

Brief Contents

Part One Genes, Chromosomes, and Heredity

- 1 Introduction to Genetics 1
- 2 Mitosis and Meiosis 17
- 3 Mendelian Genetics 39
- 4 Extensions of Mendelian Genetics 66
- 5 Chromosome Mapping in Eukaryotes 100
- 6 Genetic Analysis and Mapping in Bacteria and Bacteriophages 137
- 7 Sex Determination and Sex Chromosomes 165
- 8 Chromosome Mutations: Variation in Chromosome Number and Arrangement 187
- 9 Extranuclear Inheritance 214

Part Two DNA: Structure, Replication, and Variation

- 10 DNA Structure and Analysis 231
- 11 DNA Replication and Recombination 263
- 12 DNA Organization in Chromosomes 286

Part Three Expression and Regulation of Genetic Information

- 13 The Genetic Code and Transcription 306
- 14 Translation and Proteins 334
- 15 Gene Mutation, DNA Repair, and Transposition 361
- 16 Regulation of Gene Expression in Prokaryotes 392
- 17 Regulation of Gene Expression in Eukaryotes 411
- 18 Cell Cycle Regulation and Cancer 434

Part Four Genomic Analysis

- 19 Recombinant DNA Technology 457
- 20 Genomics and Proteomics 484
- 21 Dissection of Gene Function: Mutational Analysis in Model Organisms 516
- 22 Applications and Ethics of Biotechnology 549

Part Five Genetics of Organisms and Populations

- 23 Developmental Genetics of Model Organisms 575
- 24 Quantitative Genetics and Multifactorial Traits 599
- 25 Population Genetics 617
- 26 Evolutionary Genetics 640
- 27 Conservation Genetics 663

Appendix A Glossary A-1

Appendix B Answers to Selected Problems A-17

Contents

Preface xxiv

Part ONE Genes, Chromosomes, and Heredity

1 Introduction to Genetics 1

1.1 From Mendel to DNA in Less Than a Century 2

- Mendel's Work on Transmission of Traits 2
- The Chromosome Theory of Inheritance:
Uniting Mendel and Meiosis 3
- Genetic Variation 4
- The Search for the Chemical Nature of Genes:
DNA or Protein? 4

1.2 Discovery of the Double Helix Launched the Recombinant DNA Era 5

- The Structure of DNA and RNA 5
- Gene Expression: From DNA to Phenotype 5
- Proteins and Biological Function 6
- Linking Genotype to Phenotype:
Sickle-Cell Anemia 6

1.3 Genomics Grew Out of Recombinant DNA Technology 7

- Making Recombinant DNA Molecules
and Cloning DNA 7
- Sequencing Genomes: The Human
Genome Project 8

1.4 The Impact of Biotechnology Is Growing 9

- Plants, Animals, and the Food Supply 9
- Who Owns Transgenic Organisms? 10
- Biotechnology in Genetics and Medicine 10

1.5 Genetic Studies Rely On the Use of Model Organisms 11

- The Modern Set of Genetic Model Organisms 12
- Model Organisms and Human Diseases 13

1.6 We Live in the "Age of Genetics" 14

Genetics, Technology, and Society 14

Chapter Summary 15

Problems and Discussion Questions 15

Selected Readings 16

2 Mitosis and Meiosis 17

2.1 Cell Structure Is Closely Tied to Genetic Function 18

- Cell Boundaries 18
- The Nucleus 18
- The Cytoplasm and Cellular Organelles 19

2.2 In Diploid Organisms, Chromosomes Exist in Homologous Pairs 20

2.3 Mitosis Partitions Chromosomes into Dividing Cells 23

- Interphase and the Cell Cycle 23
- Prophase 25
- Prometaphase and Metaphase 26
- Anaphase 26
- Telophase 26

2.4 Meiosis Reduces the Chromosome Number from Diploid to Haploid in Germ Cells and Spores 27

- An Overview of Meiosis 28
- The First Meiotic Division: Prophase I 28
- Metaphase, Anaphase, and Telophase I 29
- The Second Meiotic Division 29

2.5 The Development of Gametes Varies during Spermatogenesis and Oogenesis 31

2.6 Meiosis Is Critical to the Successful Sexual Reproduction of All Diploid Organisms 32

2.7 Electron Microscopy Has Revealed the Cytological Nature of Mitotic and Meiotic Chromosomes 33

- Chromatin and Chromosomes 33
- The Synaptonemal Complex 34

Chapter Summary 35

Insights and Solutions 36

Problems and Discussion Questions 37

Extra-Spicy Problems 38

Selected Readings 38



3 Mendelian Genetics 39

- 3.1 Mendel Used a Model Experimental Approach to Study Patterns of Inheritance 40
- 3.2 The Monohybrid Cross Reveals How One Trait Is Transmitted from Generation to Generation 40
 - Mendel's First Three Postulates 41
 - Modern Genetic Terminology 42
 - Mendel's Analytical Approach 42
 - Punnett Squares 43
 - The Testcross: One Character 43
- 3.3 Mendel's Dihybrid Cross Revealed His Fourth Postulate: Independent Assortment 44
 - Independent Assortment 44
 - The Testcross: Two Characters 47
- 3.4 The Trihybrid Cross Demonstrates That Mendel's Principles Apply to Inheritance of Multiple Traits 47
 - The Forked-Line Method, or Branch Diagram 47
- 3.5 Mendel's Work Was Rediscovered in the Early 20th Century 49
- 3.6 The Correlation of Mendel's Postulates with the Behavior of Chromosomes Formed the Foundation of Modern Transmission Genetics 49
 - Unit Factors, Genes, and Homologous Chromosomes 49
- 3.7 Independent Assortment Leads to Extensive Genetic Variation 51
- 3.8 Laws of Probability Help to Explain Genetic Events 51
 - The Product Law and the Sum Law 51
 - Conditional Probability 52
 - The Binomial Theorem 52
- 3.9 Chi-Square Analysis Evaluates the Influence of Chance on Genetic Data 54
 - Interpreting χ^2 Calculations 56
- 3.10 Pedigrees Reveal Patterns of Inheritance in Humans 56
 - Pedigree Conventions 56
 - Pedigree Analysis 57

Genetics, Technology, and Society 59

Tay-Sachs Disease: A Recessive Molecular Disorder in Humans 59

Chapter Summary 59

Insights and Solutions 60



Problems and Discussion Questions 62

Extra-Spicy Problems 64

Selected Readings 65

4 Extensions of Mendelian Genetics 66

- 4.1 Alleles Alter Phenotypes in Different Ways 67
- 4.2 Geneticists Use a Variety of Symbols for Alleles 68
- 4.3 In Incomplete Dominance, Neither Allele Is Dominant 68
- 4.4 In Codominance, the Influence of Both Alleles in a Heterozygote Is Clearly Evident 69
- 4.5 Multiple Alleles of a Gene May Exist in a Population 70
 - The ABO Blood Groups 70
 - The A and B Antigens 71
 - The Bombay Phenotype 71
 - The *white* Locus in *Drosophila* 72
- 4.6 Lethal Alleles Represent Essential Genes 72
 - Dominant Lethal Mutations 73
- 4.7 Combinations of Two Gene Pairs Involving Two Modes of Inheritance Modify the 9:3:3:1 Ratio 74
- 4.8 Phenotypes Are Often Affected by More Than One Gene 75
 - Epistasis 75
 - Unique Inheritance Patterns 75
 - Novel Phenotypes 78
 - Other Modified Dihybrid Ratios 79
- 4.9 Expression of a Single Gene May Have Multiple Effects 80
- 4.10 X-Linkage Describes Genes on the X Chromosome 81
 - X-Linkage in *Drosophila* 81
 - X-Linkage in Humans 82
 - Lesch-Nyhan Syndrome: The Molecular Basis of a Rare X-Linked Recessive Disorder 84
- 4.11 In Sex-Limited and Sex-Influenced Inheritance, an Individual's Sex Influences the Phenotype 84
- 4.12 Phenotypic Expression Is Not Always a Direct Reflection of the Genotype 85
 - Penetrance and Expressivity 85
 - Genetic Background: Suppression and Position Effects 86

