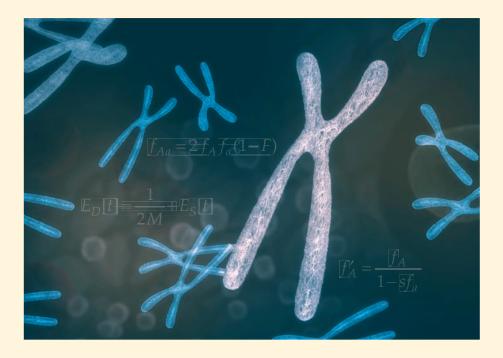
An Introduction to Population Genetics

THEORY AND APPLICATIONS



Rasmus Nielsen • Montgomery Slatkin



© 2013 Sinauer Associates, Inc. This material cannot be copied, reproduced, manufactured or disseminated in any form without express written permission from the publisher.

Brief Contents

Chapter 1	Allele Frequencies, Genotype Frequencies, and Hardy–Weinberg Equilibrium 5
Chapter 2	Genetic Drift and Mutation 21
Chapter 3	Coalescence Theory: Relating Theory to Data 35
Chapter 4	Population Subdivision 59
Chapter 5	Inferring Population History and Demography 77
Chapter 6	Linkage Disequilibrium and Gene Mapping 107
Chapter 7	Selection I 129
Chapter 8	Selection in a Finite Population 153
Chapter 9	The Neutral Theory and Tests of Neutrality 179
Chapter 10	Selection II: Interactions and Conflict 195
Chapter 11	Quantitative Genetics 215
Appendix A	Basic Probability Theory 233
Appendix B	The Exponential Distribution and Coalescence Times 245
Appendix C	Maximum Likelihood and Bayesian Estimation 249
Appendix D	Critical Values of the Chi-Square Distribution with <i>d</i> Degrees of Freedom 255

Contents

Preface xi

Introduction 1 Types of Genetic Data 1 Detecting Differences in Genotype 2

CHAPTER 1

Allele Frequencies, Genotype Frequencies, and Hardy–Weinberg Equilibrium 5

Allele Frequencies 6 Genotype Frequencies 6 K-Allelic Loci 7 Example: The MC1R Gene 7 Hardy-Weinberg Equilibrium 8 The MC1R Gene Revisited 9 BOX 1.1 Probability and Independence 10 BOX 1.2 Derivation of HWE Genotype Frequencies 11 Tay–Sachs Disease 11 Extensions and Generalizations of HWE 12 Deviations from HWE 1: Assortative Mating 12 Deviations from HWE 2: Inbreeding 13 Deviations from HWE 3: Population Structure 13 Deviations from HWE 4: Selection 14 The Inbreeding Coefficient 15 Testing for Deviations from HWE 16 BOX 1.3 The Chi-Square Test 17 Using Allele Frequencies to Identify Individuals 18

CHAPTER 2	Genetic Drift and Mutation 21 The Wright–Fisher Model 22 Genetic Drift and Expected Allele Frequencies 23 BOX 2.1 Expectation 24 Patterns of Genetic Drift in the Wright–Fisher Model 24 Effect of Population Size in the Wright–Fisher Model 25 Mutation 27 Effects of Mutation on Allele Frequency 28 Probability of Fixation 29 Species Divergence and the Rate of Substitution 30 The Molecular Clock 30 Dating the Human Chimpanzan Divergence Time, 21
	Dating the Human–Chimpanzee Divergence Time 31
CHAPTER 3	Coalescence Theory: Relating Theory to Data 35
	Coalescence in a Sample of Two Chromosomes $(n = 2)$ 36
	Coalescence in Large Populations 38 Mutation, Genetic Variability, and Population Size 40
	Infinite Sites Model 41
	The Tajima's Estimator 42
	The Concept of Effective Population Size 43
	Interpreting Estimates of θ 46
	The Infinite Alleles Model and Expected Heterozygosity 47
	The Coalescence Process in a Sample of <i>n</i> Individuals 49
	The Coalescence Tree and the tMRCA 50
	Total Tree Length and the Number of Segregating Sites 51
	The Site Frequency Spectrum (SFS) 53
	Tree Shape as a Function of Population Size 55
CHAPTER 4	Population Subdivision 59
	The Wahlund Effect 59
	F _{st} : Quantifying Population Subdivision 60
	The Wright–Fisher Model with Migration 63
	The Coalescence Process with Migration 64
	Expected Coalescence Times for $n = 2$ 66
	F _{st} and Migration Rates 68
	Divergence Models 70
	Expected Coalescence Times, Pairwise Difference and F _{ST} in Divergence Models 71
	Isolation by Distance 72

