

ESSENTIAL BIOCHEMISTRY

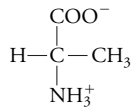
FOURTH EDITION

CHARLOTTE W. PRATT ● KATHLEEN CORNELLY

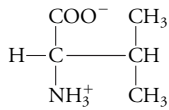
WILEY

AMINO ACID STRUCTURES AND ABBREVIATIONS

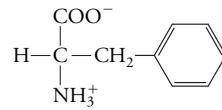
Hydrophobic amino acids



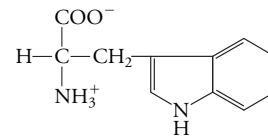
Alanine (Ala, A)



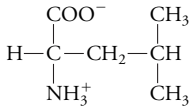
Valine (Val, V)



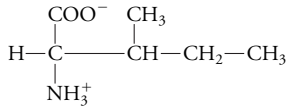
Phenylalanine (Phe, F)



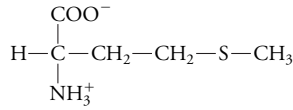
Tryptophan (Trp, W)



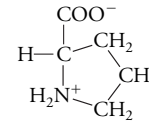
Leucine (Leu, L)



Isoleucine (Ile, I)

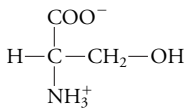


Methionine (Met, M)

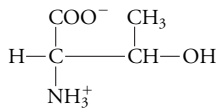


Proline (Pro, P)

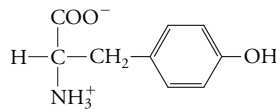
Polar amino acids



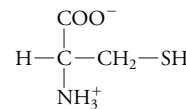
Serine (Ser, S)



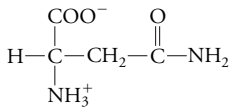
Threonine (Thr, T)



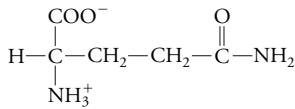
Tyrosine (Tyr, Y)



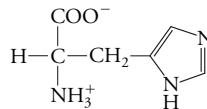
Cysteine (Cys, C)



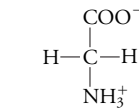
Asparagine (Asn, N)



Glutamine (Gln, Q)

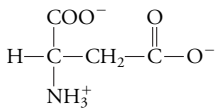


Histidine (His, H)

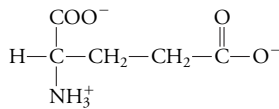


Glycine (Gly, G)

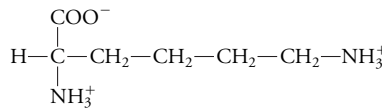
Charged amino acids



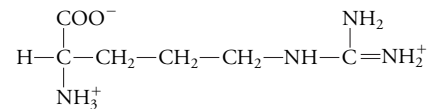
Aspartate (Asp, D)



Glutamate (Glu, E)



Lysine (Lys, K)



Arginine (Arg, R)

Essential Biochemistry

Fourth Edition

CHARLOTTE W. PRATT

Seattle Pacific University

KATHLEEN CORNELLY

Providence College

WILEY

VICE PRESIDENT, PUBLISHER	Petra Recter
SPONSORING EDITOR	Joan Kalkut
ASSOCIATE DEVELOPMENT EDITOR	Laura Rama
SENIOR MARKETING MANAGER	Kristine Ruff
PRODUCT DESIGNER	Sean Hickey
SENIOR DESIGNER	Thomas Nery
SENIOR PHOTO EDITOR	Billy Ray
EDITORIAL ASSISTANT	Mili Ali
PRODUCT DESIGN ASSISTANT	Alyce Pellegrino
MARKETING ASSISTANT	Maggie Joest
SENIOR PRODUCTION EDITOR	Elizabeth Swain

Cover image: The active site of RNA polymerase, based on a structure determined by Yuan He, Chunli Yan, Jie Fang, Carla Inouye, Robert Tjian, Ivaylo Ivanov, and Eva Nogales (pdb 5IYD).

This book was typeset by Aptara and printed and bound by Quad Graphics Versailles. The cover was printed by Quad Graphics Versailles.

Copyright © 2018, 2014, 2011, 2004 John Wiley and Sons, Inc. All rights reserved.

No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, scanning or otherwise, except as permitted under Sections 107 or 108 of the 1976 United States Copyright Act, without either the prior written permission of the Publisher or authorization through payment of the appropriate per-copy fee to the Copyright Clearance Center, 222 Rosewood Drive, Danvers, MA 01923, (978) 750-8400, fax (978) 646-8600. Requests to the Publisher for permission should be addressed to the Permissions Department, John Wiley Sons, Inc., 111 River Street, Hoboken, NJ 07030-5774, (201) 748-6011, fax (201) 748-6008.

Evaluation copies are provided to qualified academics and professionals for review purposes only, for use in their courses during the next academic year. These copies are licensed and may not be sold or transferred to a third party. Upon completion of the review period, please return the evaluation copy to Wiley. Return instructions and a free of charge return shipping label are available at www.wiley.com/go/returnlabel. Outside of the United States, please contact your local representative.

ISBN 978-1-119-31933-7

The inside back cover will contain printing identification and country of origin if omitted from this page. In addition, if the ISBN on the back cover differs from the ISBN on this page, the one on the back cover is correct.

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

About the Authors

CHARLOTTE PRATT received a B.S. in biology from the University of Notre Dame and a Ph.D. in biochemistry from Duke University. She is a protein chemist who has conducted research in blood coagulation and inflammation at the University of North Carolina at Chapel Hill. She is currently Associate Professor in the Biology Department at Seattle Pacific University. Her interests include molecular evolution, enzyme action, and the relationship between metabolic processes and disease. She has written numerous research and review articles, has worked as a textbook editor, and is a co-author, with Donald Voet and Judith G. Voet, of *Fundamentals of Biochemistry*, published by John Wiley & Sons, Inc.

KATHLEEN CORNELLY holds a B.S. in chemistry from Bowling Green (Ohio) State University, an M.S. in biochemistry from Indiana University, and a Ph.D. in nutritional biochemistry from Cornell University. She currently serves as a Professor in the Department of Chemistry and Biochemistry at Providence College where she has focused on expanding the use of case studies and guided inquiry across a broad spectrum of classes. Her interest in active pedagogy has led to her involvement in national programs including Project Kaleidoscope, the POGIL Project, and the Howard Hughes Medical Institute SEA PHAGES program, which has also fueled her current experimental research in phage genomics. She has been a member of the editorial board of *Biochemistry and Molecular Biology Education* and has served for several years as coordinator of the undergraduate poster competition at the annual meeting of the American Society for Biochemistry and Molecular Biology.

Brief Contents

PREFACE xi

Part 1 Foundations

- 1 The Chemical Basis of Life 1
- 2 Aqueous Chemistry 24

Part 2 Molecular Structure and Function

- 3 From Genes to Proteins 52
- 4 Protein Structure 85
- 5 Protein Function 119
- 6 How Enzymes Work 154
- 7 Enzyme Kinetics and Inhibition 183
- 8 Lipids and Membranes 215
- 9 Membrane Transport 235
- 10 Signaling 260
- 11 Carbohydrates 283

Part 3 Metabolism

- 12 Metabolism and Bioenergetics 301
- 13 Glucose Metabolism 329
- 14 The Citric Acid Cycle 362
- 15 Oxidative Phosphorylation 385
- 16 Photosynthesis 411
- 17 Lipid Metabolism 432
- 18 Nitrogen Metabolism 464
- 19 Regulation of Mammalian Fuel Metabolism 497

Part 4 Genetic Information

- 20 DNA Replication and Repair 519
- 21 Transcription and RNA 551
- 22 Protein Synthesis 580

Part 1 Foundations

1 The Chemical Basis of Life 1

- 1.1 What Is Biochemistry?** 1
- 1.2 Biological Molecules** 3
Cells contain four major types of biomolecules 3
There are three major kinds of biological polymers 6
- Box 1.A Units Used in Biochemistry** 7
- 1.3 Energy and Metabolism** 10
Enthalpy and entropy are components of free energy 10
 ΔG is less than zero for a spontaneous process 11
Life is thermodynamically possible 12
- 1.4 The Origin and Evolution of Life** 14
The prebiotic world 14
Origins of modern cells 16
- Box 1.B How Does Evolution Work?** 17

2 Aqueous Chemistry 24

- 2.1 Water Molecules and Hydrogen Bonds** 24
Hydrogen bonds are one type of electrostatic force 26
- Box 2.A Why Do Some Drugs Contain Fluorine?** 28
Water dissolves many compounds 28
- 2.2 The Hydrophobic Effect** 29
Amphiphilic molecules experience both hydrophilic interactions and the hydrophobic effect 31
The hydrophobic core of a lipid bilayer is a barrier to diffusion 31
- Box 2.B Sweat, Exercise, and Sports Drinks** 32
- 2.3 Acid–Base Chemistry** 33
[H⁺] and [OH⁻] are inversely related 33
The pH of a solution can be altered 34
- Box 2.C Atmospheric CO₂ and Ocean Acidification** 35
A pK value describes an acid's tendency to ionize 36
The pH of a solution of acid is related to the pK 37
- 2.4 Tools and Techniques: Buffers** 40
- 2.5 Clinical Connection: Acid–Base Balance in Humans** 42

Part 2 Molecular Structure and Function

3 From Genes to Proteins 52

- 3.1 Nucleotides** 52
Nucleic acids are polymers of nucleotides 53
Some nucleotides have other functions 54

- 3.2 Nucleic Acid Structure** 56
DNA is a double helix 56
RNA is single-stranded 59
Nucleic acids can be denatured and renatured 59
- 3.3 The Central Dogma** 61
DNA must be decoded 62
A mutated gene can cause disease 63
- 3.4 Genomics** 64
Gene number is roughly correlated with organismal complexity 65
Genes are identified by comparing sequences 66
Genomic data reveal biological functions 67
- 3.5 Tools and Techniques: Manipulating DNA** 68
Cutting and pasting generates recombinant DNA 69
The polymerase chain reaction amplifies DNA 71
- Box 3.A Genetically Modified Organisms** 72
- Box 3.B DNA Fingerprinting** 74
DNA sequencing uses DNA polymerase to make a complementary strand 74
DNA can be altered 76

4 Protein Structure 85

- 4.1 Amino Acids, the Building Blocks of Proteins** 86
The 20 amino acids have different chemical properties 87
- Box 4.A Does Chirality Matter?** 88
- Box 4.B Monosodium Glutamate** 90
Peptide bonds link amino acids in proteins 90
The amino acid sequence is the first level of protein structure 93
- 4.2 Secondary Structure: The Conformation of the Peptide Group** 94
The α helix exhibits a twisted backbone conformation 95
The β sheet contains multiple polypeptide strands 95
Proteins also contain irregular secondary structure 96
- 4.3 Tertiary Structure and Protein Stability** 97
Proteins have hydrophobic cores 98
Protein structures are stabilized mainly by the hydrophobic effect 99
Other interactions help stabilize proteins 100
Protein folding begins with the formation of secondary structures 101
Some proteins have more than one conformation 102
- 4.4 Quaternary Structure** 104
- 4.5 Clinical Connection: Protein Misfolding and Disease** 105
- 4.6 Tools and Techniques: Analyzing Protein Structure** 107
Chromatography takes advantage of a polypeptide's unique properties 107

Mass spectrometry reveals amino acid sequences 109
 Protein structures are determined by X-ray
 crystallography, electron crystallography, and
 NMR spectroscopy 110

Box 4.C Mass Spectrometry Applications 110

5 Protein Function 119

5.1 Myoglobin and Hemoglobin: Oxygen-Binding Proteins 120

Oxygen binding to myoglobin depends on the oxygen concentration 120
 Myoglobin and hemoglobin are related by evolution 121
 Oxygen binds cooperatively to hemoglobin 123
 A conformational shift explains hemoglobin's cooperative behavior 124

