

UNIT 1 BASIC CHEMICAL AND BIOLOGICAL PRINCIPLES 1

CHAPTER 1 *Cells and Organisms* 2

| | |
|--|----|
| 1. What Is Life? | 3 |
| 2. Living Creatures Are Made of Cells | 4 |
| 3. Eubacteria and Archaea Are Genetically Distinct | 8 |
| 4. Eukaryotic Cells Are Subdivided into Compartments | 9 |
| 5. The Diversity of Eukaryotes | 13 |
| 6. Haploidy, Diploidy, and the Eukaryote Cell Cycle | 14 |
| 7. Organisms Are Classified | 15 |
| 8. Some Widely-Studied Organisms Serve as Models | 16 |
| 9. Basic Characteristics of a Model Organism | 27 |
| 10. Purifying DNA from Model Organisms | 27 |
| 11. Viruses Are Not Living Cells | 29 |
| 12. Bacterial Viruses Infect Bacteria | 30 |
| 13. Human Viral Diseases Are Common | 32 |
| 14. A Variety of Subcellular Genetic Entities Exist | 32 |
| Key Concepts | 34 |
| Review Questions | 35 |
| Conceptual Questions | 36 |

CHAPTER 2 *Basic Genetics* 37

| | |
|--|----|
| 1. Gregor Mendel, The Father of Classical Genetics | 37 |
| 2. Genes Determine Each Step in Biochemical Pathways | 39 |
| 3. Mutants Result from Alterations in Genes | 40 |
| 4. Phenotypes and Genotypes | 41 |
| 5. Chromosomes Are Long, Thin Molecules That Carry Genes | 42 |
| 6. Dominant and Recessive Alleles | 45 |
| 7. Genes from Both Parents Are Mixed by Sexual Reproduction | 48 |
| 8. Neighboring Genes Are Linked During Inheritance Unless the DNA Recombines | 52 |
| 9. Identifying Genes that Cause Human Diseases | 57 |
| Key Concepts | 58 |
| Review Questions | 59 |
| Conceptual Questions | 60 |

CHAPTER 3 *DNA, RNA, and Protein* 62

| | |
|---|----|
| 1. History of DNA as the Genetic Material | 62 |
| 2. Nucleic Acid Molecules Carry Genetic Information | 63 |
| 3. Chemical Structure of Nucleic Acids | 63 |
| 4. Double-Stranded DNA Forms a Double Helix | 67 |

| | |
|---|----|
| 5. Constituents of Chromosomes | 75 |
| 6. The Central Dogma Outlines the Flow of Genetic Information | 78 |
| 7. Ribosomes Read the Genetic Code | 81 |
| 8. Various Classes of RNA Have Different Functions | 82 |
| 9. Proteins Carry Out Many Cell Functions | 84 |
| Key Concepts | 91 |
| Review Questions | 92 |
| Conceptual Questions | 93 |

CHAPTER 4 *Genomes and DNA* 94

| | |
|--|-----|
| 1. Genome Organization | 94 |
| 2. Repeated Sequences Are a Feature of Eukaryotic DNA | 100 |
| 3. Palindromes, Inverted Repeats, and Stem and Loop Structures | 105 |
| 4. Multiple A-Tracts Cause DNA to Bend | 106 |
| 5. Supercoiling Is Necessary for Packaging of Bacterial DNA | 106 |
| 6. Separation of DNA Fragments by Electrophoresis | 111 |
| 7. Alternative Helical Structures of DNA Occur | 113 |
| 8. Packaging DNA in Eukaryotic Nuclei | 116 |
| Key Concepts | 121 |
| Review Questions | 122 |
| Conceptual Questions | 123 |

CHAPTER 5 *Manipulation of Nucleic Acids* 125

| | |
|--|-----|
| 1. Manipulating DNA | 126 |
| 2. Chemical Synthesis of DNA | 135 |
| 3. Measuring the Concentration of DNA and RNA with Ultraviolet Light | 143 |
| 4. Radioactive Labeling of Nucleic Acids | 144 |
| 5. Fluorescence in the Detection of DNA and RNA | 146 |
| 6. The Electron Microscope | 149 |
| 7. Hybridization of DNA and RNA | 151 |
| Key Concepts | 158 |
| Review Questions | 158 |
| Conceptual Questions | 159 |

