GLOBAL EDITION

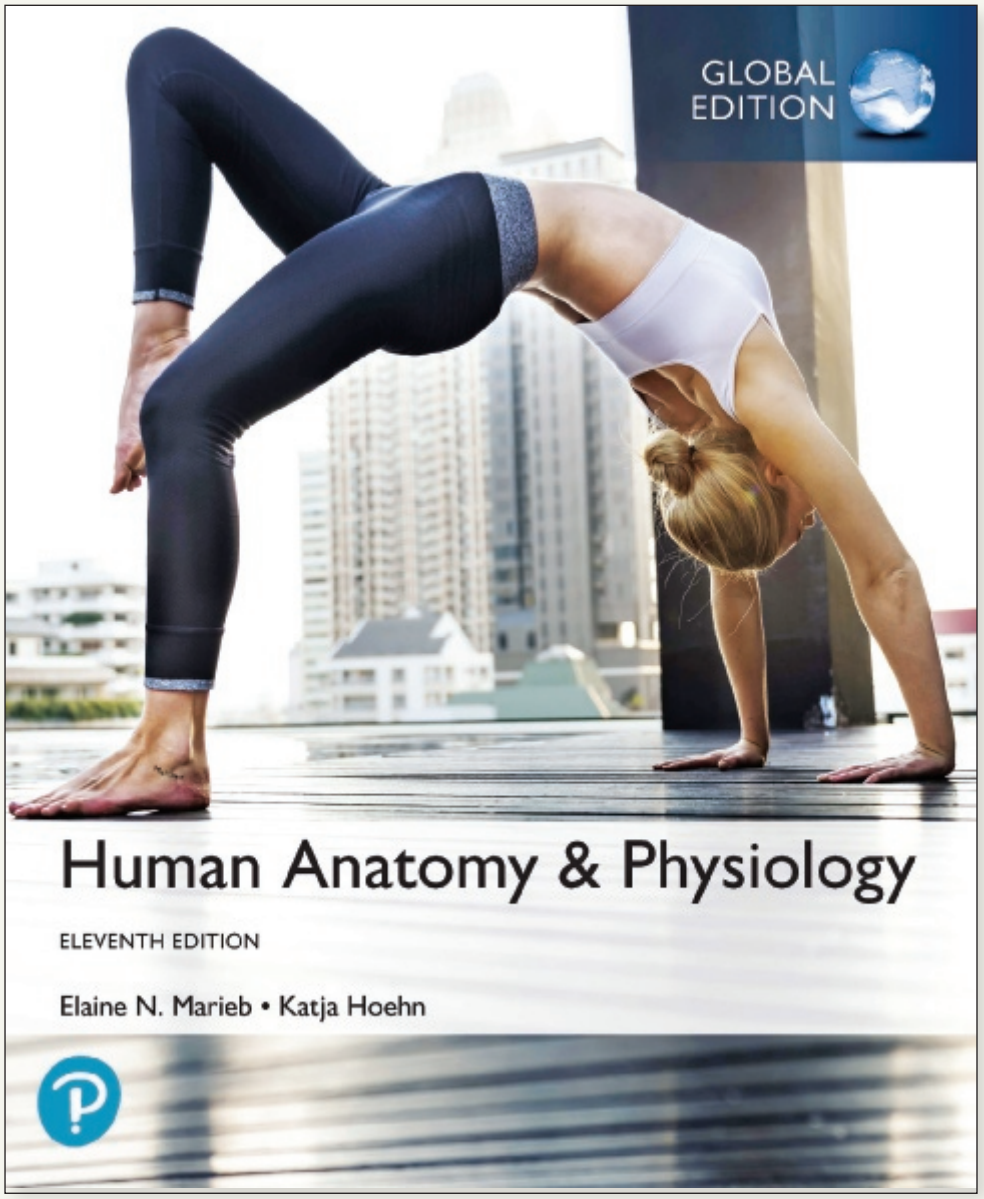
Human Anatomy & Physiology

ELEVENTH EDITION

Elaine N. Marieb • Katja Hoehn

Equipping You with 21st-Century Skills to Succeed in A&P *and Beyond...*

The **11th Edition** of Elaine Marieb and Katja Hoehn's best-selling A&P text and media program motivates and supports both novice learners and expert students, more than ever before. Each carefully-paced chapter guides you in advancing from mastering terminology to applying knowledge in clinical scenarios, to practicing the critical thinking and problem-solving skills that are required for entry to nursing, allied health, and exercise science programs.



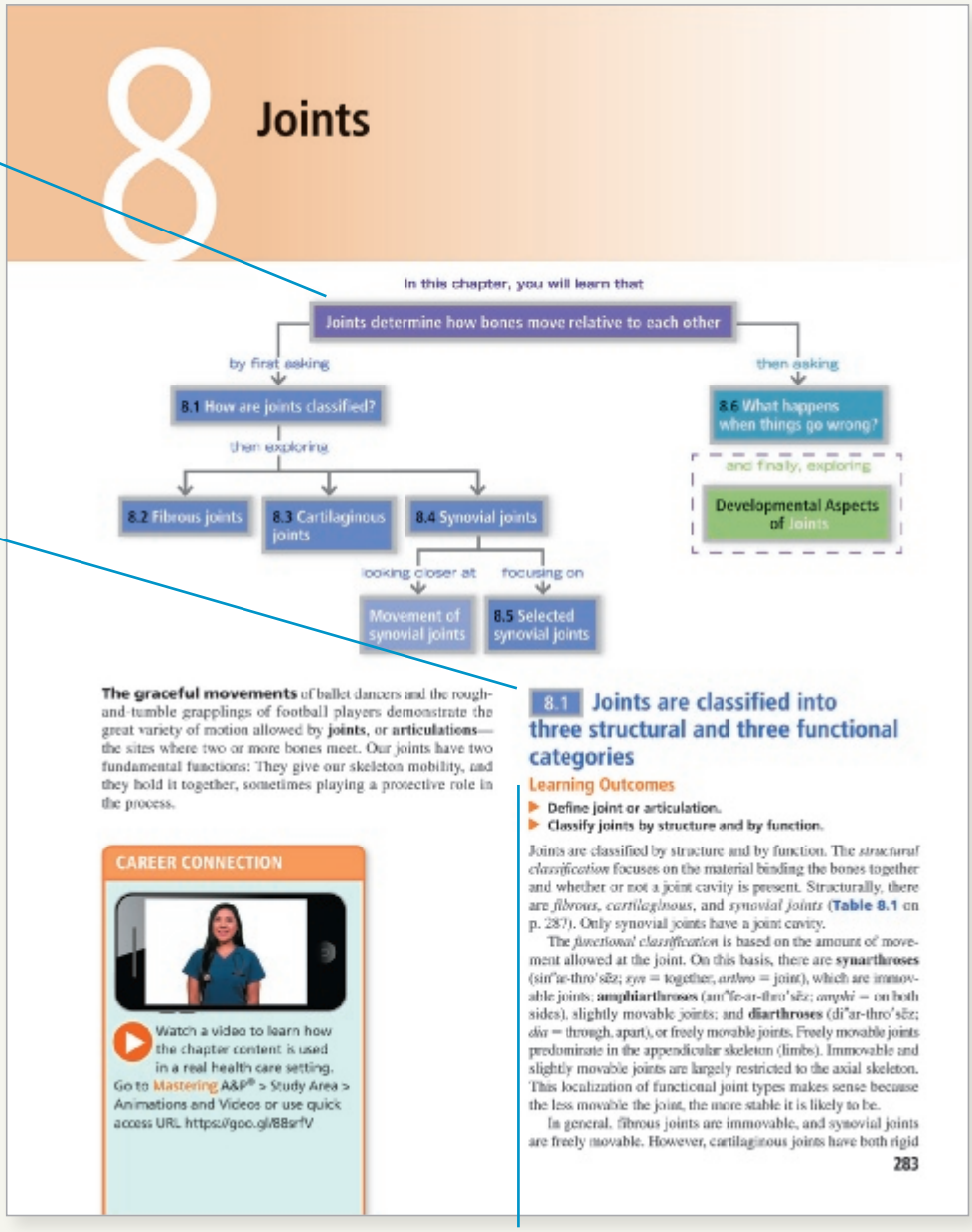
Pearson

Identify "Big Picture" Concepts Before Exploring Details

Before you look up details and information within a chapter, read the **Chapter-Opening Roadmap**, which visually groups and organizes "big picture" concepts and shows how they are related. To focus your studying, review the numbered **Key Concept Headings**, **Learning Outcomes**, and summaries.

UNIQUE! Chapter Roadmaps provide a visual overview of the key concepts in the chapter and show how they relate to each other. Each key concept "brick" in the roadmap corresponds to a numbered section within the chapter.

Each numbered section within the chapter begins with a **Key Concept Heading** that helps you quickly grasp the "big idea" of the discussion that follows.



8 Joints

In this chapter, you will learn that

Joints determine how bones move relative to each other

by first asking

8.1 How are joints classified?

then exploring

8.2 Fibrous joints

8.3 Cartilaginous joints

8.4 Synovial joints

looking closer at

Movement of synovial joints

focusing on

8.5 Selected synovial joints

then asking

8.6 What happens when things go wrong?

and finally, exploring

Developmental Aspects of Joints

The graceful movements of ballet dancers and the rough-and-tumble grapplings of football players demonstrate the great variety of motion allowed by **joints**, or **articulations**—the sites where two or more bones meet. Our joints have two fundamental functions: They give our skeleton mobility, and they hold it together, sometimes playing a protective role in the process.

CAREER CONNECTION

Watch a video to learn how the chapter content is used in a real health care setting. Go to Mastering A&P® > Study Area > Animations and Videos or use quick access URL https://goo.gl/88srfV

8.1 Joints are classified into three structural and three functional categories

Learning Outcomes

- Define joint or articulation.
- Classify joints by structure and by function.

Joints are classified by structure and by function. The *structural classification* focuses on the material binding the bones together and whether or not a joint cavity is present. Structurally, there are *fibrous*, *cartilaginous*, and *synovial joints* (Table 8.1 on p. 287). Only synovial joints have a joint cavity.

The *functional classification* is based on the amount of movement allowed at the joint. On this basis, there are **synarthroses** (sin"ar-thro'sēz; *syn* = together, *arthro* = joint), which are immovable joints; **amphiarthroses** (am"fe-ar-thro'sēz; *amphi* = on both sides), slightly movable joints; and **diarthroses** (di"ar-thro'sēz; *dia* = through, apart), or freely movable joints. Freely movable joints predominate in the appendicular skeleton (limbs). Immovable and slightly movable joints are largely restricted to the axial skeleton. This localization of functional joint types makes sense because the less movable the joint, the more stable it is likely to be.

In general, fibrous joints are immovable, and synovial joints are freely movable. However, cartilaginous joints have both rigid

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UPDATED! Career Connection Videos feature a health care professional who describes how the chapter content relates to their everyday work. You can access all of the Career Connections videos through an open access web page at https://goo.gl/88srfV.

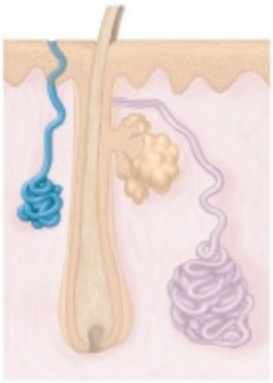
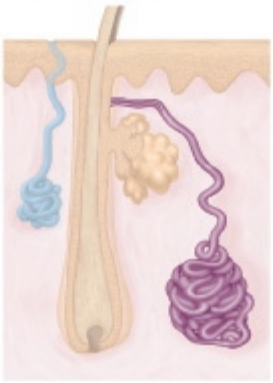
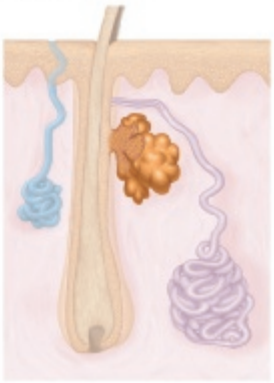
See p. 283

Learning Outcomes are presented at the beginning of each chapter section to give you a preview of essential information to study.

Pace Yourself:
Learn & Review the Basics

EXPANDED! Summary Tables present key information and serve as "one-stop shopping" study tools. 13 new Summary Tables have been added to this edition.

Table 5.1 Summary of Cutaneous Glands

	ECCRINE SWEAT GLANDS	APOCRINE SWEAT GLANDS	SEBACEOUS GLANDS
			
Functions	• Temperature control • Some antibacterial properties	May act as sexual scent glands	• Lubricate skin and hair • Help prevent water loss • Antibacterial properties
Type of Secretion	Hypotonic filtrate of blood plasma	Filtrate of blood plasma with added proteins and fatty substances	Sebum (an oily secretion)
Method of Secretion	Merocrine (exocytosis)	Merocrine (exocytosis)	Holocrine
Secretion Exits Duct At	Skin surface	Usually upper part of hair follicle; rarely, skin surface	Usually upper part of hair follicle; sometimes, skin surface
Body Location	Everywhere, but especially palms, soles, forehead	Mostly axillary and anogenital regions	Everywhere *except* palms and soles

See p. 194

Sebaceous Glands

The **sebaceous glands** (se-ba′shus; "greasy"), or *oil glands* (Figure 5.9a), are simple branched alveolar glands that are found all over the body except in the thick skin of the palms and soles. They are small on the body trunk and limbs, but quite large on the face, neck, and upper chest. These glands secrete an oily substance called **sebum** (se′bum). The central cells of the alveoli accumulate oily lipids until they become so engorged that they burst, so functionally these glands are *holocrine glands* (◀ p. 158). The accumulated lipids and cell fragments constitute sebum.

NEW! Text Recall icons guide you to review specific pages where a concept was first introduced.

See p. 195

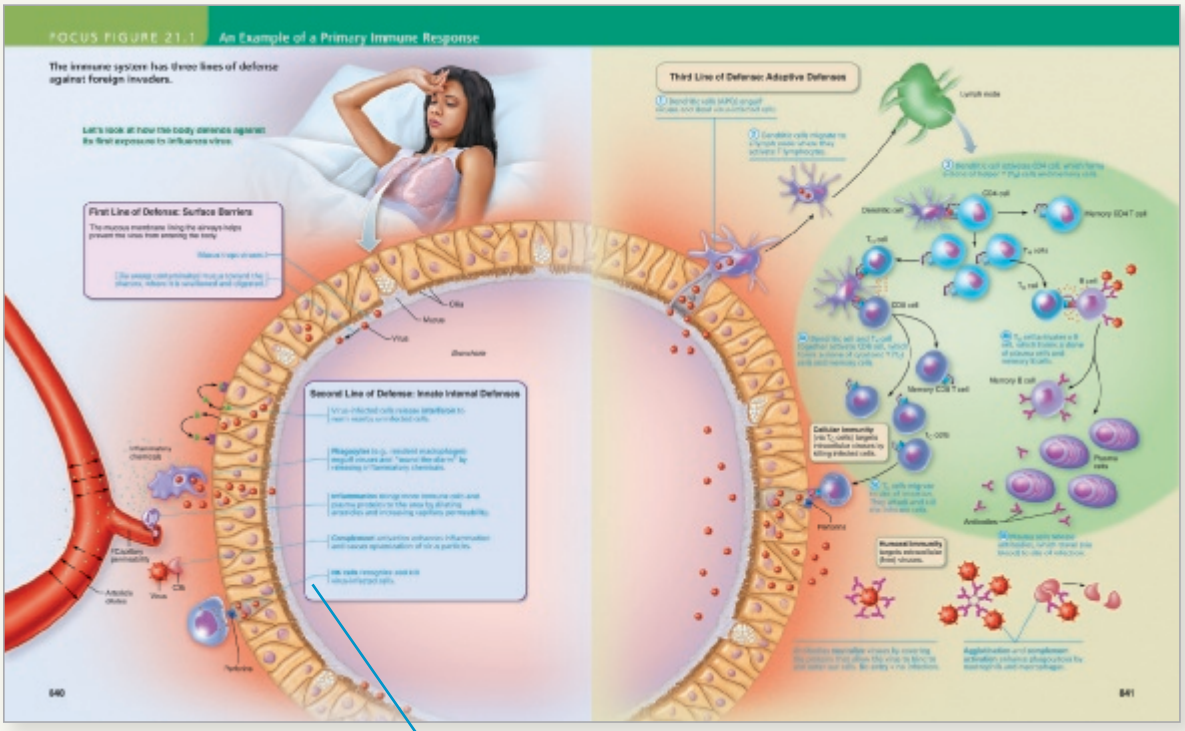
NEW! Building Vocabulary Coaching Activities in Mastering A&P® are a fun way to learn word roots and A&P terminology while building and practicing important language skills.

Study the Figures as You Read the Text

Anatomy and Physiology is a visual science. To succeed, you need to practice and develop visual literacy skills for understanding and interpreting information. To help you achieve this goal, the text and associated figures are tightly integrated so that you never have to flip pages back and forth to connect visuals with words.

EXPANDED! 6 new Focus Figures (for a total of 26) walk you through complex processes using exceptionally clear, easy-to-follow illustrations with integrated text explanations.

NEW Focus Figures are as follows:
3.1 The Plasma Membrane, *pp. 96–97*
11.4 Postsynaptic Potentials and Their Summation, *pp. 450–451*
16.2 Stress and the Adrenal Gland, *pp. 660–661*
18.2 The Cardiac Cycle, *pp. 726–727*
21.1 An Example of a Primary Immune Response, *pp. 840–841*
28.2 Fetal and Newborn Circulation, *pp. 1140–1141*



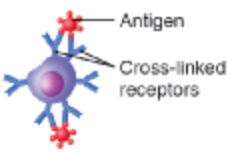
See pp. 840–841

NEW! Focus Figure "Mini-Animation" Coaching Activities bring the 6 new Focus Figures to life using short video segments.

Blue text represents the voice of an A&P instructor, highlighting important points to remember.

Activation and Differentiation of B Cells

An immunocompetent but naive B lymphocyte is *activated* when matching antigens bind to its surface receptors and cross-link adjacent receptors together. Antigen binding is quickly followed by receptor-mediated endocytosis of the cross-linked antigen-receptor complexes. As we described previously, this is called *clonal selection* and is fol-



EXPANDED! 31 unique In-Line Figures are strategically placed within the text to visually reinforce the text discussion.

See p. 828

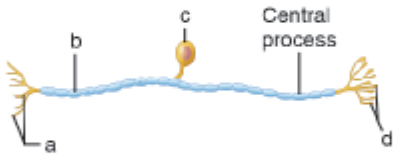
Apply Your Knowledge to a Range & Variety of Questions

As you build your knowledge and confidence in A&P, practice responding to the more challenging questions—you are likely to encounter similar questions on a test or licensing exam. Your extra effort will pay off at exam time!

NEW! A greater **variety and range of self-assessment questions** have been added to the **Check Your Understanding** sections within each chapter and include **Apply**, **Predict**, **What If?**, **Draw**, and **Make Connections**. Dozens of new **visual questions** ask you to label structures or interpret visual information.

Check Your Understanding

5. How does a nucleus within the brain differ from a nucleus within a neuron?
6. How is a myelin sheath formed in the CNS, and what is its function?
7. What is the structural classification of the neuron shown below? What is its usual functional classification? Name the parts labeled a–d.



8. APPLY Which structural and functional type of neuron is activated first when you burn your finger? Which type is activated last to move your finger away from the source of heat?
9. MAKE CONNECTIONS Which part of the neuron is its fiber? How do nerve fibers differ from the fibers of connective tissue (see Chapter 4) and the fibers in muscle (see Chapter 9)?

For answers, see Answers Appendix.

See p. 432

NEW! **"Draw" questions** ask you to create visuals that reinforce important concepts by drawing a structure, annotating a figure, or creating a summary table.

3. DRAW Create a summary table to help you study the pharynx by comparing and contrasting its three parts. For each part, identify what it conducts (air, food, or both), the type of epithelium found there, and the associated tonsils.

	Conducts	Epithelium	Tonsils
Nasopharynx	Air	Pseudostratified ciliated columnar	Pharyngeal Tubal
Oropharynx	Air and food	Stratified squamous	Palatine Lingual
Laryngopharynx	Air and food	Stratified squamous	—— (none)

See p. 856 and Answers Appendix

NEW! All of the **End-of-Chapter Review questions** are now organized into 3 levels of difficulty based on **Bloom's Taxonomy categories**:
Level 1: Remember/Understand
Level 2: Apply/Analyze
Level 3: Evaluate/Synthesize

Prepare for Your Future Career & Practice Solving Real-World Problems

The authors of this text, Elaine Marieb and Katja Hoehn, share insights from their own clinical experience to help you prepare for your future career in health care. All clinical examples and applications are signaled with an easy-to-find "Clinical" label.

UPDATED! Homeostatic Imbalance discussions alert you to the consequences of body systems not functioning optimally. Relevant photos have been added to selected discussions for visual reinforcement.

HOMEOSTATIC IMBALANCE 5.6 CLINICAL

Changes in nail appearance can help diagnose certain conditions. For example, yellow-tinged nails may indicate a respiratory or thyroid gland disorder. (Thickened yellow nails are usually due to a fungus infecting the nail.) An outward concavity of the nail (*koilonychia* or "spoon nail," **Figure 5.8**) may signal an iron deficiency. Horizontal lines (Beau's lines) across the nails can be a sign of severe illness that affects the whole body such as uncontrolled diabetes, a heart attack, or cancer chemotherapy.

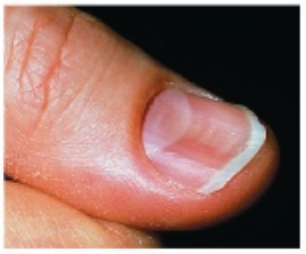


Figure 5.8 Koilonychia.

See p. 193

UPDATED! Clinical Case Studies are provided at the end of Chapters 5–29 and challenge you to apply your knowledge to realistic clinical scenarios.

CLINICAL CASE STUDY

One-Year-Old Girl with Retarded Growth

Miriam gave birth to a twin boy and girl a year ago. She is concerned about Theresa, her daughter, since her growth and development is much slower than that of her brother. Miriam visits a pediatric outpatient clinic, where she informs the physician that, apart from having retarded growth, Theresa has a poor appetite, suffers from constipation, and is lethargic. The physician orders blood tests to check Theresa's growth hormone (GH), thyroid-stimulating hormone (TSH), and thyroxine (T_4) levels.

