

# **CONTENTS**

## **I. INTRODUCTION AND BACKGROUND 1**

### **1. Life 2**

1. Prokaryotes 3
2. Eukaryotes 7
3. Biochemistry: A Prologue 14
4. Origin of Life 18
5. The Biochemical Literature 24

### **2. Aqueous Solutions 29**

1. Properties of Water 30
2. Acids, Bases, and Buffers 35

### **3. Thermodynamic Principles: A Review 42**

1. First Law of Thermodynamics: Energy Is Conserved 43
2. Second Law of Thermodynamics: The Universe Tends Towards Maximum Disorder 44
3. Free Energy: The Indicator of Spontaneity 48
4. Chemical Equilibria 49
- Appendix: Concentration Dependence of Free Energy 52

## **II. BIOMOLECULES 57**

### **4. Amino Acids 59**

1. Amino Acids of Proteins 62
2. Optical Activity 66
3. "Nonstandard" Amino Acids 71

### **5. Techniques of Protein Purification 75**

1. Protein Isolation 76
2. Solubilities of Proteins 79
3. Chromatographic Separations 81
4. Electrophoresis 94
5. Ultracentrifugation 100

### **6. Covalent Structures of Proteins 108**

1. Primary Structure Determination 109
2. Protein Modification 122
3. Chemical Evolution 126
4. Peptide Synthesis 136

### **7. Three-Dimensional Structures of Proteins 144**

1. Secondary Structure 144
2. Fibrous Proteins 156
3. Globular Proteins 165
4. Protein Stability 175
5. Quaternary Structure 182
- Appendix: Viewing Stereo Pictures 187

### **8. Protein Folding, Dynamics, and Structural Evolution 193**

1. Protein Folding: Theory and Experiment 194
2. Protein Dynamics 202
3. Structural Evolution 204

### **9. Hemoglobin: Protein Function in Microcosm 210**

1. Hemoglobin Function 211
2. Structure and Mechanism 217
3. Abnormal Hemoglobins 228
4. Allosteric Regulation 234
- Appendix: Derivation of Symmetry Model Equations 240

### **10. Sugars and Polysaccharides 245**

1. Monosaccharides 246
2. Polysaccharides 252
3. Glycoproteins 260

### **11. Lipids and Membranes 271**

1. Lipid Classification 272
2. Properties of Lipid Aggregates 279
3. Biological Membranes 284
4. Lipoproteins 304

### III. MECHANISMS OF ENZYME ACTION 315

#### 12. Introduction to Enzymes 316

1. Historical Perspective 317
2. Substrate Specificity 317
3. Coenzymes 320
4. Regulation of Enzymatic Activity 322
5. A Primer of Enzyme Nomenclature 326

#### 13. Rates of Enzymatic Reactions 329

1. Chemical Kinetics 330
  2. Enzyme Kinetics 335
  3. Inhibition 340
  4. Effects of pH 344
  5. Bisubstrate Reactions 346
- Appendix: Derivations of Michaelis–Menten Equation Variants 350

#### 14. Enzymatic Catalysis 355

1. Catalytic Mechanisms 356
2. Lysozyme 365
3. Serine Proteases 373
4. Glutathione Reductase 382

### IV. METABOLISM 393

#### 15. Introduction to Metabolism 394

1. Metabolic Pathways 396
2. Organic Reaction Mechanisms 397
3. Experimental Approaches to the Study of Metabolism 403
4. Thermodynamics of Phosphate Compounds 409
5. Oxidation–Reduction Reactions 415
6. Thermodynamics of Life 418

#### 16. Glycolysis 425

1. The Glycolytic Pathway 426
2. The Reactions of Glycolysis 429
3. Fermentation: The Anaerobic Fate of Pyruvate 444
4. Control of Metabolic Flux 448
5. Metabolism of Hexoses Other Than Glucose 454

#### 17. Glycogen Metabolism 461

1. Glycogen Breakdown 462
  2. Glycogen Synthesis 467
  3. Control of Glycogen Metabolism 470
  4. Glycogen Storage Diseases 479
- Appendix: Kinetics of a Cyclic Cascade 481

#### 18. Transport through Membranes 484

1. Thermodynamics of Transport 484
2. Kinetics and Mechanism of Transport 485

3. ATP-Driven Active Transport 493
4. Ion Gradient-Driven Active Transport 500

#### 19. The Citric Acid Cycle 506

1. Cycle Overview 506
2. Metabolic Sources of Acetyl-Coenzyme A 509
3. Enzymes of the Citric Acid Cycle 514
4. Regulation of the Citric Acid Cycle 522
5. The Amphibolic Nature of the Citric Acid Cycle 524