- Temperature Effects 87
- Nutritional Effects 87
- Onset of Genetic Expression 88
- Genetic Anticipation 88
- Genomic (Parental) Imprinting 88

Genetics, Technology, and Society 90

Improving the Genetic Fate of Purebred Dogs 90

Chapter Summary 91

Insights and Solutions 91

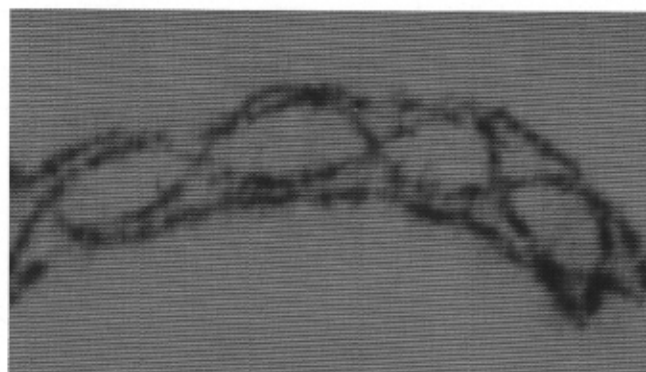
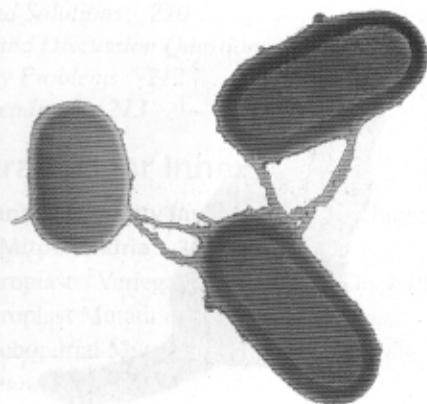
Problems and Discussion Questions 93

Extra-Spicy Problems 96

Selected Readings 99

5 Chromosome Mapping in Eukaryotes 100

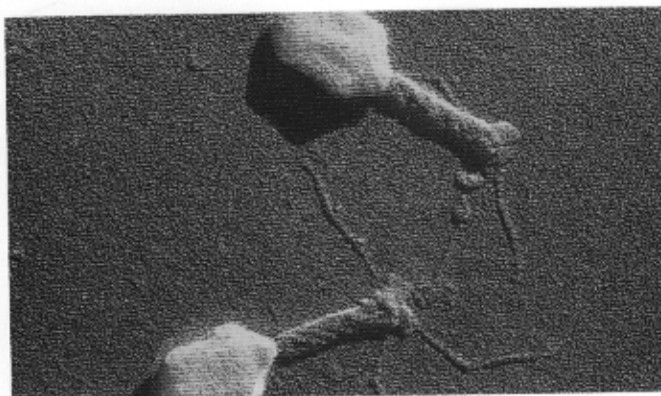
- 5.1 Genes Linked on the Same Chromosome Segregate Together 101
 - The Linkage Ratio 102
- 5.2 Crossing Over Serves as the Basis of Determining the Distance between Genes during Chromosome Mapping 104
 - Morgan and Crossing Over 104
 - Sturtevant and Mapping 104
 - Single Crossovers 106
- 5.3 Determining the Gene Sequence during Mapping Relies on the Analysis of Multiple Crossovers 107
 - Multiple Exchanges 107
 - Three-Point Mapping in *Drosophila* 108
 - Determining the Gene Sequence 110
 - A Mapping Problem in Maize 111
- 5.4 Interference Affects the Recovery of Multiple Exchanges 114
- 5.5 As the Distance between Two Genes Increases, Mapping Experiments Become More Inaccurate 115
- 5.6 *Drosophila* Genes Have Been Extensively Mapped 116
- 5.7 Crossing Over Involves a Physical Exchange between Chromatids 117
- 5.8 Recombination Occurs between Mitotic Chromosomes 118



- 5.9 Exchanges Also Occur between Sister Chromatids 120
- 5.10 Linkage Analysis and Mapping Can Be Performed in Haploid Organisms 120
 - Gene-to-Centromere Mapping 121
 - Ordered versus Unordered Tetrad Analysis 123
 - Linkage and Mapping 124
- 5.11 Lod Score Analysis and Somatic Cell Hybridization Were Historically Important in Creating Human Chromosome Maps 126
- 5.12 Gene Mapping Is Now Possible Using Molecular Analysis of DNA 128
 - Gene Mapping Using Annotated Computer Databases 128
- 5.13 Did Mendel Encounter Linkage? 128
 - Why Didn't Gregor Mendel Find Linkage? 129
 - Chapter Summary 129
 - Insights and Solutions 130
 - Problems and Discussion Questions 132
 - Extra-Spicy Problems 135
 - Selected Readings 136

6 Genetic Analysis and Mapping in Bacteria and Bacteriophages 137

- 6.1 Bacteria Mutate Spontaneously and Grow at an Exponential Rate 138
- 6.2 Conjugation Is One Means of Genetic Recombination in Bacteria 139
 - F^+ and F^- Bacteria 140
 - Hfr Bacteria and Chromosome Mapping 141
 - Recombination in $F^+ \times F^-$ Matings: A Reexamination 144
 - The F' State and Merozygotes 145
- 6.3 Mutational Analysis Led to the Discovery of the Rec Proteins Essential to Bacterial Recombination 146
- 6.4 F Factors Are Plasmids 146
- 6.5 Transformation Is Another Process Leading to Genetic Recombination in Bacteria 147
 - The Transformation Process 147
 - Transformation and Linked Genes 147



- 6.6 **Bacteriophages Are Bacterial Viruses** 148
 - Phage T4: Structure and Life Cycle 148
 - The Plaque Assay 149
 - Lysogeny 150
- 6.7 **Transduction Is Virus-Mediated Bacterial DNA Transfer** 151
 - The Lederberg–Zinder Experiment 151
 - The Nature of Transduction 152
 - Transduction and Mapping 153
- 6.8 **Bacteriophages Undergo Intergenic Recombination** 153
 - Mapping in Bacteriophages 154
- 6.9 **Intragenic Recombination Occurs in Phage T4** 154
 - The *rII* Locus of Phage T4 154
 - Complementation by *rII* Mutations 155
 - Recombinational Analysis 156
 - Deletion Testing of the *rII* Locus 156
 - The *rII* Gene Map 157

Genetics, Technology, and Society 159

Bacterial Genes and Disease: From Gene Expression to Edible Vaccines 159

Chapter Summary 160

Insights and Solutions 160

Problems and Discussion Questions 161

Extra-Spicy Problems 163

Selected Readings 164

7 Sex Determination and Sex Chromosomes 165

- 7.1 **Sexual Differentiation and Life Cycles** 166
 - Chlamydomonas* 166
 - Zea mays* 167
 - Caenorhabditis elegans* 168
- 7.2 **X and Y Chromosomes Were First Linked to Sex Determination Early in the 20th Century** 169
- 7.3 **The Y Chromosome Determines Maleness in Humans** 170
 - Klinefelter and Turner Syndromes 171
 - 47,XXX Syndrome 172
 - 47,XYY Condition 172
 - Sexual Differentiation in Humans 173
 - The Y Chromosome and Male Development 173

- 7.4 **The Ratio of Males to Females in Humans Is Not 1.0** 175
- 7.5 **Dosage Compensation Prevents Excessive Expression of X-Linked Genes in Humans and Other Mammals** 175
 - Barr Bodies 176
 - The Lyon Hypothesis 176
 - The Mechanism of Inactivation 178
- 7.6 **The Ratio of X Chromosomes to Sets of Autosomes Determines Sex in *Drosophila*** 178
 - Dosage Compensation in *Drosophila* 180
 - Drosophila* Mosaics 180
- 7.7 **Temperature Variation Controls Sex Determination in Reptiles** 181
- Chapter Summary 182