1. + NCLEX-STYLE Theresa's retarded growth could be due to:
   - **a.** The positive feedback of GH on the hypothalamus
   - **b.** A pituitary tumor that is causing hypersecretion of GH
   - **c.** Hypersecretion of growth hormone–releasing hormone (GHRH) by the hypothalamus
   - **d.** Hyposecretion of GH by the anterior pituitary

Theresa's blood tests indicate that her GH levels are normal, but her TSH levels are elevated, and her T_4 levels are low. The physician tells Miriam that since Theresa's GH levels are normal, her retarded growth is not due to pituitary dwarfism.

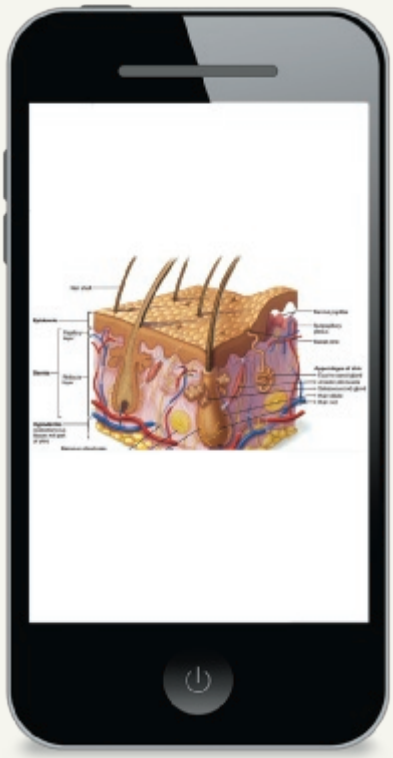
See p. 673

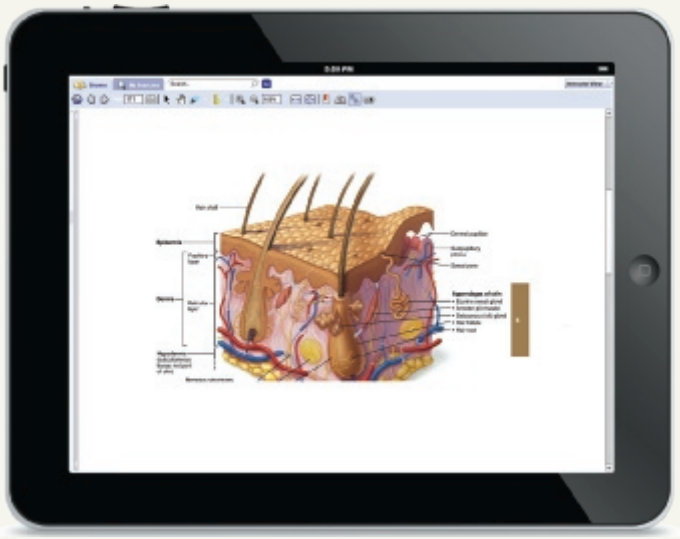
NEW! Each Clinical Case Study includes **"NCLEX-Style" questions** for practice with the kinds of challenge questions that you will eventually encounter on a licensing exam. Practice answering these questions on your own or in collaboration with classmates. Your instructor can also assign **new NCLEX-Style questions in Mastering A&P®**, along with Homeostatic Imbalance questions, Clinical Case Study Coaching Activities, and Nurses Need Physiology Case Studies.

Access the Complete Textbook Online Using the Pearson eText

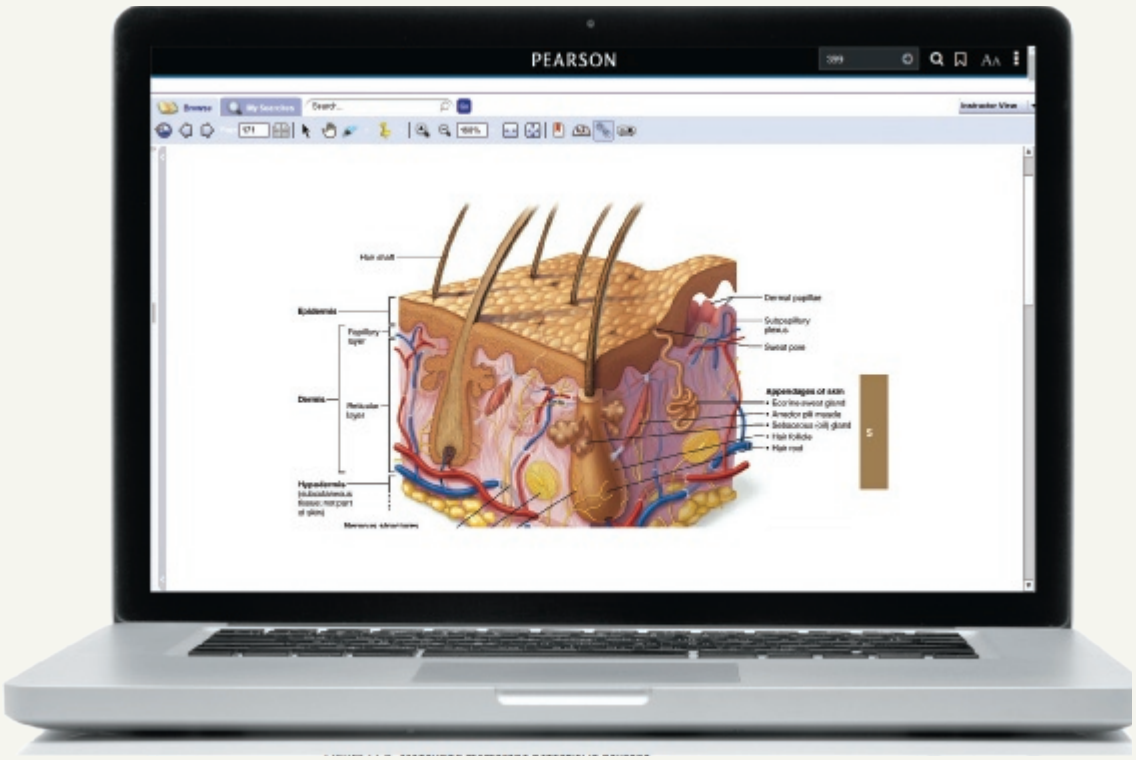
You can read your textbook without having to add weight to your bookbag!

The Pearson eText mobile app offers offline access and can be downloaded for most iOS and Android phones and tablets from the Apple App or Google Play stores.





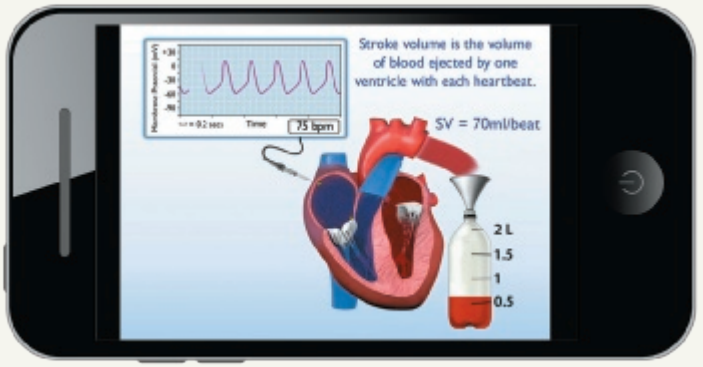
Powerful interactive and customization functions include instructor and student note-taking, highlighting, bookmarking, search, and links to glossary terms.



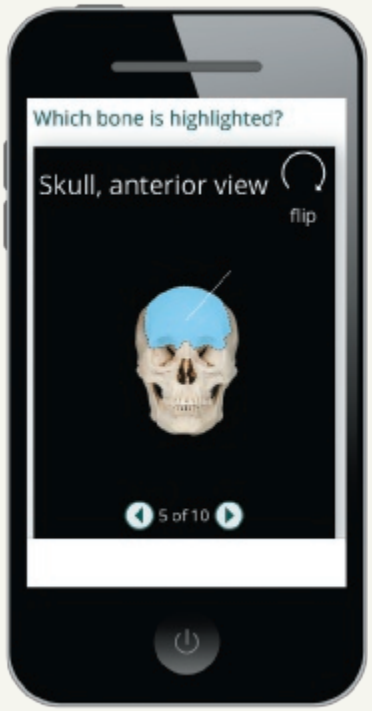
Get Online Practice and Coaching with Mastering A&P®

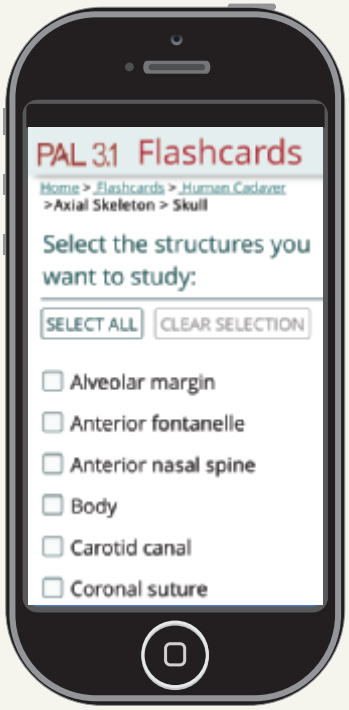
Mastering A&P® provides tutorials and review questions that you can access before, during, and after class.

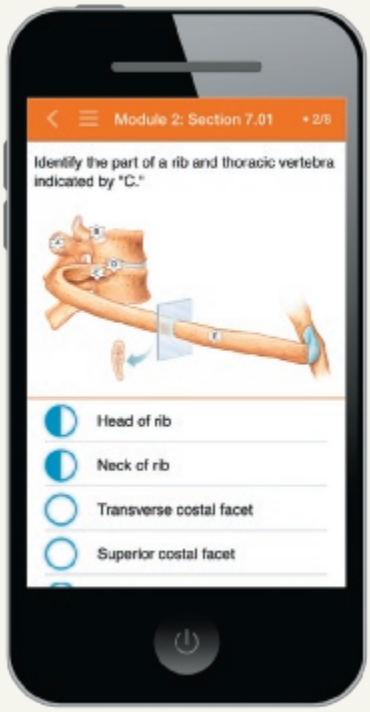
EXPANDED! Interactive Physiology 2.0 Coaching Activities teach complex physiology processes using exceptionally clear animations, interactive tutorials, games, and quizzes. IP2 features new graphics, quicker navigation, and a mobile-friendly design. New topics include Generation of an Action Potential and Cardiac Cycle. IP2 and IP animations can be assigned from the Mastering A&P® item library or accessed through the Study Area.



NEW! PAL 3.1 Customizable Flashcards allow you to create a personalized, mobile-friendly deck of flashcards and quizzes using images from Practice Anatomy Lab. Use the checklist to select only those structures covered in your course.







Dynamic Study Modules are manageable, mobile-friendly sets of questions with extensive feedback for you to test, learn, and retest yourself on basic concepts. **NEW!** Instructors can select or deselect specific questions for assignments from more than 3,000 questions, organized by chapter section.

New for Instructors:
Ready-to-Go Teaching Modules

NEW! Ready-to-Go Teaching Modules help instructors efficiently make use of the best teaching tools before, during, and after class. Accessed through the Instructor Resources area of Mastering A&P® and prepared by expert A&P instructors, each module includes a variety of teaching ideas and ready-to-use resources for teaching 10 challenging course topics.

Learning Catalytics allows students to use their smartphone, tablet, or laptop to respond to questions in class. Visit learningcatalytics.com to learn more.

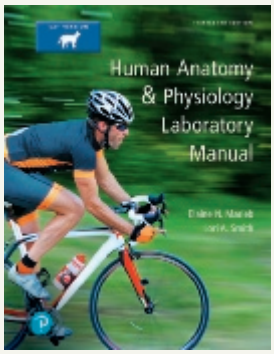
Additional Support for Students & Instructors

Mastering A&P® offers thousands of tutorials, activities, and questions that can be assigned for homework and practice. Highlights of new assignment options include:

- **NEW! Building Vocabulary Coaching Activities** give you practice learning and using word roots in context as you learn new A&P terms.
- **NEW! Focus Figure "Mini-Animation" Coaching Activities** bring the 6 new Focus Figures to life and include assessment questions.
- **IMPROVED! Concept Map Coaching Activities** support the concept maps in the text without requiring students to submit their own concept map for grading.
- **NEW! NCLEX-Style Questions** give students practice with the kinds of questions that will eventually appear on a licensing exam.

The Mastering A&P® Instructor Resources Area includes the following downloadable tools for instructors who adopt the Eleventh Edition for their classes:

- **NEW! Ready-to-Go Teaching Modules** provide teaching tools for 10 challenging topics in A&P.
- **Customizable PowerPoint® lecture outlines** include customizable images and provide a springboard for lecture prep.
- **All of the figures, photos, and tables from the text** are available in JPEG and PowerPoint® formats, in labeled and unlabeled versions, and with customizable labels and leader lines.
- **Test bank** provides thousands of customizable questions across Bloom's Taxonomy levels. Each question is tagged to chapter learning outcomes that can also be tracked within Mastering A&P® assessments. Available in Microsoft® Word and TestGen® formats.
- **Animations and videos** bring A&P concepts to life and include A&P Flix 3-D Animations.



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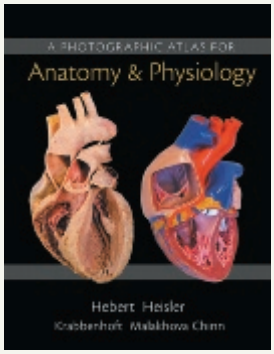

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About the Authors

We dedicate this work to our students both present and past, who always inspire us to "push the envelope."

Elaine N. Marieb

After receiving her Ph.D. in zoology from the University of Massachusetts at Amherst, Elaine N. Marieb joined the faculty of the Biological Science Division of Holyoke Community College. While teaching at Holyoke Community College, where many of her students were pursuing nursing degrees, she developed a desire to better understand the relationship between the scientific study of the human body and the clinical aspects of the nursing practice. To that end, while continuing to teach full time, Dr. Marieb pursued her nursing education, which culminated in a Master of Science degree with a clinical specialization in gerontology from the University of Massachusetts. It is this experience that has informed the development of the unique perspective and accessibility for which her publications are known.

Dr. Marieb has given generously to provide opportunities for students to further their education. She funds the E.N. Marieb Science Research Awards at Mount Holyoke College, which promotes research by undergraduate science majors, and has underwritten renovation of the biology labs in Clapp Laboratory at that college. Dr. Marieb also contributes to the University of Massachusetts at Amherst, where she provided funding for reconstruction and instrumentation of a cutting-edge cytology research laboratory. Recognizing the severe national shortage of nursing faculty, she underwrites the Nursing Scholars of the Future Grant Program at the university.

In 2012 and 2017, Dr. Marieb gave generous philanthropic support to Florida Gulf Coast University as a long-term investment in education, research, and training for healthcare and human services professionals in the local community. In honor of her contributions, the university is now home to the Elaine Nicpon Marieb College of Health and Human Services.

Katja Hoehn

Dr. Katja Hoehn is a professor in the Department of Biology at Mount Royal University in Calgary, Canada. Dr. Hoehn's first love is teaching. Her teaching excellence has been recognized by several awards during her 24 years at Mount Royal University. These include a PanCanadian Educational Technology Faculty Award (1999), a Teaching Excellence Award from the Students' Association of Mount Royal (2001), and the Mount Royal Distinguished Faculty Teaching Award (2004).

Dr. Hoehn received her M.D. (with Distinction) from the University of Saskatchewan, and her Ph.D. in Pharmacology from Dalhousie University. In 1991, the Dalhousie Medical Research Foundation presented her with the Max Forman (Jr.) Prize for excellence in medical research. During her Ph.D. and postdoctoral studies, she also pursued her passion for teaching by presenting guest lectures to first- and second-year medical students at Dalhousie University and at the University of Calgary.

Dr. Hoehn has been a contributor to several books, written numerous research papers in Neuroscience and Pharmacology, and has co-authored the previous four editions of this textbook. For many years, she has also reviewed and authored electronic media that accompanies Pearson anatomy and physiology books.

Following Dr. Marieb's example, Dr. Hoehn provides financial support for students in the form of a scholarship that she established in 2006 for nursing students at Mount Royal University.

Dr. Hoehn is also actively involved in the Human Anatomy and Physiology Society (HAPS) and is a member of the American Association of Anatomists. When not teaching, she likes to spend time outdoors with her husband and two sons. She also enjoys competing in long-course triathlons, and playing Irish flute down at the local pub.

Preface

Today's students have access to an enormous amount of information about anatomy and physiology. As educators, our biggest challenge is to help students focus on mastering the basic concepts of this field. Providing this firm foundation will help students to become lifelong learners who can critically evaluate new information, connect that information to the foundation they have already established, and apply it in a clinical setting. How can we help students build a strong foundation in anatomy and physiology? We believe that this new edition of our textbook will help learners by building on the strengths of previous editions while using new and innovative ways to help students visualize connections between various concepts.

Unifying Themes

Three unifying themes that have helped to organize and set the tone of this textbook continue to be valid and are retained in this edition. These themes are:

Interrelationships of body organ systems. This theme emphasizes the fact that nearly all regulatory mechanisms have interactions with several organ systems. The respiratory system, for example, cannot carry out its role of gas exchange in the body if there are problems with the cardiovascular system that prevent the normal delivery of blood throughout the body. The System Connections feature and Make Connections questions throughout the book help students connect new information to old information and think of the body as a community of dynamic parts instead of a number of independent units.

Homeostasis. Homeostasis is the normal and most desirable condition of the body. Its loss is always associated with past or present pathology. This theme is not included to emphasize pathological conditions, but rather to illustrate what happens in the body "when things go wrong" and homeostasis is lost. Whenever students see a red balance beam symbol accompanied by an associated clinical topic, their understanding of how the body works to stay in balance is reinforced.

Complementarity of structure and function. This theme encourages students to understand the structure of some body part (ranging from a molecule to an organ) in order to understand the function of that structure. For example, muscle cells can produce movement because they are contractile cells.

New to the Eleventh Edition

New and augmented elements aim to help learners in the following ways.

To help students make connections between new and previously learned material. In order for students to master new concepts, they must link these new concepts with concepts they already understand. In this edition, we help them do this by adding:

- **Text recall icons (◀).** These icons direct the student back to the specific pages where a concept was first introduced.
- **Make Connections questions.** We've added more of this type of question to the Check Your Understanding review questions that follow each module within a chapter. To answer these questions, the student must employ concepts learned previously (most often in previous chapters).
- **New kinds of higher-level questions.** Each chapter now has at least five higher-level questions that require students to think more deeply, pulling together strands from multiple concepts. These questions are clearly identified as APPLY, DRAW, PREDICT, MAKE CONNECTIONS, and WHAT IF? questions.
- **New summary tables.** Students have told us that they want more summary tables. In response, 13 new summary tables (two with illustrations) have been added in order to help students see the big picture.

To enhance students' visual literacy. Anatomy is and has always been taught principally through images. Increasingly, however, physiological data is also represented as images, whether it be molecular interactions or graphical descriptions of

processes. Throughout their future health care careers, students will need to be able to understand and interpret information presented visually. In this edition, we help them do this by:

- **Adding new Focus figures.** Focus figures are illustrations that use a "big picture" layout and dramatic art to guide the student through difficult physiological processes in a step-by-step way. Our previous Focus figures have been a hit with both students and instructors. In response to requests for additional Focus figures, we are pleased to present six new two-page features.
- **Adding DRAW questions in each chapter.** Students often think that they understand an illustration simply by looking at it, but to truly comprehend an illustration and cement its concepts requires a more active learning approach. For this reason we now include at least one higher-level review question within each chapter that requires a student either to draw an illustration or to add to an existing diagram.
- **Adding questions about illustrations.** To help students practice their visual literacy skills, we have added 47 new Check Your Understanding questions that include an illustration as part of the question. Some of these are as simple as labeling exercises, but many require more advanced interpretation.
- **Updating art to improve its teaching effectiveness.** As always, this is a major part of the revision. Today's students are accustomed to seeing sophisticated photorealistically rendered images. However, many students are not adept at extracting, and thinking critically about, the relevant information contained in such illustrations. With this in mind we continue to refine and update our illustrations as students' needs change, improving their ability to teach important concepts. In many cases we have added blue "instructor's voice" text within the figure to guide a student through it, replacing much of the more remote figure legend. In addition, new photos were painstakingly chosen and labeled to enhance the learning process.
- **Adding new illustrations to existing tables and adding new illustrated tables.** Students find illustrated tables particularly effective because they provide a visual cue that helps them remember a topic. In this edition, we have added illustrations to two tables and added two new illustrated tables.
- **Adding in-line figures.** These are small (less than a half-column wide) illustrations or photos strategically located within the text that discuss the concept they illustrate. This edition now has 31 such in-line figures, most of them newly added.

To help students clinically apply what they have learned

- **Updated Homeostatic Imbalance features.** Many of the Homeostatic Imbalance features have been updated and relevant photos have been added to some. All have been reviewed for accuracy and relevancy. In addition, the updated book design makes these features stand out more clearly.
- **Updated Clinical Case Studies in Chapters 5-29 with added new NCLEX-STYLE questions.** The end-of-chapter review questions, which are now organized into three levels of difficulty based on Bloom's Taxonomy categories, culminate in a clinical case study that allows students to apply some of the concepts they have learned to a clinical scenario. These case studies have been extensively revised and each case study has two questions that are similar in style to those in the NCLEX exam.
- **New clinically relevant photos.** We have added or updated a number of photos that have clinical relevance (procedures, conditions, etc.) that will help students apply what they are reading to real-life situations and to their future careers.

In this edition, certain chapters have received the bulk of our attention and have been more heavily revised. As you can see in the Highlights of New Content (below), these are Chapters 2–4, 9, and 27–29.