UNIT 2 THE GENOME 162

CHAPTER 6 *Polymerase Chain Reaction* 163

| | |
|--|-----|
| 1. Fundamentals of the Polymerase Chain Reaction | 164 |
| 2. Inverse PCR | 171 |

| | |
|---|-----|
| 3. Randomly Amplified Polymorphic DNA (RAPD) | 172 |
| 4. Reverse Transcriptase PCR | 174 |
| 5. Differential Display PCR | 175 |
| 6. Rapid Amplification of cDNA Ends (RACE) | 176 |
| 7. PCR in Genetic Engineering | 179 |
| 8. Directed Mutagenesis | 179 |
| 9. Engineering Deletions and Insertions by PCR | 181 |
| 10. Real-Time Fluorescent PCR | 182 |
| 11. Molecular Beacons and Scorpion Primers | 184 |
| 12. Use of PCR in Medical Diagnosis | 188 |
| 13. Environmental Analysis by PCR | 189 |
| 14. Rescuing DNA from Extinct Life Forms by PCR | 190 |
| Key Concepts | 191 |
| Review Questions | 192 |
| Conceptual Questions | 193 |

CHAPTER 7 *Cloning Genes for Analysis* 194

| | |
|---|-----|
| 1. Properties of Cloning Vectors | 195 |
| 2. Detecting Insertions in Vectors | 199 |
| 3. Moving Genes Between Organisms: Shuttle Vectors | 201 |
| 4. Bacteriophage Lambda Vectors | 205 |
| 5. Cosmid Vectors | 206 |
| 6. Yeast Artificial Chromosomes | 208 |
| 7. Bacterial and P1 Artificial Chromosomes | 208 |
| 8. Recombineering Increases the Speed of Gene Cloning | 209 |
| 9. A DNA Library is a Collection of Genes from One Source | 212 |
| 10. Cloning Complementary DNA Avoids Introns | 215 |
| 11. Chromosome Walking | 217 |
| 12. Cloning by Subtractive Hybridization | 219 |
| 13. Expression Vectors | 220 |
| Key Concepts | 223 |
| Review Questions | 224 |
| Conceptual Questions | 225 |

CHAPTER 8 *DNA Sequencing* 227

| | |
|---|-----|
| 1. DNA Sequencing—General Principles for Chain Termination Sequencing | 228 |
| 2. Primer Walking Along a Strand of DNA | 234 |
| 3. Automated Sequencing | 235 |
| 4. Cycle Sequencing | 236 |
| 5. The Emergence of DNA Chip Technology | 237 |
| 6. Pyrosequencing | 239 |
| 7. Second-Generation Sequencing | 239 |

| | |
|--------------------------------|-----|
| 8. Third-Generation Sequencing | 242 |
| 9. Nanopore Detectors for DNA | 243 |
| Key Concepts | 244 |
| Review Questions | 246 |
| Conceptual Questions | 246 |

CHAPTER 9 *Genomics & Systems Biology* 248

| | |
|---|-----|
| 1. Large-Scale Mapping with Sequence Tags | 249 |
| 2. Assembling Small Genomes by Shotgun Sequencing | 250 |
| 3. Race for the Human Genome | 253 |
| 4. Survey of the Human Genome | 255 |
| 5. Pharmacogenomics—Genetically-Individualized Drug Treatment | 263 |
| 6. Personal Genomics and Comparative Genomics | 264 |
| 7. Bioinformatics and Computer Analysis | 265 |
| 8. Systems Biology | 266 |
| 9. Metagenomics and Community Sampling | 268 |
| 10. Epigenetics and Epigenomics | 268 |
| Key Concepts | 269 |
| Review Questions | 271 |
| Conceptual Questions | 271 |