Box 5.A Carbon Monoxide Poisoning 124

H⁺ ions and bisphosphoglycerate regulate oxygen binding to hemoglobin *in vivo* 126

5.2 Clinical Connection: Hemoglobin Variants 127

5.3 Structural Proteins 130

Actin filaments are most abundant 130
 Actin filaments continuously extend and retract 131
 Tubulin forms hollow microtubules 132
 Some drugs affect microtubules 134
 Keratin is an intermediate filament 135
 Collagen is a triple helix 136

Box 5.B Vitamin C Deficiency Causes Scurvy 137

Collagen molecules are covalently cross-linked 139

Box 5.C Bone and Collagen Defects 139

5.4 Motor Proteins 141

Myosin has two heads and a long tail 141
 Myosin operates through a lever mechanism 142
 Kinesin is a microtubule-associated motor protein 143

Box 5.D Myosin Mutations and Deafness 144

Kinesin is a processive motor 146

6 How Enzymes Work 154

6.1 What Is an Enzyme? 154

Enzymes are usually named after the reaction they catalyze 157

6.2 Chemical Catalytic Mechanisms 158

A catalyst provides a reaction pathway with a lower activation energy barrier 159
 Enzymes use chemical catalytic mechanisms 160

Box 6.A Depicting Reaction Mechanisms 162

The catalytic triad of chymotrypsin promotes peptide bond hydrolysis 164

6.3 Unique Properties of Enzyme Catalysts 166

Enzymes stabilize the transition state 166
 Efficient catalysis depends on proximity and orientation effects 168
 The active-site microenvironment promotes catalysis 168

6.4 Chymotrypsin in Context 169

Not all serine proteases are related by evolution 170
 Enzymes with similar mechanisms exhibit different substrate specificity 170

Chymotrypsin is activated by proteolysis 171
 Protease inhibitors limit protease activity 172

6.5 Clinical Connection: Blood Coagulation 173

7 Enzyme Kinetics and Inhibition 183

7.1 Introduction to Enzyme Kinetics 183

7.2 Derivation and Meaning of the Michaelis–Menten Equation 186

Rate equations describe chemical processes 186
 The Michaelis–Menten equation is a rate equation for an enzyme-catalyzed reaction 187
 K_M is the substrate concentration at which velocity is half-maximal 189
 The catalytic constant describes how quickly an enzyme can act 190
 k_{cat}/K_M indicates catalytic efficiency 190
 K_M and V_{max} are experimentally determined 191
 Not all enzymes fit the simple Michaelis–Menten model 192

7.3 Enzyme Inhibition 194

Some inhibitors act irreversibly 195
 Competitive inhibition is the most common form of reversible enzyme inhibition 195
 Transition state analogs inhibit enzymes 197

Box 7.A Inhibitors of HIV Protease 198

Other types of inhibitors affect V_{max} 199
 Allosteric enzyme regulation includes inhibition and activation 200
 Several factors may influence enzyme activity 203

7.4 Clinical Connection: Drug Development 204

8 Lipids and Membranes 215

8.1 Lipids 215

Fatty acids contain long hydrocarbon chains 216

Box 8.A Omega-3 Fatty Acids 216

Some lipids contain polar head groups 217
 Lipids perform a variety of physiological functions 219

Box 8.B The Lipid Vitamins A, D, E, and K 221

8.2 The Lipid Bilayer 222

The bilayer is a fluid structure 223
 Natural bilayers are asymmetric 224

8.3 Membrane Proteins 225

Integral membrane proteins span the bilayer 225
 An α helix can cross the bilayer 226
 A transmembrane β sheet forms a barrel 226
 Lipid-linked proteins are anchored in the membrane 227

8.4 The Fluid Mosaic Model 228

Membrane glycoproteins face the cell exterior 229

9 Membrane Transport 235

9.1 The Thermodynamics of Membrane Transport 235

Ion movements alter membrane potential 237
 Membrane proteins mediate transmembrane ion movement 237

9.2 Passive Transport 240

Porins are β barrel proteins 240
 Ion channels are highly selective 241

Box 9.A Pores Can Kill 242

Gated channels undergo conformational changes 242
 Aquaporins are water-specific pores 243
 Some transport proteins alternate between conformations 244

9.3 Active Transport 245

The Na,K-ATPase changes conformation as it pumps ions across the membrane 246
 ABC transporters mediate drug resistance 247
 Secondary active transport exploits existing gradients 247

9.4 Membrane Fusion 248**Box 9.B Antidepressants Block Serotonin Transport 250**

SNAREs link vesicle and plasma membranes 251
 Endocytosis is the reverse of exocytosis 252

Box 9.C Exosomes 253**10 Signaling 260****10.1 General Features of Signaling Pathways 260**

A ligand binds to a receptor with a characteristic affinity 261

Box 10.A Bacterial Quorum Sensing 262

Most signaling occurs through two types of receptors 263
 The effects of signaling are limited 264

10.2 G Protein Signaling Pathways 265

G protein-coupled receptors include seven transmembrane helices 265
 The receptor activates a G protein 265
 Adenylate cyclase generates the second messenger cyclic AMP 266
 Cyclic AMP activates protein kinase A 267
 Signaling pathways are also switched off 267
 The phosphoinositide signaling pathway generates two second messengers 269
 Calmodulin mediates some Ca^{2+} signals 270

10.3 Receptor Tyrosine Kinases 270

The insulin receptor dimer binds one insulin 271
 The receptor undergoes autophosphorylation 271

Box 10.B Cell Signaling and Cancer 273**10.4 Lipid Hormone Signaling 274**

Eicosanoids are short-range signals 275

Box 10.C Aspirin and Other Inhibitors of Cyclooxygenase 276**11 Carbohydrates 283****11.1 Monosaccharides 283**

Most carbohydrates are chiral compounds 284
 Cyclization generates α and β anomers 285
 Monosaccharides can be derivatized in many different ways 286

11.2 Polysaccharides 287

Lactose and sucrose are the most common disaccharides 288

Starch and glycogen are fuel-storage molecules 288

Cellulose and chitin provide structural support 289

Box 11.A Cellulosic Biofuel 290

Bacterial polysaccharides form a biofilm 291

11.3 Glycoproteins 291

Oligosaccharides are *N*-linked or *O*-linked 292
 Oligosaccharide groups are biological markers 293

Box 11.B The ABO Blood Group System 293

Proteoglycans contain long glycosaminoglycan chains 294

Bacterial cell walls are made of peptidoglycan 295

Part 3 Metabolism**12 Metabolism and Bioenergetics 301****12.1 Food and Fuel 301**

Cells take up the products of digestion 302

Box 12.A Dietary Guidelines 303

Monomers are stored as polymers 304
 Fuels are mobilized as needed 304

12.2 Metabolic Pathways 306

Some major metabolic pathways share a few common intermediates 307
 Many metabolic pathways include oxidation-reduction reactions 308
 Metabolic pathways are complex 310

Box 12.B The Transcriptome, the Proteome, and the Metabolome 311

Human metabolism depends on vitamins 312

12.3 Free Energy Changes in Metabolic Reactions 314

The free energy change depends on reactant concentrations 314
 Unfavorable reactions are coupled to favorable reactions 316
 Free energy can take different forms 318

Box 12.C Powering Human Muscles 320

Regulation occurs at the steps with the largest free energy changes 321

13 Glucose Metabolism 329**13.1 Glycolysis 330**

Reactions 1–5 are the energy-investment phase of glycolysis 330
 Reactions 6–10 are the energy-payoff phase of glycolysis 336

Box 13.A Catabolism of Other Sugars 340

Pyruvate is converted to other substances 341

Box 13.B Alcohol Metabolism 342**13.2 Gluconeogenesis 344**

Four gluconeogenic enzymes plus some glycolytic enzymes convert pyruvate to glucose 345
 Gluconeogenesis is regulated at the fructose bisphosphatase step 346

13.3 Glycogen Synthesis and Degradation 347

Glycogen synthesis consumes the free energy of UTP 348
 Glycogen phosphorylase catalyzes glycogenolysis 349

13.4 The Pentose Phosphate Pathway 350

The oxidative reactions of the pentose phosphate pathway produce NADPH 350
 Isomerization and interconversion reactions generate a variety of monosaccharides 351
 A summary of glucose metabolism 352

13.5 Clinical Connection: Disorders of Carbohydrate Metabolism 353

Glycogen storage diseases affect liver and muscle 354

14 The Citric Acid Cycle 362**14.1 The Pyruvate Dehydrogenase Reaction 362**

The pyruvate dehydrogenase complex contains multiple copies of three different enzymes 363
 Pyruvate dehydrogenase converts pyruvate to acetyl-CoA 363

14.2 The Eight Reactions of the Citric Acid Cycle 365

1. Citrate synthase adds an acetyl group to oxaloacetate 366
2. Aconitase isomerizes citrate to isocitrate 368
3. Isocitrate dehydrogenase releases the first CO₂ 369
4. α -Ketoglutarate dehydrogenase releases the second CO₂ 369
5. Succinyl-CoA synthetase catalyzes substrate-level phosphorylation 370
6. Succinate dehydrogenase generates ubiquinol 370
7. Fumarase catalyzes a hydration reaction 371
8. Malate dehydrogenase regenerates oxaloacetate 371

14.3 Thermodynamics of the Citric Acid Cycle 372

The citric acid cycle is an energy-generating catalytic cycle 372
 The citric acid cycle is regulated at three steps 372
 The citric acid cycle probably evolved as a synthetic pathway 373

Box 14.A Mutations in Citric Acid Cycle Enzymes 373

14.4 Anabolic and Catabolic Functions of the Citric Acid Cycle 375

Citric acid cycle intermediates are precursors of other molecules 375
 Anaplerotic reactions replenish citric acid cycle intermediates 376

Box 14.B The Glyoxylate Pathway 377

15 Oxidative Phosphorylation 385**15.1 The Thermodynamics of Oxidation–Reduction Reactions 385**

Reduction potential indicates a substance's tendency to accept electrons 386
 The free energy change can be calculated from the change in reduction potential 388

15.2 Mitochondrial Electron Transport 390

Mitochondrial membranes define two compartments 390
 Complex I transfers electrons from NADH to ubiquinone 392
 Other oxidation reactions contribute to the ubiquinol pool 394

Complex III transfers electrons from ubiquinol to cytochrome *c* 394

Complex IV oxidizes cytochrome *c* and reduces O₂ 397

Box 15.A Free Radicals and Aging 398

15.3 Chemiosmosis 399

Chemiosmosis links electron transport and oxidative phosphorylation 400
 The proton gradient is an electrochemical gradient 400

15.4 ATP Synthase 401

ATP synthase rotates as it translocates protons 401
 The binding change mechanism explains how ATP is made 403
 The P:O ratio describes the stoichiometry of oxidative phosphorylation 403

Box 15.B Uncoupling Agents Prevent ATP Synthesis 404

The rate of oxidative phosphorylation depends on the rate of fuel catabolism 404

16 Photosynthesis 411**16.1 Chloroplasts and Solar Energy 411**

Pigments absorb light of different wavelengths 412
 Light-harvesting complexes transfer energy to the reaction center 414

16.2 The Light Reactions 415

Photosystem II is a light-activated oxidation–reduction enzyme 416
 The oxygen-evolving complex of Photosystem II oxidizes water 417
 Cytochrome *b₆f* links Photosystems I and II 418
 A second photooxidation occurs at Photosystem I 419
 Chemiosmosis provides the free energy for ATP synthesis 421

16.3 Carbon Fixation 422

Rubisco catalyzes CO₂ fixation 422

Box 16.A The C₄ Pathway 424

The Calvin cycle rearranges sugar molecules 424
 The availability of light regulates carbon fixation 426
 Calvin cycle products are used to synthesize sucrose and starch 426