As in the previous edition, we have taken painstaking care to ensure that almost all the text and the associated art are covered on the same two-page spread. Although this sounds like a simple goal, it actually takes a great deal of work and has not usually been achieved by other textbooks. We make this effort because it is invaluable to student learning to not have to flip pages back and forth between art and text. Finally, you will notice the appearance of new icons referencing MasteringA&P® interspersed within the text. This guides students to go to the relevant on-line activities to supplement their learning.

Other Highlights of New Content

Chapter 1 The Human Body: An Orientation

- New Figure 1.1 illustrates complementarity of structure and function.
- Updated *A Closer Look* feature on types of medical imaging and added five new photos.
- New Homeostatic Imbalance features about hiatal hernias and about "wrong site surgery."

Chapter 2 Chemistry Comes Alive

- New Homeostatic Imbalance feature about patient's pH predicting outcome of CPR.
- New figures illustrate triglyceride structure (2.16); the difference between saturated and unsaturated fatty acids (2.17); phospholipids (2.18); and protein functions (2.20).
- Revised Figures 2.6 (formation of ionic bonds) and 2.12 (dissociation of salt in water) teach more effectively.
- New summary tables reinforce information about chemical bonds (Table 2.2) and about macromolecules and their monomers and polymers (Table 2.5).

Chapter 3 Cells: The Living Units

- Added Focus Figure 3.1 about the plasma membrane, and reorganized accompanying text.
- Reorganized text about passive membrane transport for improved clarity; updated and reorganized discussion of autophagy and apoptosis.
- Updated information about Tay-Sachs disease.

- New micrographs show micro- and intermediate filaments (Figure 3.20).
- Improved teaching effectiveness of Figures 3.5 (diffusion), 3.17 (processing and distribution of newly synthesized proteins), and 3.30 (stages of transcription).
- New information about telomeres in cancer cells.
- New Homeostatic Imbalance feature about progeria.

Chapter 4 Tissue: The Living Fabric

- New images of cilia show the difference between transmission and scanning electron microscopy (Figure 4.2).
- New in-line figure illustrates apical and basal surfaces of epithelial cells.
- Revised art for epithelial and connective tissue for clarity (Figures 4.4 and 4.11).
- New Figure 4.5 shows how exocrine and endocrine glands differ, and new Figure 4.10 gives an overview of the classification of connective tissue.
- Updated *A Closer Look* feature about cancer.

Chapter 5 The Integumentary System

- New illustrated summary table comparing cutaneous glands (Table 5.1).
- Revised Figures 5.3 and 5.4 for better teaching effectiveness.
- Updated information about skin color and disease states.
- Updated Homeostatic Imbalance features about hirsutism and about hair loss.
- New Homeostatic Imbalance feature about nail changes with disease.
- Updated statistics for and treatment of melanoma, with new photo (Figure 5.11c).

Chapter 6 Bones and Skeletal Tissues

- New summary Table 6.1 compares cartilage and bone tissue.
- New photos of an osteoclast (Figure 6.7); of a femur in longitudinal section to show compact and spongy bone (Figure 6.3); and of a section of a flat bone (skull bone) (Figure 6.4 top).
- Extensive revision of Figure 6.12, which teaches bone growth at epiphyseal plates, including new X ray to show epiphyseal plates, and new photomicrograph of epiphyseal cartilage.
- Updated information about bone remodeling, hormonal regulation of bone growth, and osteoporosis.

Chapter 7 The Skeleton

- New drawings to illustrate the location of the true and false pelves, and the pelvic inlet and outlet (Figure 7.33).
- Updated Homeostatic Imbalance features about pes planus (flat feet) and about developmental dysplasia of the hip.
- New photos of bimalleolar fracture (Figure 7.35) and of cleft lip and palate (Figure 7.39).

Chapter 8 Joints

- New Homeostatic Imbalance feature about shoulder dislocations.
- New Table 8.3 summarizes movements at synovial joints.
- Revised Figure 8.4 (bursae and tendon sheaths).
- Updated *A Closer Look* about prostheses.

Chapter 9 Muscles and Muscle Tissue

- New "Background and Overview" section begins the discussion of the mechanisms of excitation and contraction of skeletal muscle, including a new "big picture" overview in Figure 9.7.
- New introduction to ion channels with art helps students understand skeletal muscle excitation and contraction.
- Reorganized discussions of graded muscle contractions and of smooth muscle, including new Figure 9.24 showing calcium sources for smooth muscle contraction.
- Updated discussion of muscle fatigue.
- Updated Homeostatic Imbalance feature on Duchenne muscular dystrophy.
- Updated *A Closer Look* feature about anabolic steroids.

Chapter 10 The Muscular System

- Revised art about levers for clarity (Figure 10.2 and 10.3).
- New cadaver dissection photos show dissection of muscles of the anterior neck and throat, superficial muscles of the thorax and shoulder in posterior view, and posterior muscles of the thigh and hip (Figures 10.9, 10.14, and 10.21).
- New photos illustrate thumb movements and show torticollis.

Chapter 11 Fundamentals of the Nervous System and Nervous Tissue

- New Focus Figure 11.4 illustrates postsynaptic potentials and their summation.
- Improved teaching effectiveness of Figure 11.12 (coding of action potentials for stimulus intensity) and Figure 11.19 (illustrating a reflex).
- New information about synthetic opiates in *A Closer Look*, with new PET scans showing effects of drug addiction.
- Added new research findings associating synaptic pruning and development of schizophrenia.

Chapter 12 The Central Nervous System

- New Figure 12.26 and revised text teach more effectively about the blood brain barrier.
- New Figure 12.30 shows spinal cord segment location in relation to vertebral column.
- New Table 12.2 summarizes spinal cord cross-sectional anatomy.
- Updated Homeostatic Imbalance features about hypothalamic disorders, cerebral palsy, anencephaly, and spina bifida, and about narcolepsy and insomnia, including new use of orexin receptor antagonists to treat insomnia.
- New type of MRI photo shows fiber tracts in brain and spinal cord.

Chapter 13 The Peripheral Nervous System and Reflex Activity

- New drawings of nerves of cervical, brachial, lumbar, and sacral plexuses show their position in relationship to the vertebrae (and hip bone in some cases) (Figures 13.9–13.12).

- New images illustrating the results of damage to the ulnar and radial nerves.
- New summary table of nerve plexuses (Table 13.7).
- New Homeostatic Imbalance feature and photo about an abnormal plantar reflex (Babinski's sign).
- Redrawn figure illustrating crossed-extensor reflex for improved student understanding.

Chapter 14 The Autonomic Nervous System

- New Figure 14.8 shows sympathetic innervation of the adrenal medulla.
- Clarified section about visceral sensory neurons.
- New photo illustrates Raynaud's disease.
- Revised Figure 14.5 on the sympathetic trunk for better teaching effectiveness.

Chapter 15 The Special Senses

- Revised Figure 15.2 (the lacrimal apparatus) for better teaching effectiveness.
- New photo of fundus of retina (Figure 15.7).

Chapter 16 The Endocrine System

- New Table 16.1 compares the endocrine and nervous systems.
- New Focus Figure 16.2 describes short- and long-term stress responses.
- Figures 16.5 (effects of growth hormone) and 16.9 (synthesis of thyroid hormone) revised for clarity.
- Updated information about diabetes mellitus, Addison's disease, and thyroid deficiency in childhood.

Chapter 17 Blood

- Updated information about anticoagulant medications.
- New photo shows petechiae resulting from thrombocytopenia (Figure 17.16).

Chapter 18 The Cardiovascular System: The Heart

- New Focus Figure 18.2 teaches students how to understand the cardiac cycle, with accompanying text reorganized.
- New photo shows an individual having an ECG (Figure 18.16).

Chapter 19 The Cardiovascular System: Blood Vessels

- New "drinking straw" analogy and art to explain resistance.
- New Figure 19.4 shows the structure of most capillary beds according to current understanding, and new text describes those capillary beds.
- Revised Figure 19.6 on proportions of blood volume throughout the vascular tree for greater teaching effectiveness.
- New illustration of cerebral arterial circle (circle of Willis) (Figure 19.24).

Chapter 20 The Lymphatic System and Lymphoid Organs and Tissues

- New illustrated Table 20.1 summarizes key characteristics of the major lymphoid organs.
- Revised Figure 20.9 with orientation diagrams helps students locate Peyer's patches (aggregated lymphoid nodules).
- Updated information about lymphatic drainage of the CNS.

Chapter 21 The Immune System: Innate and Adaptive Body Defenses

- New Focus Figure 21.1 gives an example of a primary immune response and summarizes innate and adaptive defenses.
- New illustrated Table 21.8 summarizes the components of adaptive immunity and complements the new Focus figure.
- New photo of a macrophage engulfing bacteria.
- Revised Figure 21.4 and text on inflammation, Figure 21.6 on complement activation, and Figure 21.11 on clonal selection of a B cell for greater teaching effectiveness.

Chapter 22 The Respiratory System

- New Figure 22.1 illustrates the four respiratory processes.
- Added section about sleep apnea.
- New scanning electron micrographs of emphysematous and normal lung tissue (Figure 22.22).
- Updated statistics about lung cancer and trends in asthma prevalence.

Chapter 23 The Digestive System

- New Figure 23.25 teaches the enterohepatic circulation of bile salts, and new Figure 23.30 shows the macroscopic anatomy of the small intestine.
- Improved teaching effectiveness of Figure 23.7 (neural reflex pathways in the gastrointestinal tract) and 23.16 (microscopic anatomy of the stomach).
- Added Homeostatic Imbalance features about dry mouth (xerostomia) and about tooth decay in primary teeth.
- Updated Homeostatic Imbalance feature about acute appendicitis to state that surgery is no longer always the first choice of treatment.

Chapter 24 Nutrition, Metabolism, and Energy Balance

- New Figure 24.24 shows the size and composition of various lipoproteins.
- Improved teaching effectiveness of Figure 24.21 (insulin effects during the postabsorptive stage).
- Updated Homeostatic Imbalance features with mechanism of cell death in frostbite, and diet recommendations for individuals with phenylketonuria.
- New information about environmental factors that may contribute to the obesity epidemic in *A Closer Look*.
- Updated nutritional information about lipids, and updated statistics about the prevalence of obesity in adults and children and about the prevalence of diabetes mellitus.

Chapter 25 The Urinary System

- New Figure 25.18 shows the medullary osmotic gradient and interstitial fluid osmolalities in the renal cortex and medulla.
- New Table 25.1 summarizes the regulation of glomerular filtration rate.
- Improved teaching effectiveness of Figures 25.9 (blood vessels of the renal cortex), 25.12 (the filtration membrane), 25.15 (routes for tubular reabsorption), and 25.16 (tubular reabsorption of water and nutrients).

- New pyelogram shows anatomy of kidneys, ureters, and urinary bladder (Figure 25.23).
- Added Homeostatic Imbalance feature about renal trauma.
- Updated Homeostatic Imbalance feature about kidney stones.

Chapter 26 Fluid, Electrolyte, and Acid-Base Balance

- New Figure 26.12 summarizes the body's chemical buffers.
- Improved teaching effectiveness of Figure 26.1 (major fluid compartments of the body), 26.2 (electrolyte composition of blood plasma, interstitial fluid, and intracellular fluid), and 26.7 (disturbances in water balance).
- Clarified definitions of sensible and insensible water loss.

Chapter 27 The Reproductive System

- This chapter has been extensively updated, revised, and reorganized. Almost every figure has been reconceptualized and several new figures have been added. These changes have been made for better teaching effectiveness.
- New opening module now compares male and female reproductive system anatomy and physiology and highlights common features, allowing students to make connections more easily. Homologous structures, patterns of hormone release, and meiosis are included in this section.
- New Figure 27.1 illustrates the basic pattern of interactions along the hypothalamic-pituitary-gonadal (HPG) axis in both males and females.
- The section about meiosis has been extensively rewritten to help increase student understanding. New in-line figures help introduce the basic terminology and some of the concepts before meiosis is discussed in detail.
- A new big-picture overview of meiosis introduces the major events before the details of each step are presented.
- Figures 27.22 (events of oogenesis) and 27.24 (regulation of the ovarian cycle) are extensively revised and updated for increased teaching effectiveness and accuracy.
- New Figure 27.26 depicts the genetic determination of sex.

Chapter 28 Pregnancy and Human Development

- New photo of sperm surrounding an oocyte (Figure 28.2).
- New Figure 28.5 illustrates implantation of a blastocyst.
- New photo of a 22-day embryo illustrates lateral folding (Figure 28.10d).
- Figure 28.12 (neurulation and early mesodermal differentiation) revised for clarity.
- New Focus Figure 28.2 (*Focus on Fetal and Newborn Circulation*) teaches the special features of fetal circulation and changes that occur in this circulation after birth.
- New Table 28.1 summarizes the special structures of the fetal circulation, their functions, and their postnatal structure.
- Updated information about placental hormone secretion and about the hormonal control of the initiation of labor.
- New information about fetal cells that enter the maternal circulation.
- New Homeostatic Imbalance feature about preeclampsia.

Chapter 29 Heredity

- Added Punnett square showing X-linked inheritance.
- Figure 29.1 (preparing a karyotype) and 29.4 (genotype and phenotype probabilities) revised for clarity.
- New photo of a couple with achondroplasia.
- Updated information about small noncoding RNAs.
- It has become increasingly clear that very few benign traits in humans follow a simple dominant-recessive inheritance pattern. Tongue rolling, astigmatism, freckles, dimples, phenylthiocarbamide tasting, widow's peak, and double-jointed thumb were all at one time thought to follow this pattern of inheritance. Closer examination has revealed compelling evidence against each of these. Consequently, the examples throughout the chapter have changed.

Acknowledgments

Producing a new edition of this book is an enormous undertaking. Let us take you through the steps and introduce you to the people behind the scenes that have helped make this book what it is. Every new edition begins with a revision plan. We'd like to thank all of the students and instructors who have provided the feedback (gathered by our editorial team) that forms the basis of this plan. Once this plan was in place, Barbara Price (our text Development Editor) scoured each chapter. This was Barbara's first exposure to the book and her fresh eyes on the text found opportunities to further clarify the presentation. In addition, she noted places where additional chunking of the text (such as bulleted lists) would help the students. Her excellent work has made this text better. We incorporated her ideas, and reviewer feedback, together with our own updates and ideas for reorganization of the text and art. Thanks to Patricia Bowne for contributing to the Clinical Case Studies and Wendy Mercier for reviewing all of the Case Studies. We also very much appreciate the help of Karen Dougherty, who used her expertise as a physician and educator to review all of the Homeostatic Imbalance features and help us revise and update them.

We then laid out each chapter to maintain text-art correlation before passing the manuscript off to Michele Mangelli. Michele wore many different hats during this revision. She was both the Program Manager for the editorial side of things as well as the Goddess of Production. She reviewed the revised manuscript before she sent it to ace copyeditor Anita Hueftle. Anita saved us on many occasions from public embarrassment by finding our spelling and grammar errors, our logical lapses, and various other inconsistencies. We can't thank Anita enough for her meticulous and outstanding work! (Any remaining errors are our fault.)

At the same time the text was in revision, the art program was going through a similar process. This book would not be what it is without the help of Laura Southworth, our superb Art Development Editor. Laura's creativity, attention to detail, and her sense of what will teach well and what won't have helped us immensely. She has worked tirelessly to make our Focus figures and other art even better. Finding good, usable photos is never easy, and we are grateful for the hard work of Kristin Piljay (Photo Researcher). It was also a pleasure to work with Jean Lake again, who expertly juggled the administrative aspects of the art program and kept us all on track. This team ensured that the artists at Imagineering had all the information they needed to produce beautiful final art products.

As the manuscript made the transition from Editorial to Production, Michelle Mangelli (wearing a different hat—this one as the Production and Design Manager) took over again. As head honcho and skilled handler of all aspects of production, everyone answered to her from this point on. Kudos to our excellent production coordinator, Karen Gulliver, who did much of the hands-on handling, routing, and scheduling of the manuscript. We'd also like to thank Martha Ghent (Proofreader), Betsy Dietrich (Art Proofreader), Sallie Steele (Indexer), Alicia Elliot (Project Manager at Imagineering), and Cenveo (Compositor). Izak Paul meticulously read every chapter for scientific accuracy, and we are very grateful for his careful work. Thanks also to Gary Hespenheide for his stunning design work on the cover, chapter opening pages, and the text.

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Kudos to our entire team. We feel we have once again prepared a superb textbook. We hope you agree.

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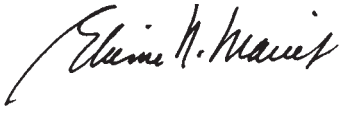

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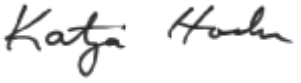

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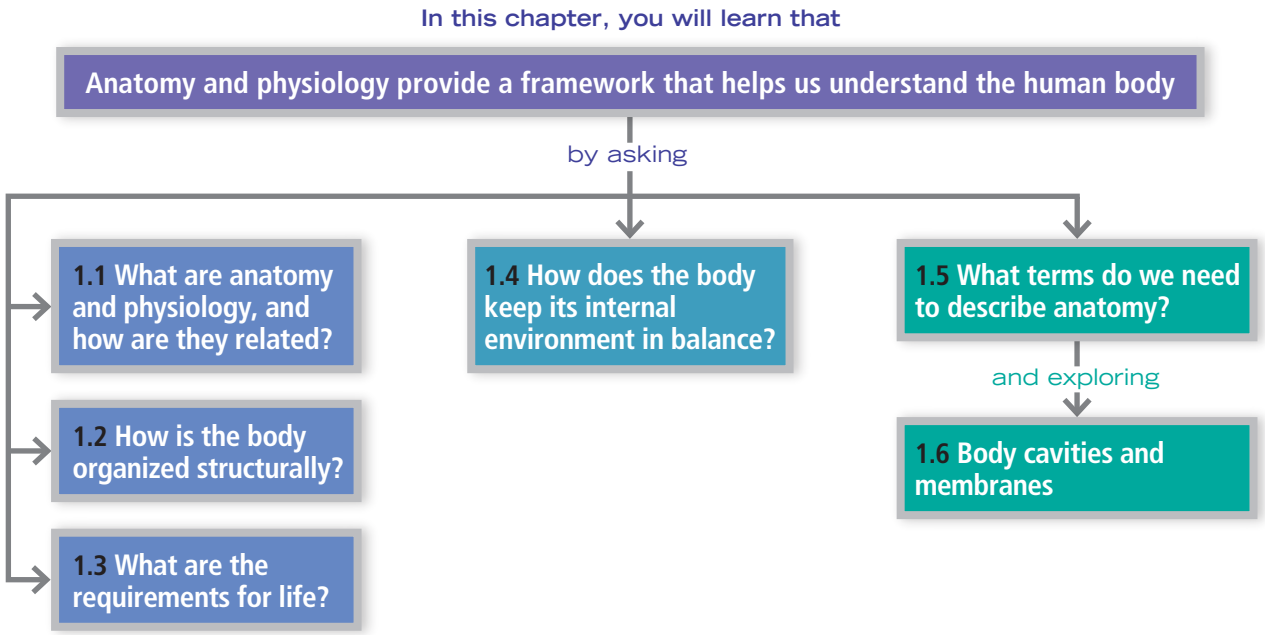
UNIT 3 Regulation and Integration of the Body

1 The Human Body: An Orientation



Welcome to the study of one of the most fascinating subjects possible—your own body. Such a study is not only highly personal, but timely as well. We get news of some medical advance almost daily. To appreciate emerging discoveries in molecular genetics, to understand new techniques for detecting and treating disease, and to make use of published facts on how to stay healthy, you'll find it helps to learn about the workings of your body. If you are preparing for a career in the health sciences, the study of anatomy and physiology has added rewards because it provides the essential foundation for your clinical experiences.

In this chapter we define and contrast anatomy and physiology and discuss how the human body is organized. Then we review needs and processes common to all living organisms. Three essential concepts—*the complementarity of structure and function, the hierarchy of structural organization,* and *homeostasis*—will unify and form the bedrock for your study of the human body. And finally you'll learn the language of anatomy—terminology that anatomists use to describe the body and its parts.

CAREER CONNECTION

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1.1 Form (anatomy) determines function (physiology)

Learning Outcomes

- **Define anatomy and physiology and describe their subdivisions.**
- **Explain the principle of complementarity.**

1

Two complementary branches of science—anatomy and physiology—provide the concepts that help us to understand the human body. **Anatomy** studies the *structure* of body parts and their relationships to one another. Anatomy has a certain appeal because it is concrete. Body structures can be seen, felt, and examined closely. You don't need to imagine what they look like.

Physiology concerns the *function* of the body, in other words, how the body parts work and carry out their life-sustaining activities. When all is said and done, physiology is explainable only in terms of the underlying anatomy.

For simplicity, when we refer to body structures and physiological values (body temperature, heart rate, and the like), we will assume that we are talking about a healthy young *reference man* weighing about 155 lb [70 kilograms (kg)] or a healthy young *reference woman* weighing about 125 lb (57 kg).

Although we use the reference values and common directional and regional terms to refer to all human bodies, you know from observing the faces and body shapes of people around you that we humans differ in our external anatomy. The same kind of variability holds for internal organs as well. In one person, for example, a nerve or blood vessel may be somewhat out of place, or a small muscle may be missing. Nonetheless, well over 90% of all structures present in any human body match the textbook descriptions. We seldom see extreme anatomical variations because they are incompatible with life.

Topics of Anatomy

Anatomy is a broad field with many subdivisions, each providing enough information to be a course in itself. **Gross**, or **macroscopic**, **anatomy** is the study of large body structures visible to the naked eye, such as the heart, lungs, and kidneys. Indeed, the term *anatomy* (from Greek, meaning "to cut apart") relates most closely to gross anatomy because in such studies preserved animals or their organs are dissected (cut up) to be examined.

Gross anatomy can be approached in different ways.

- In **regional anatomy**, all the structures (muscles, bones, blood vessels, nerves, etc.) in a particular region of the body, such as the abdomen or leg, are examined at the same time.
- In **systemic anatomy** (sis-tem′ik),* body structure is studied system by system. For example, when studying the cardiovascular system, you would examine the heart and the blood vessels of the entire body.
- Another subdivision of gross anatomy is **surface anatomy**, the study of internal structures as they relate to the overlying skin surface. You use surface anatomy when you identify the bulging muscles beneath a bodybuilder's skin, and clinicians use it to locate appropriate blood vessels in which to feel pulses and draw blood.