UNIT 3 THE CENTRAL DOGMA OF MOLECULAR BIOLOGY 273

CHAPTER 10 *Cell Division and DNA Replication* 274

| | |
|---|-----|
| 1. Cell Division and Reproduction Are Not Always Identical | 275 |
| 2. DNA Replication Occurs at the Replication Fork | 275 |
| 3. Properties of DNA Polymerase | 279 |
| 4. Nucleotides Are the Precursors for DNA Synthesis | 280 |
| 5. DNA Polymerase Elongates DNA Strands | 282 |
| 6. The Complete Replication Fork Is Complex | 285 |
| 7. Discontinuous Synthesis of the Lagging Strand | 286 |
| 8. Chromosome Replication Initiates at <i>oriC</i> | 289 |
| 9. Chromosome Replication Terminates at <i>terC</i> | 292 |
| 10. Cell Division in Bacteria Occurs after Replication of Chromosomes | 293 |
| 11. The Concept of the Replicon | 297 |
| 12. Replicating Linear DNA in Eukaryotes | 298 |
| 13. Cell Division in Higher Organisms | 304 |
| Key Concepts | 305 |
| Review Questions | 307 |
| Conceptual Questions | 308 |

CHAPTER 11 *Transcription of Genes* 309

| | |
|---|-----|
| 1. Genes Are Expressed by Making RNA | 310 |
| 2. How Is the Beginning of a Gene Recognized? | 312 |
| 3. Manufacturing the Message | 314 |
| 4. RNA Polymerase Knows Where to Stop | 316 |
| 5. How Does the Cell Know Which Genes to Turn On? | 318 |
| 6. Transcription in Eukaryotes Is More Complex | 324 |
| Key Concepts | 333 |
| Review Questions | 334 |
| Conceptual Questions | 335 |

CHAPTER 12 *Processing of RNA* 336

| | |
|--|-----|
| 1. RNA Is Processed in Several Ways | 336 |
| 2. Coding and Non-Coding RNA | 338 |
| 3. Processing of Ribosomal and Transfer RNA | 338 |
| 4. Eukaryotic Messenger RNA Contains a Cap and a Tail | 340 |
| 5. Introns Are Removed from RNA by Splicing | 344 |
| 6. Alternative Splicing Produces Multiple Forms of RNA | 349 |
| 7. Inteins and Protein Splicing | 352 |
| 8. Base Modification of rRNA Requires Guide RNA | 355 |
| 9. RNA Editing Alters the Base Sequence | 358 |
| 10. Transport of RNA out of the Nucleus | 360 |
| 11. Degradation of mRNA | 361 |
| Key Concepts | 366 |
| Review Questions | 367 |
| Conceptual Questions | 367 |

CHAPTER 13 *Protein Synthesis* 369

| | |
|---|-----|
| 1. Overview of Protein Synthesis | 370 |
| 2. Proteins Are Chains of Amino Acids | 371 |
| 3. Decoding the Genetic Information | 376 |
| 4. The Ribosome: The Cell's Decoding Machine | 381 |
| 5. Three Possible Reading Frames Exist | 386 |
| 6. The tRNA Occupies Three Sites During Elongation of the Polypeptide | 389 |
| 7. Bacterial mRNA Can Code for Several Proteins | 394 |
| 8. Some Ribosomes Become Stalled and Are Rescued | 395 |
| 9. Differences between Eukaryotic and Prokaryotic Protein Synthesis | 397 |
| 10. Protein Synthesis Is Halted When Resources Are Scarce | 401 |
| 11. A Signal Sequence Marks a Protein for Export from the Cell | 403 |

| | |
|---|-----|
| 12. Protein Synthesis Occurs in Mitochondria and Chloroplasts | 405 |
| 13. Mistranslation Usually Results in Mistakes in Protein Synthesis | 407 |
| 14. Many Antibiotics Work by Inhibiting Protein Synthesis | 408 |
| 15. Post-Translational Modifications of Proteins | 408 |
| 16. Selenocysteine and Pyrrolysine: Rare Amino Acids | 410 |
| 17. Degradation of Proteins | 412 |
| Key Concepts | 415 |
| Review Questions | 415 |
| Conceptual Questions | 416 |