17 Lipid Metabolism 432**17.1 Lipid Transport 432****17.2 Fatty Acid Oxidation 435**

Fatty acids are activated before they are degraded 435
 Each round of β oxidation has four reactions 436
 Degradation of unsaturated fatty acids requires isomerization and reduction 439
 Oxidation of odd-chain fatty acids yields propionyl-CoA 440
 Some fatty acid oxidation occurs in peroxisomes 442

17.3 Fatty Acid Synthesis 443

Acetyl-CoA carboxylase catalyzes the first step of fatty acid synthesis 444
 Fatty acid synthase catalyzes seven reactions 445
 Other enzymes elongate and desaturate newly synthesized fatty acids 447

- Box 17.A** Fats, Diet, and Heart Disease 448
Fatty acid synthesis can be activated and inhibited 449
- Box 17.B** Inhibitors of Fatty Acid Synthesis 450
Acetyl-CoA can be converted to ketone bodies 450
- 17.4 Synthesis of Other Lipids 452**
Triacylglycerols and phospholipids are built from acyl-CoA groups 452
Cholesterol synthesis begins with acetyl-CoA 454
A summary of lipid metabolism 457

18 Nitrogen Metabolism 464

- 18.1 Nitrogen Fixation and Assimilation 464**
Nitrogenase converts N_2 to NH_3 465
Ammonia is assimilated by glutamine synthetase and glutamate synthase 466
Transamination moves amino groups between compounds 467
- Box 18.A** Transaminases in the Clinic 469
- 18.2 Amino Acid Biosynthesis 469**
Several amino acids are easily synthesized from common metabolites 470
Amino acids with sulfur, branched chains, or aromatic groups are more difficult to synthesize 471
- Box 18.B** Glyphosate, the Most Popular Herbicide 473
Amino acids are the precursors of some signaling molecules 475
- Box 18.C** Nitric Oxide 476
- 18.3 Amino Acid Catabolism 476**
Amino acids are glucogenic, ketogenic, or both 477
- Box 18.D** Diseases of Amino Acid Metabolism 480
- 18.4 Nitrogen Disposal: The Urea Cycle 480**
Glutamate supplies nitrogen to the urea cycle 481
The urea cycle consists of four reactions 482
- 18.5 Nucleotide Metabolism 485**
Purine nucleotide synthesis yields IMP and then AMP and GMP 485
Pyrimidine nucleotide synthesis yields UTP and CTP 486
Ribonucleotide reductase converts ribonucleotides to deoxyribonucleotides 487
Thymidine nucleotides are produced by methylation 488
Nucleotide degradation produces uric acid or amino acids 489

19 Regulation of Mammalian Fuel Metabolism 497

- 19.1 Integration of Fuel Metabolism 498**
Organs are specialized for different functions 498
Metabolites travel between organs 499
- Box 19.A** The Intestinal Microbiome Contributes to Metabolism 500
- 19.2 Hormonal Control of Fuel Metabolism 501**
Insulin is released in response to glucose 502
Insulin promotes fuel use and storage 503
Glucagon and epinephrine trigger fuel mobilization 504

- Additional hormones influence fuel metabolism 505
AMP-dependent protein kinase acts as a fuel sensor 506

- 19.3 Disorders of Fuel Metabolism 507**
The body generates glucose and ketone bodies during starvation 507
- Box 19.B** Marasmus and Kwashiorkor 507
Obesity has multiple causes 508
Diabetes is characterized by hyperglycemia 509
The metabolic syndrome links obesity and diabetes 511
- 19.4 Clinical Connection: Cancer Metabolism 511**
Aerobic glycolysis supports biosynthesis 512
Cancer cells consume large amounts of glutamine 512

Part 4 Genetic Information

20 DNA Replication and Repair 519

- 20.1 The DNA Replication Machinery 519**
Replication occurs in factories 520
Helicases convert double-stranded DNA to single-stranded DNA 521
DNA polymerase faces two problems 522
DNA polymerases share a common structure and mechanism 523
DNA polymerase proofreads newly synthesized DNA 525
An RNase and a ligase are required to complete the lagging strand 525
- 20.2 Telomeres 528**
Telomerase extends chromosomes 529
- Box 20.A** HIV Reverse Transcriptase 530
Is telomerase activity linked to cell immortality? 531
- 20.3 DNA Damage and Repair 531**
DNA damage is unavoidable 531
Repair enzymes restore some types of damaged DNA 533
Base excision repair corrects the most frequent DNA lesions 533
Nucleotide excision repair targets the second most common form of DNA damage 535
Double-strand breaks can be repaired by joining the ends 535
Recombination also restores broken DNA molecules 536
- 20.4 Clinical Connection: Cancer as a Genetic Disease 538**
Tumor growth depends on multiple events 538
DNA repair pathways are closely linked to cancer 539
- 20.5 DNA Packaging 540**
DNA is negatively supercoiled 541
Topoisomerases alter DNA supercoiling 541
Eukaryotic DNA is packaged in nucleosomes 543

21 Transcription and RNA 551

- 21.1 Initiating Transcription 552**
What is a gene? 552
DNA packaging affects transcription 553
DNA also undergoes covalent modification 555
Transcription begins at promoters 555
Transcription factors recognize eukaryotic promoters 557

Enhancers and silencers act at a distance from the promoter 558

Box 21.A DNA-Binding Proteins 558

Prokaryotic operons allow coordinated gene expression 560

21.2 RNA Polymerase 562

RNA polymerases have a common structure and mechanism 562

RNA polymerase is a processive enzyme 564

Transcription elongation requires a conformational change in RNA polymerase 564

Transcription is terminated in several ways 565

21.3 RNA Processing 567

Eukaryotic mRNAs receive a 5' cap and a 3' poly(A) tail 567

Splicing removes introns from eukaryotic RNA 567

mRNA turnover and RNA interference limit gene expression 569

rRNA and tRNA processing includes the addition, deletion, and modification of nucleotides 572

RNAs have extensive secondary structure 573

22 Protein Synthesis 580

22.1 tRNA and the Genetic Code 580

The genetic code is redundant 581

tRNAs have a common structure 581

tRNA aminoacylation consumes ATP 582

Some synthetases have proofreading activity 584

tRNA anticodons pair with mRNA codons 584

Box 22.A The Genetic Code Expanded 585

22.2 Ribosome Structure 586

The ribosome is mostly RNA 586

Three tRNAs bind to the ribosome 587

22.3 Translation 589

Initiation requires an initiator tRNA 589

The appropriate tRNAs are delivered to the ribosome during elongation 590

The peptidyl transferase active site catalyzes peptide bond formation 593

Box 22.B Antibiotic Inhibitors of Protein Synthesis 594

Release factors mediate translation termination 595

Translation is efficient *in vivo* 596

22.4 Post-Translational Events 597

Chaperones promote protein folding 597

The signal recognition particle targets some proteins for membrane translocation 599

Many proteins undergo covalent modification 600

GLOSSARY G-1

ODD-NUMBERED SOLUTIONS S-1

INDEX I-1

Several years ago, we set out to write a short biochemistry textbook that combined succinct, clear chapters with extensive problem sets. We believed that students would benefit from a modern approach involving broad but not overwhelming coverage of biochemical facts, focusing on the chemistry behind biology, and providing students with practical knowledge and problem-solving opportunities. Our experience in the classroom continues to remind us that effective learning also requires students to become as fully engaged with the material as possible. To that end, we have embraced a strategy of posing questions and suggesting study activities throughout each chapter, so that students will not simply read and memorize but will explore and discover on their own—a truer reflection of how biochemists approach their work in the laboratory or clinic.

As always, we view our textbook as a guidebook for students, providing a solid foundation in biochemistry, presenting complete, up-to-date information, and showing the practical aspects of biochemistry as it applies to human health, nutrition, and disease. We hope that students will develop a sense of familiarity and comfort as they encounter new material, explore it, and test their understanding through problem solving.

New to This Edition

Many details in the text and illustration program have been updated, with virtually no section left untouched. Some significant changes are worth mentioning: Chapter 3 includes an updated discussion of genomics and a completely new presentation of DNA sequencing technologies and the use of CRISPR-Cas to edit genes. Other new items include a discussion of archaeal lipids, details on the GLUT membrane transport protein, a box on exosomes, new illustrations of respiratory cilia and bacterial peptidoglycan, new molecular graphics of mitochondrial respiratory complexes, an updated presentation of the ribonucleotide reductase mechanism, and more information on the microbiome, cancer, and obesity. Descriptions of DNA replication and transcription have been extensively modified, with numerous new diagrams to present a more realistic picture of these processes. The histone code and readers, writers, and erasers are explained. New details on RNA splicing and protein translocation round out the revised text.

Eight health-related topics that were previously confined to short boxes have been updated and expanded to **Clinical Connection** sections to give them the appropriate attention: 2.5 Acid–Base Balance in Humans, 4.5 Protein Misfolding and Disease, 5.2 Hemoglobin Variants, 6.5 Blood Coagulation, 7.4 Drug Development, 13.5 Disorders of Carbohydrate Metabolism, 19.4 Cancer Metabolism, and 20.4 Cancer as a Genetic Disease.

With the same goal of making it easy for students to navigate complex topics, some material within sections has been reorganized, and several new sections of text now focus on key content areas: 14.3 Thermodynamics of the Citric Acid Cycle, 17.1 Lipid Transport, 18.5 Nucleotide Metabolism, 20.5 DNA Packaging, 21.1 Initiating Transcription, and 22.1 tRNA and the Genetic Code.

Above all, the focus of the fourth edition is ease of use, particularly for students and instructors taking advantage of new ways to assess student understanding. New **Learning Objectives** at the start of every section are based on verbs, giving students an indication of what they need to be able to *do*, not just *know*. **Before You Go On** study hints at end of each section reinforce the activities that support learning. The **end-of-chapter problem sets** have been refreshed, with a total of 1,624 problems (averaging 74 per chapter, an increase of 18% over the previous edition). Problems are grouped by section and offered in pairs, with the answers to odd-numbered problems provided in an appendix.

Traditional Pedagogical Strengths

- “Do You Remember?” **review questions** start each chapter, to help students tie new topics to what they have already studied.
- **Figure Questions** that accompany key tables and figures prompt students to inspect information more closely.
- **Key sentences** summarizing main points are printed in italics to assist with quick visual identification.
- **Tools and Techniques Sections** appear at the end of Chapters 2, 3, and 4, to showcase practical aspects of biochemistry and provide an overview of experimental techniques that students will encounter in their reading or laboratory experience.
- **Metabolism overview figures** introduced in Chapter 12 and revisited in subsequent chapters help students place individual metabolic pathways into a broader context.
- Chapter **Summaries**, organized by major section headings, highlight important concepts to guide students to the most important points within each section.
- **Key terms** are in boldface. Their definitions are also included in the **Glossary**.
- An annotated list of **Selected Readings** for each chapter includes recent short papers, mostly reviews, that students are likely to find useful as sources of additional information.

Organization

We have chosen to focus on aspects of biochemistry that tend to receive little coverage in other courses or present a challenge to many students. Thus, in this textbook, we devote proportionately more space to topics such as acid–base chemistry, enzyme mechanisms, enzyme kinetics, oxidation–reduction reactions, oxidative phosphorylation, photosynthesis, and the enzymology of DNA replication, transcription, and translation. At the same time, we appreciate that students can become overwhelmed with information. To counteract this tendency, we have intentionally left out some details, particularly in the chapters on metabolic pathways, in order to emphasize some general themes, such as the stepwise nature of pathways, their evolution, and their regulation.

The 22 chapters of *Essential Biochemistry* are relatively short, so that students can spend less time reading and more time extending their learning through active problem-solving. Most of the problems require some analysis rather than simple recall of facts. Many problems based on research data provide students a glimpse of the “real world” of science and medicine.

Although each chapter of *Essential Biochemistry, Fourth Edition* is designed to be self-contained so that it can be covered at any point in the syllabus, the 22 chapters are organized into four parts that span the major themes of biochemistry, including some chemistry background, structure–function relationships, the transformation of matter and energy, and how genetic information is stored and made accessible.