Microscopic anatomy deals with structures too small to be seen with the naked eye. For most such studies, exceedingly thin slices of body tissues are stained and mounted on glass slides to be examined under the microscope. Subdivisions of microscopic anatomy include **cytology** (si-tol′o-je), which considers the cells of the body, and **histology** (his-tol′o-je), the study of tissues.

Developmental anatomy traces structural changes that occur throughout the life span. **Embryology** (em″bre-ol′o-je), a subdivision of developmental anatomy, concerns developmental changes that occur before birth.

Some highly specialized branches of anatomy are used primarily for medical diagnosis and scientific research. For example, *pathological anatomy* studies structural changes caused by disease. *Radiographic anatomy* studies internal structures as visualized by X-ray images or specialized scanning procedures.

Studying Anatomy

One essential tool for studying anatomy is a mastery of anatomical terminology. Other tools are observation, manipulation, and, in a living person, *palpation* (feeling organs with your hands) and *auscultation* (listening to organ sounds with a stethoscope). A simple example illustrates how some of these tools work together in an anatomical study.

Let's assume that your topic is freely movable joints of the body. In the laboratory, you will be able to *observe* an animal joint, noting how its parts fit together. You can work the joint (*manipulate* it) to determine its range of motion. Using *anatomical terminology*, you can name its parts and describe how they are related so that other students (and your instructor) will have no trouble understanding you. The list of word roots (at the back of the book) and the glossary will help you with this special vocabulary.

Although you will make most of your observations with the naked eye or with the help of a microscope, medical technology has developed a number of sophisticated tools that can peer into the body without disrupting it. See **A Closer Look** on pp. 48–49.

Topics of Physiology

Like anatomy, physiology has many subdivisions. Most of them consider the operation of specific organ systems. For example, **renal physiology** concerns kidney function and urine production. **Neurophysiology** explains the workings of the nervous system. **Cardiovascular physiology** examines the operation of the heart and blood vessels. While anatomy provides us with a static image of the body's architecture, physiology reveals the body's dynamic and animated workings.

Physiology often focuses on events at the cellular or molecular level. This is because the body's abilities depend on those of its individual cells, and cells' abilities ultimately depend on the chemical reactions that go on within them. Physiology also rests on principles of physics, which help to explain electrical

* For the pronunciation guide rules, see the first page of the glossary in the back of the book.

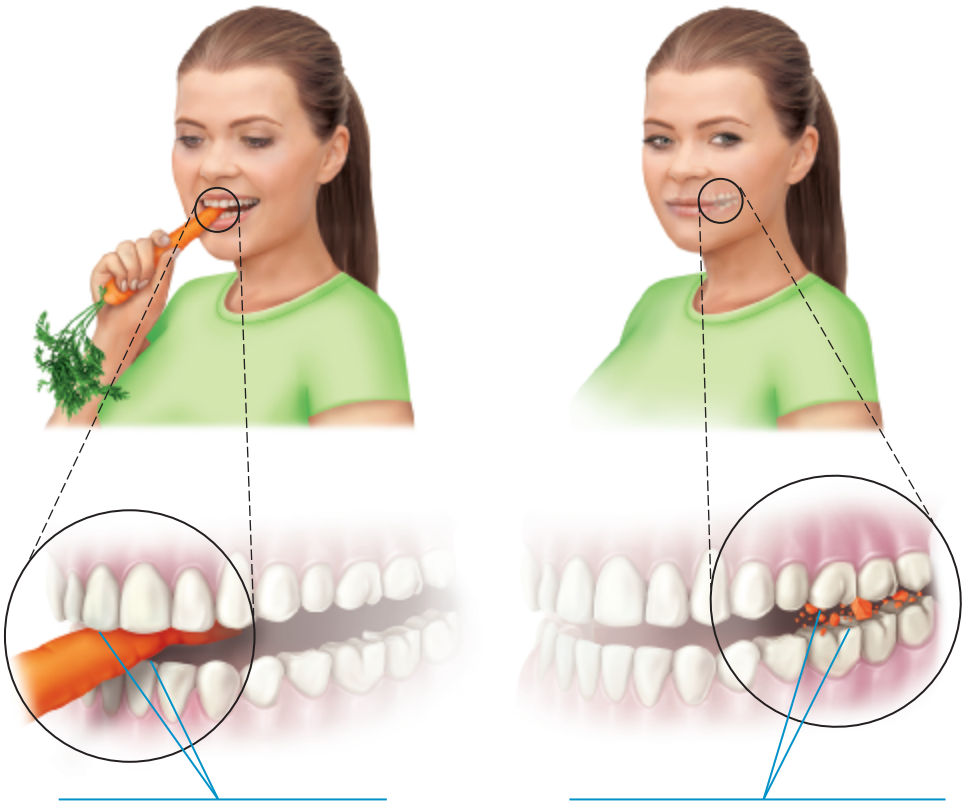


Figure 1.1 **Complementarity of structure and function.**

currents, blood pressure, and the way muscles use bones to cause body movements, among other things. We present basic chemical and physical principles in Chapter 2 and throughout the book as needed to explain physiological topics.

Complementarity of Structure and Function

Although it is possible to study anatomy and physiology individually, they are really inseparable because function always reflects structure. That is, what a structure can do depends on its specific form. This key concept is called the **principle of complementarity of structure and function**.

For example, bones can support and protect body organs because they contain hard mineral deposits. Blood flows in one direction through the heart because the heart has valves that prevent backflow. Another example is how the various shapes of our teeth reflect their different actions, as shown in **Figure 1.1**. Throughout this book, we accompany a description of a structure's anatomy with an explanation of its function, and we emphasize structural characteristics contributing to that function.

Check Your Understanding

1. In what way does physiology depend on anatomy?
2. Would you be studying anatomy or physiology if you investigated how muscles shorten? If you explored the location of the lungs in the body?
3. APPLY Use the word root definitions located at the back of this book to define each of the following terms: gastritis, leukocyte, nephropathy.

For answers, see Answers Appendix.

1.2 The body's organization ranges from atoms to the entire organism

Learning Outcomes

- **Name the different levels of structural organization that make up the human body, and explain their relationships.**
- **List the 11 organ systems of the body, identify their components, and briefly explain the major function(s) of each system.**

The human body has many levels of structural organization (**Figure 1.2**). The simplest level of the structural hierarchy is the **chemical level**, which we study in Chapter 2. At this level, *atoms*, tiny building blocks of matter, combine to form *molecules* such as water and proteins. Molecules, in turn, associate in specific ways to form *organelles* that are the basic components of cells. *Cells* are the smallest units of living things. We examine the **cellular level** in Chapter 3. All cells share some common functions, but individual cells vary widely in size and shape, reflecting their unique functions in the body.

The simplest living creatures are single cells, but in complex organisms such as human beings, the hierarchy continues on to the **tissue level**. *Tissues* are groups of similar cells that have a common function. The four basic tissue types in the human body

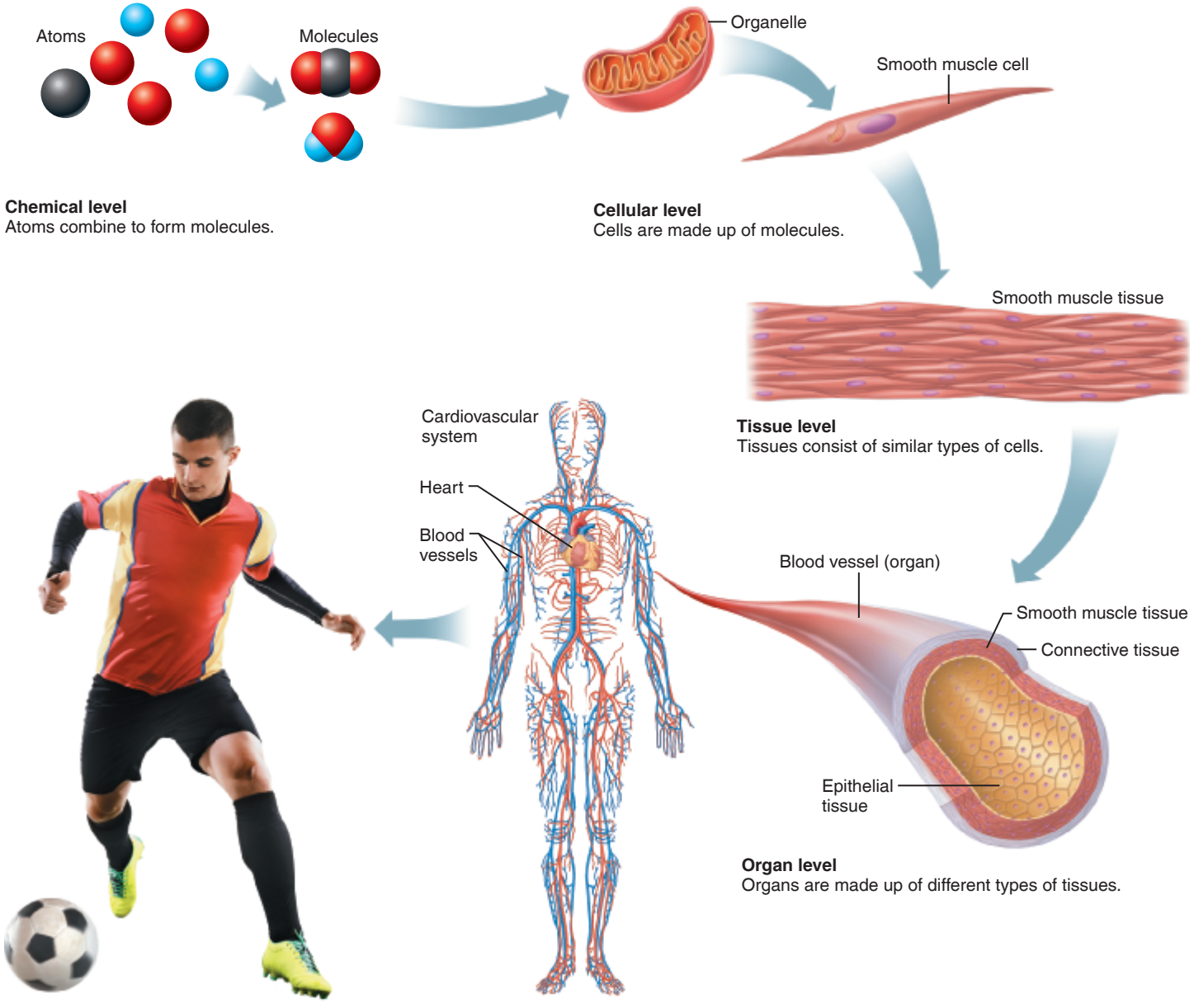


Figure 1.2 Levels of structural organization. Components of the cardiovascular system are used to illustrate the levels of structural organization in a human being.

are epithelial tissue, muscle tissue, connective tissue, and nervous tissue.

Each tissue type has a characteristic role in the body, which we explore in Chapter 4. Briefly, epithelial tissue covers the body surface and lines its cavities. Muscle tissue provides movement. Connective tissue supports and protects body organs. Nervous tissue provides a means of rapid internal communication by transmitting electrical impulses.

An *organ* is a discrete structure composed of at least two tissue types (four is more common) that performs a specific function for the body. The liver, the brain, and a blood vessel are very different from the stomach, but each is an organ. You can think of each organ of the body as a specialized functional center responsible for a necessary activity that no other organ can perform.

At the **organ level**, extremely complex functions become possible. Let's take the stomach for an example. Its lining is an epithelium that produces digestive juices. The bulk of its wall is muscle, which churns and mixes stomach contents (food). Its connective tissue reinforces the soft muscular walls. Its nerve fibers increase digestive activity by stimulating the muscle to contract more vigorously and the glands to secrete more digestive juices.

The next level of organization is the **organ system level**. Organs that work together to accomplish a common purpose make up an *organ system*. For example, the heart and blood vessels of the cardiovascular system circulate blood continuously to carry oxygen and nutrients to all body cells. Besides the cardiovascular system, the other organ systems of the body are the integumentary, skeletal, muscular, nervous, endocrine, lymphatic, respiratory, digestive, urinary, and reproductive systems. (Note that the immune system is closely associated with the lymphatic system.) Look ahead to Figure 1.4 on pp. 38–39 for an overview of the 11 organ systems.

The highest level of organization is the *organism*, the living human being. The **organismal level** represents the sum total of all structural levels working together to keep us alive.

Check Your Understanding

4. What level of structural organization is typical of a cytologist's field of study?
5. What is the correct structural order for the following terms: tissue, organism, organ, cell?

For answers, see Answers Appendix.

1.3 What are the requirements for life?

Learning Outcomes

- **List the functional characteristics necessary to maintain life in humans.**
- **List the survival needs of the body.**

Necessary Life Functions

Now that you know the structural levels of the human body, the question that naturally follows is: What does this highly organized human body do?

Like all complex animals, humans maintain their boundaries, move, respond to environmental changes, take in and digest nutrients, carry out metabolism, dispose of wastes, reproduce themselves, and grow. We will introduce these necessary life functions here and discuss them in more detail in later chapters.

We cannot emphasize too strongly that all body cells are interdependent. This interdependence is due to the fact that humans are multicellular organisms and our vital body functions are parceled out among different organ systems. Organ systems, in turn, work cooperatively to promote the well-being of the entire body. **Figure 1.3** identifies some of the organ systems making major contributions to necessary life functions. Also, as you read this section, check **Figure 1.4** on pp. 38–39 for more detailed descriptions of the body's organ systems.

(Text continues on p. 40.)

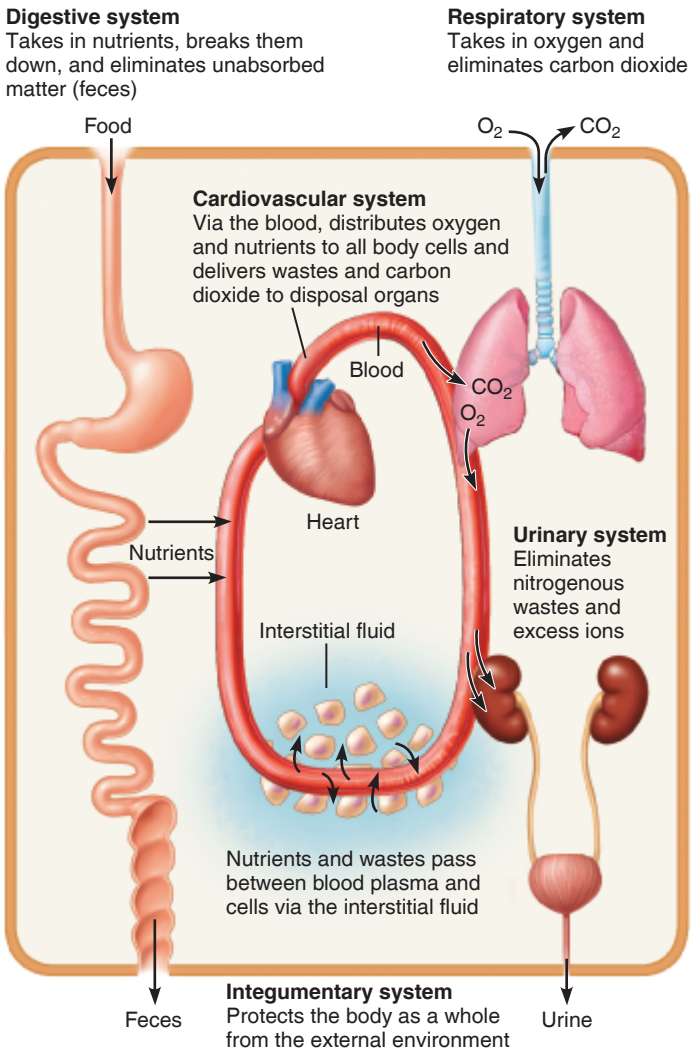
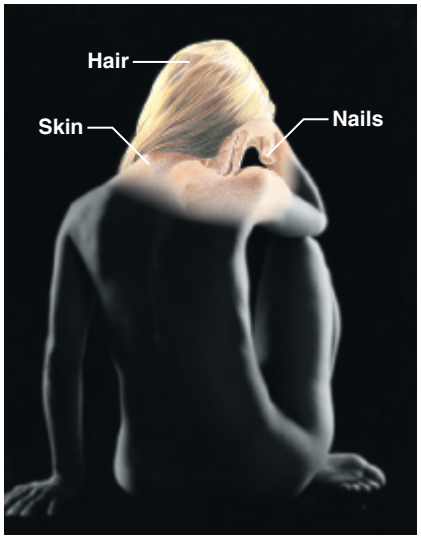
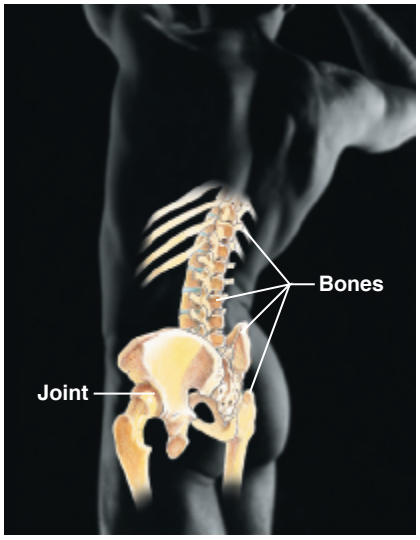


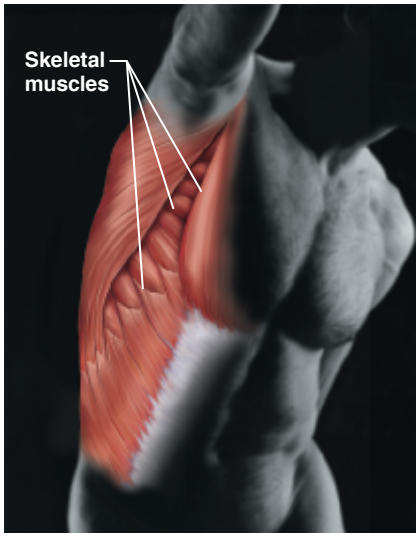
Figure 1.3 Examples of interrelationships among body organ systems.



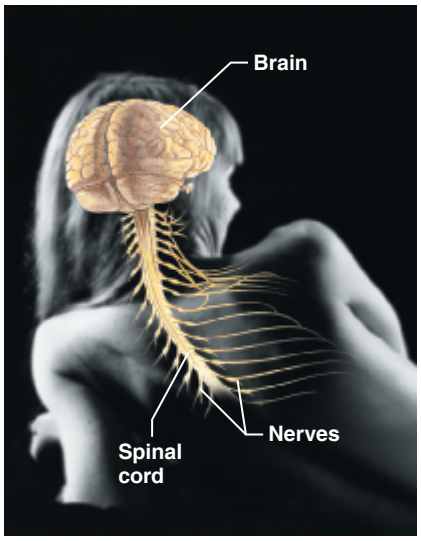
(a) Integumentary System
Forms the external body covering, and protects deeper tissues from injury. Synthesizes vitamin D, and houses cutaneous (pain, pressure, etc.) receptors, and sweat and oil glands.



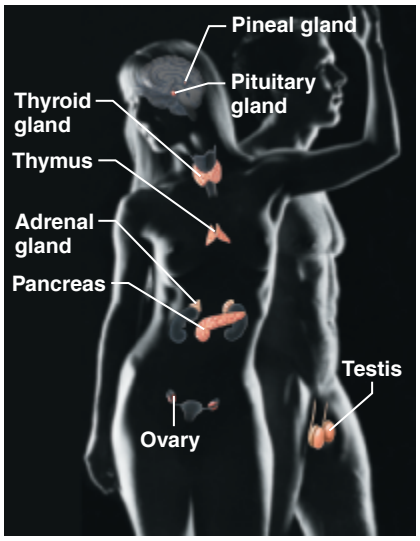
(b) Skeletal System
Protects and supports body organs, and provides a framework the muscles use to cause movement. Blood cells are formed within bones. Bones store minerals.



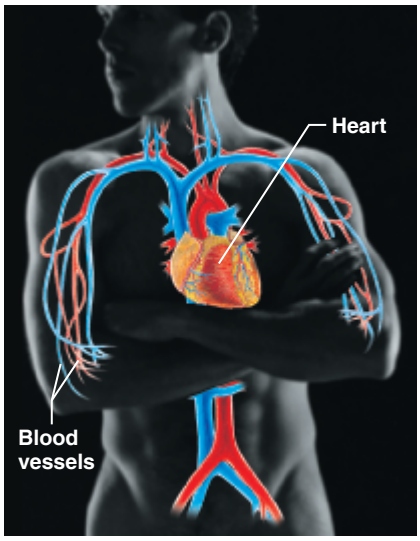
(c) Muscular System
Allows manipulation of the environment, locomotion, and facial expression. Maintains posture, and produces heat.



(d) Nervous System
As the fast-acting control system of the body, it responds to internal and external changes by activating appropriate muscles and glands.

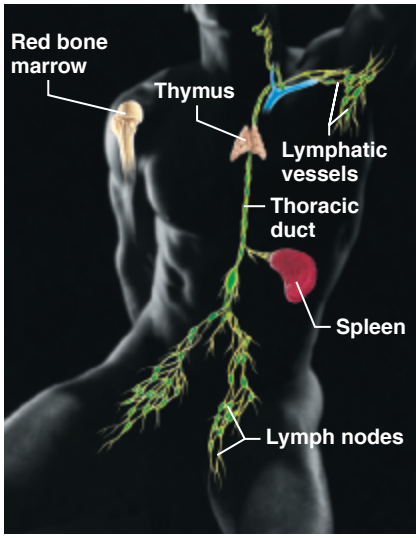


(e) Endocrine System
Glands secrete hormones that regulate processes such as growth, reproduction, and nutrient use (metabolism) by body cells.