Genetics, Technology, and Society 183

A Question of Gender: Sex Selection in Humans 183

Insights and Solutions 184

Problems and Discussion Questions 184

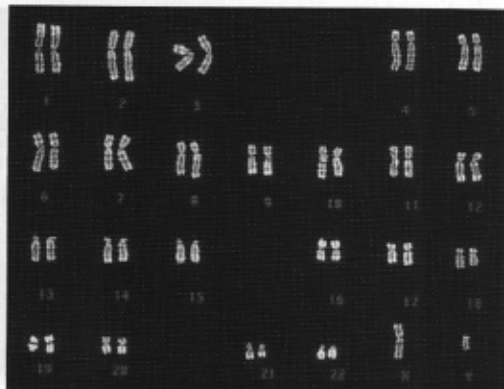
Extra-Spicy Problems 185

Selected Readings 186

8 Chromosome Mutations: Variation in Chromosome Number and Arrangement 187

- 8.1 **Specific Terminology Describes Variations in Chromosome Number** 188
- 8.2 **Variation in the Number of Chromosomes Results from Nondisjunction** 188
- 8.3 **Monosomy, the Loss of a Single Chromosome, May Have Severe Phenotypic Effects** 189
 - Partial Monosomy in Humans: The Cri-du-Chat Syndrome 189
- 8.4 **Trisomy Involves the Addition of a Chromosome to a Diploid Genome** 190
 - Down Syndrome 191
 - Patau Syndrome 193
 - Edwards Syndrome 193
 - Viability in Human Aneuploidy 193





- 8.5 Polyploidy, in Which More Than Two Haploid Sets of Chromosomes Are Present, Is Prevalent in Plants** 194
 Autopolyploidy 195
 Allopolyploidy 196
 Endopolyploidy 198
- 8.6 Variation Occurs in the Structure and Arrangement of Chromosomes** 198
- 8.7 A Deletion Is a Missing Region of a Chromosome** 199
- 8.8 A Duplication Is a Repeated Segment of the Genetic Material** 200
 Gene Redundancy and Amplification: Ribosomal RNA Genes 200
 The Bar-Eye Mutation in *Drosophila* 201
 The Role of Gene Duplication in Evolution 201
- 8.9 Inversions Rearrange the Linear Gene Sequence** 203
 Consequences of Inversions during Gamete Formation 203
 Position Effects of Inversions 204
 Evolutionary Advantages of Inversions 205
- 8.10 Translocations Alter the Location of Chromosomal Segments in the Genome** 206
 Translocations in Humans: Familial Down Syndrome 206
- 8.11 Fragile Sites in Humans Are Susceptible to Chromosome Breakage** 208
 Fragile X Syndrome (Martin-Bell Syndrome) 208

Genetics, Technology, and Society 209

The Link between Fragile Sites and Cancer 209

Chapter Summary 210

Insights and Solutions 210

Problems and Discussion Questions 211

Extra-Spicy Problems 212

Selected Readings 213

9 Extranuclear Inheritance 214

- 9.1 Organelle Heredity Involves DNA in Chloroplasts and Mitochondria** 215
 Chloroplasts: Variegation in Four O'Clock Plants 215
 Chloroplast Mutations in *Chlamydomonas* 216
 Mitochondrial Mutations: The Case of *poky* in *Neurospora* 216
 Petites in *Saccharomyces* 217

- 9.2 Knowledge of Mitochondrial and Chloroplast DNA Helps Explain Organelle Heredity** 218
 Organelle DNA and the Endosymbiotic Theory 218
 Molecular Organization and Gene Products of Chloroplast DNA 219
 Molecular Organization and Gene Products of Mitochondrial DNA 220
- 9.3 Mutations in Mitochondrial DNA Cause Human Disorders** 221
- 9.4 Infectious Heredity Is Based on a Symbiotic Relationship between Host Organism and Invader** 222
 Kappa in *Paramecium* 222
 Infective Particles in *Drosophila* 224
- 9.5 In Maternal Effect, the Maternal Genotype Has a Strong Influence during Early Development** 224
Ephesia Pigmentation 224
Linnaea Coiling 224
 Embryonic Development in *Drosophila* 225

Genetics, Technology, and Society 226

Mitochondrial DNA and the Mystery of the Romanovs 226

Chapter Summary 227

Insights and Solutions 228

Problems and Discussion Questions 228

Extra-Spicy Problems 229

Selected Readings 230

Part Two

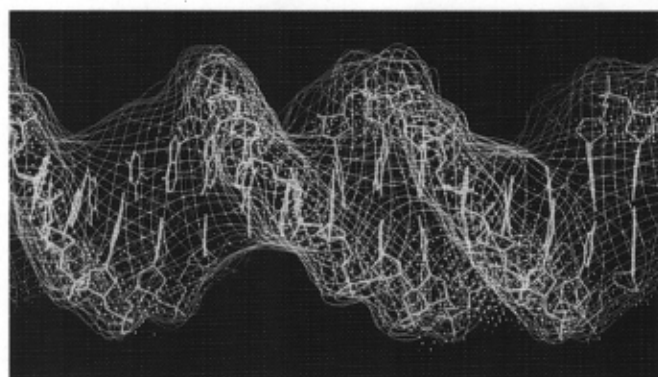
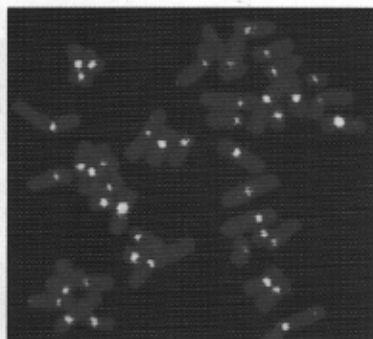
DNA: Structure, Replication, and Variation

10 DNA Structure and Analysis 231

- 10.1 The Genetic Material Must Exhibit Four Characteristics** 232
- 10.2 Until 1944, Observations Favored Protein as the Genetic Material** 233
- 10.3 Evidence Favoring DNA as the Genetic Material Was First Obtained during the Study of Bacteria and Bacteriophages** 233
 Transformation: Early Studies 233



Transformation: The Avery, MacLeod, and McCarty Experiment	235
The Hershey–Chase Experiment	236
Transfection Experiments	239
10.4 Indirect and Direct Evidence Supports the Concept that DNA Is the Genetic Material in Eukaryotes	239
Indirect Evidence: Distribution of DNA	239
Indirect Evidence: Mutagenesis	239
Direct Evidence: Recombinant DNA Studies	240
10.5 RNA Serves as the Genetic Material in Some Viruses	240
10.6 Knowledge of Nucleic Acid Chemistry Is Essential to the Understanding of DNA Structure	241
Nucleotides: Building Blocks of Nucleic Acids	241
Nucleoside Diphosphates and Triphosphates	243
Polynucleotides	243
10.7 The Structure of DNA Holds the Key to Understanding Its Function	243
Base Composition Studies	244
X-Ray Diffraction Analysis	245
The Watson–Crick Model	245
10.8 Alternative Forms of DNA Exist	248
10.9 The Structure of RNA Is Chemically Similar to DNA, but Single Stranded	249
<i>Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid</i>	250
10.10 Many Analytical Techniques Have Been Useful during the Investigation of DNA and RNA	251
Absorption of Ultraviolet Light (UV)	251
Sedimentation Behavior	251
Denaturation and Renaturation of Nucleic Acids	253
Molecular Hybridization	254
Fluorescent <i>in situ</i> Hybridization (FISH)	255
Reassociation Kinetics and Repetitive DNA	255
Electrophoresis of Nucleic Acids	257
Genetics, Technology, and Society	258
The Twists and Turns of the Helical Revolution	258
Chapter Summary	259
Insights and Solutions	259
Problems and Discussion Questions	260
Extra-Spicy Problems	261
Selected Readings	262



