

Contents

Preface xv

1 Biochemistry: An Introduction 1

1.1 What Is Life? 2

1.2 Biomolecules 4

Functional Groups of Organic Biomolecules 5

Major Classes of Small Biomolecules 6

1.3 Is the Living Cell a Chemical Factory? 13

Biochemical Reactions 13

Energy 18

Overview of Metabolism 19

Biological Order 20

1.4 Systems Biology 21

Emergence 22

Robustness 22

Systems Biology Model Concepts 23

Biochemistry IN THE LAB

An Introduction 25

Chapter Summary 25

Key Words 26

Review Questions 26

Thought Questions 28

2 Living Cells 30

2.1 Basic Themes 31

Water 32

Biological Membranes 32

Self-Assembly 33

Molecular Machines 33

Macromolecular Crowding 34

Proteostasis 34

Signal Transduction 35

2.2 Structure of Prokaryotic Cells 37

Cell Wall 37

Plasma Membrane 38

Cytoplasm 39

Pili and Flagella 39

2.3 Structure of Eukaryotic Cells 40

Plasma Membrane 40

Endoplasmic Reticulum 43

Golgi Apparatus 44

Vesicular Organelles and Lysosomes:

The Endocytic Pathway 47

Nucleus 50

Mitochondria 52

Peroxisomes 55

Chloroplasts 56

Cytoskeleton 56

Biochemistry IN PERSPECTIVE

Primary Cilia and Human Disease 60

Biochemistry IN THE LAB

Cell Technology 61

Chapter Summary 63

Key Words 64

Review Questions 64

Thought Questions 66

3 Water: The Matrix of Life 67

3.1 Molecular Structure of Water 68

3.2 Noncovalent Bonding 70

Ionic Interactions 70

Hydrogen Bonds 70

Van der Waals Forces 71

3.3 Thermal Properties of Water 72

3.4 Solvent Properties of Water 74

Hydrophilic Molecules, Cell Water

Structuring, and Sol-Gel Transitions 74

Hydrophobic Molecules and the

Hydrophobic Effect 77

Amphipathic Molecules 78

Osmotic Pressure 78

3.5 Ionization of Water 82

Acids, Bases, and pH 82

Buffers 84

Physiological Buffers 90

Biochemistry IN PERSPECTIVE

Cell Volume Regulation and Metabolism 92

Chapter Summary 93

Key Words 94

Review Questions 94

Thought Questions 95

4 Energy 97

4.1 Thermodynamics 99

First Law of Thermodynamics 100

Second Law of Thermodynamics 102

4.2 Free Energy 104

- Standard Free Energy Changes 105
- Coupled Reactions 106
- The Hydrophobic Effect Revisited 108

4.3 The Role of ATP 108

Biochemistry IN PERSPECTIVE

Nonequilibrium Thermodynamics and the
Evolution of Life 112

Chapter Summary 113

Key Words 113

Review Questions 113

Thought Questions 114

5 Amino Acids, Peptides, and Proteins 116

5.1 Amino Acids 118

- Amino Acid Classes 118
- Biologically Active Amino Acids 121
- Modified Amino Acids in Proteins 122
- Amino Acid Stereoisomers 122
- Titration of Amino Acids 123
- Amino Acid Reactions 127

5.2 Peptides 130

5.3 Proteins 132

- Other Protein Classifications 133
- Protein Structure 134
- The Folding Problem 148
- Fibrous Proteins 152
- Globular Proteins 156

5.4 Molecular Machines 160

- Motor Proteins 161

Biochemistry IN PERSPECTIVE

Spider Silk and Biomimetics 162

Biochemistry IN THE LAB

Protein Technology 164

Chapter Summary 169

Key Words 170

Review Questions 170

Thought Questions 171

6 Enzymes 173

6.1 Properties of Enzymes 174

- Enzyme Catalysts: The Basics 174
- Enzymes: Activation Energy and Reaction
Equilibrium 175
- Enzymes and Macromolecular Crowding
Effects 176
- Enzyme Specificity 177