CHAPTER 14 *Protein Structure and Function* 417

| | |
|--|-----|
| 1. The Structure of Proteins Reflects Four Levels of Organization | 417 |
| 2. Determining Protein Structures | 428 |
| 3. Nucleoproteins, Lipoproteins, and Glycoproteins Are Conjugated Proteins | 430 |
| 4. Proteins Serve Numerous Cellular Functions | 433 |
| 5. Protein (Nano)-Machines | 436 |
| 6. Enzymes Catalyze Metabolic Reactions | 437 |
| 7. Binding of Proteins to DNA Occurs in Several Different Ways | 450 |
| 8. Denaturation of Proteins | 454 |
| Key Concepts | 455 |
| Review Questions | 456 |
| Conceptual Questions | 457 |

CHAPTER 15 *Proteomics: The Global Analysis of Proteins* 459

| | |
|--|-----|
| 1. The Proteome | 460 |
| 2. Antibodies Are Essential Proteomics Tools | 464 |
| 3. Western Blotting of Proteins | 465 |
| 4. Isolating Proteins with Chromatography | 466 |
| 5. Mass Spectrometry for Protein Identification | 468 |
| 6. Protein-Tagging Systems | 470 |
| 7. Selection by Phage Display | 474 |
| 8. Protein Interactions: The Yeast Two-Hybrid System | 478 |
| 9. Protein Interaction by Co-Immunoprecipitation | 483 |
| 10. Protein Arrays | 484 |
| 11. Metabolomics | 487 |
| Key Concepts | 489 |
| Review Questions | 490 |
| Conceptual Questions | 491 |

UNIT 4 REGULATING GENE EXPRESSION 492**CHAPTER 16 *Regulation of Transcription in Prokaryotes* 493**

1. Gene Regulation Ensures a Physiological Response 493
2. Regulation at the Level of Transcription Involves Several Steps 496
3. Alternative Sigma Factors in Prokaryotes Recognize Different Sets of Genes 497
4. Activators and Repressors Participate in Positive and Negative Regulation 502
5. Two-Component Regulatory Systems 511
6. Specific versus Global Control 515
7. Accessory Factors and Nucleoid-Binding Proteins 517
8. Anti-Termination as a Control Mechanism 520
- Key Concepts 523
- Review Questions 524
- Conceptual Questions 524

CHAPTER 17 *Regulation of Transcription in Eukaryotes* 526

1. Transcriptional Regulation in Eukaryotes Is More Complex Than in Prokaryotes 526
2. Specific Transcription Factors Regulate Protein-Encoding Genes 527
3. Negative Regulation of Transcription Occurs in Eukaryotes 533
4. Heterochromatin Blocks Access to DNA in Eukaryotes 537
5. Methylation of Eukaryotic DNA Controls Gene Expression 543
6. X-Chromosome Inactivation Occurs in Female XX Animals 547
- Key Concepts 550
- Review Questions 550
- Conceptual Questions 551

CHAPTER 18 *Regulation at the RNA Level* 553

1. Regulation at the Level of mRNA 553
2. Basic Principles of RNA Interference (RNAi) 564
3. Long Non-coding Regulatory RNA 572
4. CRISPR: Anti-Viral Defense in Bacteria 573

5. Premature Termination Causes Attenuation of RNA Transcription 574
6. Riboswitches—RNA Acting Directly as a Control Mechanism 576
- Key Concepts 579
- Review Questions 579
- Conceptual Questions 580

CHAPTER 19 *Analysis of Gene Expression* 581

1. Monitoring Gene Expression 581
2. Reporter Genes for Monitoring Gene Expression 582
3. Deletion Analysis of the Upstream Region 590
4. DNA-Protein Complexes Can Be Isolated by Chromatin Immunoprecipitation 594
5. Location of the Start of Transcription by Primer Extension 596
6. Transcriptome Analysis 600
7. DNA Microarrays for Gene Expression 601
8. TaqMan Quantitative PCR to Assay Gene Expression 608
9. Serial Analysis of Gene Expression (SAGE) 610
- Key Concepts 613
- Review Questions 613
- Conceptual Questions 614

UNIT 5 SUBCELLULAR LIFE FORMS 615**CHAPTER 20 *Plasmids* 616**

1. Plasmids as Replicons 616
2. General Properties of Plasmids 619
3. Plasmid DNA Replicates by Two Alternative Methods 622
4. Many Plasmids Help their Host Cells 628
5. Plasmids may Provide Aggressive Characters 635
6. Ti Plasmids are Transferred from Bacteria to Plants 640
7. The 2 μ Plasmid of Yeast 644
8. Certain DNA Molecules May Behave as Viruses or Plasmids 645
- Key Concepts 646
- Review Questions 647
- Conceptual Questions 648