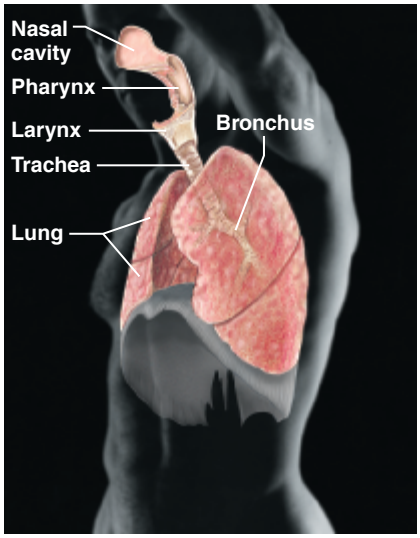


(f) Cardiovascular System
Blood vessels transport blood, which carries oxygen, carbon dioxide, nutrients, wastes, etc. The heart pumps blood.

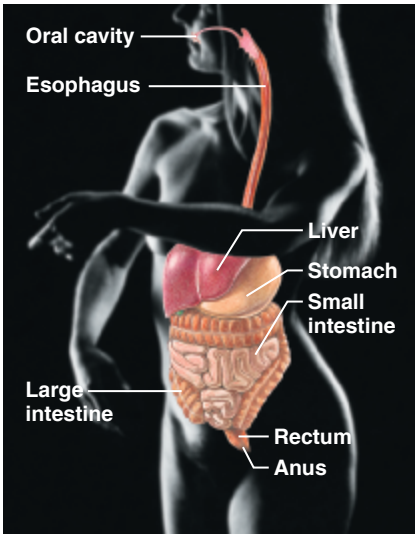
Figure 1.4 The body's organ systems and their major functions.



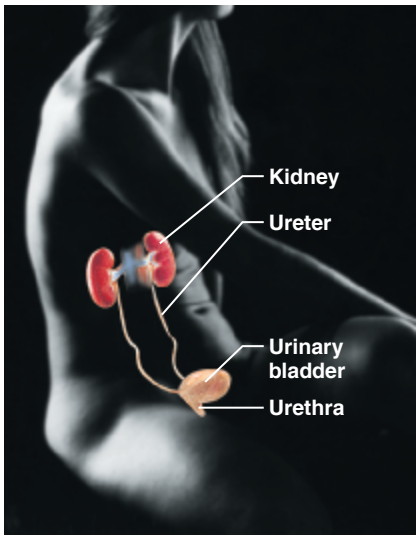
(g) Lymphatic System/Immunity
Picks up fluid leaked from blood vessels and returns it to blood. Disposes of debris in the lymphatic stream. Houses white blood cells (lymphocytes) involved in immunity. The immune response mounts the attack against foreign substances within the body.



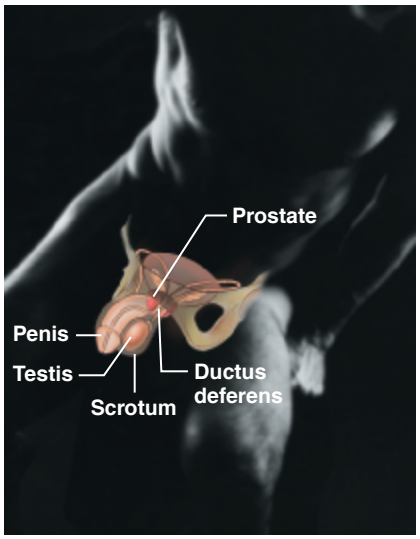
(h) Respiratory System
Keeps blood constantly supplied with oxygen and removes carbon dioxide. These exchanges occur through the walls of the air sacs of the lungs.



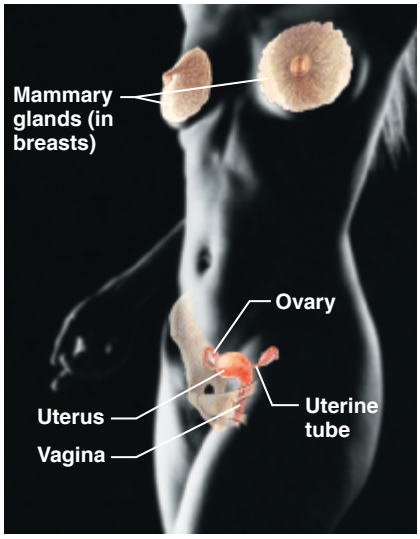
(i) Digestive System
Breaks down food into absorbable units that enter the blood for distribution to body cells. Indigestible foodstuffs are eliminated as feces.



(j) Urinary System
Eliminates nitrogenous wastes from the body. Regulates water, electrolyte, and acid-base balance of the blood.



(k) Male Reproductive System



(l) Female Reproductive System

Overall function is production of offspring. Testes produce sperm and male sex hormone, and male ducts and glands aid in delivery of sperm to the female reproductive tract. Ovaries produce eggs and female sex hormones. The remaining female structures serve as sites for fertilization and development of the fetus. Mammary glands of female breasts produce milk to nourish the newborn.

Figure 1.4 *(continued)*

Maintaining Boundaries

Every living organism must **maintain its boundaries** so that its internal environment (its inside) remains distinct from the external environment (its outside). In single-celled organisms, the external boundary is a limiting membrane that encloses its contents and lets in needed substances while restricting entry of potentially damaging or unnecessary substances. Similarly, all body cells are surrounded by a selectively permeable *plasma membrane*.

The plasma membrane separates the *intracellular fluid* inside cells from the *extracellular fluid* outside. Part of the extracellular fluid (blood *plasma*) is enclosed in blood vessels. The remainder, the *interstitial fluid*, surrounds and bathes all of our cells (see Figure 1.3 on p. 37).

Another important boundary, the integumentary system, or skin, encloses the body as a whole (Figure 1.4a). This system protects our internal organs from drying out (a fatal change), infection, and the damaging effects of heat, sunlight, and an unbelievable number of chemicals in the external environment.

Movement

Movement includes the activities promoted by the muscular system, such as propelling ourselves from one place to another by running or swimming, and manipulating the external environment with our nimble fingers (Figure 1.4c). The skeletal system provides the bony framework that the muscles pull on as they work (Figure 1.4b). Movement also occurs when substances such as blood, foodstuffs, and urine are propelled through internal organs of the cardiovascular, digestive, and urinary systems, respectively. On the cellular level, the muscle cell's ability to move by shortening is more precisely called **contractility**.

Responsiveness

Responsiveness, or **excitability**, is the ability to sense changes (stimuli) in the environment and then respond to them. For example, if you cut your hand on broken glass, a *withdrawal reflex* occurs—you involuntarily pull your hand away from the painful stimulus (the broken glass). You don't have to think about it—it just happens! Likewise, when carbon dioxide in your blood rises to dangerously high levels, chemical sensors respond by sending messages to brain centers controlling respiration, and you breathe more rapidly.

Because nerve cells are highly excitable and communicate rapidly with each other via electrical impulses, the nervous system is most involved with responsiveness (Figure 1.4d). However, all body cells are excitable to some extent.

Digestion

Digestion is the breaking down of ingested foodstuffs to simple molecules that can be absorbed into the blood. The nutrient-rich blood is then distributed to all body cells by the cardiovascular system. In a simple, one-celled organism such as an amoeba, the cell itself is the "digestion factory," but in the multicellular human body, the digestive system performs this function for the entire body (Figure 1.4i).

Metabolism

Metabolism (mĕ-tab′o-lizm; "a state of change") is a broad term that includes all chemical reactions that occur within body cells. It includes breaking down substances into simpler building blocks (the process of *catabolism*), synthesizing more complex substances from simpler building blocks (*anabolism*), and using nutrients and oxygen to produce (via *cellular respiration*) ATP, the energy-rich molecules that power cellular activities. Metabolism depends on the digestive and respiratory systems to make nutrients and oxygen available to the blood, and on the cardiovascular system to distribute them throughout the body (Figure 1.4i, h, and f, respectively). Metabolism is regulated largely by hormones secreted by endocrine system glands (Figure 1.4e).

Excretion

Excretion is the process of removing wastes, or *excreta* (ek-skre′tah), from the body. If the body is to operate as we expect it to, it must get rid of nonuseful substances produced during digestion and metabolism.

Several organ systems participate in excretion. For example, the digestive system rids the body of indigestible food residues in feces, and the urinary system disposes of nitrogen-containing metabolic wastes, such as urea, in urine (Figure 1.4i and j). Carbon dioxide, a by-product of cellular respiration, is carried in the blood to the lungs, where it leaves the body in exhaled air (Figure 1.4h).

Reproduction

Reproduction occurs at the cellular and the organismal level. In cellular reproduction, the original cell divides, producing two identical daughter cells that may then be used for body growth or repair. Reproduction of the human organism, or making a whole new person, is the major task of the reproductive system. When a sperm unites with an egg, a fertilized egg forms and develops into a baby within the mother's body. The reproductive system is directly responsible for producing offspring, but its function is exquisitely regulated by hormones of the endocrine system (Figure 1.4e).

Because males produce sperm and females produce eggs (ova), there is a division of labor in reproduction, and the reproductive organs of males and females are different (Figure 1.4k, l). Additionally, the female's reproductive structures provide the site for fertilization of eggs by sperm, and then protect and nurture the developing fetus until birth.

Growth

Growth is an increase in size of a body part or the organism as a whole. It is usually accomplished by increasing the number of cells. However, individual cells also increase in size when not dividing. For true growth to occur, constructive activities must occur at a faster rate than destructive ones.

Survival Needs

The ultimate goal of all body systems is to maintain life. However, life is extraordinarily fragile and requires several factors.

These **survival needs** include nutrients (food), oxygen, water, and appropriate temperature and atmospheric pressure.

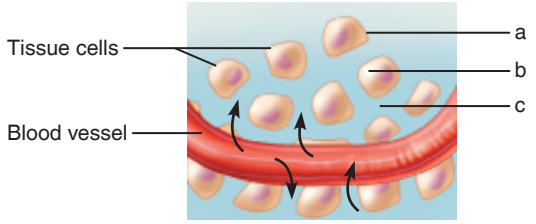
- **Nutrients. Nutrients**, taken in via the diet, contain the chemical substances used for energy and cell building. Most plant-derived foods are rich in carbohydrates, vitamins, and minerals, whereas most animal foods are richer in proteins and fats.

  Carbohydrates are the major energy fuel for body cells. Proteins, and to a lesser extent fats, are essential for building cell structures. Fats also provide a reserve of energy-rich fuel. Selected minerals and vitamins are required for the chemical reactions that go on in cells and for oxygen transport in the blood. The mineral calcium helps to make bones hard and is required for blood clotting.
- **Oxygen.** All the nutrients in the world are useless unless **oxygen** is also available. Because the chemical reactions that release energy from foods are *oxidative* reactions that require oxygen, human cells can survive for only a few minutes without oxygen. Approximately 20% of the air we breathe is oxygen. The cooperative efforts of the respiratory and cardiovascular systems make oxygen available to the blood and body cells.
- **Water. Water** accounts for 50–60% of our body weight and is the single most abundant chemical substance in the body. It provides the watery environment necessary for chemical reactions and the fluid base for body secretions and excretions. We obtain water from ingested foods and liquids. We lose it from the body by evaporation from the lungs and skin and in body excretions.
- **Normal body temperature.** If chemical reactions are to continue at life-sustaining rates, **normal body temperature** must be maintained. As body temperature drops below 37°C (98.6°F), metabolic reactions become slower and slower, and finally stop. When body temperature is too high, chemical reactions occur at a frantic pace and body systems stop functioning. At either extreme, death occurs. The activity of the muscular system generates most body heat.
- **Appropriate atmospheric pressure. Atmospheric pressure** is the force that air exerts on the surface of the body. Breathing and gas exchange in the lungs depend on *appropriate* atmospheric pressure. At high altitudes, where atmospheric pressure is lower and the air is thin, gas exchange may be inadequate to support cellular metabolism.

The mere presence of these survival factors is not sufficient to sustain life. They must be present in the proper amounts. Too much and too little may be equally harmful. For example, oxygen is essential, but excessive amounts are toxic to body cells. Similarly, the food we eat must be of high quality and in proper amounts. Otherwise, nutritional disease, obesity, or starvation is likely. Also, while the needs listed here are the most crucial, they do not even begin to encompass all of the body's needs. For example, we can live without gravity if we must, but the quality of life suffers.

Check Your Understanding

6. What separates living beings from nonliving objects?
7. What name is given to all chemical reactions that occur within body cells?
8. The image below shows tissue cells and part of a blood vessel. The cells' nutrients and wastes are exchanged across an important boundary between two fluid compartments. Name the boundary (a) and the fluid in the compartments (b and c). Be specific.



For answers, see Answers Appendix.

1.4 Homeostasis is maintained by negative feedback

Learning Outcomes

- **Define homeostasis and explain its significance.**
- **Describe how negative and positive feedback maintain body homeostasis.**
- **Describe the relationship between homeostatic imbalance and disease.**

When you think about the fact that your body contains trillions of cells in nearly constant activity, and that remarkably little usually goes wrong with it, you begin to appreciate what a marvelous machine your body is. Walter Cannon, an American physiologist of the early twentieth century, spoke of the "wisdom of the body," and he coined the word **homeostasis** (ho″me-o-sta′sis) to describe its ability to maintain relatively stable internal conditions even though the outside world changes continuously.

Although the literal translation of homeostasis is "unchanging," the term does not really mean a static, or unchanging, state. Rather, it indicates a *dynamic* state of equilibrium, or a balance, in which internal conditions vary, but always within relatively narrow limits. In general, the body is in homeostasis when its needs are adequately met and it is functioning smoothly.

Maintaining homeostasis is more complicated than it appears at first glance. Virtually every organ system plays a role in maintaining the constancy of the internal environment. Adequate blood levels of vital nutrients must be continuously present, and heart activity and blood pressure must be constantly monitored and adjusted so that the blood is propelled to all body tissues. Also, wastes must not be allowed to accumulate, and body temperature must be precisely controlled. A wide variety of chemical, thermal, and neural factors act and interact in complex ways—sometimes helping and sometimes hindering the body as it works to maintain its "steady rudder."

Homeostatic Control

Communication within the body is essential for homeostasis. Communication is accomplished chiefly by the nervous and endocrine systems, which use neural electrical impulses or bloodborne hormones, respectively, as information carriers. We cover the details of how these two great regulating systems operate in later chapters, but here we explain the basic characteristics of control systems that promote homeostasis.

The **variable** is the factor or event being regulated. All homeostatic control mechanisms are processes involving at least three components that work together to regulate the variable (**Figure 1.5**).

1. The **receptor** is the first component. It is a sensor that monitors the environment. It responds to *stimuli* (changes) by sending information (input) along the *afferent pathway* to the second component, the *control center*.
2. The **control center** determines the *set point*, which is the level (or range of levels) at which a variable is to be maintained. It analyzes the input it receives by comparing it to the set point and determines the appropriate response. Information (output) then flows from the control center along the *efferent pathway* to the third component, the *effector*. (To help you remember the difference between "afferent" and "efferent," note that information traveling along the afferent pathway *approaches* the control center and efferent information *exits* from the control center.)
3. The **effector** carries out the control center's response to the stimulus. The results of the response then *feed back* to influence the effect of the stimulus, either reducing it so that the whole control process is shut off, or enhancing it so that the whole process continues at an even faster rate.

Negative Feedback Mechanisms

Most homeostatic control mechanisms are **negative feedback mechanisms**. In these systems, the output shuts off the original effect of the stimulus or reduces its intensity. These mechanisms cause the variable to change in a direction *opposite* to that of the initial change, returning it to its "ideal" value.

Let's start with an example of a nonbiological negative feedback system: a home heating system connected to a temperature-sensing thermostat. The thermostat houses both the receptor (thermometer) and the control center. If the thermostat is set at 20°C (68°F), the heating system (effector) is triggered ON when the house temperature drops below that setting. As the furnace produces heat and warms the air, the temperature rises, and when it reaches 20°C or slightly higher, the thermostat triggers the furnace OFF. This process results in a cycling of the furnace between "ON" and "OFF" so that the temperature in the house stays very near the desired temperature. Your body "thermostat," located in a part of your brain called the hypothalamus, operates in a similar fashion (**Figure 1.6**).

Regulation of body temperature is only one of the many ways the nervous system maintains the constancy of the internal environment. Another type of neural control mechanism is seen in the *withdrawal reflex* mentioned earlier, in which the hand is jerked away from a painful stimulus such as broken glass.

The endocrine system is equally important in maintaining homeostasis. A good example of a hormonal negative feedback mechanism is the control of blood sugar (glucose) by insulin. As blood sugar rises, receptors in the body sense this change, and the pancreas (the control center) secretes insulin into the blood. This change in turn prompts body cells to absorb more glucose, removing it from the bloodstream. As blood sugar falls, the stimulus for insulin release ends.

The body's ability to regulate its internal environment is fundamental. All negative feedback mechanisms have the same goal: preventing severe changes within the body. Body temperature and blood sugar are only two of the variables that need to

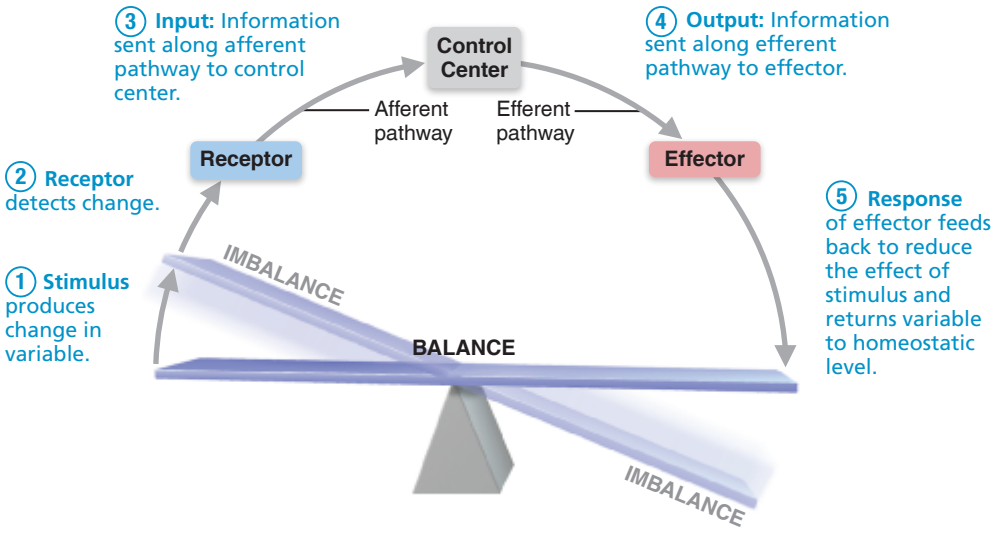


Figure 1.5 Interactions among the elements of a homeostatic control system maintain stable internal conditions.

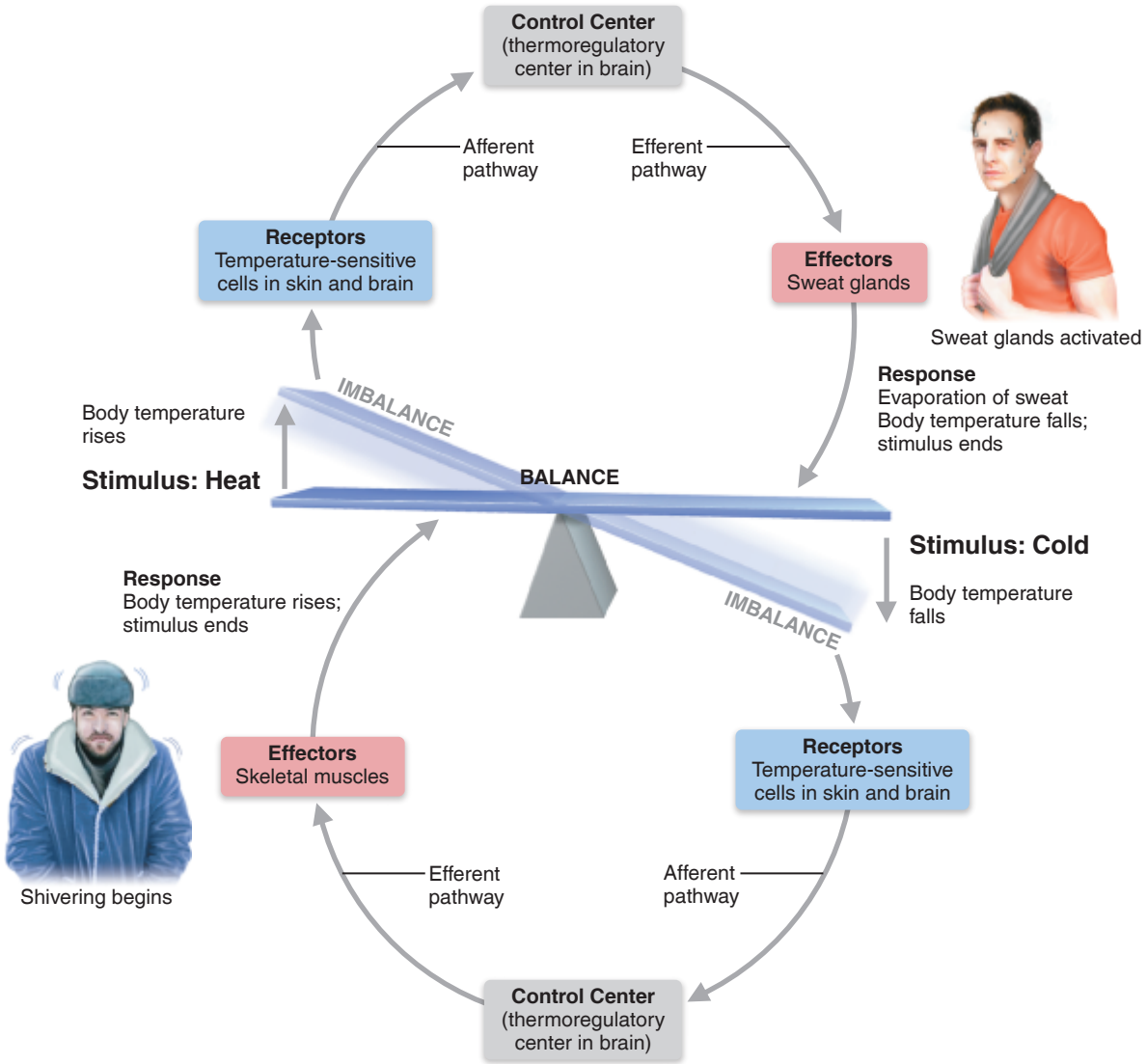


Figure 1.6 **Body temperature is regulated by a negative feedback mechanism.**

be regulated. There are many! Other negative feedback mechanisms regulate heart rate, blood pressure, the rate and depth of breathing, and blood levels of oxygen, carbon dioxide, and minerals.

