

CONTENTS

PREFACE XV

CHAPTER 1 **MODELS OF EVOLUTION 1**

BASIC SEQUENCE TERMINOLOGY 2

MODELS OF EVOLUTIONARY PROCESSES 3

Models of populations 3

The effective size of a population 6

Models of mutation 7

Models of recombination 11

Models of natural selection 12

Models of migration 14

Models of mating 17

MODELS OF MOLECULAR EVOLUTION 18

The neutral theory of molecular evolution 18

Misunderstanding and misuse of the neutral theory 21

Alternative models of molecular evolution 23

CHAPTER 2

EXPERIMENTAL DESIGN 25

POPULATION SAMPLING 25

DNA SEQUENCING 26

Sanger sequencing 27

Haplotypes 30

Next-generation sequencing 31

The effect of short sequence reads 33

The effect of high error rates 35

Diverse experimental designs for next-generation genome sequencing 36

GENOTYPING 40

CHAPTER 3

DESCRIBING VARIATION 43

MEASURES OF SEQUENCE DIVERSITY 44

Common estimators of θ for SNPs under the infinite sites model 44

The frequency spectrum of alleles 47

Estimators of θ for SNPs under finite sites models and incorporating sequencing error 50

Interpreting measures of nucleotide variation 53

ADDITIONAL MEASURES OF DIVERSITY 55

Microsatellite variation 55

Haplotype variation 57

CHAPTER 4

RECOMBINATION 59

MEASURING LINKAGE DISEQUILIBRIUM 59

Linkage and linkage disequilibrium 59

Measures of pairwise linkage disequilibrium 61

Summarizing pairwise linkage disequilibrium 63

*Extensions to multiple alleles, multiple loci,
and genotypes* 66

ESTIMATING RECOMBINATION 68

*Finding the minimum number of recombination
events in a sample* 68

The population recombination parameter 70

Estimating the population recombination parameter 71

GENE CONVERSION 77

CHAPTER 5

POPULATION STRUCTURE 79

POPULATION DIFFERENTIATION 79

Populations, subpopulations, and demes 79

The Wahlund effect 80

MEASURING POPULATION DIFFERENTIATION 81

Measuring population differentiation using F_{ST} 81

Alternative measures of population differentiation 86

Is there evidence for population differentiation at a locus? 89

THE EFFECT OF EVOLUTIONARY PROCESSES ON DIFFERENTIATION 91

The effects of natural selection on population differentiation 91

*The effects of migration and drift on population
differentiation* 93

Distinguishing between migration and drift:

The isolation-with-migration model 97

*Additional methods for detecting migration
between pairs of populations* 100

DEFINING POPULATIONS 104

Identifying populations and the individuals within them 104

Using the Wahlund effect to identify population structure 105

*Evolutionary inference from the determination
of population structure* 107

CHAPTER 6

THE COALESCENT 111

SIMULATING SAMPLES OF DNA SEQUENCES 111

SIMULATING THE COALESCENT 114

Coalescent genealogies 114

Genealogies and phylogenies 118

UNDERSTANDING THE COALESCENT 118

Important genealogical quantities 118

The coalescent and measures of polymorphism 120

The effects of ascertainment bias on the allele frequency spectrum 122

EXTENDING THE COALESCENT 124

The coalescent with recombination 124

The coalescent and reference genomes 128

CHAPTER 7

DIRECT SELECTION 131

THE ACCUMULATION OF SEQUENCE DIVERGENCE 131

The rate of nucleotide substitution 131

Estimating sequence divergence 134

DETECTING SELECTION USING DIVERGENCE 137

d_N , d_S , and d_N/d_S 137

Interpreting d_N/d_S 141

DETECTING SELECTION USING POLYMORPHISM 145

The effect of selection on the frequency of polymorphism 145

π_N/π_S 148

DETECTING SELECTION USING POLYMORPHISM AND DIVERGENCE 149

The McDonald-Kreitman test 149

Experimental design for the McDonald-Kreitman test 149

Expectations for levels of polymorphism and divergence	151
Interpreting the McDonald-Kreitman test	152
Methodological extensions of the MK test	154
Assumptions of the MK test	156
Biological extensions of the MK test	159
Summarizing selection across the genome	160