Part 1 of the textbook includes an introductory chapter and a chapter on water. Students with extensive exposure to chemistry can use this material for review. For students with little previous experience, these two chapters provide the chemistry background they will need to appreciate the molecular structures and metabolic reactions they will encounter later.

Part 2 begins with a chapter on the genetic basis of macromolecular structure and function (Chapter 3, From Genes to Proteins). This is followed by chapters on protein structure (Chapter 4) and protein function (Chapter 5), with coverage of myoglobin and hemoglobin, and cytoskeletal and motor proteins. An explanation of how enzymes work (Chapter 6) precedes a discussion of enzyme kinetics (Chapter 7), an arrangement that allows students to grasp the importance of enzymes and to focus on the chemistry of enzyme-catalyzed reactions before delving into the more quantitative aspects of enzyme kinetics. A chapter on lipid chemistry (Chapter 8, Lipids and Membranes) is followed by two chapters that discuss critical biological functions of membranes (Chapter 9, Membrane Transport, and Chapter 10, Signaling). The section ends with a chapter on carbohydrate chemistry (Chapter 11), completing the survey of molecular structure and function.

Part 3 begins with an introduction to metabolism that provides an overview of fuel acquisition, storage, and mobilization as well as the thermodynamics of metabolic reactions (Chapter 12). This is followed, in traditional fashion, by chapters on glucose and glycogen metabolism (Chapter 13); the citric acid cycle (Chapter 14); electron transport and oxidative

phosphorylation (Chapter 15); the light and dark reactions of photosynthesis (Chapter 16); lipid catabolism and biosynthesis (Chapter 17); and pathways involving nitrogen-containing compounds, including the synthesis and degradation of amino acids, the synthesis and degradation of nucleotides, and the nitrogen cycle (Chapter 18). The final chapter of Part 2 explores the integration of mammalian metabolism, with extensive discussions of hormonal control of metabolic pathways, disorders of fuel metabolism, and cancer (Chapter 19).

Part 4, the management of genetic information, includes three chapters, covering DNA replication and repair (Chapter 20), transcription (Chapter 21), and protein synthesis (Chapter 22). Because these topics are typically also covered in other courses, Chapters 20–22 emphasize the relevant biochemical details, such as topoisomerase action, nucleosome structure, mechanisms of polymerases and other enzymes, structures of accessory proteins, proofreading strategies, and chaperone-assisted protein folding.

The WileyPLUS Advantage

WileyPLUS is a research-based online environment for effective teaching and learning. WileyPLUS is packed with interactive study tools and resources, including the complete online textbook.

NEW Ten Guided Tours cover the major topics of the course. These multi-part tutorials explain biochemistry in time and space. Interactive questions at the end of each tour reinforce learning.

NEW Assignable End-of-Chapter Questions, over 20 per chapter, can be assigned to students through WileyPLUS.

NEW Twenty-four Sample Calculation Videos walk students through each step of the sample calculations.

NEW Brief Bioinformatics Exercises crafted by Rakesh Mogul at California State Polytechnic University, Pomona, provide detailed instructions for novices to access and use bioinformatics databases and software tools. Each of the 57 exercises includes multiple-choice questions to help students gauge their success in learning from these resources.

NEW Do You Remember Practice Quizzes help students prepare for new material by reinforcing relevant topics from previous chapters.

NEW Concept Check Questions for each section allow students to test their knowledge.

NEW Discussion Questions are thought-provoking questions that serve as a point of departure for student discussion and engagement with content.

NEW Twenty-three Animated Process Diagrams bring multi-step figures to life.

NEW ORION Biology and Chemistry Refresher offers ORION’s diagnostics and adaptive practice for foundational topics, to support Biochemistry students who come to the course with differing levels of background knowledge.

UPDATED Bioinformatics Projects, written by Paul Craig at Rochester Institute of Technology, provide guidance

for 12 extended explorations of online databases, with questions, many open-ended, for students to learn on their own.

Additional Instructor Resources in WileyPLUS

- PowerPoint Art Slides.
- Exercise Questions with immediate descriptive feedback updated for the fourth edition by Rachel Milner, University of Alberta; Adrienne Wright, University of Alberta; and Mary Peek, Georgia Institute of Technology.
- Test Bank Questions by Scott Lefler, Arizona State University.
- Practice and Pre-Lecture Questions by Steven Vik, Southern Methodist University, and Mary Peek, Georgia Institute of Technology.
- PowerPoint Lecture Slides with Answer Slides by Mary Peek, Georgia Institute of Technology.
- Personal Response System (“Clicker”) Questions by Gail Grabner, University of Texas at Austin, and Mary Peek, Georgia Institute of Technology.

Acknowledgments

We would like to thank everyone who helped develop *Essential Biochemistry, Fourth Edition*, including Biochemistry Editor Joan Kalkut, Product Designer Sean Hickey, Associate Development Editor Laura Rama, Senior Production Editor Elizabeth Swain, Senior Designer Tom Nery, and Senior Photo Editor Billy Ray.

We also thank all the reviewers who provided essential feedback on manuscript and media, corrected errors, and made valuable suggestions for improvements that have been so important in the writing and development of *Essential Biochemistry, Fourth Edition*.

Fourth Edition Reviews

Arkansas

Anne Grippo, *Arkansas State University*

California

Rakesh Mogul, *California State Polytechnic University, Pomona*
Brian Sato, *University of California, Irvine*

Colorado

Andrew Bonham, *Metropolitan State University of Denver*

Hawaii

Jon-Paul Bingham, *University of Hawaii-Manoa, College of Tropical Agriculture and Human Resources*

Florida

David Brown, *Florida Gulf Coast University*

Georgia

Chavonda Mills, *Georgia College*
Rich Singiser, *Clayton State University*

Illinois

Jon Friesen, *Illinois State University*
Stanley Lo, *Northwestern University*
Kristi McQuade, *Bradley University*

Indiana

Mohammad Qasim, *Indiana University Purdue, Fort Wayne*

Kansas

Peter Gegenheimer, *The University of Kansas*

Louisiana

Jeffrey Temple, *Southeastern Louisiana University*

Michigan

Kathleen Foley, *Michigan State University*
Deborah Heyl-Clegg, *Eastern Michigan University*

Mississippi

Arthur Chu, *Delta State University*

Missouri

Nuran Ercal, *Missouri University of Science and Technology*

Nebraska

Jodi Kreiling, *University of Nebraska, Omaha*

New Jersey

Bryan Speigelberg, *Rider University*
Yufeng Wei, *Seton Hall University*

New York

Sergio Abreu, *Fordham University*
Susan Rotenberg, *Queens College of CUNY*

Oregon

Jeannine Chan, *Pacific University*

Pennsylvania

Mahrukh Azam, *West Chester University of Pennsylvania*
Robin Ertl, *Marywood University*
Amy Hark, *Muhlenberg College*
Sandra Turchi-Dooley, *Millersville University*
Laura Zapanta, *University of Pittsburgh*

Rhode Island

Erica Oduaran, *Roger Williams University*

South Carolina

Weiguo Cao, *Clemson University*
Kerry Smith, *Clemson University*

Tennessee

Meagan Mann, *Austin Peay State University*

Texas

Johannes Bauer, *Southern Methodist University*

Utah

Craig Thulin, *Utah Valley University*

Previous Edition Reviews

Arkansas

Anne Grippo, *Arkansas State University*

Arizona

Allan Bieber, *Arizona State University*
Matthew Gage, *Northern Arizona University*
Scott Lefler, *Arizona State University, Tempe*
Allan Scruggs, *Arizona State University, Tempe*
Richard Posner, *Northern Arizona State University*

California

Elaine Carter, *Los Angeles City College*
Daniel Edwards, *California State University, Chico*

Gregg Jongeward, *University of the Pacific*
 Pavan Kadandale, *University of California, Irvine*
 Paul Larsen, *University of California, Riverside*
 Rakesh Mogul, *California State Polytechnic University, Pomona*

Colorado

Paul Azari, *Colorado State University*
 Andrew Bonham, *Metropolitan State University of Denver*
 Johannes Rudolph, *University of Colorado*

Connecticut

Matthew Fisher, *Saint Vincent's College*

Florida

David Brown, *Florida Gulf Coast University*

Georgia

Chavonda Mills, *Georgia College*
 Mary E. Peek, *Georgia Tech University*
 Rich Singiser, *Clayton State University*

Hawaii

Jon-Paul Bingham, *University of Hawaii-Manoa, College
 of Tropical Agriculture and Human Resources*

Illinois

Lisa Wen, *Western Illinois University*
 Gary Roby, *College of DuPage*
 Jon Friesen, *Illinois State University*
 Constance Jeffrey, *University of Illinois, Chicago*

Indiana

Brenda Blacklock, *Indiana University-Purdue University
 Indianapolis*
 Todd Hrubey, *Butler University*
 Christine Hrycyna, *Purdue University*
 Mohammad Qasim, *Indiana University-Purdue University*

Iowa

Don Heck, *Iowa State University*

Kansas

Peter Gegenheimer, *The University of Kansas*
 Ramaswamy Krishnamoorthi, *Kansas State University*

Louisiana

James Moroney, *Louisiana State University*
 Jeffrey Temple, *Southeastern Louisiana University*

Maine

Robert Gundersen, *University of Maine, Orono*

Massachusetts

Jeffrey Nichols, *Worcester State University*

Michigan

Marilee Benore, *University of Michigan*
 Kim Colvert, *Ferris State University*
 Kathleen Foley, *Michigan State University*
 Deborah Heyl-Clegg, *Eastern Michigan University*
 Melvin Schindler, *Michigan State University*
 Jon Stoltzfus, *Michigan State University*
 Mark Thomson, *Ferris State University*

Minnesota

Sandra Olmsted, *Augsburg College*
 Tammy Stobb, *St. Cloud State University*

Mississippi

Jeffrey Evans, *University of Southern Mississippi*
 James R. Heitz, *Mississippi State University*

Missouri

Karen Bame, *University of Missouri, Kansas City*

Nuran Ercal, *Missouri University of Science & Technology*

Nebraska

Jodi Kreiling, *University of Nebraska, Omaha*
 Madhavan Soundararajan, *University of Nebraska*
 Russell Rasmussen, *Wayne State College*

New Jersey

Yufeng Wei, *Seton Hall University*
 Bryan Spiegelberg, *Rider University*

New Mexico

Beulah Woodfin, *University of New Mexico*

New York

Wendy Pogozeleski, *SUNY Geneseo*
 Susan Rotenberg, *Queens College of CUNY*

Ohio

Edward Merino, *University of Cincinnati*
 Heeyoung Tai, *Miami University*
 Lai-Chu Wu, *The Ohio State University*

Oklahoma

Charles Crittall, *East Central University*

Oregon

Jeannine Chan, *Pacific University*
 Steven Sylvester, *Oregon State University*

Pennsylvania

Mahrukh Azam, *West Chester University of Pennsylvania*
 Jeffrey Brodsky, *University of Pittsburgh*
 David Edwards, *University of Pittsburgh School of Pharmacy*
 Robin Ertl, *Marywood University*
 Amy Hark, *Muhlenberg College*
 Justin Huffman, *Pennsylvania State University, Altoona*
 Michael Sypes, *Pennsylvania State University*
 Sandra Turchi-Dooley, *Millersville University*

Rhode Island

Lenore Martin, *University of Rhode Island*
 Erica Oduaran, *Roger Williams University*

South Carolina

Carolyn S. Brown, *Clemson University*
 Weiguo Cao, *Clemson University*
 Ramin Radfar, *Wofford College*
 Paul Richardson, *Coastal Carolina University*
 Kerry Smith, *Clemson University*

Tennessee

Meagan Mann, *Austin Peay State University*

Texas

Johannes Bauer, *Southern Methodist University*
 David W. Eldridge, *Baylor University*
 Edward Funkhouser, *Texas A&M University*
 Gail Grabner, *University of Texas, Austin*
 Barrie Kitto, *University of Texas at Austin*
 Marcos Oliveira, *Feik School of Pharmacy, University of the
 Incarnate Word*
 Richard Sheardy, *Texas Woman's University*
 Linette Watkins, *Southwest Texas State University*

