

PREFACE

With the emerging recognition that the expression of most characters is influenced by multiple genes and multiple environmental factors, quantitative genetics has become the central paradigm for the analysis of phenotypic variation and evolution. The historical development of the field is like that of a braided stream whose final destination has not been reached. Virtually all of quantitative genetics draws upon basic theoretical foundations laid down in the first third of this century, largely by Ronald Fisher and Sewall Wright. However, practical applications of this theory did not become common until the 1950s, and these were restricted almost entirely to agricultural settings. Plant and animal breeders subsequently diverged towards radically different modes of experimental design and analysis, perhaps because of the different population structures of crop plants and domesticated animals, but possibly also because of the historical segregation of the study of plants and animals in academia. Even today, at many major universities, separate courses in quantitative genetics are taught in departments of plant and animal science.

Only in the 1970s and 1980s did evolutionary biologists begin to fully embrace quantitative genetics as a major tool in both theoretical and empirical analysis. Many evolutionary quantitative geneticists are only vaguely aware of the extent to which the statistical machinery of the field traces to earlier work by animal and plant breeders as well as to work by the statistician Karl Pearson (an ardent non-Mendelian) at the turn of the century. Over the past few decades, human geneticists have also been progressively adopting quantitative-genetic approaches as the primary mode of analysis of genetic disorders. This work is largely unknown to (and generally uninformed by) those in the fields of breeding and evolutionary genetics.

In the mid 1980s, we realized that an integration of these disparate and semi-independent subdisciplines might be a useful contribution to the field of quantitative genetics at large. Our goal was to bring together the diverse array of theoretical and empirical applications of quantitative genetics under one cover, in a way that would be both comprehensive and accessible to anyone with a rudimentary understanding of statistics and genetics. As we ventured into a lot of unfamiliar territory, we gradually discovered that we had substantially underestimated the enormity of the task. So here we are, a decade later, about halfway to our final destination. What we originally envisioned as a single volume has now become two, with the focus of this first book being on the basic biology and methods of analysis of quantitative characters.

We have tried to write this book in a way that will encourage its use as a textbook in quantitative genetics. But the book also provides a thorough enough coverage of the literature so that it should be useful as a basic reference. Throughout, we have attempted to develop central theoretical concepts from first principles. To aid the less statistically sophisticated reader, we have included several chapters and appendices that review essentially all of the statistical tools employed in the book. Wherever possible, we have illustrated theoretical and analytical concepts with empirical examples from diverse settings. Both of our backgrounds are in evolutionary genetics, however, and a certain amount of bias may have crept in.

Today's quantitative genetics is not the science that it was 25 (or even 10) years ago. Three major developments are particularly noteworthy. First, largely motivated by the work of Russell Lande in the 1970s and early 1980s, there has been an explosive influx of quantitative-genetic thinking into evolutionary biology. It was, in fact, this dramatic refocusing of many evolutionary problems that first precipitated our interest in producing a book — most existing texts in quantitative genetics give little (and often no) attention to the great accomplishments that have been made in evolutionary biology. Thus, it is now ironic that much of our discussion of this work will be postponed to our second volume, *Evolution and Selection of Quantitative Traits*.

A second major development occurred in animal breeding. Here, enormous strides have been made in the development of new techniques for estimating breeding values (for the purposes of identifying elite individuals in selection programs) and for estimating variance components from samples of complex pedigrees. Although the foundation for many of these techniques was outlined in a remarkable series of papers by Charles Henderson in the 1960s and 1970s, their widespread application awaited the development of high-speed computers. Numerous technical treatises exist on these techniques, but their general absence from basic textbooks has endowed them with a certain mystique. In the last two chapters of this book, we have attempted to outline the basic principles of complex pedigree analysis, without getting greatly bogged down in technical details.

Third, in the past five years, as molecular markers have become widely available and economically feasible, there has been a rapid proliferation of new methods for detecting, locating, and characterizing quantitative-trait loci (QTLs). Currently one of the most active fields of quantitative-genetic research, QTL analysis was a mere dream when we embarked on this book. Thus, one benefit of our slow writing is the fact that we have been able to provide an up-to-date report on the exciting achievements of QTL analysis. Although a full integration of quantitative genetics and molecular genetics is still a long way off, with the recruitment of molecular biologists into the field we can anticipate great advances in the near future.