Positive Feedback Mechanisms

In **positive feedback mechanisms**, the initial response enhances the original stimulus so that further responses are even greater. This feedback mechanism is "positive" because the change that results proceeds in the *same* direction as the initial change, causing the variable to deviate further and further from its original value or range.

In contrast to negative feedback controls, which maintain some physiological function or keep blood chemicals within narrow ranges, positive feedback mechanisms usually control infrequent events that do not require continuous adjustments. Typically, they set off a linked sequence of events. Once initiated, the results of each reaction feed into the next like a series of waterfalls on a river. Because of these characteristics, positive feedback mechanisms are often referred to as *cascades* (from the Italian word meaning "to fall") that amplify the original stimulus. Two familiar examples are the enhancement of labor contractions during birth and blood clotting.

Chapter 28 describes the positive feedback mechanism in which oxytocin, a hypothalamic hormone, intensifies labor contractions during the birth of a baby (see Figure 28.16, p. 1146). Oxytocin causes the contractions to become both more frequent and more powerful. The increased contractions cause more oxytocin to be released, which causes more contractions, and so on until the baby is born. The birth ends the stimulus for oxytocin release and shuts off the positive feedback mechanism.

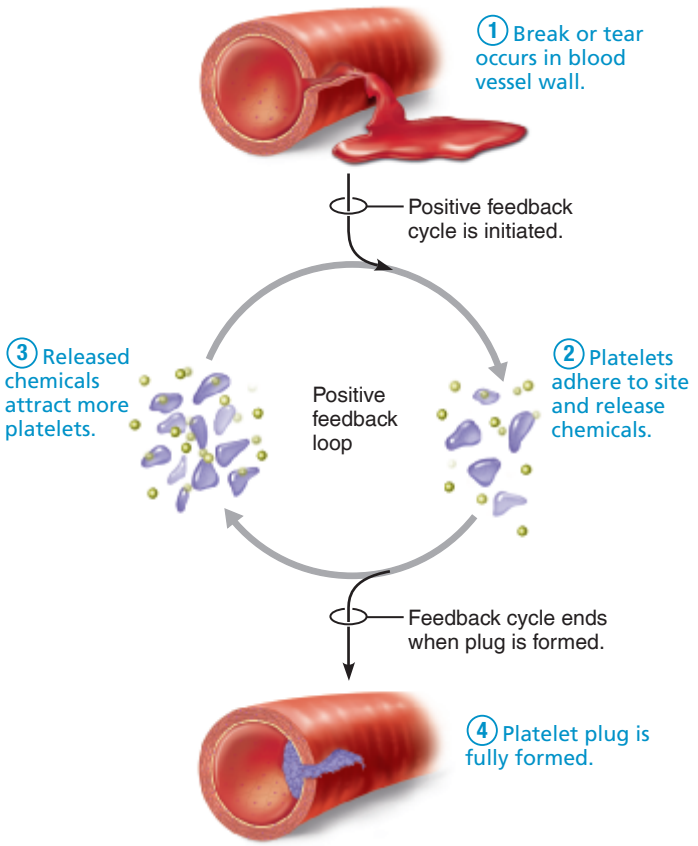


Figure 1.7 A positive feedback mechanism regulates formation of a platelet plug.

Blood clotting is a normal response to a break in the wall of a blood vessel and is an excellent example of an important body function controlled by positive feedback. Once a vessel has been damaged, blood elements called platelets immediately begin to cling to the injured site and release chemicals that attract more platelets. This rapidly growing pileup of platelets temporarily "plugs" the tear and initiates the sequence of events that finally forms a clot (**Figure 1.7**).

Positive feedback mechanisms are likely to race out of control, so they are rarely used to promote the moment-to-moment well-being of the body. Some positive feedback mechanisms, including this one, may have only local effects. For example, blood clotting is accelerated in injured vessels, but does not normally spread to the entire circulation.

Homeostatic Imbalance

Homeostasis is so important that most disease can be regarded as a result of its disturbance, a condition called **homeostatic imbalance**. As we age, our body's control systems become less efficient, and our internal environment becomes less and less stable. These events increase our risk for illness and produce the changes we associate with aging.

Another important source of homeostatic imbalance occurs when the usual negative feedback mechanisms are overwhelmed and destructive positive feedback mechanisms take over. Some instances of heart failure reflect this phenomenon.

Examples of homeostatic imbalance appear throughout this book to enhance your understanding of normal physiological mechanisms. This symbol  introduces the homeostatic imbalance sections and alerts you to the fact that we are describing an abnormal condition. Each Homeostatic Imbalance section is numbered to correspond with critical thinking questions available in the Study Area of Mastering A&P®—visit the website to find Homeostatic Imbalance questions and other helpful study tools.

Check Your Understanding

9. What process allows us to adjust to either extreme heat or extreme cold?

10. Why is the control system shown in Figure 1.7 called a positive feedback mechanism? What event ends it?

11. APPLY When we begin to get dehydrated, we usually get thirsty, which causes us to drink fluids. Is thirst part of a negative or a positive feedback control system? Explain your choice.

For answers, see Answers Appendix.

1.5 Anatomical terms describe body directions, regions, and planes

Learning Outcomes

- **Describe the anatomical position.**
- **Use correct anatomical terms to describe body directions, regions, and body planes or sections.**

Most of us are naturally curious about our bodies, but our interest sometimes dwindles when we are confronted with the terminology of anatomy and physiology. Let's face it—you can't just pick up an anatomy and physiology book and read it as though it were a novel. Unfortunately, confusion is likely without precise, specialized terminology. To prevent misunderstanding, anatomists use universally accepted terms to identify body structures precisely and with a minimum of words. We present and explain the language of anatomy next.

Anatomical Position and Directional Terms

To describe body parts and position accurately, we need an initial reference point, and we must indicate direction. The anatomical reference point is a standard body position called the **anatomical position**. In the anatomical position, the body is erect with feet slightly apart. This position is easy to remember because it resembles "standing at attention," except that the palms face forward and the thumbs point away from the body. You can see the anatomical position in **Figure 1.8a** and **Table 1.1** (top) on p. 46.

It is essential to understand the anatomical position because most of the directional terms used in this book refer to the body

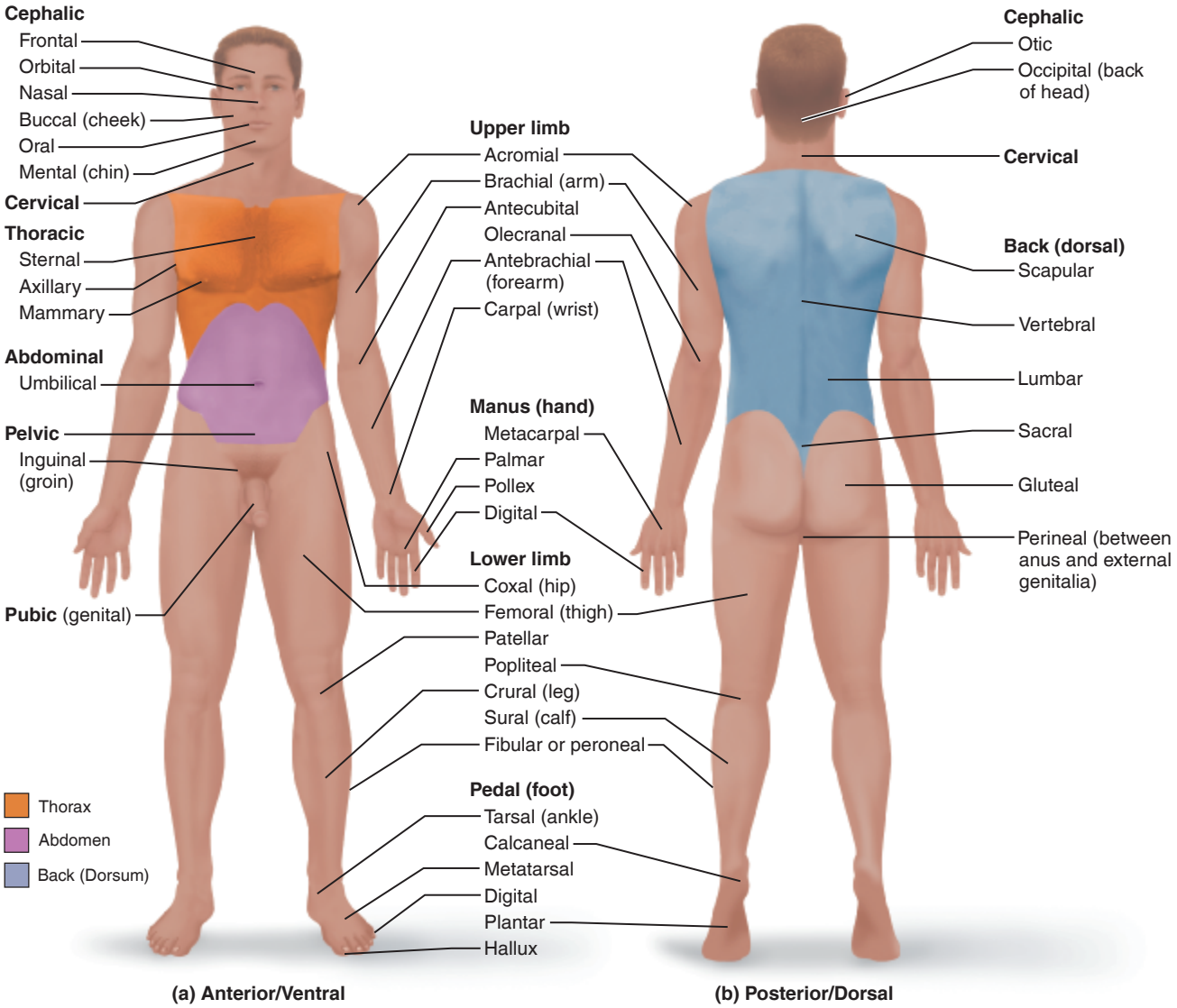


Figure 1.8 Regional terms used to designate specific body areas. Common terms are shown in parentheses. **(a)** Anatomical position. **(b)** The heels are raised to show the plantar surface of the foot.

as if it were in this position, regardless of its actual position. Another point to remember is that the terms "right" and "left" refer to those sides of the person or the cadaver being viewed—not those of the observer.

Directional terms allow us to explain where one body structure is in relation to another. For example, we could describe the relationship between the ears and the nose by stating, "The ears are located on each side of the head to the right and left of the nose." Using anatomical terminology, this becomes "The ears are lateral to the nose." Using anatomical terms saves words and is less ambiguous.

Commonly used orientation and directional terms are defined and illustrated in Table 1.1. Many of these terms are also used in everyday conversation, but remember as you study them that their anatomical meanings are very precise.

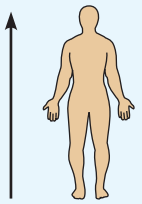
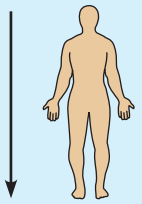
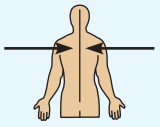
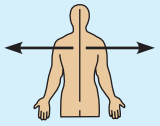
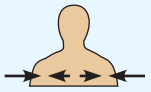
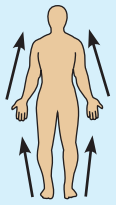
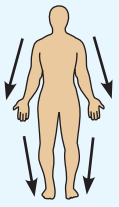
Regional Terms

The two fundamental divisions of our body are its *axial* and *appendicular* (ap″en-dik′u-lar) parts. The **axial part**, which makes up the main *axis* of our body, includes the head, neck, and trunk. The **appendicular part** consists of the *appendages*, or *limbs*, which are attached to the body's axis. **Regional terms** used to designate specific areas within these major body divisions are indicated in Figure 1.8.

Body Planes and Sections

For anatomical studies, the body is often cut, or *sectioned*, along a flat surface called a *plane*. The most frequently used body planes are *sagittal*, *frontal*, and *transverse* planes, which

Table 1.1 Orientation and Directional Terms

TERM	DEFINITION	EXAMPLE	
Superior (cranial)	Toward the head end or upper part of a structure or the body; above		The head is superior to the abdomen.
Inferior (caudal)	Away from the head end or toward the lower part of a structure or the body; below		The navel is inferior to the chin.
Anterior (ventral)*	Toward or at the front of the body; in front of		The breastbone is anterior to the spine.
Posterior (dorsal)*	Toward or at the back of the body; behind		The heart is posterior to the breastbone.
Medial	Toward or at the midline of the body; on the inner side of		The heart is medial to the arm.
Lateral	Away from the midline of the body; on the outer side of		The arms are lateral to the chest.
Intermediate	Between a more medial and a more lateral structure		The collarbone is intermediate between the breastbone and shoulder.
Proximal	Closer to the origin of the body part or the point of attachment of a limb to the body trunk		The elbow is proximal to the wrist.
Distal	Farther from the origin of a body part or the point of attachment of a limb to the body trunk		The knee is distal to the thigh.
Superficial (external)	Toward or at the body surface		The skin is superficial to the skeletal muscles.
Deep (internal)	Away from the body surface; more internal		The lungs are deep to the skin.

*The terms *ventral* and *anterior* are synonymous in humans, but this is not the case in four-legged animals. *Anterior* refers to the leading portion of the body (abdominal surface in humans, head in a cat), but *ventral* specifically refers to the "belly" of a vertebrate animal, so it is the inferior surface of four-legged animals. Likewise, although the dorsal and posterior surfaces are the same in humans, the term *dorsal* specifically refers to an animal's back (as in the dorsal fin of a shark). Thus, the dorsal surface of four-legged animals is their superior surface.

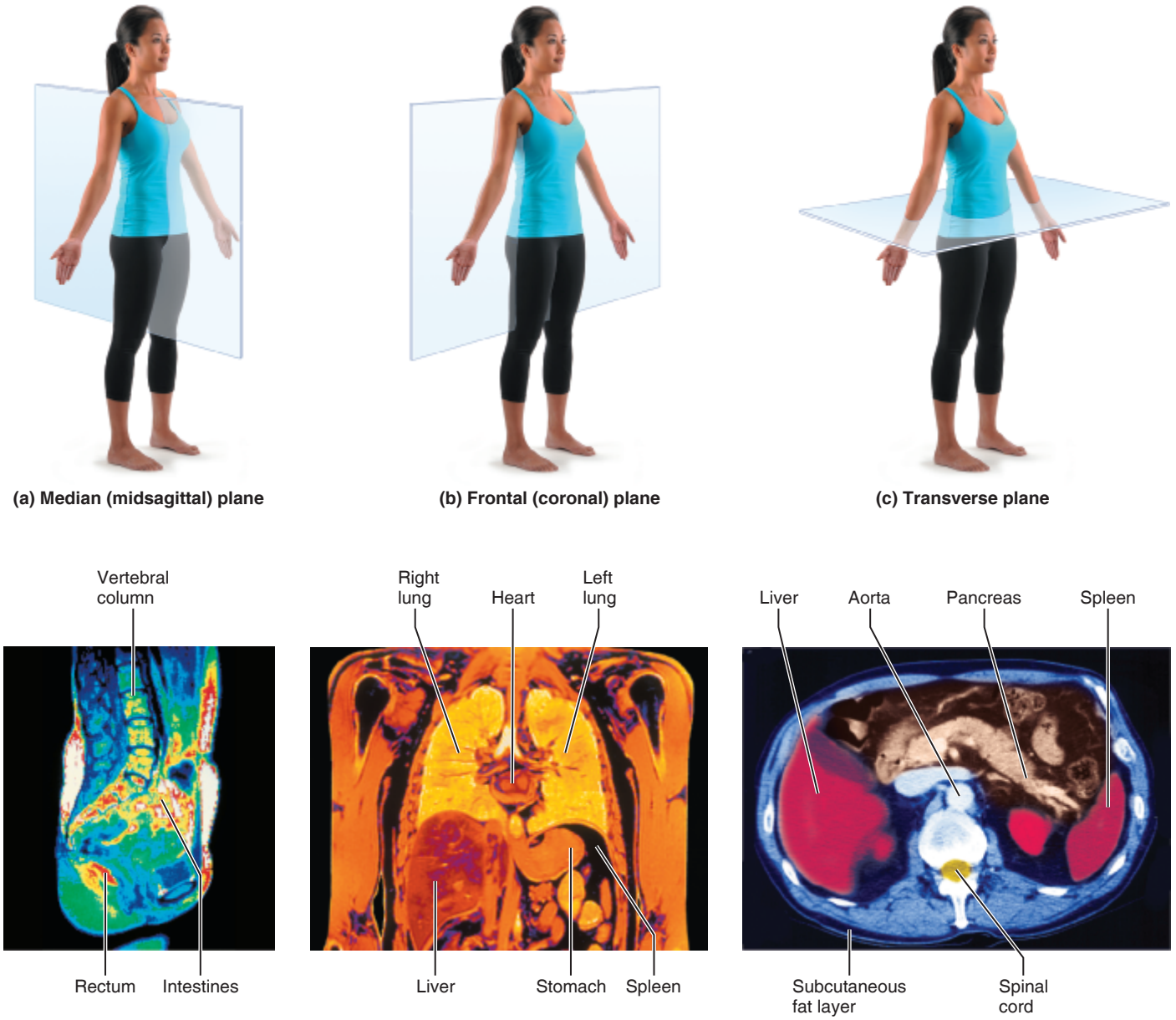


Figure 1.9 **Planes of the body with corresponding magnetic resonance imaging (MRI) scans.**

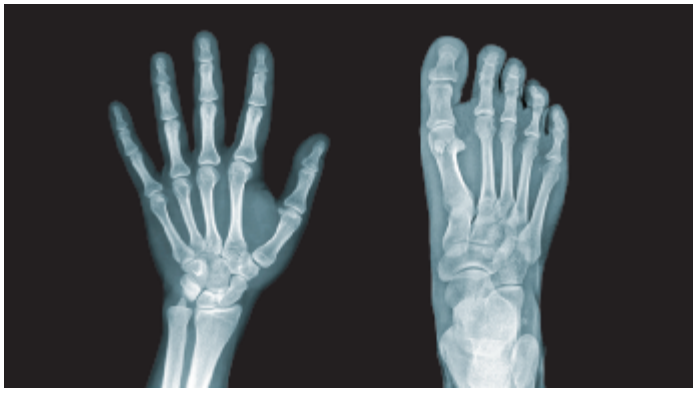
lie at right angles to one another (**Figure 1.9**). A section is named for the plane along which it is cut. Thus, a cut along a sagittal plane produces a sagittal section.

- A **sagittal plane** (saj′ĭ-tal; "arrow") is a vertical plane that divides the body into right and left parts. A sagittal plane that lies exactly in the midline is the **median plane**, or **midsagittal plane** (Figure 1.9a). All other sagittal planes, offset from the midline, are **parasagittal planes** (*para* = near).
- **Frontal planes**, like sagittal planes, lie vertically. Frontal planes, however, divide the body into anterior and posterior parts (Figure 1.9b). A frontal plane is also called a **coronal plane** (kŏ-ro′nal; "crown").
- A **transverse**, or **horizontal**, **plane** runs horizontally from right to left, dividing the body into superior and inferior parts (Figure 1.9c). Of course, many different transverse planes exist, at every possible level from head to foot. A transverse section is also called a **cross section**.
- **Oblique sections** are cuts made diagonally between the horizontal and the vertical planes. Because oblique sections are often confusing and difficult to interpret, they are seldom used.

Figure 1.9 includes examples of magnetic resonance imaging (MRI) scans that correspond to the three sections shown in the figure. Clinically, the ability to interpret sections made through the body, especially transverse sections, is important. Additionally, certain medical imaging devices (*A Closer Look*, pp. 48–49) produce sectional images rather than three-dimensional images.

It takes practice to determine an object's overall shape from sectioned material. Sectioning the body or an organ along different planes often results in very different views. For example,

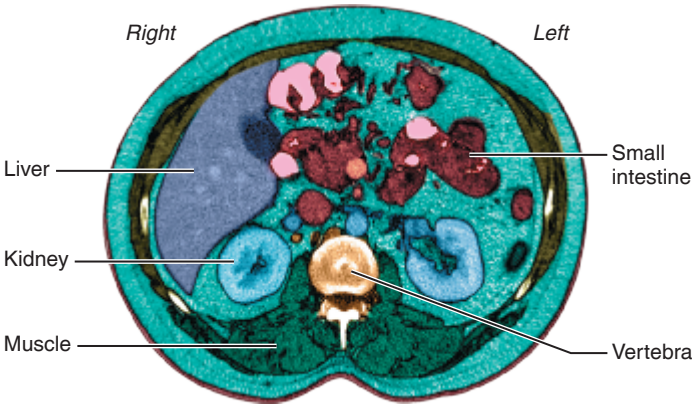
Medical Imaging: Illuminating the Body



X rays of a hand and foot

X-Ray Imaging

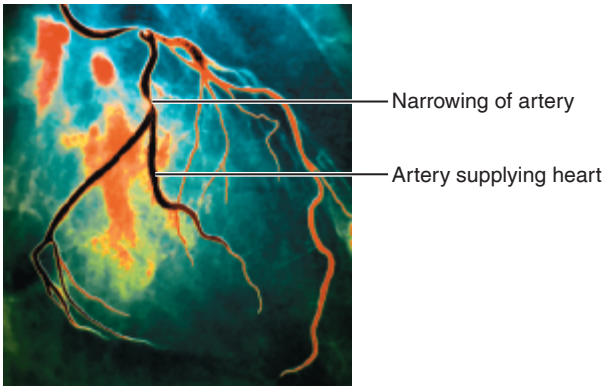
- Uses X rays (very short-wavelength electromagnetic waves).
- Dense structures (e.g., bones) appear as light areas.
- Hollow air-containing organs (e.g., lungs) and fat appear as dark areas.
- **Used for:** Detecting broken bones; finding breast tumors (mammography); measuring density of bones to screen for osteoporosis (porous bones).
- **Not used for:** Most soft tissue problems except when used with a contrast medium such as barium.
- **Cons:** Radiation exposure; images are two-dimensional.