Utah

Craig Thulin, *Utah Valley University*

Wisconsin

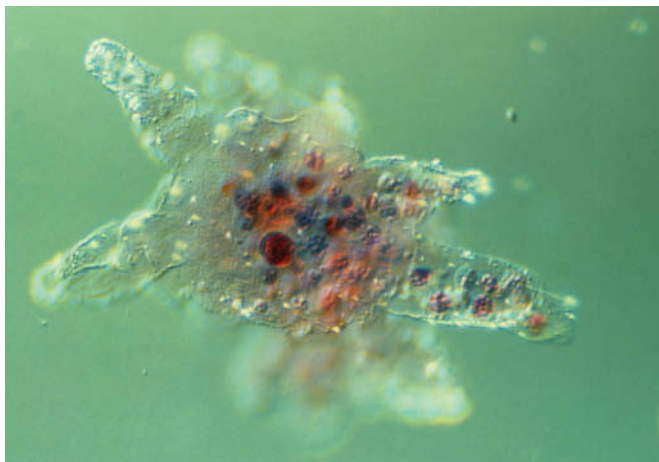
Sandy Grunwald, *University of Wisconsin La Crosse*

Canada

Isabelle Barrette-Ng, *University of Calgary*

The Chemical Basis of Life

Astrid & Hanns-Frieder Michler /
Science Source Images



While no one has yet succeeded in reproducing all of a cell's chemical reactions in a test tube, it is possible to identify and quantify the thousands of molecules present in a cell, such as this amoeba. Understanding the structures and functions of those molecules is key to understanding how cells live, move, grow, and reproduce.

This first chapter offers a preview of the study of biochemistry, broken down into three sections that reflect how topics in this book are organized. First come brief descriptions of the four major types of small biological molecules and their polymeric forms. Next is a summary of the thermodynamics that apply to metabolic reactions. Finally, there is a discussion of the origin of self-replicating life-forms and their evolution into modern cells. These short discussions introduce some of the key players and major themes of biochemistry and provide a foundation for the topics that will be encountered in subsequent chapters.

1.1 What Is Biochemistry?

Biochemistry is the scientific discipline that seeks to explain life at the molecular level. It uses the tools and terminology of chemistry to describe the various attributes of living organisms. Biochemistry offers answers to such fundamental questions as “What are we made of?” and “How do we work?” Biochemistry is also a practical science: It generates powerful techniques that underlie advances in other fields, such as genetics, cell biology, and immunology; it offers insights into the treatment of diseases such as cancer and diabetes; and it improves the efficiency of industries such as wastewater treatment, food production, and drug manufacturing.

Some aspects of biochemistry can be approached by studying individual molecules isolated from cells. A thorough understanding of each molecule's physical structure and chemical reactivity helps lead to an understanding of how molecules cooperate and combine to form larger functional units and, ultimately, the intact organism (Fig. 1.1). But just as a clock completely disassembled no longer resembles a clock, information about a multitude of biological molecules does not necessarily reveal how an organism lives. Biochemists therefore investigate how organisms behave under different conditions or when a particular molecule is modified or absent. In addition, they collect vast amounts of information about molecular structures and functions—information that is stored and analyzed by computer, a field of study known as **bioinformatics**. A biochemist's laboratory is as likely to hold racks of test tubes as flasks of bacteria or computers.

LEARNING OBJECTIVE

Recognize the main themes of biochemistry.

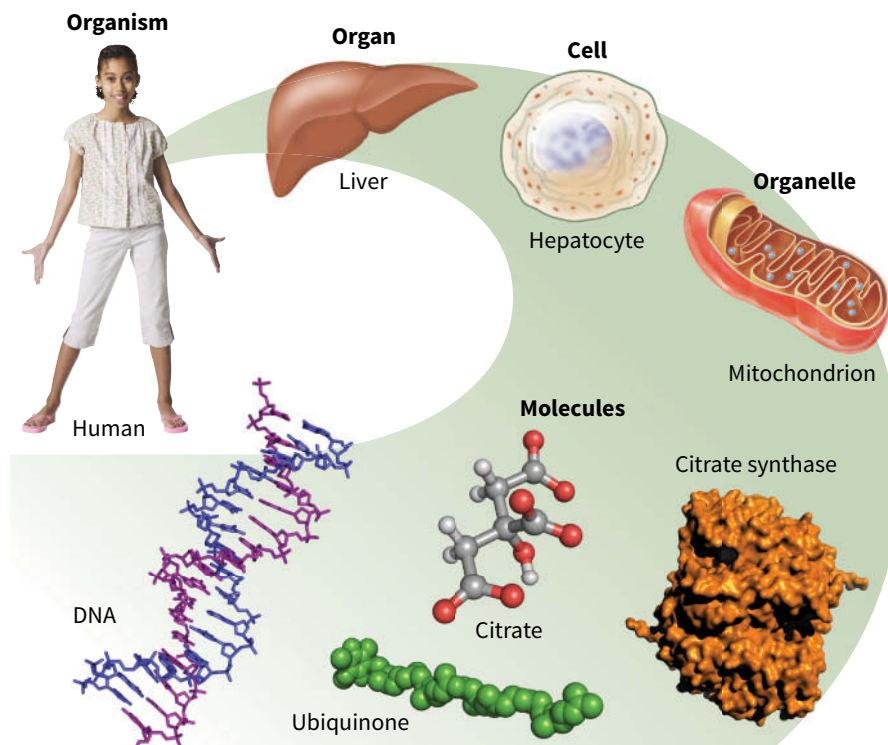


FIGURE 1.1 Levels of organization in a living organism. Biochemistry focuses on the structures and functions of molecules. Interactions between molecules give rise to higher-order structures (for example, organelles), which may themselves be components of larger entities, leading ultimately to the entire organism. [Photodisc/Rubberball/Getty Images]

Chapters 3 through 22 of this book are divided into three groups that roughly correspond to three major themes of biochemistry:

1. *Living organisms are made of macromolecules.* Some molecules are responsible for the physical shapes of cells. Others carry out various activities in the cell. (For convenience, we often use cell interchangeably with organism since the simplest living entity is a single cell.) In all cases, the structure of a molecule is intimately linked to its function. Understanding a molecule's structural characteristics is therefore an important key to understanding its functional significance.
2. *Organisms acquire, transform, store, and use energy.* The ability of a cell to carry out metabolic reactions—to synthesize its constituents and to move, grow, and reproduce—requires the input of energy. A cell must extract this energy from the environment and spend it or store it in a manageable form.
3. *Biological information is transmitted from generation to generation.* Modern human beings look much like they did 100,000 years ago. Certain bacteria have persisted for millions, if not billions, of years. In all organisms, the genetic information that specifies a cell's structural composition and functional capacity must be safely maintained and transmitted each time the cell divides.

Several other themes run throughout biochemistry, and we will highlight these where appropriate.

4. *Cells maintain a state of homeostasis.* Even within its own lifetime, a cell may dramatically alter its shape or metabolic activities, but it does so within certain limits. And in order to remain in a steady, non-equilibrium state—**homeostasis**—the cell must recognize changing internal and external conditions and regulate its activities.
5. *Organisms evolve.* Over long periods of time, the genetic composition of a population of organisms changes. Examining the molecular makeup of living organisms allows biochemists to identify the genetic features that distinguish groups of organisms and to trace their evolutionary history.
6. *Diseases can be explained at the biochemical level.* Identifying the molecular defects that underlie human diseases, or investigating the pathways that allow one organism to infect another, is the first step in diagnosing, treating, preventing, or curing a host of ailments.

1.2 Biological Molecules

Even the simplest organisms contain a staggering number of different molecules, yet this number represents only an infinitesimal portion of all the molecules that are chemically possible. For one thing, *only a small subset of the known elements are found in living systems* (Fig. 1.2). The most abundant of these are C, N, O, and H, followed by Ca, P, K, S, Cl, Na, and Mg. Certain **trace elements** are also present in very small quantities.

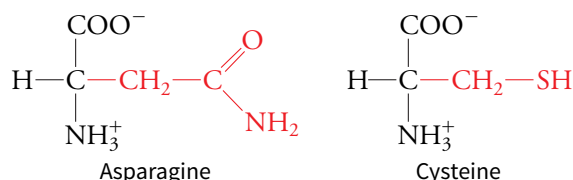
Virtually all the molecules in a living organism contain carbon, so biochemistry can be considered to be a branch of organic chemistry. In addition, biological molecules are constructed from H, N, O, P, and S. Most of these molecules belong to one of a few structural classes, which are described below.

Similarly, *the chemical reactivity of biomolecules is limited relative to the reactivity of all chemical compounds*. A few of the functional groups and intramolecular linkages that are common in biochemistry are listed in Table 1.1. Familiarity with these functional groups is essential for understanding the behavior of the different types of biological molecules we will encounter throughout this book.

Cells contain four major types of biomolecules

Most of the cell's small molecules can be divided into four classes. Although each class contains many members, *they are united under a single structural or functional definition*. Identifying a particular molecule's class may help predict its chemical properties and possibly its role in the cell.

1. Amino Acids Among the simplest compounds are the **amino acids**, so named because they contain an amino group ($-\text{NH}_2$) and a carboxylic acid group ($-\text{COOH}$). Under physiological conditions, these groups are actually ionized to $-\text{NH}_3^+$ and $-\text{COO}^-$. The common amino acid alanine—like other small molecules—can be depicted in different ways, for example, by a structural formula, a ball-and-stick model, or a space-filling model (Fig. 1.3). Other amino acids resemble alanine in basic structure, but instead of a methyl group ($-\text{CH}_3$), they have another group—called a side chain or R group—that may also contain N, O, or S; for example,



1 H																
		5 B	6 C	7 N	8 O	9 F										
11 Na	12 Mg	13 Al	14 Si	15 P	16 S	17 Cl										
19 K	20 Ca	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	33 As	34 Se	35 Br				
			42 Mo						48 Cd				53 I			
			74 W													

FIGURE 1.2 Elements found in biological systems. The most abundant elements are most darkly shaded; trace elements are most lightly shaded. Not every organism contains every trace element. Biological molecules primarily contain H, C, N, O, P, and S.

LEARNING OBJECTIVES

Identify the major classes of biological molecules.

- List the elements found in biological molecules.
- Draw and name the common functional groups in biological molecules.
- Draw and name the common linkages in biological molecules.
- Distinguish the main structural features of carbohydrates, amino acids, nucleotides, and lipids.
- Identify the monomers and linkages in polysaccharides, polypeptides, and nucleic acids.
- Summarize the biological functions of the major classes of biological molecules.