11 DNA Replication and Recombination 263

11.1 DNA Is Reproduced by Semiconservative Replication	264
The Meselson–Stahl Experiment	265
Semiconservative Replication in Eukaryotes	266
Origins, Forks, and Units of Replication	266
11.2 DNA Synthesis in Bacteria Involves Five Polymerases, as well as Other Enzymes	268
DNA Polymerase I	268
Synthesis of Biologically Active DNA	269
DNA Polymerase II, III, IV, and V	270
11.3 Many Complex Issues Must Be Resolved during DNA Replication	271
11.4 The DNA Helix Must Be Unwound	271
11.5 Initiation of DNA Synthesis Requires an RNA Primer	272
11.6 Antiparallel Strands Require Continuous and Discontinuous DNA Synthesis	272
11.7 Concurrent Synthesis Occurs on the Leading and Lagging Strands	273
11.8 Proofreading and Error Correction Are an Integral Part of DNA Replication	273
11.9 A Coherent Model Summarizes DNA Replication	273
11.10 Replication Is Controlled by a Variety of Genes	274
11.11 Eukaryotic DNA Synthesis Is Similar to Synthesis in Prokaryotes, but More Complex	275
Multiple Replication Origins	275
Eukaryotic DNA Polymerases	275
11.12 The Ends of Linear Chromosomes Are Problematic during Replication	276
11.13 DNA Recombination, Like DNA Replication, Is Directed by Specific Enzymes	278
11.14 Gene Conversion Is a Consequence of DNA Recombination	279

Genetics, Technology, and Society 281

Telomerase: The Key to Immortality? 281

Chapter Summary 282

Insights and Solutions 282

Problems and Discussion Questions 283

Extra-Spicy Problems 284

Selected Readings 285

12 DNA Organization in Chromosomes 286

12.1 Viral and Bacterial Chromosomes Are Relatively Simple DNA Molecules 287

12.2 Supercoiling Is Common in the DNA of Viral and Bacterial Chromosomes 289

12.3 Specialized Chromosomes Reveal Variations in Structure 290

Polytene Chromosomes 290

Lampbrush Chromosomes 291

12.4 DNA Is Organized into Chromatin in Eukaryotes 292

Chromatin Structure and Nucleosomes 292

High Resolution Studies of the Nucleosome Core 294

Heterochromatin 295

12.5 Chromosome Banding Differentiates Regions along the Mitotic Chromosome 296

12.6 Eukaryotic Chromosomes Demonstrate Complex Organization Characterized by Repetitive DNA 297

Repetitive DNA and Satellite DNA 297

Centromeric DNA Sequences 298

Telomeric DNA Sequences 299

Middle Repetitive Sequences: VNTRs and Dinucleotide Repeats 300

Repetitive Transposed Sequences: SINES and LINES 300

Middle Repetitive Multiple-Copy Genes 301

12.7 The Vast Majority of a Eukaryotic Genome Does Not Encode Functional Genes 301

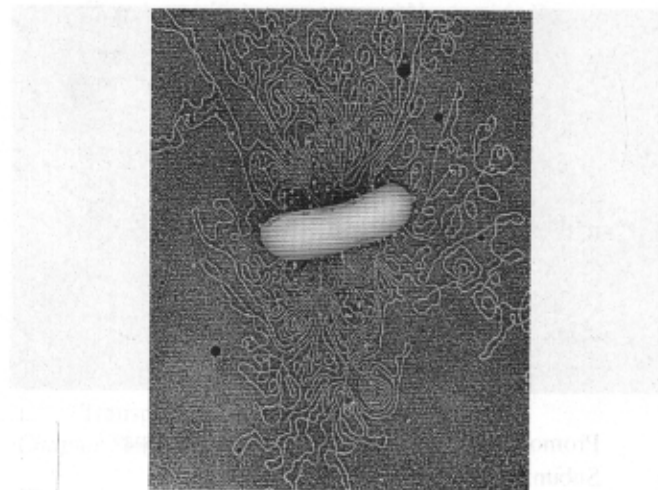
Chapter Summary 301

Insights and Solutions 302

Problems and Discussion Questions 302

Extra-Spicy Problems 303

Selected Readings 305



Part THREE

Expression and Regulation of Genetic Information

13 The Genetic Code and Transcription 306

13.1 The Genetic Code Exhibits a Number of Characteristics 307

13.2 Early Studies Established the Basic Operational Patterns of the Code 307

The Triplet Nature of the Code 308

The Nonoverlapping Nature of the Code 308

The Commaless and Degenerate Nature of the Code 309

13.3 Studies by Nirenberg, Matthaei, and Others Led to Deciphering of the Code 309

Synthesizing Polypeptides in a Cell-Free System 309

Homopolymer Codes 310

Mixed Copolymers 310

The Triplet Binding Assay 311

Repeating Copolymers 312

13.4 The Coding Dictionary Reveals Several Interesting Patterns among the 64 Codons 313

Degeneracy and the Wobble Hypothesis 313

The Ordered Nature of the Code 314

Initiation, Termination, and Suppression 314

13.5 The Genetic Code Has Been Confirmed in Studies of Phage MS2 315

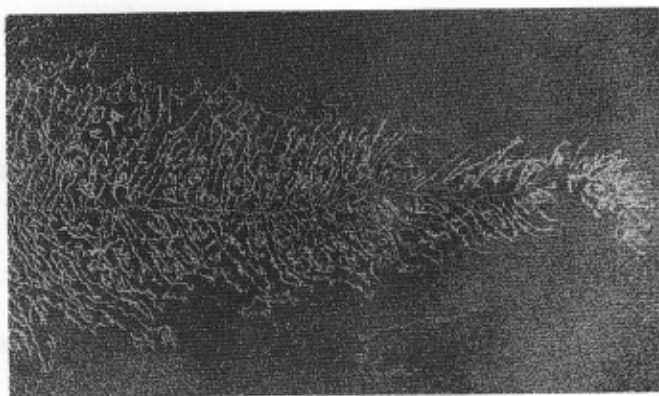
13.6 The Genetic Code Is Nearly Universal 315

13.7 Different Initiation Points Create Overlapping Genes 316

13.8 Transcription Synthesizes RNA on a DNA Template 317

13.9 Studies with Bacteria and Phages Provided Evidence for the Existence of mRNA 317

13.10 RNA Polymerase Directs RNA Synthesis 318



Promoters, Template Binding, and the Sigma Subunit 318

Initiation, Elongation, and Termination of RNA Synthesis 319

13.11 Transcription in Eukaryotes Differs from Prokaryotic Transcription in Several Ways 320

Initiation of Transcription in Eukaryotes 320

Recent Discoveries Concerning RNA Polymerase Function 321

Heterogeneous Nuclear RNA and Its Processing: Caps and Tails 322

13.12 The Coding Regions of Eukaryotic Genes Are Interrupted by Intervening Sequences 323

Splicing Mechanisms: Autocatalytic RNAs 324

Splicing Mechanisms: The Spliceosome 325

RNA Editing 326

13.13 Transcription Has Been Visualized by Electron Microscopy 326

Genetics, Technology, and Society 328

Antisense Oligonucleotides: Attacking the Messenger 328

Chapter Summary 329

Insights and Solutions 329

Problems and Discussion Questions 330

Extra-Spicy Problems 331

Selected Readings 333

14 Translation and Proteins 334

14.1 Translation of mRNA Depends on Ribosomes and Transfer RNAs 335

Ribosomal Structure 335

tRNA Structure 336

Charging tRNA 337

14.2 Translation of mRNA Can Be Divided into Three Steps 338

Initiation 338

Elongation 339

Termination 340

Polyribosomes 341

14.3 Crystallographic Analysis Has Revealed Many Details about the Functional Prokaryotic Ribosome 342

14.4 Translation Is More Complex in Eukaryotes 342

14.5 The Initial Insight That Proteins Are Important in Heredity Was Provided by the Study of Inborn Errors of Metabolism 343