CHAPTER 21 *Viruses* 649

1. Viruses Are Infectious Packages of Genetic Information 650
2. The Great Diversity of Viruses 658

| | |
|---|-----|
| 3. Viruses with RNA Genomes Have Very Few Genes | 666 |
| 4. Retroviruses Use both RNA and DNA | 672 |
| 5. Subviral Infectious Agents | 678 |
| Key Concepts | 684 |
| Review Questions | 684 |
| Conceptual Questions | 685 |

CHAPTER 22 *Mobile DNA* 686

| | |
|--|-----|
| 1. Subcellular Genetic Elements as Gene Creatures | 686 |
| 2. Most Mobile DNA Consists of Transposable Elements | 687 |
| 3. Retroelements Make an RNA Copy | 703 |
| 4. The Multitude of Transposable Elements | 708 |
| 5. Junk DNA and Selfish DNA | 716 |
| Key Concepts | 717 |
| Review Questions | 718 |
| Conceptual Questions | 719 |

UNIT 6 CHANGING THE DNA BLUEPRINT 720

CHAPTER 23 *Mutations and Repair* 721

| | |
|---|-----|
| 1. Mutations Alter the DNA Sequence | 721 |
| 2. The Major Types of Mutation | 722 |
| 3. Chemical Mutagens Damage DNA | 733 |
| 4. Overview of DNA Repair | 742 |
| 5. Mutations Occur More Frequently at Hotspots | 758 |
| 6. Reversions Are Genetic Alterations That Change the Phenotype Back to Wild-Type | 759 |
| 7. Site-Directed Mutagenesis | 763 |
| Key Concepts | 764 |
| Review Questions | 765 |
| Conceptual Questions | 766 |

CHAPTER 24 *Recombination* 767

| | |
|--|-----|
| 1. Overview of Recombination | 767 |
| 2. Molecular Basis of Homologous Recombination | 769 |

| | |
|--------------------------------------|-----|
| 3. Site-Specific Recombination | 773 |
| 4. Recombination in Higher Organisms | 776 |
| 5. Gene Conversion | 778 |
| Key Concepts | 781 |
| Review Questions | 781 |
| Conceptual Questions | 782 |

CHAPTER 25 *Bacterial Genetics* 783

| | |
|---|-----|
| 1. Reproduction versus Gene Transfer | 783 |
| 2. Fate of the Incoming DNA after Uptake | 784 |
| 3. Transformation Is Gene Transfer by Naked DNA | 785 |
| 4. Gene Transfer by Virus—Transduction | 792 |
| 5. Transfer of Plasmids between Bacteria | 795 |
| 6. Gene Transfer among Gram-Positive Bacteria | 801 |
| 7. Archaeal Genetics | 804 |
| 8. Whole-Genome Sequencing | 805 |
| Key Concepts | 808 |
| Review Questions | 809 |
| Conceptual Questions | 810 |

CHAPTER 26 *Molecular Evolution* 812

| | |
|---|-----|
| 1. Getting Started—Formation of the Earth | 812 |
| 2. Oparin's Theory of the Origin of Life | 814 |
| 3. Origin of Informational Macromolecules | 818 |
| 4. The Autotrophic Theory of the Origin of Metabolism | 823 |
| 5. Evolution of DNA, RNA, and Protein Sequences | 824 |
| 6. Different Proteins Evolve at Very Different Rates | 830 |
| 7. Symbiotic Origin of Eukaryotic Cells | 835 |
| 8. DNA Sequencing and Biological Classification | 841 |
| 9. Evolving Sideways: Horizontal Gene Transfer | 847 |
| Key Concepts | 850 |
| Review Questions | 851 |
| Conceptual Questions | 852 |

| | |
|-----------------|------------|
| Glossary | 855 |
|-----------------|------------|

| | |
|--------------|------------|
| Index | 883 |
|--------------|------------|