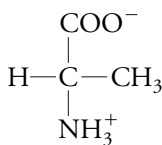
TABLE 1.1 Common Functional Groups and Linkages in Biochemistry

COMPOUND NAME	STRUCTURE ^a	FUNCTIONAL GROUP
Amine ^b	$\left\{ \begin{array}{l} \text{RNH}_2 \text{ or } \text{RNH}_3^+ \\ \text{R}_2\text{NH} \text{ or } \text{R}_2\text{NH}_2^+ \\ \text{R}_3\text{N} \text{ or } \text{R}_3\text{NH}^+ \end{array} \right.$	$-\text{N} \begin{array}{l} \diagdown \\ \diagup \end{array} \text{ or } \begin{array}{c} \\ -\text{N}^+- \\ \end{array} \text{ (amino group)}$
Alcohol	ROH	—OH (hydroxyl group)
Thiol	RSH	—SH (sulfhydryl group)
Ether	ROR	—O— (ether linkage)
Aldehyde	$\begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{H} \end{array}$	$\begin{array}{c} \text{O} \\ \\ -\text{C}- \end{array} \text{ (carbonyl group), } \begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}- \end{array} \text{ (acyl group)}$
Ketone	$\begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{R} \end{array}$	$\begin{array}{c} \text{O} \\ \\ -\text{C}- \end{array} \text{ (carbonyl group), } \begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}- \end{array} \text{ (acyl group)}$
Carboxylic acid ^b (Carboxylate)	$\left\{ \begin{array}{l} \begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{OH} \end{array} \text{ or } \\ \begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{O}^- \end{array} \end{array} \right.$	$\left\{ \begin{array}{l} \begin{array}{c} \text{O} \\ \\ -\text{C}-\text{OH} \end{array} \text{ (carboxyl group) or } \\ \begin{array}{c} \text{O} \\ \\ -\text{C}-\text{O}^- \end{array} \text{ (carboxylate group)} \end{array} \right.$
Ester	$\begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{OR} \end{array}$	$\begin{array}{c} \text{O} \\ \\ -\text{C}-\text{O}- \end{array} \text{ (ester linkage)}$
Amide	$\left\{ \begin{array}{l} \begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{NH}_2 \\ \text{O} \\ \\ \text{R}-\text{C}-\text{NHR} \\ \text{O} \\ \\ \text{R}-\text{C}-\text{NR}_2 \end{array} \end{array} \right.$	$\begin{array}{c} \text{O} \\ \\ -\text{C}-\text{N} \begin{array}{l} \diagdown \\ \diagup \end{array} \end{array} \text{ (amido group)}$
Imine ^b	$\begin{array}{l} \text{R}=\text{NH} \text{ or } \text{R}=\text{NH}_2^+ \\ \text{R}=\text{NR} \text{ or } \text{R}=\text{NHR}^+ \end{array}$	$\begin{array}{l} \diagdown \text{C}=\text{N}- \text{ or } \diagdown \text{C}=\text{N}^+ \begin{array}{l} \text{H} \\ \diagup \end{array} \end{array} \text{ (imino group)}$
Phosphoric acid ester ^b	$\left\{ \begin{array}{l} \begin{array}{c} \text{O} \\ \\ \text{R}-\text{O}-\text{P}-\text{OH} \\ \\ \text{OH} \end{array} \text{ or } \\ \begin{array}{c} \text{O} \\ \\ \text{R}-\text{O}-\text{P}-\text{O}^- \\ \\ \text{O}^- \end{array} \end{array} \right.$	$\begin{array}{l} \begin{array}{c} \text{O} \\ \\ -\text{O}-\text{P}-\text{O}- \\ \\ \text{OH} \end{array} \text{ (phosphoester linkage)} \\ \begin{array}{c} \text{O} \\ \\ -\text{P}-\text{OH} \\ \\ \text{OH} \end{array} \text{ or } \begin{array}{c} \text{O} \\ \\ -\text{P}-\text{O}^- \\ \\ \text{O}^- \end{array} \text{ (phosphoryl group, P}_i\text{)} \end{array}$
Diphosphoric acid ester ^b	$\left\{ \begin{array}{l} \begin{array}{c} \text{O} \quad \text{O} \\ \quad \\ \text{R}-\text{O}-\text{P}-\text{O}-\text{P}-\text{OH} \\ \quad \\ \text{OH} \quad \text{OH} \end{array} \text{ or } \\ \begin{array}{c} \text{O} \quad \text{O} \\ \quad \\ \text{R}-\text{O}-\text{P}-\text{O}-\text{P}-\text{O}^- \\ \quad \\ \text{O}^- \quad \text{O}^- \end{array} \end{array} \right.$	$\begin{array}{l} \begin{array}{c} \text{O} \quad \text{O} \\ \quad \\ -\text{O}-\text{P}-\text{O}-\text{P}-\text{O}- \\ \quad \\ \text{OH} \quad \text{OH} \end{array} \text{ (phosphoanhydride linkage)} \\ \begin{array}{c} \text{O} \quad \text{O} \\ \quad \\ -\text{P}-\text{O}-\text{P}-\text{OH} \\ \quad \\ \text{OH} \quad \text{OH} \end{array} \text{ or } \begin{array}{c} \text{O} \quad \text{O} \\ \quad \\ -\text{P}-\text{O}-\text{P}-\text{O}^- \\ \quad \\ \text{O}^- \quad \text{O}^- \end{array} \end{array} \text{ (diphosphoryl group, pyrophosphoryl group, PP}_i\text{)}$

^aR represents any carbon-containing group. In a molecule with more than one R group, the groups may be the same or different.

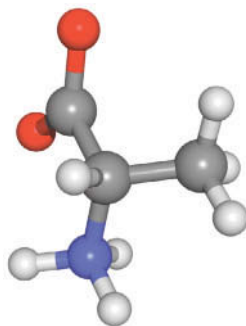
^bUnder physiological conditions, these groups are ionized and hence bear a positive or negative charge.

Q Cover the Structure column and draw the structure for each compound listed on the left. Do the same for each functional group.



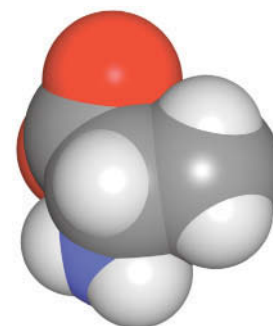
(a)

In a structural formula, some bonds, such as the C—O and N—H bonds, are implied. Around the central carbon, the horizontal bonds extend slightly above the plane of the page, and the vertical bonds extend slightly behind it.



(b)

The atoms are color-coded by convention: C gray, N blue, O red, and H white. A ball-and-stick representation reveals the identities of the atoms and their positions in space.



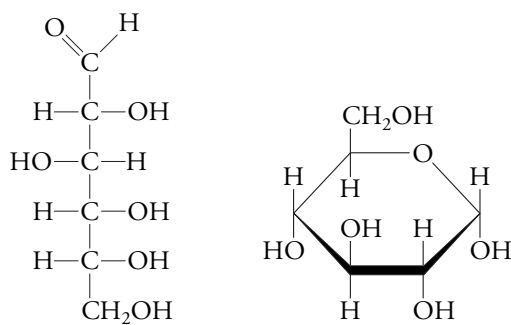
(c)

In a space-filling model, each atom is presented as a sphere whose radius (the van der Waals radius) corresponds to the distance of closest approach by another atom.

FIGURE 1.3 Representations of alanine. The structural formula (a) indicates all the atoms and the major bonds. Because the central carbon atom has tetrahedral geometry, its four bonds do not lie flat in the plane of the paper. This tetrahedral arrangement is more

accurately depicted in the ball-and-stick model (b), although the relative sizes and electrical charges of atoms are not shown. A space-filling model (c) best represents the actual shape of the molecule but may obscure some of its atoms and linkages.

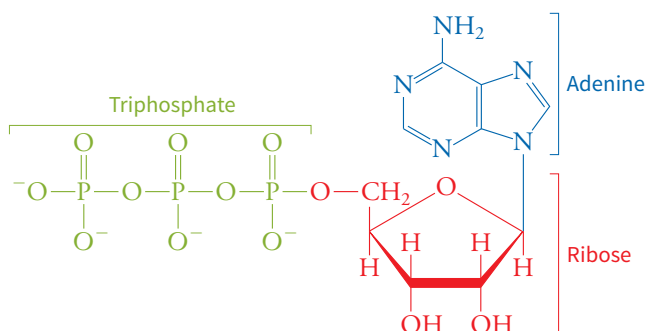
2. Carbohydrates Simple **carbohydrates** (also called **monosaccharides** or just sugars) have the formula $(\text{CH}_2\text{O})_n$, where n is ≥ 3 . Glucose, a monosaccharide with six carbon atoms, has the formula $\text{C}_6\text{H}_{12}\text{O}_6$. It is sometimes convenient to draw it as a ladder-like chain (*left*); however, glucose forms a cyclic structure in solution (*right*):



Glucose

In the representation of the cyclic structure, the darker bonds project in front of the page and the lighter bonds project behind it. In many monosaccharides, one or more hydroxyl groups are replaced by other groups, but the ring structure and multiple —OH groups of these molecules allow them to be easily recognized as carbohydrates.

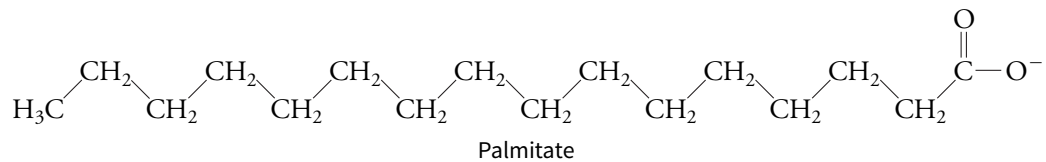
3. Nucleotides A five-carbon sugar, a nitrogen-containing ring, and one or more phosphate groups are the components of **nucleotides**. For example, adenosine triphosphate (ATP) contains the nitrogenous group adenine linked to the monosaccharide ribose, to which a triphosphate group is also attached:



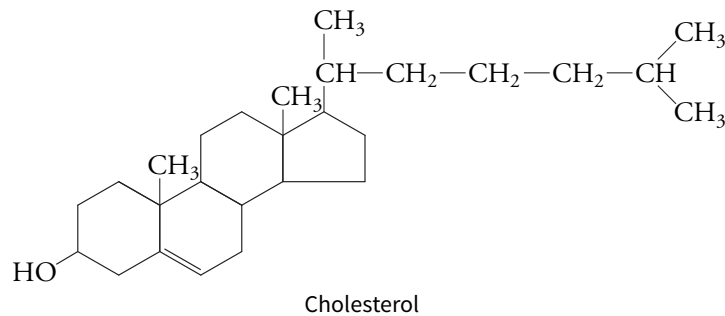
Adenosine triphosphate (ATP)

The most common nucleotides are mono-, di-, and triphosphates containing the nitrogenous ring compounds (or “bases”) adenine, cytosine, guanine, thymine, or uracil (abbreviated A, C, G, T, and U).

4. Lipids The fourth major group of biomolecules consists of the **lipids**. These compounds cannot be described by a single structural formula since they are a diverse collection of molecules. However, they all tend to be poorly soluble in water because the bulk of their structure is hydrocarbon-like. For example, palmitic acid consists of a highly insoluble chain of 15 carbons attached to a carboxylic acid group, which is ionized under physiological conditions. The anionic lipid is therefore called palmitate.



Cholesterol, although it differs significantly in structure from palmitate, is also poorly soluble in water because of its hydrocarbon-like composition.

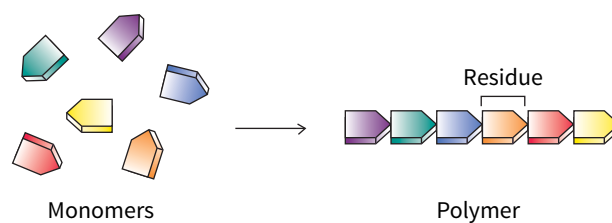


Cells also contain a few other small molecules that cannot be easily classified into the groups above or that are constructed from molecules belonging to more than one group.

There are three major kinds of biological polymers

In addition to small molecules consisting of relatively few atoms, organisms contain macromolecules that may consist of thousands of atoms. Such huge molecules are not synthesized in one piece but are built from smaller units. This is a universal feature of nature: *A few kinds of building blocks can be combined in different ways to produce a wide variety of larger structures.* This is advantageous for a cell, which can get by with a limited array of raw materials. In addition, the very act of chemically linking individual units (**monomers**) into longer strings (**polymers**) is a way of encoding information (the sequence of the monomeric units) in a stable form. Biochemists use certain units of measure to describe both large and small molecules (**Box 1.A**).