Phenylketonuria 344

14.6 Studies of *Neurospora* Led to the One-Gene: One-Enzyme Hypothesis 344

Analysis of *Neurospora* Mutants by Beadle and Tatum 344

Genes and Enzymes: Analysis of Biochemical Pathways 346

14.7 Studies of Human Hemoglobin Established That One Gene Encodes One Polypeptide 346

Sickle-Cell Anemia 347

Human Hemoglobins 348

14.8 The Nucleotide Sequence of a Gene and the Amino Acid Sequence of the Corresponding Protein Exhibit Colinearity 349

14.9 Protein Structure Is the Basis of Biological Diversity 349

Posttranslational Modification 352

14.10 Protein Function Is Directly Related to the Structure of the Molecule 353

14.11 Proteins Are Made Up of One or More Functional Domains 354

Exon Shuffling and the Origin of Protein Domains 354

Genetics, Technology, and Society 356

Mad Cow Disease: The Prion Story 356

Chapter Summary 357

Insights and Solutions 357

Problems and Discussion Questions 357

Extra-Spicy Problems 358

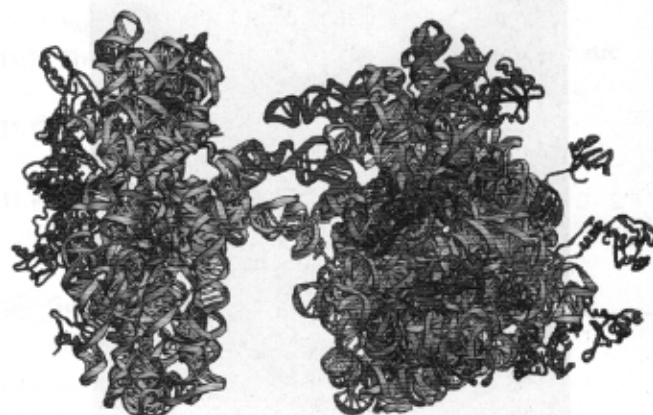
Selected Readings 360

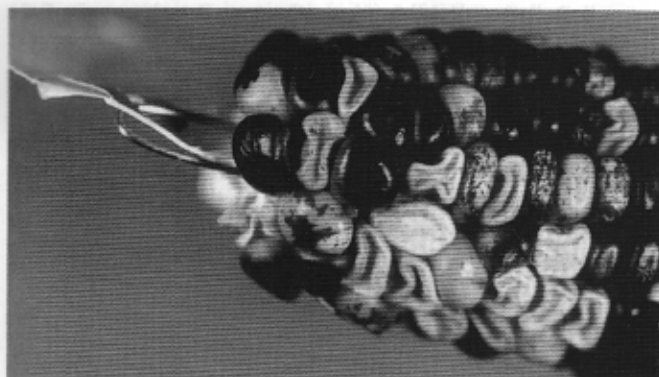
15 Gene Mutation, DNA Repair, and Transposition 361

15.1 Mutations Are Classified in Various Ways 362

Spontaneous, Induced, and Adaptive Mutations 362

Classification Based on Location of Mutation 363





Classification Based on Type of Molecular Change 364

Classification Based on Phenotypic Effects 364

15.2 The Spontaneous Mutation Rate Varies Greatly among Organisms 365

Deleterious Mutations in Humans 365

15.3 Spontaneous Mutations Arise from Replication Errors and Base Modifications 366

DNA Replication Errors 366

Replication Slippage 366

The Odds of Losing at Genetic Roulette 367

Tautomeric Shifts 368

Depurination and Deamination 368

Oxidative Damage 369

Transposons 369

15.4 Induced Mutations Arise from DNA Damage Caused by Chemicals and Radiation 369

Base Analogs 370

Alkylating Agents 370

Acridine Dyes and Frameshift Mutations 370

Ultraviolet Light and Thymine Dimers 371

Ionizing Radiation 372

15.5 Genomics and Gene Sequencing Have Enhanced Our Understanding of Mutations in Humans 372

ABO Blood Types 373

Muscular Dystrophy 373

Trinucleotide Repeats in Fragile X Syndrome, Myotonic Dystrophy, and Huntington Disease 373

15.6 Genetic Techniques, Cell Cultures, and Pedigree Analysis Are All Used to Detect Mutations 375

Detection in Bacteria and Fungi 375

Detection in Plants 375

Detection in Humans 375

15.7 The Ames Test Is Used to Assess the Mutagenicity of Compounds 377

15.8 Organisms Use DNA Repair Systems to Counteract Mutations 377

Proofreading and Mismatch Repair 377

Postreplication Repair and the SOS Repair System 378

Photoreactivation Repair: Reversal of UV Damage in Prokaryotes 379

Base and Nucleotide Excision Repair 379

Xeroderma Pigmentosum and Nucleotide Excision Repair in Humans 380

Double-Strand Break Repair in Eukaryotes 381

15.9 Transposable Elements Move within the Genome and May Disrupt Genetic Function 382

Insertion Sequences 382

Bacterial Transposons 382

The *Ac-Ds* System in Maize 383

Mobile Genetic Elements and Wrinkled Peas: Mendel Revisited 384

Copia Elements in *Drosophila* 385

P Element Transposons in *Drosophila* 385

Transposable Elements in Humans 386

Chapter Summary 386

Genetics, Technology, and Society 387

Chernobyl's Legacy 387

Insights and Solutions 388

Problems and Discussion Questions 389

Extra-Spicy Problems 390

Selected Readings 391

16 Regulation of Gene Expression in Prokaryotes 392

16.1 Prokaryotes Exhibit Efficient Genetic Mechanisms to Respond to Environmental Conditions 393

16.2 Lactose Metabolism in *E. coli* Is Regulated by an Inducible System 393

Structural Genes 394

The Discovery of Regulatory Mutations 394

The Operon Model: Negative Control 395

Genetic Proof of the Operon Model 395

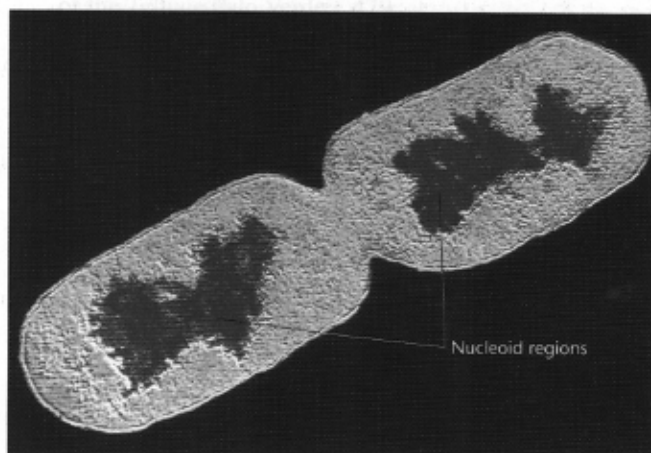
Isolation of the Repressor 397

16.3 The Catabolite-Activating Protein (CAP) Exerts Positive Control over the *lac* Operon 398

16.4 Crystal Structure Analysis of Repressor Complexes Has Confirmed the Operon Model 399

16.5 The tryptophan (*trp*) Operon in *E. coli* Is a Repressible Gene System 401

Evidence for the *trp* Operon 401



- 16.6 Attenuation Is a Critical Process during the Regulation of the *trp* Operon in *E. coli* 402
- 16.7 TRAP and AT Proteins Govern Attenuation in *B. subtilis* 403
- 16.8 The *ara* Operon Is Controlled by a Regulator Protein That Exerts Both Positive and Negative Control 404

Genetics, Technology, and Society 406

Quorum Sensing: How Bacteria Talk to One Another 406

Chapter Summary 407

Insights and Solutions 407

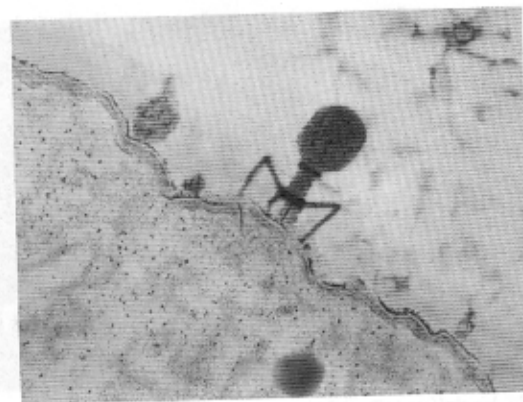
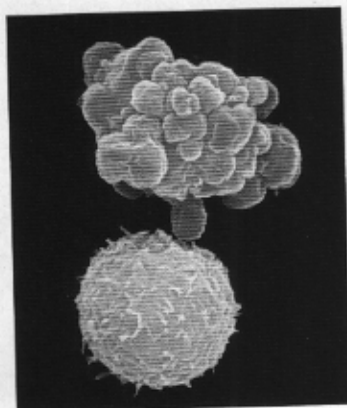
Problems and Discussion Questions 408