CHAPTER 8

LINKED SELECTION 165

DETECTING SELECTION USING THE AMOUNT OF POLYMORPHISM 165

The effects of positive selection on levels of linked neutral variation	165
The effects of balancing selection and strongly deleterious alleles on levels of linked neutral variation	168
The most underappreciated result in molecular population genetics	170
Detecting selection via levels of polymorphism: The HKA test	171
Experimental design for the HKA test	172
Interpreting the HKA test	173

DETECTING SELECTION USING THE ALLELE FREQUENCY SPECTRUM 175

The effects of positive selection on the allele frequency spectrum	176
The effects of balancing selection on the allele frequency spectrum	177
Detecting selection using the allele frequency spectrum: Tajima's D and related tests	179
Interpreting Tajima's D and related tests of the frequency spectrum	181
Detecting selection using the allele frequency spectrum: Fay and Wu's H	185
The power to detect natural selection using tests of the frequency spectrum	186

DETECTING SELECTION USING PATTERNS OF LINKAGE DISEQUILIBRIUM 189

The effects of balancing selection on linkage disequilibrium 189

The effects of completed sweeps on linkage disequilibrium 190

The effects of partial sweeps on linkage disequilibrium 191

Detecting selection using linkage disequilibrium: Haplotype summary statistics 194

Detecting selection using linkage disequilibrium: Measures of pairwise LD 195

Detecting selection using linkage disequilibrium: Haplotype homozygosity 196

Interpreting tests based on haplotype structure and linkage disequilibrium 200

CAVEATS TO TESTS OF LINKED SELECTION 201

CHAPTER 9

DEMOGRAPHIC HISTORY 203

THE DEMOGRAPHIC HISTORY OF SINGLE POPULATIONS 204

Nonequilibrium demographic histories 204

The effect of changing population size on gene genealogies 206

The effect of changing population size on the allele frequency spectrum 208

The effect of changing population size on other measures of variation 210

Types of data and computational methods used in demographic inference 214

Inferring nonequilibrium population histories 217

THE DEMOGRAPHIC HISTORY OF MULTIPLE POPULATIONS 222

The effect of population structure on gene genealogies 223

The effect of population structure on the allele frequency spectrum 225

Inferring demographic histories for multiple populations 228

<i>Multi-population histories as networks</i>	230
<i>The analysis of multiple populations in space</i>	234

POPULATION GENETICS WITHOUT POLYMORPHISM 239

<i>Ancestral parameters inferred from two species</i>	239
<i>Ancestral parameters inferred from gene tree discordance</i>	240
<i>Introgression inferred from gene tree discordance</i>	244

CAVEATS TO INFERENCES OF DEMOGRAPHIC HISTORY 247

CHAPTER 10

POPULATION GENOMICS 249

GENOME-WIDE SCANS FOR SELECTION 250

<i>Motivating questions</i>	250
<i>Selection versus demography</i>	251
<i>General approaches for identifying targets of selection</i>	254

METHODS FOR CARRYING OUT GENOME-WIDE SCANS FOR SELECTION 258

<i>Detecting selection using a sample from a single population</i>	258
<i>Detecting selection using samples from multiple populations</i>	262

CAVEATS ABOUT NON-INDEPENDENCE IN POPULATION GENOMICS 266

FUTURE APPROACHES 268

<i>The application of machine learning to population genetics</i>	268
<i>Ancient DNA and genetic variation through time</i>	270
<i>Populations of whole assembled genomes</i>	271
<i>Deep population sequencing</i>	273

REFERENCES 275

INDEX 315