CT scan of the abdomen. By convention, cross sections such as this are shown as if the patient were lying on their back and viewed from the feet toward the head.

Computed Tomography (CT) Scans

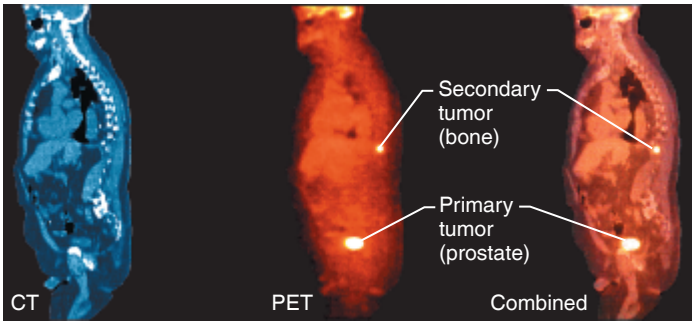
- Computerized reconstruction of a series of X-ray images.
- Provide detailed cross-sectional pictures of scanned body regions.
- **Used for:** Images of bone, soft tissues, and blood vessels.
- **Less useful for:** Nervous tissue and joint structure (e.g., knee and shoulder).
- **Cons:** More radiation exposure than X rays—may be a concern if used repeatedly.



A DSA image of the arteries that supply the heart.

Digital Subtraction Angiography

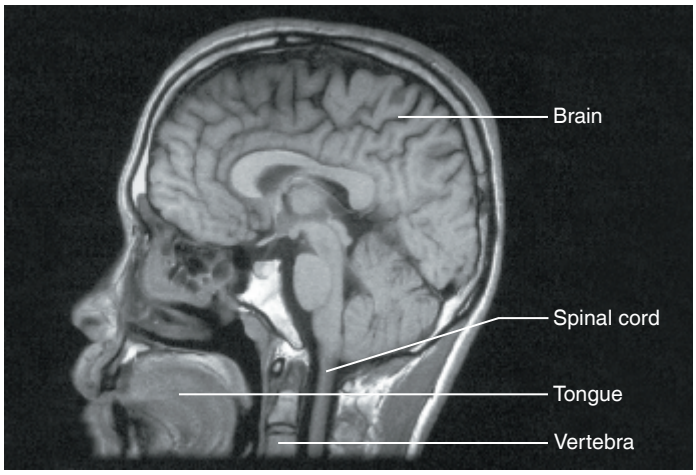
- Angiography is visualizing blood vessels (*angi* = vessel) by X ray or CT scan.
- Requires injection of an X-ray-absorbing contrast agent.
- Digitally subtracting images from before and after injection of the contrast agent yields very clear images of blood vessels.
- **Used for:** Detecting blood vessel abnormalities such as blockages in the arteries that supply the heart.
- **Cons:** Time-consuming and expensive. Adverse reactions to the contrast medium can occur.



PET scans are used to monitor the spread of cancers. In this case, a CT scan (left) and PET scan (center) are combined to create the final image (right).

Positron Emission Tomography (PET) Scans

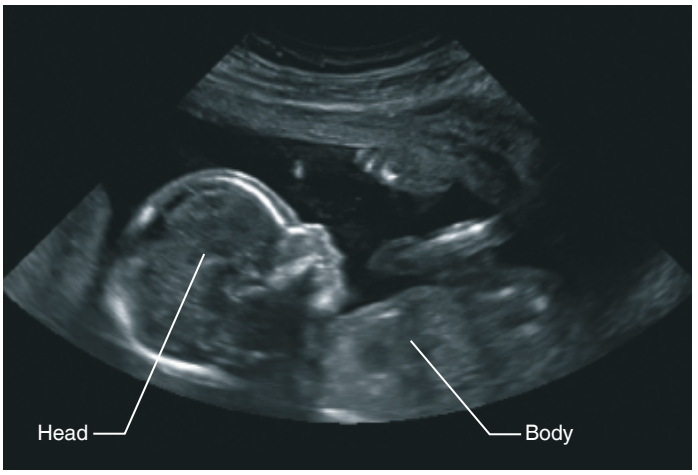
- Uses gamma rays that are emitted by radioactively tagged tracer molecules that are injected into the body.
- The radioactive tracer molecule used depends on the reason for doing the scan. Radioactive *glucose* is used to locate cells with the highest metabolic activity, such as cancer cells. *Florbetapir* is used to visualize beta-amyloid plaques in the brain that are associated with Alzheimer's disease.
- **Used for:** Detecting the spread of cancer or monitoring the response to cancer treatment. Sometimes used to help diagnose Alzheimer's disease, and as a research tool to explore brain function.
- **Cons:** Radiation exposure; relatively poor image resolution.



MRI showing a midsagittal section of the head.

Magnetic Resonance Imaging (MRI)

- Uses powerful magnets and radio waves to image the location of hydrogen atoms in the body (most of which are in water).
- Distinguishes body tissues based on water content. Structures with low water content such as bones are not readily visible.
- Produces high-contrast images of soft tissues, particularly those that are obscured by bone in CT scans.
- Functional MRI (fMRI) tracks blood flow into various parts of the brain.
- **Used for:** Imaging of brain, spinal cord, and nerves to detect abnormalities such as tumors; assessing joint, ligament, cartilage, and other soft tissues; fMRI allows visualization of the activity in specific brain regions.
- **Not used for:** Bones.
- **Cons:** More expensive and much slower than CT scans. Cannot be used in patients with most types of metal implant.



Ultrasound image of a fetus in the uterus.

Ultrasound Imaging

- Uses high-frequency sound waves that reflect (echo) off of the body's tissues.
- Does not use X rays, so thought to be safe for imaging a developing fetus.
- Can monitor movement in real time (such as heart valve motion and blood flow through vessels and the heart).
- Inexpensive and easy to use.
- **Used for:** Monitoring a fetus during pregnancy; diagnosing abdominal or pelvic disorders such as gallbladder disease; can detect atherosclerosis (thickening and hardening of the arterial walls) and heart valve disorders.
- **Not used for:** Air-filled structures (such as the lungs) and structures surrounded by bone (such as the brain and spinal cord).
- **Cons:** Images tend to be lower resolution (blurry), although their sharpness is being improved.

a transverse section of the body trunk at the level of the kidneys would show kidney structure in cross section very nicely. A frontal section of the body trunk would show a different view of kidney anatomy, and a midsagittal section would miss the kidneys completely. With experience, you will gradually learn to relate two-dimensional sections to three-dimensional shapes.

Check Your Understanding

12. What is the anatomical position? Why is it important that *you* learn this position?

13. The axillary and acromial regions are both in the general area of the shoulder. Where specifically is each located?

14. What type of cut would separate the brain into anterior and posterior parts?

15. DRAW Draw the outline that you would get if you made midsagittal, coronal, and transverse sections of the banana at the right.

For answers, see Answers Appendix.

1.6 Many internal organs lie in membrane-lined body cavities

Learning Outcomes

- **Locate and name the major body cavities and their subdivisions and associated membranes, and list the major organs contained within them.**
- **Name the four quadrants or nine regions of the abdominopelvic cavity and list the organs they contain.**

Anatomy and physiology textbooks typically describe two sets of internal body cavities called the dorsal and ventral body cavities. These cavities are closed to the outside and provide different degrees of protection to the organs within them. Because these two cavities differ in their mode of embryonic development and their lining membranes, the dorsal body cavity is not recognized as such in many anatomical references. However, the idea of two sets of internal body cavities is a useful learning concept and we use it here.

Dorsal Body Cavity

The **dorsal body cavity**, which protects the fragile nervous system organs, has two subdivisions (**Figure 1.10**, gold areas). The **cranial cavity**, in the skull, encases the brain. The **vertebral**, or **spinal**, **cavity**, which runs within the bony vertebral column, encloses the delicate spinal cord. The spinal cord is essentially a continuation of the brain, and the cranial and spinal cavities are continuous with one another. Both the brain and the spinal cord are covered by membranes called meninges.

Ventral Body Cavity

The more anterior and larger of the closed body cavities is the **ventral body cavity** (Figure 1.10, deep-red areas). Like the dorsal cavity, it has two major subdivisions, the *thoracic cavity* and the *abdominopelvic cavity*. The ventral body cavity houses internal organs collectively called the **viscera** (vis′er-ah; *viscus* = an organ in a body cavity), or visceral organs.

The superior subdivision, the **thoracic cavity** (tho-ras′ik), is surrounded by the ribs and muscles of the chest. The thoracic cavity is further subdivided into lateral **pleural cavities** (ploo′ral), each enveloping a lung, and the medial **mediastinum** (me″de-ah-sti′num). The mediastinum contains the **pericardial cavity** (per″ĭ-kar′de-al), which encloses the heart, and it also surrounds the remaining thoracic organs (esophagus, trachea, and others).

The thoracic cavity is separated from the more inferior **abdominopelvic cavity** (ab-dom′ĭ-no-pel′vic) by the diaphragm, a dome-shaped muscle important in breathing. The abdominopelvic cavity, as its name suggests, has two parts. However, these regions are not physically separated by a muscular or membrane wall. Its superior portion, the **abdominal cavity**, contains the stomach, intestines, spleen, liver, and other organs. The inferior part, the **pelvic cavity**, lies in the bony pelvis and contains the urinary bladder, some reproductive organs, and the rectum. The abdominal and pelvic cavities are not aligned with each other. Instead, the bowl-shaped pelvis tips away from the perpendicular as shown in Figure 1.10a.

HOMEOSTATIC IMBALANCE 1.1 CLINICAL

Each body cavity is uniquely suited to house its contents. Problems arrise when a structure strays into a neighboring cavity. A *hiatal hernia* occurs when part of the stomach slides through the diaphragm into the thoracic cavity, allowing stomach acid to cause heartburn (which is actually irritation of the esophagus, not the heart). Severe cases may require surgical repair.

Membranes in the Ventral Body Cavity

The walls of the ventral body cavity and the outer surfaces of the organs it contains are covered by a thin, double-layered membrane, the **serosa** (se-ro′sah), or **serous membrane**.

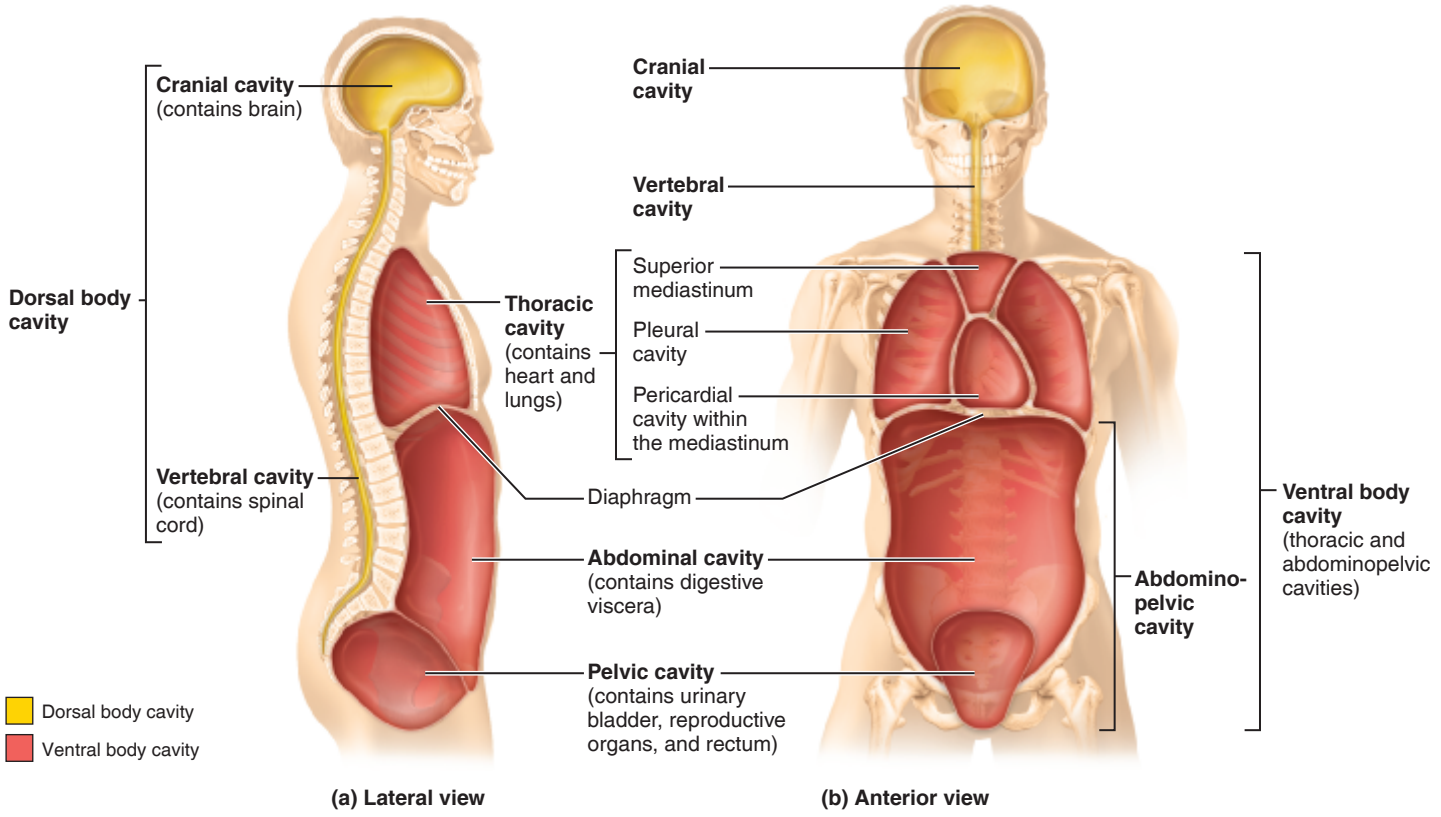
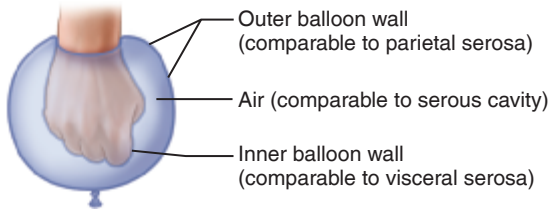
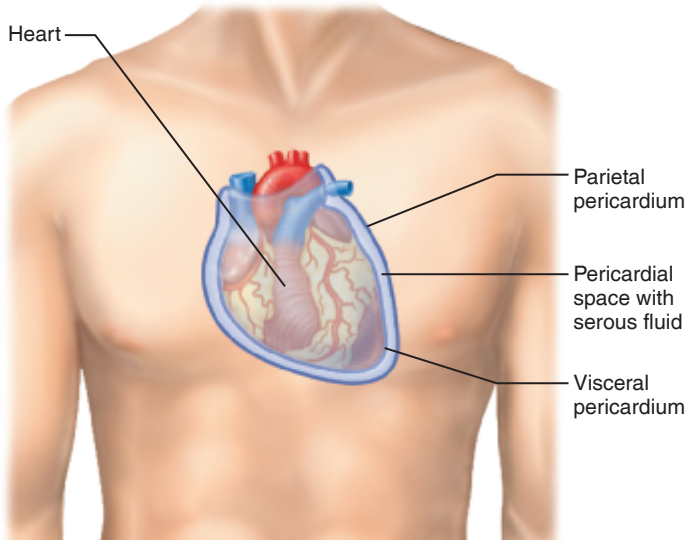


Figure 1.10 Dorsal and ventral body cavities and their subdivisions.



(a) A fist thrust into a flaccid balloon demonstrates the relationship between the parietal and visceral serous membrane layers.



(b) The serosae associated with the heart.

Figure 1.11 Serous membrane relationships.

The part of the membrane lining the cavity walls is called the **parietal serosa** (pah-ri′ĕ-tal; *parie* = wall). It folds in on itself to form the **visceral serosa**, covering the organs in the cavity.

You can visualize the relationship between the serosal layers by pushing your fist into a limp balloon (**Figure 1.11a**). The part of the balloon that clings to your fist can be compared to the visceral serosa clinging to an organ's external surface. The outer wall of the balloon represents the parietal serosa that lines the walls of the cavity. (However, unlike the balloon, the parietal serosa is never exposed but is always fused to the cavity wall.) In the body, the serous membranes are separated not by air but by a thin layer of lubricating fluid, called **serous fluid**, which is secreted by both membranes. Although there is a potential space between the two membranes, the barely present, slitlike *serous cavity* is filled with serous fluid.

The slippery serous fluid allows the organs to slide without friction across the cavity walls and one another as they carry out their routine functions. This freedom of movement is especially important for mobile organs such as the pumping heart and the churning stomach.

The serous membranes are named for the specific cavity and organs with which they are associated. For example, as shown in Figure 1.11b, the *parietal pericardium* lines the pericardial cavity and folds back as the *visceral pericardium*, which covers the heart. Likewise, the *parietal pleurae* (ploo′re) line the walls of the thoracic cavity, and the *visceral pleurae* cover the lungs. The *parietal peritoneum* (per″ĭ-to-ne′um) is associated with the walls of the abdominopelvic cavity, while the *visceral peritoneum* covers most of the organs within that cavity. (The pleural and peritoneal serosae are illustrated in Figure 4.14c on p. 174.)

HOMEOSTATIC IMBALANCE 1.2 CLINICAL

When serous membranes are inflamed, their normally smooth surfaces become roughened. This roughness causes the membranes to stick together and drag across one another. Excruciating pain results, as anyone who has experienced *pleurisy* (inflammation of the pleurae) or *peritonitis* (inflammation of the peritoneums) knows.

Abdominopelvic Regions and Quadrants

Because the abdominopelvic cavity is large and contains several organs, it helps to divide it into smaller areas for study. Medical personnel usually use a simple scheme to locate the abdominopelvic cavity organs (**Figure 1.12**). In this scheme, a transverse and a median plane pass through the umbilicus at right angles. The four resulting quadrants are named according to their positions from the subject's point of view: the **right upper quadrant (RUQ)**, **left upper quadrant (LUQ)**, **right lower quadrant (RLQ)**, and **left lower quadrant (LLQ)**.

Another division method, used primarily by anatomists, uses two transverse and two parasagittal planes. These planes,

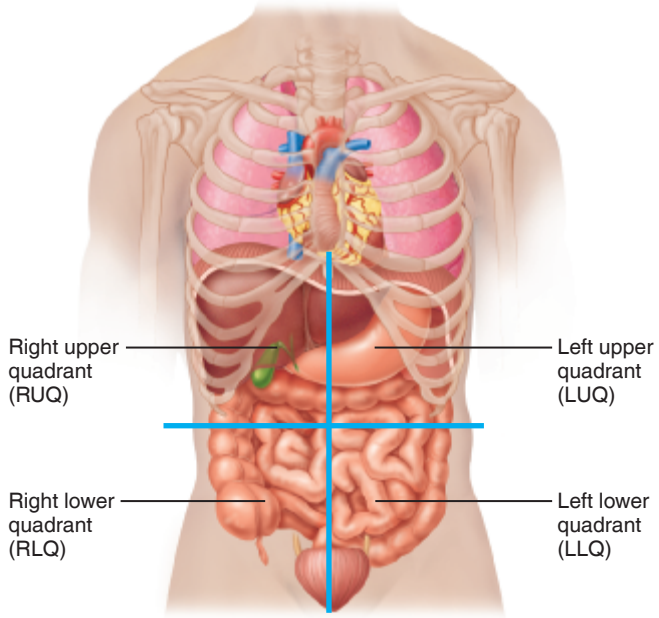
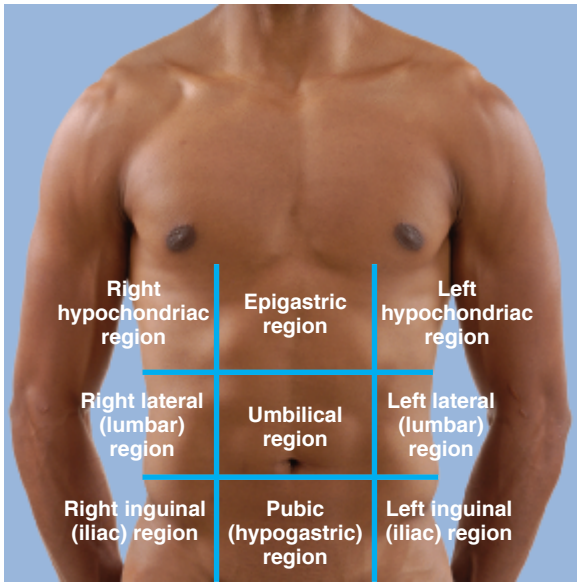
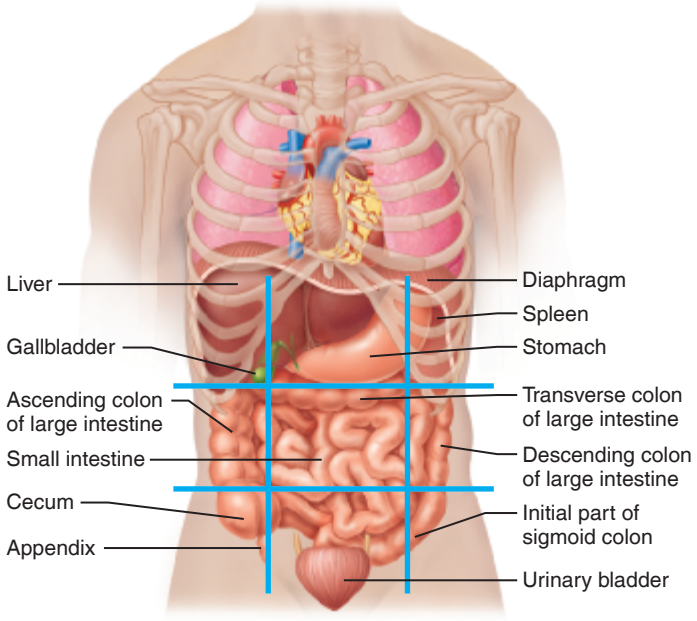


Figure 1.12 The four abdominopelvic quadrants. In this scheme, the abdominopelvic cavity is divided into four quadrants by two planes.