Extra-Spicy Problems 409

Selected Readings 410

17 Regulation of Gene Expression in Eukaryotes 411

- 17.1 Eukaryotic Gene Regulation Differs from Regulation in Prokaryotes 412
- 17.2 Chromosome Organization in the Nucleus Influences Gene Expression 412
- 17.3 Transcription Initiation Is a Major Form of Gene Regulation 413
- Promoters Have a Modular Organization 413
- Enhancers Control the Rate of Transcription 414
- 17.4 Transcription in Eukaryotes Requires Several Steps 415
- Transcription Requires Chromatin Remodeling 415
- Histone Modification Is Part of Chromatin Remodeling 416
- 17.5 Assembly of the Basal Transcription Complex Occurs at the Promoter 417
- RNA Polymerases and Transcription 417
- Formation of the Transcription Initiation Complex 417
- Activators Bind to Enhancers and Change the Rate of Transcription Initiation 418
- 17.6 Gene Regulation in a Model Organism: Positive Induction and Catabolite Repression in the *gal* Genes of Yeast 420



- 17.7 DNA Methylation and Regulation of Gene Expression 422
- 17.8 Posttranscriptional Regulation of Gene Expression 423
- Alternative Splicing Pathways for mRNA 423
- Alternative Splicing and Cell Function 423
- Alternative Splicing Amplifies the Number of Proteins Produced by a Genome 425
- RNA Silencing of Gene Expression 425
- 17.9 Alternative Splicing and mRNA Stability Also Regulate Gene Expression 426
- Sex Determination in *Drosophila*: A Model for Regulation of Alternative Splicing 426
- Controlling mRNA Stability 427

Chapter Summary 428

Genetics, Technology, and Society 429

Human Genetic Diseases and Loss of Gene Regulation 429

Insights and Solutions 430

Problems and Discussion Questions 430

Extra-Spicy Problems 432

Selected Readings 433

18 Cell Cycle Regulation and Cancer 434

- 18.1 Cancer Is a Genetic Disease 435
- What Is Cancer? 436
- The Clonal Origin of Cancer Cells 436
- Cancer As a Multistep Process, Requiring Multiple Mutations 436
- 18.2 Cancer Cells Contain Genetic Defects Affecting Genomic Stability and DNA Repair 437
- 18.3 Cancer Cells Contain Genetic Defects Affecting Cell Cycle Regulation 439
- The Cell Cycle and Signal Transduction 439
- Cell Cycle Control and Checkpoints 440
- 18.4 Many Cancer-Causing Genes Disrupt Control of the Cell Cycle 442
- The *Cyclin D1* and *Cyclin E* Proto-oncogenes 443
- The *ras* Proto-oncogenes 443
- The *p53* Tumor Suppressor Gene 444
- The *RBI* Tumor Suppressor Gene 445

- 18.5 Cancer Is a Genetic Disorder Affecting Cell–Cell Contact 446
- 18.6 Predisposition to Some Cancers Can Be Inherited 447
- 18.7 Viruses Contribute to Cancer in Both Humans and Animals 449
- 18.8 Environmental Agents Contribute to Human Cancers 451

Genetics, Technology, and Society 452

Breast Cancer: The Double-Edged Sword of Genetic Testing 452

Chapter Summary 453

Insights and Solutions 453

Problems and Discussion Questions 454

Extra-Spicy Problems 455

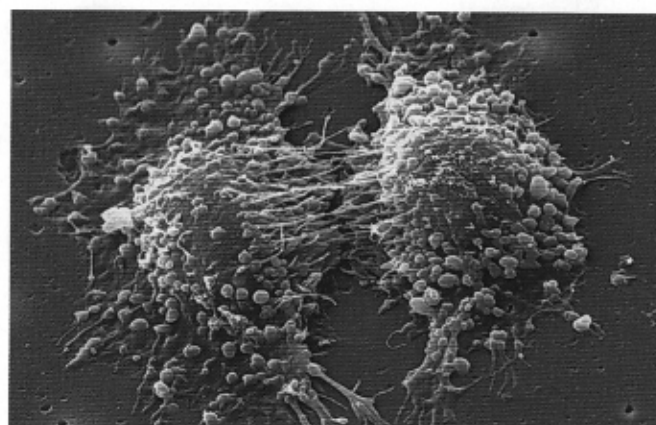
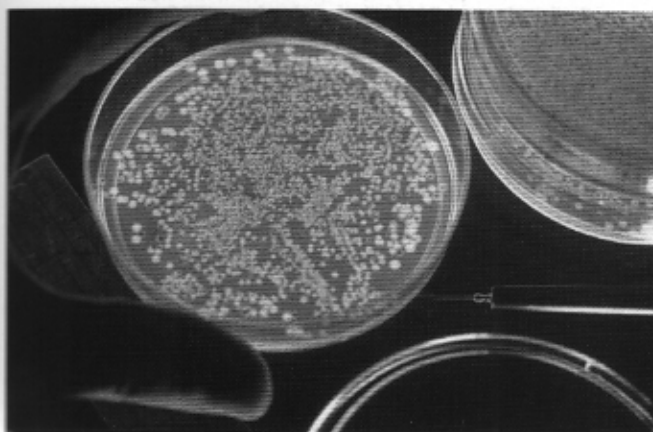
Selected Readings 456

Part FOUR

Genomic Analysis

19 Recombinant DNA Technology 457

- 19.1 Recombinant DNA Technology Combines Several Experimental Techniques 458
- 19.2 Recombinant DNA Technology Is the Foundation of Genome Analysis 458
- 19.3 Restriction Enzymes Cut DNA at Specific Recognition Sequences 458
- 19.4 Vectors Carry DNA Molecules to Be Cloned 460
 - Plasmid Vectors 460
 - Lambda (λ) Phage Vectors 461
 - Cosmid Vectors 462
 - Bacterial Artificial Chromosomes 462
 - Expression Vectors 463
- 19.5 DNA Was First Cloned in Prokaryotic Host Cells 463
- 19.6 Yeast Cells Are Used as Eukaryotic Hosts for Cloning 464



- 19.7 Genes Can Be Transferred to Eukaryotic Cells 465
 - Plant Cell Hosts 465
 - Mammalian Cell Hosts 466
 - 19.8 The Polymerase Chain Reaction Makes DNA Copies Without Host Cells 466
 - Limitations of PCR 467
 - Other Applications of PCR 468
 - 19.9 Libraries Are Collections of Cloned Sequences 468
 - Genomic Libraries 468
 - Chromosome-Specific Libraries 468
 - cDNA Libraries 469
 - 19.10 Specific Clones Can Be Recovered from a Library 470
 - Probes Identify Specific Clones 470
 - Screening a Library 471
 - 19.11 Cloned Sequences Can Be Characterized in Several Ways 471
 - Restriction Mapping 471
 - Nucleic Acid Blotting 473
 - 19.12 DNA Sequencing Is the Ultimate Way to Characterize a Clone 474
 - DNA Sequencing and Genome Projects 477
- Chapter Summary* 478