Amino acids, monosaccharides, and nucleotides each form polymeric structures with widely varying properties. In most cases, the individual monomers become covalently linked in head-to-tail fashion:



Box 1.A Units Used in Biochemistry

Biochemists follow certain conventions when quantifying objects on a molecular scale. For example, the mass of a molecule can be expressed in atomic mass units; however, the masses of biological molecules—especially very large ones—are typically given without units. Here it is understood that the mass is expressed relative to one-twelfth the mass of an atom of the common carbon isotope ^{12}C (12.011 atomic mass units). Occasionally, units of daltons (D) are used (1 dalton = 1 atomic mass unit), often with the prefix kilo, k (kD). This is useful for macromolecules such as proteins, many of which have masses in the range from 20,000 (20 kD) to over 1,000,000 (1000 kD).

The standard metric prefixes are also necessary for expressing the minute concentrations of biomolecules in living cells. Concentrations are usually given as moles per liter ($\text{mol} \cdot \text{L}^{-1}$ or M), with the appropriate prefix such as m, μ , or n:

mega (M)	10^6	nano (n)	10^{-9}
kilo (k)	10^3	pico (p)	10^{-12}
milli (m)	10^{-3}	femto (f)	10^{-15}
micro (μ)	10^{-6}		

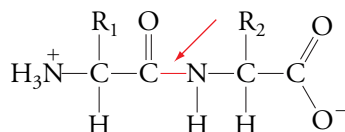
For example, the concentration of the sugar glucose in human blood is about 5 mM, but many intracellular molecules are present at concentrations of μM or less.

Distances are customarily expressed in angstroms, \AA ($1 \text{\AA} = 10^{-10} \text{ m}$) or in nanometers, nm ($1 \text{ nm} = 10^{-9} \text{ m}$). For example, the distance between the centers of carbon atoms in a C—C bond is about 1.5 \AA , and the diameter of a DNA molecule is about 20 \AA .

Q The diameter of a typical spherical bacterial cell is about 1 μm . What is the cell's volume?

The linkage between monomeric units is characteristic of each type of polymer. The monomers are called **residues** after they have been incorporated into the polymer. Strictly speaking, lipids do not form polymers, although they do tend to aggregate to form larger structures such as cell membranes.

1. Proteins Polymers of amino acids are called **polypeptides** or **proteins**. Twenty different amino acids serve as building blocks for proteins, which may contain many hundreds of amino acid residues. The amino acid residues are linked to each other by amide bonds called **peptide bonds**. A peptide bond (*arrow*) links the two residues in a dipeptide (the side chains of the amino acids are represented by R_1 and R_2).



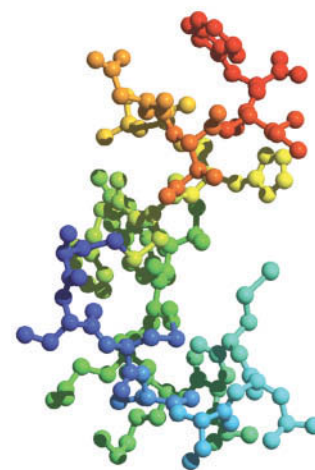
Because the side chains of the 20 amino acids have different sizes, shapes, and chemical properties, the exact **conformation** (three-dimensional shape) of the polypeptide chain depends on its amino acid composition and sequence. For example, the small polypeptide endothelin, with 21 residues, assumes a compact shape in which the polymer bends and folds to accommodate the functional groups of its amino acid residues (**Fig. 1.4**).

The 20 different amino acids can be combined in almost any order and in almost any proportion to produce myriad polypeptides, all of which have unique three-dimensional shapes. This property makes proteins as a class the most structurally variable and therefore the most functionally versatile of all the biopolymers. Accordingly, *proteins perform a wide variety of tasks in the cell, such as mediating chemical reactions and providing structural support.*

2. Nucleic Acids Polymers of nucleotides are termed **polynucleotides** or **nucleic acids**, better known as DNA and RNA. Unlike polypeptides, with 20 different amino acids available for polymerization, each nucleic acid is made from just four different nucleotides. For example, the residues in RNA contain the bases adenine, cytosine, guanine, and uracil, whereas the residues in DNA contain adenine, cytosine, guanine, and thymine. Polymerization involves the phosphate and sugar groups of the nucleotides, which become linked by **phosphodiester bonds**.



(a)



(b)

FIGURE 1.4 Structure of human endothelin. The 21 amino acid residues of this polypeptide, shaded from blue to red, form a compact structure. In (a), each amino acid residue is represented by a sphere. The ball-and-stick model (b) shows all the atoms except hydrogen. [Structure (pdb 1EDN) determined by B. A. Wallace and R. W. Jones.]

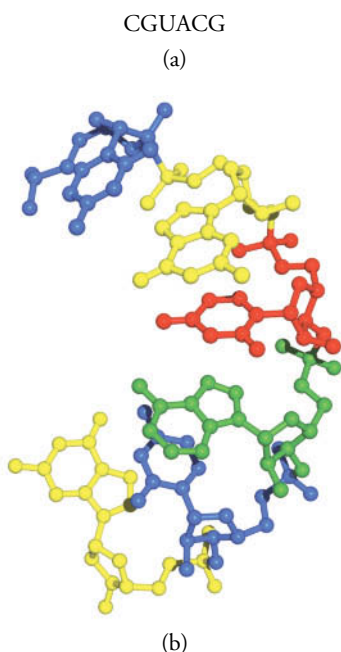
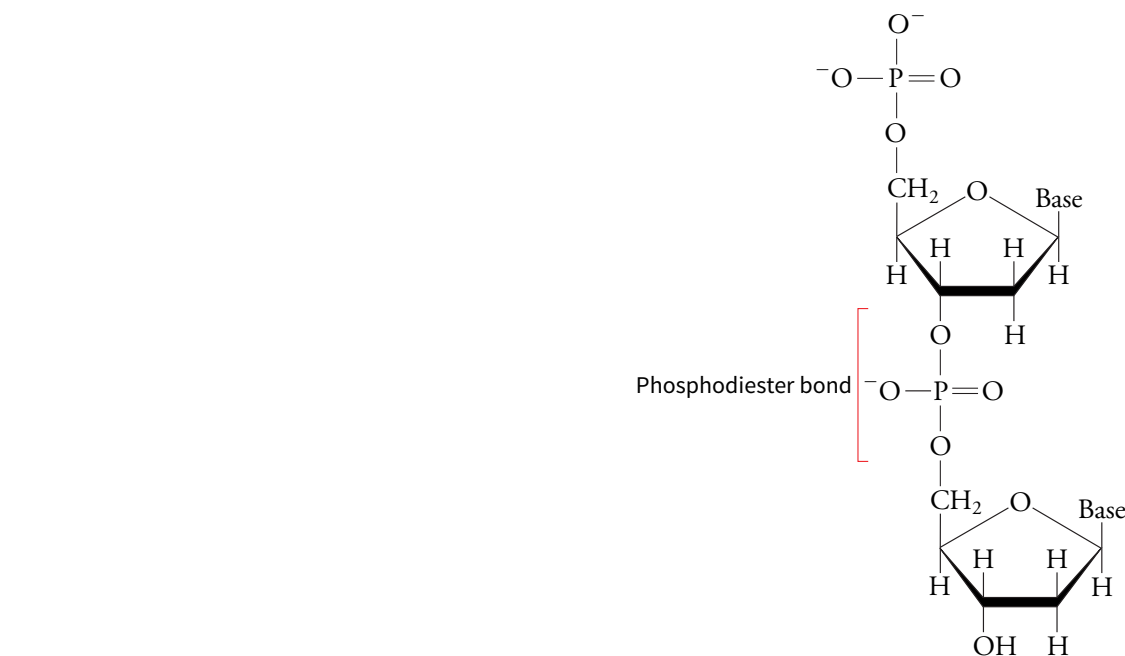
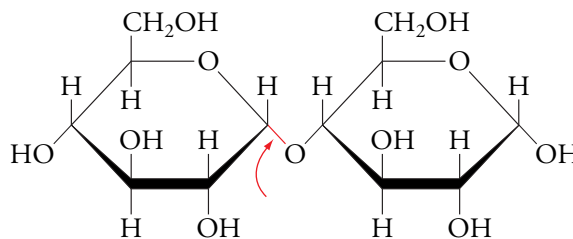


FIGURE 1.5 Structure of a nucleic acid. (a) Sequence of nucleotide residues, using one-letter abbreviations. (b) Ball-and-stick model of the polynucleotide, showing all atoms except hydrogen (this structure is a six-residue segment of RNA). [Structure (pdb ARF0108) determined by R. Biswas, S. N. Mitra, and M. Sundaralingam.]

In part because nucleotides are much less variable in structure and chemistry than amino acids, nucleic acids tend to have more regular structures than proteins. *This is in keeping with their primary role as carriers of genetic information, which is contained in their sequence of nucleotide residues rather than in their three-dimensional shape (Fig. 1.5).* Nevertheless, many nucleic acids do bend and fold into compact globular shapes, as proteins do.

3. Polysaccharides Polysaccharides usually contain only one or a few different types of monosaccharide residues, so even though a cell may synthesize dozens of different kinds of monosaccharides, most of its polysaccharides are homogeneous polymers. This tends to limit their potential for carrying genetic information in the sequence of their residues (as nucleic acids do) or for adopting a large variety of shapes and mediating chemical reactions (as proteins do). On the other hand, *polysaccharides perform essential cell functions by serving as fuel-storage molecules and by providing structural support.* For example, plants link the monosaccharide glucose, which is a fuel for virtually all cells, into the polysaccharide starch for long-term storage. The glucose residues are linked by **glycosidic bonds** (the bond is shown in red in this disaccharide):



Glucose monomers are also the building blocks for cellulose, the extended polymer that helps make plant cell walls rigid (Fig. 1.6). The starch and cellulose polymers differ in the arrangement of the glycosidic bonds between glucose residues.

The brief descriptions of biological polymers given above are generalizations, meant to convey some appreciation for the possible structures and functions of these macromolecules. *Exceptions to the generalizations abound.* For example, some small polysaccharides encode information that allows cells bearing the molecules on their surfaces to recognize each other. Likewise, some nucleic acids perform structural roles, for example, by serving as scaffolding in ribosomes, the small particles where protein synthesis takes place. Under certain conditions,

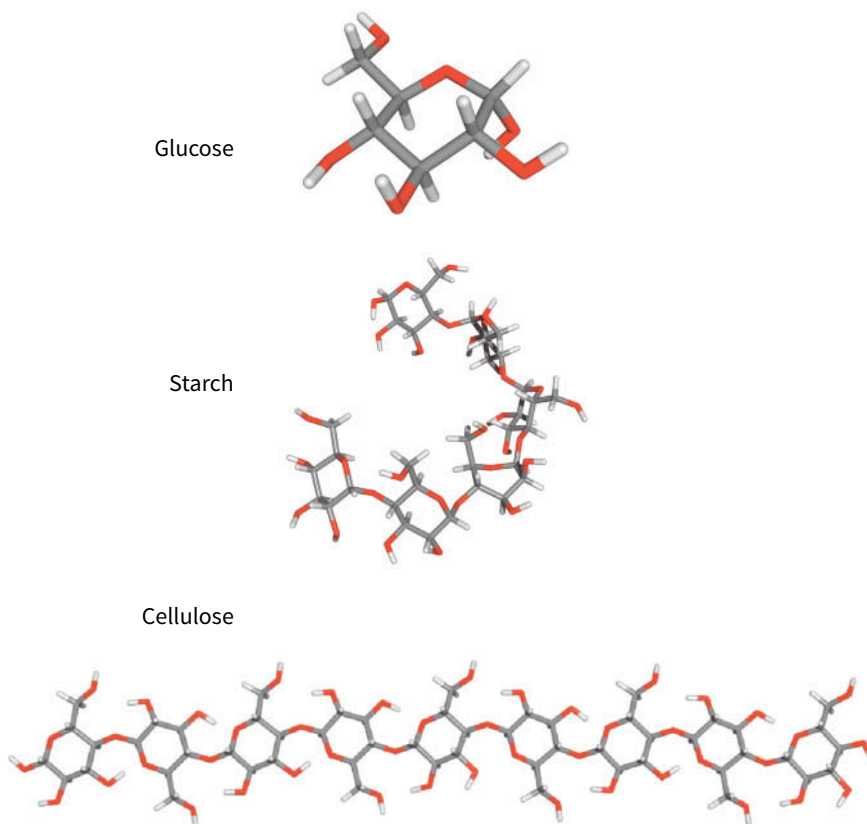


FIGURE 1.6 **Glucose and its polymers.** Both starch and cellulose are polysaccharides containing glucose residues. They differ in the type of chemical linkage between the monosaccharide units. Starch molecules have a loose helical conformation, whereas cellulose molecules are extended and relatively stiff.

proteins are called on as fuel-storage molecules. A summary of the major and minor functions of proteins, polysaccharides, and nucleic acids is presented in [Table 1.2](#).

