize genetic diseases, map risk factors for common systemic diseases, study inbreeding and its consequences with or without pedigrees, and identify genomic regions under natural selection and important for human adaptations—just a few of the applications of this old concept. The pace of these molecular and analytical advances is dizzying, so I have not written a "how to" book that would become almost immediately out-of-date, but rather a "why and when" book. Computer programs implementing these old and established principles of populations genetics are constantly being developed in new and more powerful ways, but understanding the underlying population genetic principles will help researchers answer the questions of why these programs do what they do and when they should be used—and perhaps more importantly, when they should not be used. The why and when depends not only on an understanding of population genetic principles, but also an understanding of fundamental statistical principles such as maximum likelihood (developed in the 1910s) and Bayes theorem (from the 1700s). Despite the widespread use of maximum likelihood and Bayesian statistics in human population genetics, there is still the

need to understand the why and when of programs based on these and other statistical principles. Once again, this is not a "how to" book in statistics, but rather a book designed to help the reader become a more discerning and intelligent user of the programs and analytical techniques that are continually being developed and refined.

I wish to thank Charlie Sing (my graduate mentor in Human Genetics) and Ed Rothman (my graduate mentor in Statistics) for giving me such an excellent grounding in two fields that have proven to be remarkably synergistic in my subsequent research, as well as continuing my education in these fields through collaborations after I left the University of Michigan. My love and interest of population genetics was first whetted by Dr. Harrison Stalker, my undergraduate mentor at Washington University, and Dr. Hampton Carson, both an undergraduate mentor at Washington University and a postdoctoral mentor at the University of Hawaii, and memories of these two remarkable scientists and human beings were in my mind repeatedly in the writing of this book. I also would like to thank the many younger mentors who taught me so much—a large group of creative, highly intelligent, and independent undergrads, graduate students, and postdocs who were in my lab over the years. I thank the editors at Elsevier—Christine Minihane, Lisa Eppich, Peter Linsley, and Carlos Rodriguez—for their understanding of the many delays and interruptions encountered while writing this book and for their unflagging support of the project despite those delays. Finally, I wish to thank my wife, Dr. Bonnie Templeton, for her support and encouragement over the long process of writing this book.