Genetics, Technology, and Society 479

DNA Fingerprints and Forensics: The Case of the Telltale Palo Verde 479

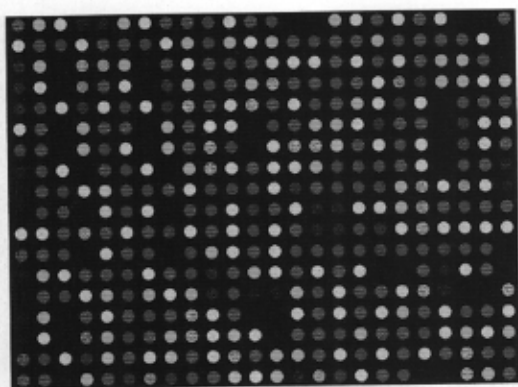
Insights and Solutions 480

Problems and Discussion Questions 480

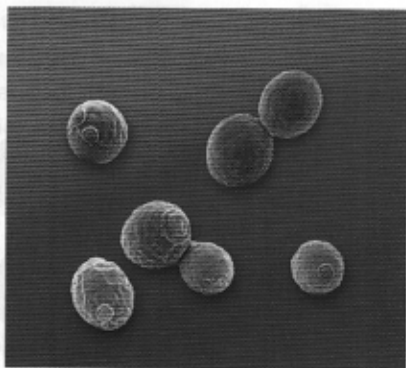
Selected Readings 483

20 Genomics and Proteomics 484

- 20.1 Genomics: Sequencing Is the Basis for Identifying and Mapping All Genes in a Genome 486
- 20.2 An Overview of Genomic Analysis 487
 - Compiling the Sequence 487
 - Annotating the Sequence 487
- 20.3 Functional Genomics Classifies Genes and Identifies Their Functions 488



- Functional Genomics of a Bacterial Genome 489
Strategies for Functional Assignments of Unknown Genes 489
- 20.4 Prokaryotic Genomes Have Some Unexpected Features 491**
Size Range of Eubacterial Genomes 491
Linear Chromosomes and Multiple Chromosomes in Bacteria 491
- 20.5 Genomes of Eubacteria 492**
Genomes of Archaea 493
- 20.6 Eukaryotic Genomes Have Several Organizational Patterns 493**
General Features of Eukaryotic Genomes 494
Transcriptional Units in the *C. elegans* Genome 494
Genomes of Higher Plants 495
- 20.7 The Human Genome: The Human Genome Project (HGP) 496**
Origins of the Human Genome Project 496
Major Features of the Human Genome 496
The Unfinished Tasks in Human Genome Sequencing 497
Chromosomal Organization of Human Genes 498
Our Genome and the Chimpanzee Genome 498
- 20.8 Comparative Genomics Is a Versatile Tool 499**
Finding New Genes Using Comparative Genomics 499
Comparative Genomics and Model Organisms 500
Comparative Analysis of Nuclear Receptors and Drug Development 501
The Minimum Genome for Living Cells 502
- 20.9 Comparative Genomics: Multigene Families Diversify Gene Function 503**
Gene Duplications 503
Evolution of Gene Families: The Globin Genes 504
- 20.10 Proteomics Identifies and Analyzes the Proteins in a Cell 505**
Reconciling the Number of Genes and the Number of Proteins 505
Proteomics Technology 506
The Bacterial Proteome Changes with Alterations in the Environment 507
Proteome Analysis of an Organelle: The Nucleolus 508
- Genetics, Technology, and Society 509**
Beyond Dolly: The Cloning of Humans 509
Chapter Summary 510
Insights and Solutions 511
Problems and Discussion Questions 511
Extra-Spicy Problems 514
Selected Readings 515
- 21 Dissection of Gene Function: Mutational Analysis in Model Organisms 516**
- 21.1 Geneticists Use Model Organisms That Are Genetically Tractable 517**
Features of Genetic Model Organisms 517
Yeast as a Genetic Model Organism 517
Drosophila as a Genetic Model Organism 519
The Mouse as a Genetic Model Organism 521
- 21.2 Geneticists Dissect Gene Function Using Mutations and Forward Genetics 523**
Generating Mutants with Radiation, Chemicals, and Transposon Insertion 523
Screening for Mutants 523
Selecting for Mutants 525
Defining the Genes 525
Dissecting Genetic Networks: Epistasis and Pathways 526
Extending the Analysis: Suppressors and Enhancers 527
Extending the Analysis: Cloning the Genes 528
Extending the Analysis: Biochemical Functions 528
- 21.3 Geneticists Dissect Gene Function Using Genomics and Reverse Genetics 529**
Genetic Analysis Beginning with a Purified Protein 529
Genetic Analysis Beginning with a Mutant Model Organism 530
Genetic Analysis Beginning with the Cloned Gene 531
Genetics Analysis Using Gene Targeting Technologies 533
- 21.4 Geneticists Dissect Gene Function Using Functional Genomic and RNAi Technologies 536**
RNAi: Genetics without Mutations 536
High-Throughput Functional Genomics Techniques 537
Gene Expression Microarrays 537
Genome-Wide Mapping of Protein-DNA Binding Sites 538
- 21.5 Geneticists Advance Our Understanding of Molecular Processes by Undertaking Genetic Research in Model Organisms: Three Case Studies 538**
Yeast: Cell Cycle Genes 539
Drosophila: The Heidelberg Screens 541
The Mouse: A Model for ALS Gene Therapy 543



- Chapter Summary 544
 Insights and Solutions 545
 Problems and Discussion Questions 546
 Extra-Spicy Problems 547
 Selected Readings 548

22 Applications and Ethics of Biotechnology 549

- 22.1 **Biotechnology Has Revolutionized Agriculture** 550
 Transgenic Crops and Herbicide Resistance 550
 Nutritional Enhancement of Crop Plants 550
 Concerns about Genetically Modified Organisms 551
- 22.2 **Pharmaceutical Products Are Synthesized in Genetically Altered Organisms** 552
 Insulin Production in Bacteria 552
 Transgenic Animal Hosts and Pharmaceutical Products 553
 Transgenic Plants and Edible Vaccines 554
- 22.3 **Biotechnology Is Used to Diagnose and Screen Genetic Disorders** 555
 Prenatal Diagnosis of Sickle-cell Anemia 555
 Single-Nucleotide Polymorphisms and Genetic Screening 556
 DNA Microarrays 557
 Drug Development 558
 Disease Diagnosis 559
 Genome Scanning 559
 Genetic Testing and Ethical Dilemmas 560
- 22.4 **Genetic Disorders Can Be Treated by Gene Therapy** 560
 Gene Therapy for Severe Combined Immunodeficiency (SCID) 561
 Problems and Failures in Gene Therapy 562
 The Future of Gene Therapy 562
- 22.5 **Gene Therapy Raises Many Ethical Concerns** 563
- 22.6 **Ethical Issues Are an Outgrowth of the Human Genome Project** 563
 The Ethical, Legal, and Social Implications (ELSI) Program 564
- 22.7 **Finding and Mapping Genes in the Human Genome with Recombinant DNA Technology** 564
 RFLPs as Genetic Markers 564
 Linkage Analysis Using RFLPs 565

- Positional Cloning: The Gene for Neurofibromatosis 565
 Fluorescent *in situ* Hybridization (FISH) Gene Mapping 566

- 22.8 **DNA Fingerprints Can Identify Individuals** 567
 Minisatellites (VNTRs) and Microsatellites (STRs) 567
 Forensic Applications 568

Genetics, Technology, and Society 569

- Gene Therapy—Two Steps Forward or Two Steps Back? 569

- Chapter Summary 570
 Insights and Solutions 570
 Problems and Discussion Questions 571
 Extra-Spicy Problems 573
 Selected Readings 574

Part Five

Genetics of Organisms and Populations

23 Developmental Genetics of Model Organisms 575

- 23.1 **Developmental Genetics Seeks to Explain How a Differentiated State Develops from an Organism's Genome** 576
- 23.2 **Conservation of Developmental Mechanisms and the Use of Model Organisms** 577
 Model Organisms in the Study of Development 577
 Analysis of Developmental Mechanisms 577
 Basic Concepts in Developmental Genetics 577
- 23.3 **Master Switch Genes Program Genomic Expression** 578
 The Control of Eye Formation 578
- 23.4 **Genetics of Embryonic Development in *Drosophila*: Specification of the Body Axis** 579
 Overview of *Drosophila* Development 579
 Genes That Regulate Formation of the Anterior–Posterior Body Axis 581
 Genetic Analysis of Embryogenesis 581