6.2 Classification of Enzymes 178

6.3 Enzyme Kinetics 180

- Michaelis-Menten Kinetics 182
- Lineweaver-Burk Plots 185
- Multisubstrate Reactions 186
- Enzyme Inhibition 187
- Enzyme Kinetics, Metabolism, and Macromolecular
Crowding 193

6.4 Catalysis 194

- Organic Reactions and the Transition State 194
- Transition State Stabilization 195
- Catalytic Mechanisms 197
- The Roles of Amino Acids in Enzyme Catalysis 200
- The Role of Cofactors in Enzyme Catalysis 201
- Effects of Temperature and pH on Enzyme-Catalysed
Reactions 204
- Detailed Mechanisms of Enzyme Catalysis 205

6.5 Enzyme Regulation 207

- Genetic Control 208
- Covalent Modification 208
- Allosteric Regulation 209
- Compartmentation 211

Biochemistry IN PERSPECTIVE

Alcohol Dehydrogenase: A Tale
of Two Species 213

Chapter Summary 214

Key Words 215

Review Questions 215

Thought Questions 216



7 Carbohydrates 218

7.1 Monosaccharides 219

- Monosaccharide Stereoisomers 220
- Cyclic Structure of Monosaccharides 220
- Reactions of Monosaccharides 223
- Important Monosaccharides 228
- Monosaccharide Derivatives 230

7.2 Disaccharides 231

7.3 Polysaccharides 232

- Homoglycans 232
- Heteroglycans 236

7.4 Glycoconjugates 237

- Proteoglycans 237
- Glycoproteins 238

7.5 The Sugar Code 240

- Lectins: Translators of the
Sugar Code 241
- The Glycome 243

Chapter Summary 244

Key Words 244

Review Questions 245

Thought Questions 246



8 Carbohydrate Metabolism 248

8.1 Glycolysis 249

The Reactions of the Glycolytic Pathway 252

The Fates of Pyruvate 257

The Energetics of Glycolysis 260

Regulation of Glycolysis 261

8.2 Gluconeogenesis 266

Gluconeogenesis Reactions 266

Gluconeogenesis Substrates 271

Gluconeogenesis Regulation 272

8.3 The Pentose Phosphate Pathway 274

8.4 Metabolism of Other Important Sugars 278

Fructose Metabolism 278

8.5 Glycogen Metabolism 280

Glycogenesis 280

Glycogenolysis 281

Regulation of Glycogen Metabolism 283

Biochemistry IN PERSPECTIVE

Saccharomyces cerevisiae
and the Crabtree Effect 262

Biochemistry IN PERSPECTIVE

Turbo Design Can Be Dangerous 268

Chapter Summary 288

Key Words 288

Review Questions 288

Thought Questions 289

9 Aerobic Metabolism I: The Citric Acid Cycle 290

9.1 Oxidation-Reduction Reactions 292

Redox Coenzymes 295

Aerobic Metabolism 299

9.2 Citric Acid Cycle 299

Conversion of Pyruvate to Acetyl-CoA 301

Reactions of the Citric Acid Cycle 304

Fate of Carbon Atoms in the Citric
Acid Cycle 308

The Amphibolic Citric Acid Cycle 308

Citric Acid Cycle Regulation 309

The Citric Acid Cycle and Human
Disease 313

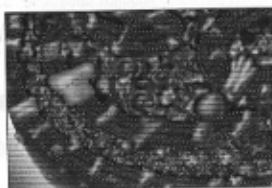
The Glyoxylate Cycle 314

Chapter Summary 316

Key Words 316

Review Questions 316

Thought Questions 317



10 Aerobic Metabolism II: Electron Transport and Oxidative Phosphorylation 318

10.1 Electron Transport 319

Electron Transport and Its Components 319

Electron Transport: The Fluid State and
Solid State Models 326

Electron Transport Inhibitors 326

10.2 Oxidative Phosphorylation 327

The Chemiosmotic Theory 327

ATP Synthesis 329

Control of Oxidative Phosphorylation 331

The Complete Oxidation of Glucose 332

Uncoupled Electron Transport 335

10.3 Oxygen, Cell Function, and Oxidative Stress 336

Reactive Oxygen Species 337

Antioxidant Enzyme Systems 341

Antioxidant Molecules 343

Biochemistry IN PERSPECTIVE

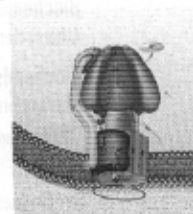
Myocardial Infarct: Ischaemia and Reperfusion 346