Over the past couple of years, we have heard a number of colleagues, some quite prominent, make statements like "quantitative genetics is dead," a rather hard thing to take when we have spent 10 years writing a treatise on the subject!

There are indeed some people who would dearly like to embrace this obituary as a rationale for ignoring a technically demanding field. However, the reality is that as a tool for the analysis of complex characters, quantitative genetics is as alive as it has ever been. What may be dead (or at least much less viable than we originally thought) is the simple caricature of traits being influenced by an effectively infinite number of loci with very small, additive effects. As we try to emphasize throughout this book, quantitative genetics is still fully capable of accommodating characters with small numbers of loci (even single loci), nonadditive genetic effects, non-Mendelian inheritance, and other genetic complexities. Indeed, the current machinery of quantitative genetics stands waiting (and its practitioners willing) to incorporate the fine genetic details of complex traits being elucidated by molecular and developmental biologists.

In spite of our best efforts, it is likely that a few errors have escaped scrutiny. Hopefully, they will be trivial and obvious, but Murphy's law suggests otherwise. Likewise, many of the methods we discuss can be computationally very demanding. To address both of these issues, we have set up a World Wide Web home page to post listings of detected errors and links to recent programs. The URL is <http://nitro.biosci.arizona.edu/zbook/book.html>; interested parties should contact BW at jbwalsh@u.arizona.edu for further information.

Acknowledgments

We have both profited considerably from interactions with numerous colleagues, most notably the clear-thinking, insights, and encouragement from Russ Lande. During the 1980s, while at the University of Illinois, ML was also highly fortunate to find company with an exceptional group of theoreticians in animal breeding (Rohan Fernando, Dan Gianola, Charles Henderson, and Mike Grossman), with whom joint participation in seminar courses was a defining experience. Collaborations with Steve Arnold, Reinhard Bürger, Wilfried Gabriel, Bill Hill, and Russ Lande also played critical roles in ML's movement into the field of quantitative genetics (from a background in limnology). BW's exposure to quantitative genetics arose from undergraduate, graduate, and postdoctoral experiences at the University of California at Davis, the University of Washington, and the University of Chicago, where he had the fortune to learn from the likes of Bob Allard, Steve Arnold, Joe Felsenstein, Russ Lande, Tom Nagylaki, Tim Prout, Monty Slatkin, Michael Turelli, and Mike Wade.

A very large number of individuals have aided in the development of this book. Most notable are Jim Crow and Bill Hill, both of whom critically evaluated nearly the entire manuscript, and in the process saved us from numerous embarrassing mistakes. The breadth of their understanding of population and quantitative genetics is a continual source of amazement to us. Large blocks of the book were reviewed by Bill Bradshaw, Doug Schemske, Ruth Shaw, and

Shizhong Xu, and comments on individual chapters were made by May Berenbaum, Hong-Wen Deng, Jim Fry, Sun-Wei Guo, Chris Haley, Jeff Hard, David Houle, Ritsert Jansen, Sara Knott, Trudy Mackay, Emília Martins, Patrick Phillips, Ahmed Rebaï, Ken Spitze, Tom Starmer, Sijne van der Beek, Sara Via, Joel Weller, John Willis, Mary Willson, and Zhao-Bang Zeng. To all of these individuals and to the many students who were victims of early drafts, we are extremely grateful for your insights.

We are especially grateful to our publisher, Andy Sinauer, who exhibited an extraordinary degree of patience (in the face of what, at times, must have been very serious doubt) as this project extended several years beyond its projected completion date. Marie Scavotto, Chris Small, and Carol Wigg were tremendously helpful during production.

As geneticists we certainly must acknowledge our parents, Bob and Bernice (ML), and Kevin and Phyllis (BW). We are especially grateful to them for providing us with an atmosphere conducive to learning and for putting up with our antics as young biologists, which can be a considerable strain to the faint-of-heart. Our sincere hope is that other budding biologists also find themselves in such supportive environments.

Finally, we thank our wives Emília Martins (ML) and Lee Fulmer (BW) for their continuous encouragement, patience, and friendship.

Mike Lynch, Eugene

J. Bruce Walsh, Tucson

October 1997