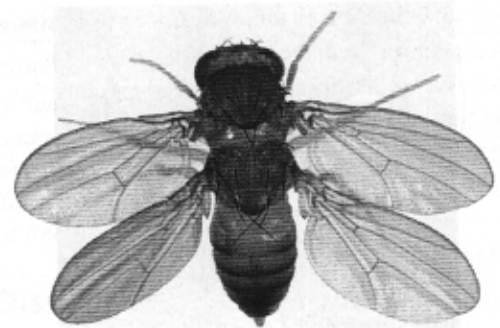
- 23.5 Zygotic Genes Program Segment Formation in *Drosophila* 583**
 Gap Genes 583
 Pair-Rule Genes 584
 Segment Polarity Genes 584
- 23.6 Homeotic Genes Control the Developmental Fate of Segments along the Anterior–Posterior Axis 585**
Hox Genes in *Drosophila* 585
Hox Genes and Human Genetic Disorders 586
 Control of *Hox* Gene Expression 587
- 23.7 Cascades of Gene Action Control Differentiation 588**
- 23.8 Plants Have Evolved Systems That Parallel the *Hox* Genes of Animals 589**
 Homeotic Genes in *Arabidopsis* 589
 Evolutionary Divergence in Homeotic Genes 590
- 23.9 Cell–Cell Interactions in *C. elegans* Development 590**
 Signaling Systems in Development 590
 The Notch Signaling Pathway 591
 Overview of *C. elegans* Development 591
 Genetic Analysis of Vulva Formation 592
- 23.10 Programmed Cell Death Is Required for Normal Development 594**

Genetics, Technology, and Society 595

- Stem Cell Wars 595
 Chapter Summary 596
 Insights and Solutions 596
 Problems and Discussion Questions 597
 Extra-Spicy Problems 598
 Selected Readings 598

24 Quantitative Genetics and Multifactorial Traits 599

- 24.1 Not All Polygenic Traits Show Continuous Variation 600**
- 24.2 Quantitative Traits Can Be Explained in Mendelian Terms 600**
 The Multiple Gene Hypothesis for Quantitative Inheritance 601
 Additive Alleles: The Basis of Continuous Variation 602
 Calculating the Number of Polygenes 602
- 24.3 The Study of Polygenic Traits Relies on Statistical Analysis 603**
 The Mean 603
 Variance 603
 Standard Deviation 604
 Standard Error of the Mean 604
 Covariance 604
 Analysis of a Quantitative Character 604



- 24.4 Heritability Estimates the Genetic Contribution to Phenotypic Variability 605**
 Broad-Sense Heritability 606
 Narrow-Sense Heritability 606
 Artificial Selection 607
- 24.5 Twin Studies Allow an Estimation of Heritability in Humans 608**
- 24.6 Quantitative Trait Loci Can Be Mapped 609**
- Chapter Summary 610

Genetics, Technology, and Society 611

- The Green Revolution Revisited 611
 Insights and Solutions 612
 Problems and Discussion Questions 613
 Extra-Spicy Problems 614
 Selected Readings 616

25 Population Genetics 617

- 25.1 Allele Frequencies in Population Gene Pools Vary in Space and Time 618**
- 25.2 The Hardy–Weinberg Law Describes the Relationship between Allele Frequencies and Genotype Frequencies in an Ideal Population 618**
- 25.3 The Hardy–Weinberg Law Can Be Applied to Human Populations 620**
 Testing for Hardy–Weinberg Equilibrium 622
- 25.4 The Hardy–Weinberg Law Can Be Used for Multiple Alleles, X-Linked Traits, and Estimating Heterozygote Frequencies 622**
 Calculating Frequencies for Multiple Alleles 622
 Calculating Frequencies for X-linked Traits 623
 Calculating Heterozygote Frequency 624
- 25.5 Natural Selection Is a Major Force Driving Allele Frequency Change 624**
 Natural Selection 624
 Fitness and Selection 625
 Selection in Natural Populations 627
 Natural Selection and Quantitative Traits 628
- 25.6 Mutation Creates New Alleles in a Gene Pool 629**
- 25.7 Migration and Gene Flow Can Alter Allele Frequencies 630**

- 25.8 Genetic Drift Causes Random Changes in Allele Frequency in Small Populations 632
- 25.9 Nonrandom Mating Changes Genotype Frequency but Not Allele Frequency 632
 - Inbreeding 633
 - Genetic Effects of Inbreeding 634

Genetics, Technology, and Society 635

Tracking Our Genetic Footprints out of Africa 635

Chapter Summary 636

Insights and Solutions 636

Problems and Discussion Questions 637

Extra-Spicy Problems 638

Selected Readings 638

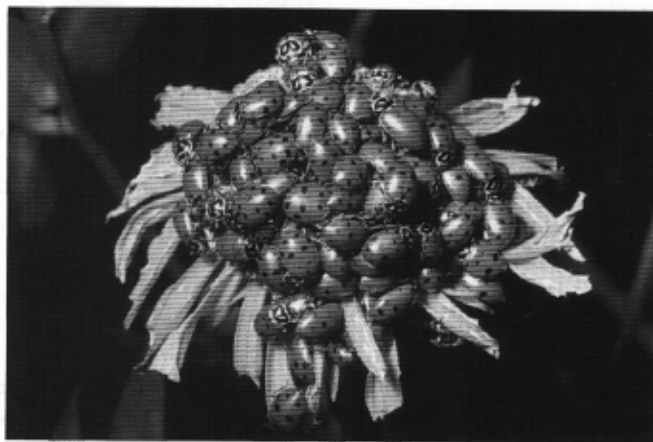
26 Evolutionary Genetics 640

- 26.1 Speciation Can Occur by Transformation or by Splitting Gene Pools 641
- 26.2 Most Populations and Species Harbor Considerable Genetic Variation 642
 - Artificial Selection 642
 - Protein Polymorphisms 642
 - Variations in Nucleotide Sequence 643
 - Explaining the High Level of Genetic Variation in Populations 644
- 26.3 The Genetic Structure of Populations Changes across Space and Time 644
- 26.4 The Definition of Species Is a Great Challenge for Evolutionary Biology 647
- 26.5 A Reduction in Gene Flow between Populations, Accompanied by Divergent Selection or Genetic Drift, Can Lead to Speciation 647
 - Examples of Speciation 649
 - The Minimum Genetic Divergence Required for Speciation 649
 - In at Least Some Instances, Speciation Is Rapid 651
- 26.6 We Can Use Genetic Differences among Populations or Species to Reconstruct Evolutionary History 653
 - A Method for Estimating Evolutionary Trees from Genetic Data 653
 - Molecular Clocks 655
- 26.7 Reconstructing Evolutionary History Allows Us to Answer a Variety of Questions 656
 - Transmission of HIV from a Dentist to His Patients 656
 - The Relationship of Neanderthals to Modern Humans 657
 - The Origin of Mitochondria 657

Chapter Summary 658

Genetics, Technology, and Society 659

What Can We Learn from the Failure of the Eugenics Movement? 659



Insights and Solutions 660

Problems and Discussion Questions 660

Extra-Spicy Problems 661

Selected Readings 662

27 Conservation Genetics 663

- 27.1 Genetic Diversity Is at the Heart of Conservation Genetics 664
 - Loss of Genetic Diversity 665
 - Identifying Genetic Diversity 666
- 27.2 Population Size Has a Major Impact on Species Survival 666
- 27.3 Genetic Effects Are More Pronounced in Small, Isolated Populations 668
 - Genetic Drift 668
 - Inbreeding 668
 - Reduction in Gene Flow 669
- 27.4 Genetic Erosion Diminishes Genetic Diversity 670
- 27.5 Conservation of Genetic Diversity Is Essential to Species Survival 670
 - Ex Situ Conservation: Captive Breeding 671
 - Captive Breeding: The Black-Footed Ferret 671
 - Ex Situ Conservation and Gene Banks 672
 - In Situ Conservation 672
 - Population Augmentation 673

Genetics, Technology, and Society 674

Gene Pools and Endangered Species:

The Plight of the Florida Panther 674

Chapter Summary 675

Insights and Solutions 675

Problems and Discussion Questions 675

Extra-Spicy Problems 676

Selected Readings 677

Appendix A

Glossary A-1

Appendix B

Answers A-17

Credits

C-1

Index

I-1