

# Contents

*Preface xi*

*Acronyms and Abbreviations xv*

## **Chapter 1 Genetic Variation 1**

Genetic and Molecular Essentials 2

*Genotype and Phenotype 2*

*Gene Expression 3*

*DNA Cleavage, Manipulation, and Amplification 5*

Types of Polymorphisms 11

*DNA Polymorphisms 11*

*Uses of DNA Polymorphisms 18*

*Protein Polymorphisms 18*

*Gene and Genotype Frequencies 20*

Organization of Genetic Variation 23

*Populations 24*

*Models 24*

*Random Mating 26*

*The Hardy-Weinberg Principle 26*

*Implications of Random Mating 29*

*Chi-square Test for HWE 29*

*Recessive Alleles Hidden in Heterozygotes 32*

*Multiple Alleles and X-Linked Genes 33*

*Multiple Loci: Linkage and Linkage Disequilibrium 36*

Inbreeding 41

*Genotype Frequencies with Inbreeding 41*

*The Inbreeding Coefficient 44*

*Inbreeding Depression 46*

*Calculation of the Inbreeding Coefficient from Pedigrees 49*

*Regular Systems of Mating 52*

Further Readings 53 • Problems 54

## **Chapter 2 The Causes of Evolution 59**

### **Mutation 59**

*Forward Mutation 60*

*Reversible Mutation 61*

*Remote Inbreeding in a Finite Population 63*

*Equilibrium Heterozygosity with Mutation 65*

### **Migration 66**

*The Island Model of Migration 67*

*How Migration Limits Genetic Divergence 68*

*Wahlund's Principle 70*

*Hierarchical Population Structure 72*

### **Natural Selection 74**

*Haploid Selection 74*

*Diploid Selection 77*

*Time Required for Changes in Gene Frequency 80*

*Overdominance and Underdominance 83*

*Mutation-Selection Balance 86*

*More Complex Modes of Selection 87*

### **Random Genetic Drift 88**

*Diffusion Approximations 88*

*Probability of Fixation and Time to Fixation 94*

*Effective Population Number 96*

### **Further Readings 98 • Problems 100**

## **Chapter 3 Molecular Population Genetics 105**

### **Molecular Polymorphisms 106**

*The Information Content of Molecular Sequences 106*

*The Coalescent 108*

*Nucleotide Polymorphism 110*

*Nucleotide Diversity 111*

*Tajima's D Statistic 112*

### **Patterns of Change in Nucleotide and Amino Acid Sequences 113**

*Synonymous and Nonsynonymous Substitutions 114*

*Codon Usage Bias 116*

*Selection for Optimal Codons and Amino Acids 117*

*Selective Sweeps versus Background Selection 120*

### **Polymorphism and Divergence 122**

*The Hudson-Kreitman-Aguadé (HKA) Test 123*

*The McDonald-Kreitman Test 126*

*Polymorphism and Divergence in a Poisson Random Field 128*

*Convergence to Adaptation 130*

### **Molecular Phylogenetics 132**

<i>The Multiple-Hit Problem</i>	134
<i>Phylogenetic Inference</i>	136
<i>Molecular Clocks</i>	138
Transposable Elements	141
<i>Insertion Sequences and Transposons in Bacteria</i>	142
<i>Transposable Elements in Eukaryotes</i>	143
Further Readings	144 • Problems 145

## **Chapter 4 The Genetic Architecture of Complex Traits 151**

Types of Complex Traits	151
Phenotypic Variation	152
Genetics and Environment	156
<i>Genotypic Variance and Environmental Variance</i>	156
<i>Broad-Sense Heritability</i>	158
<i>Genotype-Environment and Other Interactions</i>	158
<i>Genetic Effects on Complex Traits</i>	160
<i>Components of Genotypic Variation</i>	160
Artificial Selection	163
<i>Prediction Equation for Individual Selection</i>	165
<i>Genetic Basis of Complex Traits</i>	167
<i>Change in Allele Frequency</i>	169
<i>Change in Mean Phenotype</i>	170
Correlation between Relatives	172
<i>Parent-Offspring Correlation</i>	173
<i>Heritability Estimates from Resemblance between Relatives</i>	174
<i>Offspring-on-Parent Regression</i>	176
Quantitative Genetics of Natural Populations	177
<i>Directional Selection with Mutation-Selection-Drift</i>	178
<i>Stabilizing Selection with Mutation-Selection-Drift</i>	179
<i>Antagonistic Pleiotropy</i>	180
Complex Traits with Discrete Expression	181
<i>Threshold Traits: Genes as Risk Factors</i>	181
<i>Heritability of Liability</i>	182
<i>Applications to Human Disease</i>	185
<i>Linkage Analysis and Lod Scores</i>	186
Quantitative Trait Loci (QTLs)	189
<i>Number of Genes</i>	189
<i>QTL Mapping</i>	190
<i>Candidate Genes</i>	194
Further Readings	195 • Problems 196

## **Literature Cited 203**

## **Index 213**