BEFORE GOING ON

- List the six most abundant elements in biological molecules.
- Name the common functional groups and linkages shown in Table 1.1.
- Give the structural or functional definitions for amino acids, monosaccharides, nucleotides, and lipids.
- Describe the advantage of building a polymer from monomers.
- Give the structural definitions and major functions of proteins, polysaccharides, and nucleic acids.
- Name the linkage in each type of polymer.
- List the major functions of proteins, polysaccharides, and nucleic acids.

TABLE 1.2 **Functions of Biopolymers**

BIOPOLYMER	ENCODE INFORMATION	CARRY OUT METABOLIC REACTIONS	STORE ENERGY	SUPPORT CELLULAR STRUCTURES
Proteins	—	✓	✓	✓
Nucleic acids	✓	✓	—	✓
Polysaccharides	✓	—	✓	✓

✓ major function

✓ minor function

LEARNING OBJECTIVES

Explain how enthalpy, entropy, and free energy apply to biological systems.

- Define enthalpy, entropy, and free energy.
- Write the equation that links changes in enthalpy, entropy, and free energy.
- Relate changes in enthalpy and entropy to the spontaneity of a process.
- Describe the energy flow that makes living systems thermodynamically possible.

1.3

Energy and Metabolism

Assembling small molecules into polymeric macromolecules requires energy. And unless the monomeric units are readily available, a cell must synthesize the monomers, which also requires energy. In fact, *cells require energy for all the functions of living, growing, and reproducing.*

It is useful to describe the energy in biological systems using the terminology of thermodynamics (the study of heat and power). An organism, like any chemical system, is subject to the laws of thermodynamics. According to the first law of thermodynamics, energy cannot be created or destroyed. However, it can be transformed. For example, the energy of a river flowing over a dam can be harnessed as electricity, which can then be used to produce heat or perform mechanical work. Cells can be considered to be very small machines that use chemical energy to drive metabolic reactions, which may also produce heat or carry out mechanical work.

Enthalpy and entropy are components of free energy

The energy relevant to biochemical systems is called the Gibbs free energy (after the scientist who defined it) or just **free energy**. It is abbreviated G and has units of joules per mol ($\text{J} \cdot \text{mol}^{-1}$). Free energy has two components: enthalpy and entropy. **Enthalpy** (abbreviated H , with units of $\text{J} \cdot \text{mol}^{-1}$) *is taken to be equivalent to the heat content of the system.* **Entropy** (abbreviated S , with units of $\text{J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1}$) *is a measure of how the energy is dispersed within that system.* Entropy can therefore be considered to be a measure of the system's disorder or randomness, because the more ways a system's components can be arranged, the more dispersed its energy. For example, consider a pool table at the start of a game when all 15 balls are arranged in one neat triangle (a state of high order or low entropy). After play has begun, the balls are scattered across the table, which is now in a state of disorder and high entropy (Fig. 1.7).

Free energy, enthalpy, and entropy are related by the equation

$$G = H - TS \quad [1.1]$$

where T represents temperature in Kelvin (equivalent to degrees Celsius plus 273). Temperature is a coefficient of the entropy term because entropy varies with temperature; the entropy of a substance increases when it is warmed because more thermal energy has been dispersed

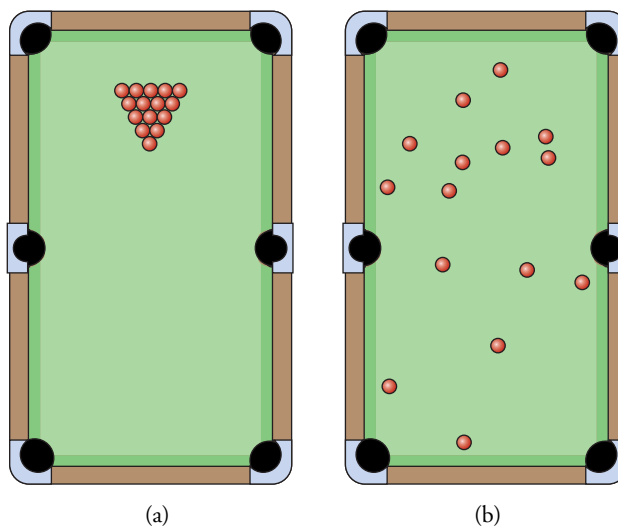


FIGURE 1.7 Illustration of entropy. Entropy is a measure of the dispersal of energy in a system, so it reflects the system's randomness or disorder. (a) Entropy is low when all the balls are arranged in a single area of the pool table. (b) Entropy is high after the balls have been scattered, because there are now a large number of different possible arrangements of the balls on the table.

Q Compare the entropy of a ball of yarn before and after a cat has played with it.

within it. The enthalpy of a chemical system can be measured, although with some difficulty, but it is next to impossible to measure a system's entropy because this would require counting all the possible arrangements of its components or all the ways its energy could be spread out among them. Therefore, it is more practical to deal with *changes* in these quantities (change is indicated by the Greek letter delta, Δ) so that

$$\Delta G = \Delta H - T\Delta S \quad [1.2]$$

Biochemists can measure how the free energy, enthalpy, and entropy of a system differ before and after a chemical reaction. For example, **exothermic reactions** are accompanied by the release of heat to the surroundings ($H_{\text{final}} - H_{\text{initial}} = \Delta H < 0$), whereas **endothermic reactions** absorb heat from the surroundings ($\Delta H > 0$). Similarly, the entropy change, $S_{\text{final}} - S_{\text{initial}} = \Delta S$, can be positive or negative. When ΔH and ΔS for a process are known, Equation 1.2 can be used to calculate the value of ΔG at a given temperature (see Sample Calculation 1.1).

SAMPLE CALCULATION 1.1

Problem

Use the information below to calculate the change in enthalpy and the change in entropy for the reaction $A \rightarrow B$.

	Enthalpy ($\text{kJ} \cdot \text{mol}^{-1}$)	Entropy ($\text{J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1}$)
A	60	22
B	75	97

Solution

$$\begin{aligned} \Delta H &= H_B - H_A \\ &= 75 \text{ kJ} \cdot \text{mol}^{-1} - 60 \text{ kJ} \cdot \text{mol}^{-1} \\ &= 15 \text{ kJ} \cdot \text{mol}^{-1} \\ &= 15,000 \text{ J} \cdot \text{mol}^{-1} \end{aligned}$$

$$\begin{aligned} \Delta S &= S_B - S_A \\ &= 97 \text{ J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1} \\ &\quad - 22 \text{ J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1} \\ &= 75 \text{ J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1} \end{aligned}$$

WileyPLUS

SEE SAMPLE
CALCULATION
VIDEOS

ΔG is less than zero for a spontaneous process

A china cup dropped from a great height will break, but the pieces will never reassemble themselves to restore the cup. The thermodynamic explanation is that the broken pieces have less free energy than the intact cup. *In order for a process to occur, the overall change in free energy (ΔG) must be negative.* For a chemical reaction, this means that the free energy of the products must be less than the free energy of the reactants:

$$\Delta G = G_{\text{products}} - G_{\text{reactants}} < 0 \quad [1.3]$$

When ΔG is less than zero, the reaction is said to be **spontaneous** or **exergonic**. A **nonspontaneous** or **endergonic** reaction has a free energy change greater than zero; in this case, the reverse reaction is spontaneous.

$A \rightarrow B$	$B \rightarrow A$
$\Delta G > 0$	$\Delta G < 0$
Nonspontaneous	Spontaneous

Note that thermodynamic spontaneity does not indicate how *fast* a reaction occurs, only whether it will occur as written. (The rate of a reaction depends on other factors, such as the concentrations of the reacting molecules, the temperature, and the presence of a catalyst.) When a reaction, such as $A \rightarrow B$, is at equilibrium, the rate of the forward reaction is equal to the rate of the reverse reaction, so there is no net change in the system. In this situation, $\Delta G = 0$.

A quick examination of Equation 1.2 reveals that *a reaction that occurs with a decrease in enthalpy and an increase in entropy is spontaneous at all temperatures because ΔG is always less than zero.* These results are consistent with everyday experience. For example, heat moves spontaneously from a hot object to a cool object, and items that are neatly arranged tend to become disordered, never the other way around. (This is a manifestation of the second law of thermodynamics, which states that energy tends to spread out.) Accordingly, reactions in which the enthalpy increases and entropy decreases do not occur. If enthalpy and entropy both increase or both decrease during a reaction, the value of ΔG then depends on the temperature, which governs whether the $T\Delta S$ term of Equation 1.2 is greater than or less than the ΔH term. This means that a large increase in entropy can offset an unfavorable (positive) change in enthalpy. Conversely, the release of a large amount of heat ($\Delta H < 0$) during a reaction can offset an unfavorable decrease in entropy (see Sample Calculation 1.2).

WileyPLUS

SEE SAMPLE
CALCULATION
VIDEOS

SAMPLE CALCULATION 1.2

Problem

Use the information given in Sample Calculation 1.1 to determine whether the reaction $A \rightarrow B$ is spontaneous at 25°C.

Solution

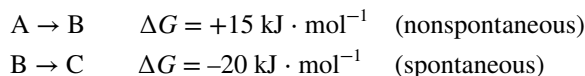
Substitute the values for ΔH and ΔS , calculated in Sample Calculation 1.1, into Equation 1.2. To express the temperature in Kelvin, add 273 to the temperature in degrees Celsius: $273 + 25 = 298$ K.

$$\begin{aligned}\Delta G &= \Delta H - T\Delta S \\ &= 15,000 \text{ J} \cdot \text{mol}^{-1} - 298 \text{ K} (75 \text{ J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1}) \\ &= 15,000 - 22,400 \text{ J} \cdot \text{mol}^{-1} \\ &= -7400 \text{ J} \cdot \text{mol}^{-1} \\ &= -7.4 \text{ kJ} \cdot \text{mol}^{-1}\end{aligned}$$

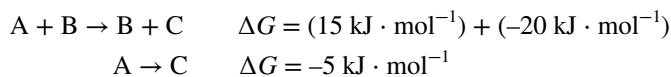
Because ΔG is less than zero, the reaction is spontaneous. Even though the change in enthalpy is unfavorable, the large increase in entropy makes ΔG favorable.

Life is thermodynamically possible

In order to exist, life must be thermodynamically spontaneous. Does this hold at the molecular level? When analyzed in a test tube (*in vitro*, literally “in glass”), many of a cell’s metabolic reactions have free energy changes that are less than zero, but some reactions do not. Nevertheless, the nonspontaneous reactions are able to proceed *in vivo* (in a living organism) because they occur in concert with other reactions that are thermodynamically favorable. Consider two reactions *in vitro*, one nonspontaneous ($\Delta G > 0$) and one spontaneous ($\Delta G < 0$):



When the reactions are combined, their ΔG values are added, so the overall process has a negative change in free energy:



This phenomenon is shown graphically in **Figure 1.8**. In effect, the unfavorable “uphill” reaction $A \rightarrow B$ is pulled along by the more favorable “downhill” reaction $B \rightarrow C$.

Cells couple unfavorable metabolic processes with favorable ones so that the net change in free energy is negative. Note that it is permissible to add ΔG values because the free energy, G ,