	٠	٠	~
VI	I	I	Contents

CHAPTER 5	Inferring Population History and Demography 77
	Inferring Demography Using Summary Statistics 77
	Coalescence Simulations and Confidence Intervals 79
	BOX 5.1 Simulating Coalescence Trees 80
	Estimating Evolutionary Trees 81
	BOX 5.2 The UPGMA Method for Estimating Trees 83
	Gene Trees vs. Species Trees 84
	Interpreting Estimated Trees from Population Genetic Data 88
	Likelihood and the Felsenstein Equation 92
	MCMC and Bayesian Methods 94
	The Effect of Recombination 97
	Population Assignment, Clustering, and Admixture 99
CHAPTER 6	Linkage Disequilibrium and Gene Mapping 107
	Linkage Disequilibrium 108
	BOX 6.1 Coefficients of Linkage Disequilibrium 109
	BOX 6.2 LD Coefficients for Two Diallelic Loci 110
	BOX 6.3 r^2 as a Correlation Coefficient 112
	Evolution of D 112 BOX 6.4 r^2 and χ^2 113
	BOX 6.5 Change in D Due to Random Mating 114
	BOX 6.6 Recurrent Mutation Reduces D' 116
	Two-Locus Wahlund Effect 116
	BOX 6.7 Two-Locus Wahlund Effect 117
	Genealogical Interpretation of LD 118
	Recombination 118
	Association Mapping 121
	BOX 6.8 Example of a Case–Control Test 123
CHAPTER 7	Selection I 129
	Selection in Haploids 129
	Selection in Diploids 132
	BOX 7.1 Haploid Selection 133
	BOX 7.2 One Generation of Viability Selection 135
	BOX 7.3 Algebraic Calculation of Allele Frequency Changes 136
	BOX 7.4 Special Cases of Selection 137
	BOX 7.5 Genic Selection 138 BOX 7.6 Heterozygote Advantage 142
	BOX 7.6 Heterozygote Advantage 142 BOX 7.7 Estimates of Selection Coefficients for the S Allele in a
	West African Population 143
	Mutation–Selection Balance 144

© 2013 Sinauer Associates, Inc. This material cannot be copied, reproduced, manufactured or disseminated in any form without express written permission from the publisher.

CHAPTER 8	Selection in a Finite Population 153
	Fixation Probabilities of New Mutations 153
	BOX 8.1 Simulating Trajectories 154
	Rates of Substitution of Selected Alleles 161
	BOX 8.2 Accounting for Multiple Substitutions 162
	BOX 8.3 Computing Synonymous and Nonsynonymous Rates 164
	Genetic Hitchhiking 166
	Selective Sweeps 166 BOX 8.4 Hitchhiking in a Haploid Population 168
	Partial Sweeps 170
	Associative Overdominance 171
	BOX 8.5 Estimating the Age of a Mutation 172
CHAPTER 9	The Neutral Theory and Tests of Neutrality 179
	The HKA Test 182
	The MacDonald–Kreitman (MK) Test 183
	The Site Frequency Spectrum (SFS) 184
	Tajima's D Test 186
	Tests Based on Genetic Differentiation among Populations 188
	Tests Using LD and Haplotype Structure 190
CHAPTER 10	Selection II: Interactions and Conflict 195
	Selection on Sex Ratio 195
	Resolving Conflicts 198
	BOX 10.1 The Prisoner's Dilemma 200
	Kin Selection 202
	Selfish Genes 205
	Meiotic Drive 205
	Transposons 207
	Species Formation 208
CHAPTER 11	Quantitative Genetics 215
	Biometrical Analysis 216
	BOX 11.1 Normal Distribution 217
	BOX 11.2 Variance of the Mid-parental Value 220
	Breeding Value 222
	Quantitative Trait Loci 224
	Multiple Quantitative Trait Loci 227

© 2013 Sinauer Associates, Inc. This material cannot be copied, reproduced, manufactured or disseminated in any form without express written permission from the publisher.

	Genotype-Environment Interactions 228 Mapping Quantitative Trait Loci 229 BOX 11.3 Mapping Alleles When Starting with Homozygous Populations 230
APPENDIX A	Basic Probability Theory 233
	The Binomial RV 234
	PMF: Bernoulli 235
	PMF: Binomial 235
	Expectation 237
	Variance 239
	The Poisson RV 240
	PMF: Poisson 240
	The Geometric RV 241
	PMF: Geometric 241
APPENDIX B	The Exponential Distribution and Coalescence Times 245
APPENDIX C	Maximum Likelihood and Bayesian Estimation 249 Bayesian Estimation 252
APPENDIX D	Critical Values of the Chi-Square Distribution with <i>d</i> Degrees of Freedom 255
	Solutions to Odd-Numbered Exercises 257
	Glossary 271
	Credits 279
	Index 281