#### 20. Electron Transport and Oxidative Phosphorylation 528

1. The Mitochondrion 529
2. Electron Transport 532
3. Oxidative Phosphorylation 544
4. Control of ATP Production 554

#### 21. Other Pathways of Carbohydrate Metabolism 561

1. Gluconeogenesis 562
2. The Glyoxylate Pathway 568
3. Biosynthesis of Oligosaccharides and Glycoproteins 568
4. The Pentose Phosphate Pathway 577

#### 22. Photosynthesis 586

1. Chloroplasts 587
2. Light Reactions 588
3. Dark Reactions 606

#### 23. Lipid Metabolism 618

1. Lipid Digestion, Absorption, and Transport 619
2. Fatty Acid Oxidation 621
3. Ketone Bodies 632
4. Fatty Acid Biosynthesis 634
5. Regulation of Fatty Acid Metabolism 641
6. Cholesterol Metabolism 645
7. Arachidonate Metabolism: Prostaglandins, Prostacyclins, Thromboxanes, and Leukotrienes 658
8. Phospholipid and Glycolipid Metabolism 665

#### 24. Amino Acid Metabolism 678

1. Amino Acid Deamination 679
2. The Urea Cycle 682
3. Metabolic Breakdown of Individual Amino Acids 686
4. Amino Acids as Biosynthetic Precursors 700
5. Amino Acid Biosynthesis 712
6. Nitrogen Fixation 724

#### 25. Energy Metabolism: Integration and Organ Specialization 730

1. Major Pathways and Strategies of Energy Metabolism: A Summary 730
2. Organ Specialization 733
3. Metabolic Adaptation 737

**26. Nucleotide Metabolism 740**

1. Chemical Structures of Nucleotides, Nucleosides, and Bases 741
2. Synthesis of Purine Ribonucleotides 741
3. Synthesis of Pyrimidine Ribonucleotides 748
4. Formation of Deoxyribonucleotides 750
5. Nucleotide Degradation 758
6. Biosynthesis of Nucleotide Coenzymes 762

**V. EXPRESSION AND TRANSMISSION OF GENETIC INFORMATION 771****27. DNA: The Vehicle of Inheritance 772**

1. Genetics: A Review 773
2. DNA Is the Carrier of Genetic Information 786

**28. Nucleic Acid Structures and Manipulation 791**

1. Chemical Structure and Base Composition 792
2. Double Helical Structures 793
3. Forces Stabilizing Nucleic Acid Structures 805
4. Nucleic Acid Fractionation 813
5. Supercoiled DNA 817
6. Nucleic Acid Sequencing 824
7. Chemical Synthesis of Oligonucleotides 836
8. Molecular Cloning 837

**29. Transcription 852**

1. The Role of RNA in Protein Synthesis 853
2. RNA Polymerase 856
3. Control of Transcription in Prokaryotes 867
4. Post-Transcriptional Processing 880

**30. Translation 893**

1. The Genetic Code 894
2. Transfer RNA 901
3. Ribosomes 913

4. Control of Eukaryotic Translation 933
5. Post-Translational Modification 935
6. Protein Degradation 938
7. Nonribosomal Polypeptide Synthesis 941

**31. DNA Replication, Repair, and Recombination 948**

1. DNA Replication: An overview 948
2. Enzymes of Replication 952
3. Prokaryotic Replication Mechanisms 957
4. Eukaryotic DNA Replication 964
5. Repair of DNA 967
6. Recombination and Mobile Genetic Elements 973
7. DNA Methylation 982

**32. Viruses: Paradigms for Cellular Functions 987**

1. Tobacco Mosaic Virus 989
2. Spherical Viruses 994
3. Bacteriophage  $\lambda$  1000
4. Influenza Virus 1016
5. Subviral Pathogens 1023

**33. Eukaryotic Gene Expression 1032**

1. Chromosome Structure 1033
2. Genomic Organization 1041
3. Control of Expression 1055
4. Cell Differentiation 1066

**34. Molecular Physiology 1086**

1. Blood Clotting 1087
2. Immunity 1095
3. Motility: Muscles, Cilia, and Flagella 1118
4. Biochemical Communications: Hormones and Neurotransmission 1139

**Index 1179**