Chapter Summary 347

Key Words 347

Review Questions 347

Thought Questions 348



11 Lipids and Membranes 350

11.1 Lipid Classes 351

Fatty Acids 351

The Eicosanoids 354

Triacylglycerols 357

Wax Esters 358

Phospholipids 358

Phospholipases 361

Sphingolipids 362

Sphingolipid Storage Diseases 364

Isoprenoids 364

Lipoproteins 367

11.2 Membranes 370

Membrane Structure 370

Membrane Function 376

Biochemistry IN PERSPECTIVE

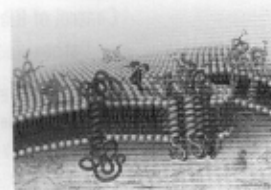
Botulism and Membrane Fusion 384

Chapter Summary 385

Key Words 386

Review Questions 386

Thought Questions 388



12 Lipid Metabolism 389

- 12.1 Fatty Acids, Triacylglycerols, and the Lipoprotein Pathways 390
 - Dietary Fat: Digestion, Absorption, and Transport 390
 - Triacylglycerol Metabolism in Adipocytes 392
 - Fatty Acid Degradation 396
 - The Complete Oxidation of a Fatty Acid 400
 - Fatty Acid Oxidation: Double Bonds and Odd Chains 401
 - Fatty Acid Biosynthesis 405
 - Regulation of Fatty Acid Metabolism in Mammals 413
 - Lipoprotein Metabolism: The Endogenous Pathway 417
- 12.2 Membrane Lipid Metabolism 417
 - Phospholipid Metabolism 417
 - Sphingolipid Metabolism 420
- 12.3 Isoprenoid Metabolism 420
 - Cholesterol Metabolism 420
 - The Cholesterol Biosynthetic Pathway and Drug Therapy 431

Biochemistry IN PERSPECTIVE

Atherosclerosis 418

Biochemistry IN PERSPECTIVE

Biotransformation 432

Chapter Summary 434

Key Words 434

Review Questions 434

Thought Questions 436

13 Photosynthesis 437

- 13.1 Chlorophyll and Chloroplasts 439
- 13.2 Light 445
- 13.3 Light Reactions 448
 - Photosystem II and Water Oxidation 450
 - Photosystem I and NADPH Synthesis 452
 - Photophosphorylation 454
- 13.4 The Light-Independent Reactions 455
 - The Calvin Cycle 455
 - Photorespiration 459
 - Alternatives to C3 Metabolism 460
- 13.5 Regulation of Photosynthesis 463
 - Light Control of Photosynthesis 463
 - Control of Ribulose-1,5-Bisphosphate Carboxylase 464

Biochemistry IN PERSPECTIVE

The Artificial Leaf: Biomimetic Photosynthesis 466

Chapter Summary 467

Key Words 467

Review Questions 468

Thought Questions 469

14 Nitrogen Metabolism I: Synthesis 470

- 14.1 Nitrogen Fixation 471
 - The Nitrogen Fixation Reaction 472
 - Nitrogen Assimilation 474
- 14.2 Amino Acid Biosynthesis 475
 - Amino Acid Metabolism Overview 475
 - Reactions of Amino Groups 476
 - Biosynthesis of the Amino Acids 480
- 14.3 Biosynthetic Reactions Involving Amino Acids 487
 - One-Carbon Metabolism 488
 - Glutathione 493
 - Neurotransmitters 494
 - Nucleotides 499
 - Haem 508

Biochemistry IN PERSPECTIVE

Gasotransmitters 497

Chapter Summary 509

Key Words 509

Review Questions 509

Thought Questions 511

15 Nitrogen Metabolism II: Degradation 512

- 15.1 Protein Turnover 513
 - Ubiquitin Proteasomal System 514
 - Autophagy-Lysosomal System 516
- 15.2 Amino Acid Catabolism 517
 - Deamination 519
 - Urea Synthesis 519
 - Control of the Urea Cycle 522
 - Catabolism of Amino Acid Carbon Skeletons 522
- 15.3 Neurotransmitter Degradation 532
- 15.4 Nucleotide Degradation 532
 - Purine Catabolism 533
 - Pyrimidine Catabolism 535

Biochemistry IN PERSPECTIVE

Disorders of Amino Acid Catabolism 531

Chapter Summary 537

Key Words 537

Review Questions 537

Thought Questions 539

16 Integration of Metabolism 540

- 16.1 Overview of Metabolism 541
- 16.2 Hormones and Intercellular Communication 543
 - Peptide Hormones 543

- Growth Factors 551
- Steroid and Thyroid Hormone Mechanisms 554

16.3 Metabolism in the Mammalian Body:

- The Feeding-Fasting Cycle 555
- The Feeding Phase 556
- The Fasting Phase 559
- Feeding Behaviour 560

Biochemistry IN PERSPECTIVE

Diabetes Mellitus 552

Biochemistry IN PERSPECTIVE

Obesity and the Metabolic Syndrome 563

Chapter Summary 564

Key Words 565

Review Questions 565

Thought Questions 566

17 Nucleic Acids 568

17.1 DNA 572

- DNA Structure: The Nature of Mutation 575
- DNA Structure: The Genetic Material 579
- DNA Structure: Variations on a Theme 579
- DNA Supercoiling 581
- Chromosomes and Chromatin 583
- Genome Structure 587

17.2 RNA 593

- Transfer RNA 596
- Ribosomal RNA 601
- Messenger RNA 603
- Noncoding RNA 604

17.3 VIRUSES 605

- Bacteriophage T4: A Viral Lifestyle 606

Biochemistry IN PERSPECTIVE

Epigenetics and the Epigenome: Genetic Inheritance beyond DNA Base Sequences 594

Biochemistry IN THE LAB

Nucleic Acid Methods 597

Biochemistry IN PERSPECTIVE

Forensic Investigations 602

Biochemistry IN PERSPECTIVE

HIV Infection 608

Chapter Summary 611

Key Words 612

Review Questions 612

Thought Questions 613

18 Genetic Information 615

18.1 Genetic Information: Replication, Repair, and Recombination 617

- DNA Replication 617
- DNA Repair 626

- Direct Repairs 628
- DNA Recombination 631

18.2 Transcription 646

- Transcription in Prokaryotes 646
- RNA Polymerase and the Prokaryotic Transcription Process 648
- Transcription in Eukaryotes 650

18.3 Gene Expression 657

- Gene Expression in Prokaryotes 659
- Gene Expression in Eukaryotes 661

Biochemistry IN THE LAB

Genomics 640

Biochemistry IN PERSPECTIVE

Carcinogenesis 669

Chapter Summary 671

Key Words 671

Review Questions 672

Thought Questions 673



19 Protein Synthesis 675

19.1 The Genetic Code 677

- Codon Usage Bias 678
- Codon-Anticodon Interactions 678
- The Aminoacyl-tRNA Synthetase Reaction 681

19.2 Protein Synthesis 682

- Prokaryotic Protein Synthesis 685
- Eukaryotic Protein Synthesis 690

19.3 The Proteostasis Network 709

- The Heat Shock Response 710
- The Proteostasis Network and Human Disease 710

Biochemistry IN PERSPECTIVE

Trapped Ribosomes: RNA to the Rescue! 692

Biochemistry IN PERSPECTIVE

Context-Dependent Coding Reassignment 698

Biochemistry IN THE LAB

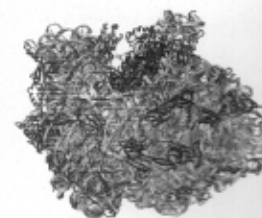
Proteomics 711

Chapter Summary 712

Key Words 712

Review Questions 713

Thought Questions 714



Appendix: Solutions A-1

Glossary G-1

Credits C-1

Index I-1