(a) Nine regions delineated by four planes



(b) Anterior view of the nine regions showing the superficial organs

Figure 1.13 The nine abdominopelvic regions. The superior transverse plane is just inferior to the ribs; the inferior transverse plane is just superior to the hip bones; and the parasagittal planes lie just medial to the nipples.

positioned like a tic-tac-toe grid on the abdomen, divide the cavity into nine regions (**Figure 1.13**):

- The **umbilical region** is the centermost region deep to and surrounding the umbilicus (navel).
- The **epigastric region** is located superior to the umbilical region (*epi* = upon, above; *gastri* = belly).
- The **pubic (hypogastric) region** is located inferior to the umbilical region (*hypo* = below).
- The **right** and **left inguinal**, or **iliac**, **regions** (ing′gwĭ-nal) are located lateral to the hypogastric region (*iliac* = superior part of the hip bone).
- The **right** and **left lateral (lumbar) regions** lie lateral to the umbilical region (*lumbus* = loin).
- The **right** and **left hypochondriac regions** lie lateral to the epigastric region and deep to the ribs (*chondro* = cartilage).

HOMEOSTATIC IMBALANCE 1.3 CLINICAL

You may have seen news stories about "wrong site surgery" and wondered how such serious mistakes can happen. Critical errors, including amputation, may result from confusion about right versus left or poor understanding of terminology. As you master the terminology of anatomy, you are helping to eliminate these blunders.

Other Body Cavities

In addition to the large closed body cavities, there are several smaller body cavities. Most of these are in the head and most open to the body exterior. Figure 1.8 provides the terms that will help you locate all but the last two cavities mentioned here.

- **Oral and digestive cavities.** The oral cavity, commonly called the mouth, contains the teeth and tongue. This cavity is part of and continuous with the cavity of the digestive organs, which opens to the body exterior at the anus.
- **Nasal cavity.** Located within and posterior to the nose, the nasal cavity is part of the respiratory system passageways.
- **Orbital cavities.** The orbital cavities (orbits) in the skull house the eyes and present them in an anterior position.
- **Middle ear cavities.** The middle ear cavities in the skull lie just medial to the eardrums. These cavities contain tiny bones that transmit sound vibrations to the hearing receptors in the inner ears.
- **Synovial cavities.** Synovial (sĭ-no′ve-al) cavities are joint cavities. They are enclosed within fibrous capsules that surround freely movable joints of the body (such as the elbow and knee joints). Like the serous membranes, membranes lining synovial cavities secrete a lubricating fluid that reduces friction as the bones move across one another.

Check Your Understanding

16. Of the uterus, small intestine, spinal cord, and heart, which is/are in the dorsal body cavity?
17. APPLY Brandon has a broken rib that punctured his right pleural cavity, but luckily his lung was not penetrated. Which serosal layer has been damaged? Why is his left pleural cavity not affected?
18. PREDICT If a surgeon is performing surgery in the right upper quadrant or the right hypochondriac region of the abdomen of a patient, which inflamed organ is he likely removing?

For answers, see Answers Appendix.

CHAPTER SUMMARY

1.1 Form (anatomy) determines function (physiology) (pp. 34–35)

1. Anatomy is the study of body structures and their relationships. Physiology is the science of how body parts function.

Topics of Anatomy (p. 34)

2. Major subdivisions of anatomy include gross anatomy, microscopic anatomy, and developmental anatomy.

Studying Anatomy (p. 34)

3. Anatomical terminology is essential for studying anatomy.

Topics of Physiology (pp. 34–35)

4. Typically, physiology concerns the functioning of specific organs or organ systems. Examples include cardiovascular physiology, renal physiology, and muscle physiology.
5. Physiology is explained by chemical and physical principles.

Complementarity of Structure and Function (p. 35)

6. Anatomy and physiology are inseparable: What a body can do depends on the unique architecture of its parts. This principle is called the complementarity of structure and function.

1.2 The body's organization ranges from atoms to the entire organism (pp. 36–37)

1. The levels of structural organization of the body, from simplest to most complex, are: chemical, cellular, tissue, organ, organ system, and organismal.
2. The 11 organ systems of the body are the integumentary, skeletal, muscular, nervous, endocrine, cardiovascular, lymphatic, respiratory, digestive, urinary, and reproductive systems. The immune system is a functional system closely associated with the lymphatic system. (For functions of these systems see pp. 38–39.)

1.3 What are the requirements for life? (pp. 37–41)

1. All living organisms carry out certain vital functional activities necessary for life, including maintenance of boundaries, movement, responsiveness, digestion, metabolism, excretion, reproduction, and growth.
2. Survival needs include nutrients, water, oxygen, and appropriate temperature and atmospheric pressure.

1.4 Homeostasis is maintained by negative feedback (pp. 41–44)

1. Homeostasis is a dynamic equilibrium of the internal environment. All body systems contribute to homeostasis, but the nervous and endocrine systems are most important. Homeostasis is necessary for health.

Homeostatic Control (pp. 41–44)

2. Control mechanisms of the body contain at least three elements that work together: receptor(s), control center, and effector(s).
3. Negative feedback mechanisms reduce the effect of the original stimulus, and are essential for maintaining homeostasis. Body temperature, heart rate, blood pressure, breathing rate and depth, and blood levels of glucose and certain ions are regulated by negative feedback mechanisms.
4. Positive feedback mechanisms intensify the initial stimulus, leading to an enhancement of the response. They rarely contribute to homeostasis, but blood clotting and labor contractions are regulated by such mechanisms.

Homeostatic Imbalance (p. 44)

5. With age, the efficiency of negative feedback mechanisms declines. These changes underlie certain disease conditions.

1.5 Anatomical terms describe body directions, regions, and planes (pp. 44–49)

Anatomical Position and Directional Terms (pp. 44–45)

1. In the anatomical position, the body is erect, facing forward, feet slightly apart, arms at sides with palms forward.
2. Directional terms allow body parts to be located precisely. Terms that describe body directions and orientation include: superior/inferior; anterior/posterior; ventral/dorsal; medial/lateral; intermediate; proximal/distal; and superficial/deep.

Regional Terms (p. 45)

3. Regional terms are used to designate specific areas of the body (see Figure 1.8).

Body Planes and Sections (pp. 45–49)

4. The body or its organs may be cut along planes to produce different types of sections. Frequently used planes are sagittal, frontal, and transverse.

1.6 Many internal organs lie in membrane-lined body cavities (pp. 49–52)

1. The body contains two major closed cavities. The dorsal cavity, subdivided into the cranial and spinal cavities, contains the brain and spinal cord. The ventral cavity is subdivided into the thoracic cavity, which houses the heart and lungs, and the abdominopelvic cavity, which contains the liver, digestive organs, and reproductive structures.
2. The walls of the ventral cavity and the surfaces of the organs it contains are covered with thin membranes, the parietal and visceral serosae, respectively. The serosae produce a thin fluid that decreases friction during organ functioning.
3. The abdominopelvic cavity may be divided by four planes into nine abdominopelvic regions (epigastric, umbilical, hypogastric, right and left iliac, right and left lumbar, and right and left hypochondriac), or by two planes into four quadrants. (For boundaries and organs contained, see Figures 1.12 and 1.13.)
4. There are several smaller body cavities. Most of these are in the head and open to the exterior.

REVIEW QUESTIONS

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(Some multiple choice questions have more than one correct answer. Select the best answer or answers from the choices given.)

Level 1 Remember/Understand

1. The correct sequence of levels forming the structural hierarchy is: **(a)** organ, organ system, cellular, chemical, tissue, organismal **(b)** chemical, cellular, tissue, organismal, organ, organ system **(c)** chemical, cellular, tissue, organ, organ system, organismal **(d)** organismal, organ system, organ, tissue, cellular, chemical
2. The structural and functional unit of life is **(a)** a cell, **(b)** an organ, **(c)** the organism, **(d)** a molecule.
3. Which of the following is a *major* functional characteristic of all organisms? **(a)** movement, **(b)** growth, **(c)** metabolism, **(d)** responsiveness, **(e)** all of these.
4. An increased rate of breathing as a result of an increased buildup of carbon dioxide in the bloodstream would be best described as an example of which of the following? **(a)** maintaining boundaries, **(b)** excretion of metabolic waste, **(c)** responsiveness, **(d)** metabolism.
5. In (a)–(e), a directional term [e.g., distal in (a)] is followed by terms indicating different body structures or locations (e.g., the elbow/the wrist). In each case, choose the structure or organ that matches the given directional term. **(a)** distal: the elbow/the wrist **(b)** lateral: the hip bone/the umbilicus **(c)** superior: the nose/the chin **(d)** anterior: the toes/the heel **(e)** superficial: the scalp/the skull
6. The diaphragm separates the thoracic cavity from the **(a)** abdominopelvic cavity, **(b)** dorsal cavity, **(c)** ventral cavity.
7. Terms that apply to the backside of the body in the anatomical position include: **(a)** ventral; anterior **(b)** back; rear **(c)** posterior; dorsal **(d)** medial; lateral
8. According to the principle of complementarity, how does anatomy relate to physiology?
9. Construct a table that lists the 11 systems of the body, names two organs of each system (if appropriate), and describes the overall or major function of each system.
10. List and describe briefly five external factors that must be present or provided to sustain life.
11. Define homeostasis.
12. Why is anatomical terminology necessary?
13. Which body region is referred to when each of the following anatomical terms is used? **(a)** tarsal, **(b)** occipital, **(c)** sural, **(d)** mental, **(e)** coxal.
14. **(a)** Make a diagram showing the nine abdominopelvic regions, and name each region. Name two organs (or parts of organs) that could be located in each of the named regions. **(b)** Make a similar sketch illustrating how the abdominopelvic cavity may be divided into quadrants, and name each quadrant.

Level 2 Apply/Analyze

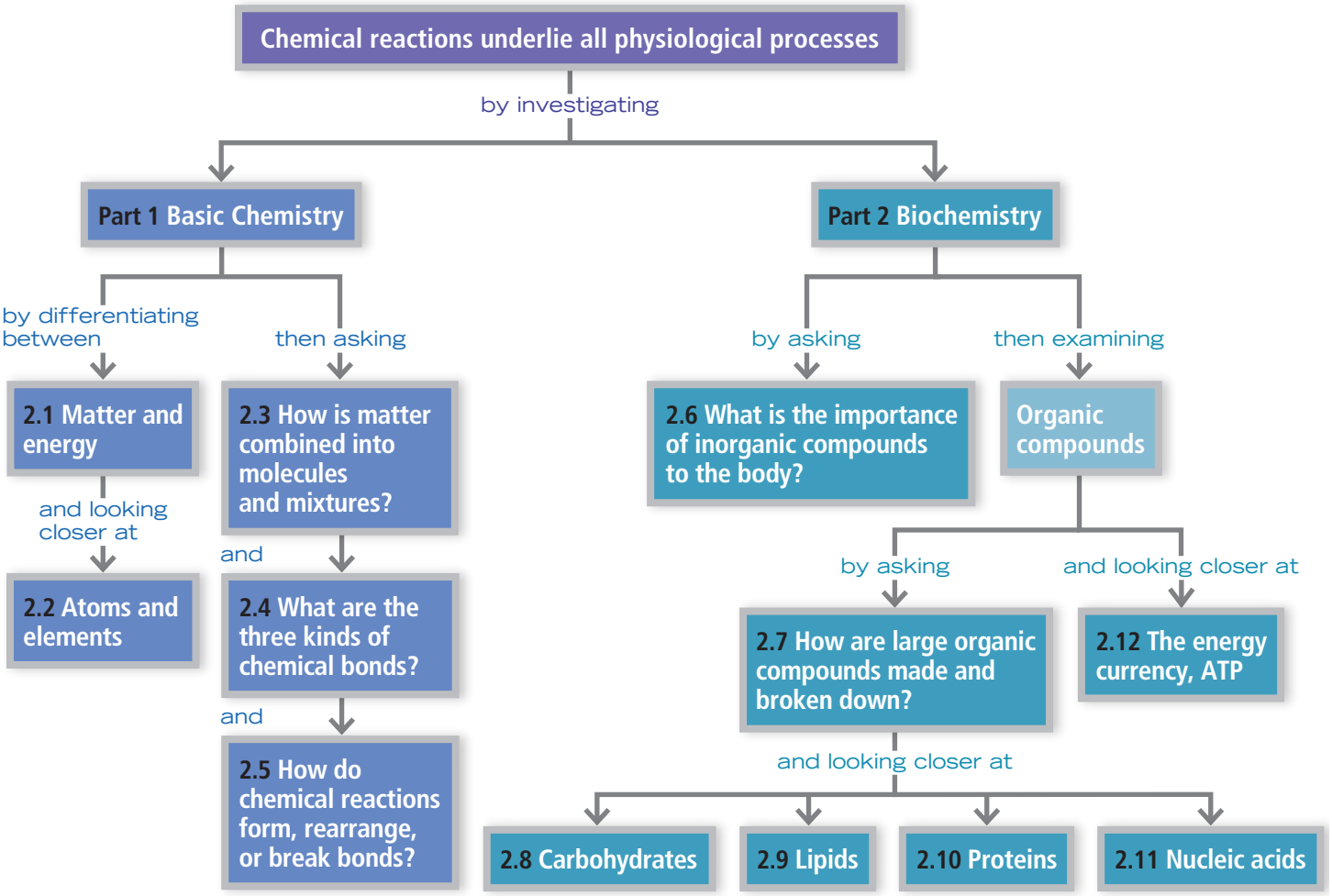
15. Assume that the body has been sectioned along three planes: **(1)** a median plane, **(2)** a frontal plane, and **(3)** a transverse plane made at the level of each of the organs listed below. Which organs would be visible in only one or two of these three cases? **(a)** urinary bladder, **(b)** brain, **(c)** lungs, **(d)** kidneys, **(e)** small intestine, **(f)** heart.
16. Relate each of the following conditions or statements to either the dorsal body cavity or the ventral body cavity. **(a)** surrounded by the bony skull and the vertebral column **(b)** includes the thoracic and abdominopelvic cavities **(c)** contains the brain and spinal cord **(d)** contains the heart, lungs, and digestive organs
17. Which of the following relationships is *incorrect*? **(a)** visceral peritoneum/outer surface of small intestine **(b)** parietal pericardium/outer surface of heart **(c)** parietal pleura/wall of thoracic cavity
18. Compare and contrast the operation of negative and positive feedback mechanisms in maintaining homeostasis. Provide two examples of variables controlled by negative feedback mechanisms and one example of a process regulated by a positive feedback mechanism.
19. Why is an understanding of the anatomical position important?
20. Use as many directional terms as you can to describe the relationship between the elbow's olecranal region and your palm.
21. At the clinic, Harry was told that blood would be drawn from his antecubital region. What body part was Harry asked to hold out? Later, the nurse came in and gave Harry a shot of penicillin in the area just distal to his acromial region. Did Harry take off his shirt or drop his pants to receive the injection? Before Harry left, the nurse noticed that Harry had a nasty bruise on his gluteal region. What part of his body was black and blue?
22. Calcium levels in Mr. Gallariani's blood are dropping to dangerously low levels. The hormone PTH is released and soon blood calcium levels begin to rise. Shortly after, PTH release slows. Is this an example of a positive or negative feedback mechanism? What is the initial stimulus? What is the result?
23. Ms. Rotich, a marathon runner, has been experiencing pain in her right foot, especially while getting out of bed. A physiotherapist diagnoses her problem as plantar fasciitis. Which part of Ms. Rotich's foot requires physical therapy?

Level 3 Evaluate/Synthesize

24. Aiden has been suffering agonizing pain with each breath and has been informed by the physician that he has pleurisy. **(a)** Specifically, what membranes are involved in this condition? **(b)** What is their usual role in the body? **(c)** Explain why Aiden's condition is so painful.
25. Mr. Rossouw has intense pain in the lower back, which made his doctor order a CT scan. The scan reveals an aneurysm in his right internal iliac artery. Where exactly is this artery located? Which additional imaging technique will the doctor use to identify the artery (and why)?

2 Chemistry Comes Alive

In this chapter, you will learn that



Why study chemistry in an anatomy and physiology course? The answer is simple. Your entire body is made up of chemicals, thousands of them, continuously interacting with one another at an incredible pace. Although it is possible to study anatomy without much reference to chemistry, chemical reactions underlie all physiological processes—movement, digestion, the pumping of your heart, and even your thoughts. This chapter presents the basic chemistry and biochemistry (the chemistry of living material) you need to understand body functions.

CAREER CONNECTION

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PART 1

BASIC CHEMISTRY

2.1 Matter is the stuff of the universe and energy moves matter

Learning Outcomes

- **Differentiate between matter and energy and between potential energy and kinetic energy.**
- **Describe the major energy forms.**

Matter

Matter is the "stuff" of the universe. More precisely, **matter** is anything that occupies space and has mass. With some exceptions, it can be seen, smelled, and felt.

We usually consider mass to be the same as weight. However, this statement is not quite accurate. The *mass* of an object is equal to the actual amount of matter in the object, and it remains constant wherever the object is. In contrast, weight varies with gravity. So while your mass is the same at sea level and on a mountaintop, you weigh just slightly less on that mountaintop. The science of chemistry studies the nature of matter, especially how its building blocks are put together and interact.

States of Matter

Matter exists in *solid*, *liquid*, and *gaseous states*. Examples of each state are found in the human body. Solids, like bones and teeth, have a definite shape and volume. Liquids such as blood plasma have a definite volume, but they conform to the shape of their container. Gases have neither a definite shape nor a definite volume. The air we breathe is a gas.

Energy

Compared with matter, energy is less tangible. It has no mass, does not take up space, and we can measure it only by its effects on matter. **Energy** is defined as the capacity to do work, or to put matter into motion. The greater the work done, the more energy is used doing it. A baseball player who has just hit the ball over the fence uses much more energy than a batter who bunts the ball back to the pitcher.

Kinetic versus Potential Energy

Energy exists in two states, and each can be transformed to the other. **Kinetic energy** (ki-net′ik) is energy in action. We see evidence of kinetic energy in the constant movement of the tiniest particles of matter (atoms) as well as in larger objects (a bouncing ball). Kinetic energy does work by moving objects, which in turn can do work by moving or pushing on other objects. For example, a push on a swinging door sets it into motion.

Potential energy is stored energy, that is, inactive energy that has the *potential*, or capability, to do work but is not presently doing so. The batteries in an unused toy have potential energy, as does water confined behind a dam. Your leg muscles have potential energy when you sit still on the couch. When potential energy is released, it becomes kinetic energy and so is capable of doing work. For example, dammed water becomes a rushing torrent when the dam is opened, and that rushing torrent can move a turbine at a hydroelectric plant and charge a battery.

Matter and energy are inseparable. Matter is the substance, and energy is the mover of the substance. All living things are composed of matter and they all require energy to grow and function. The release and use of energy by living systems gives us the elusive quality we call life. Now let's consider the forms of energy used by the body as it does its work.

Forms of Energy

- **Chemical energy** is the form stored in the bonds of chemical substances. When chemical reactions occur that rearrange the atoms of the chemicals in a certain way, the potential energy is unleashed and becomes kinetic energy, or energy in action.

  For example, some of the energy in the foods you eat is eventually converted into the kinetic energy of your moving arm. However, food fuels cannot be used to energize body activities directly. Instead, some of the food energy is captured temporarily in the bonds of a chemical called *adenosine triphosphate* (*ATP*; ah-den′o-sēn tri″fos′fāt). Later, ATP's bonds are broken and the stored energy is released as needed to do cellular work. Chemical energy in the form of ATP is the most useful form of energy in living systems because it is used to run almost all functional processes.
- **Electrical energy** results from the movement of charged particles. In your home, electrical energy is found in the flow of electrons along the household wiring. In your body, electrical currents are generated when charged particles (*ions*) move along or across cell membranes. The nervous system uses electrical currents, called *nerve impulses* (or *action potentials*), to transmit messages from one part of the body to another. Electrical currents traveling across the heart stimulate it to contract (beat) and pump blood. (This is why a strong electrical shock, which interferes with such currents, can cause death.)
- **Mechanical energy** is energy *directly* involved in moving matter. When you ride a bicycle, your legs provide the mechanical energy that moves the pedals.
- **Radiant energy**, or **electromagnetic radiation** (e-lek″tro-mag-net′ik), is energy that travels in waves. These waves, which vary in length, are collectively called the *electromagnetic spectrum*. They include radio waves, microwaves, infrared waves, visible light, ultraviolet waves, and X rays. Light energy, which stimulates the retinas of our eyes, is important in vision. Ultraviolet waves cause sunburn, but they also stimulate your body to make vitamin D.

Converting Forms of Energy

With few exceptions, energy is easily converted from one form to another. For example, the chemical energy (in gasoline) that

powers the motor of a speedboat is converted into the mechanical energy of the whirling propeller that makes the boat skim across the water.

Energy conversions are quite inefficient. Some of the initial energy supply is always "lost" to the environment as heat. It is not really lost because energy cannot be created or destroyed, but that portion given off as heat is at least partly *unusable*. It is easy to demonstrate this principle. Electrical energy is converted into light energy in a lightbulb. But if you touch a lit bulb, you will soon discover that some of the electrical energy is producing heat instead.

Likewise, all energy conversions in the body liberate heat. This heat helps to maintain our relatively high body temperature, which influences body functioning. For example, when matter is heated, the kinetic energy of its particles increases and they begin to move more quickly. The higher the temperature, the faster the body's chemical reactions occur. We will learn more about this later.

Check Your Understanding

1. What form of energy is found in the food we eat?
2. What form of energy is used to transmit messages from one part of the body to another?
3. What type of energy is available when we are still? When we are exercising?

For answers, see Answers Appendix.

2.2 The properties of an element depend on the structure of its atoms

Learning Outcomes

- **Define chemical element and list the four elements that form the bulk of body matter.**
- **Define atom. List the subatomic particles, and describe their relative masses, charges, and positions in the atom.**
- **Define atomic number, atomic mass, atomic weight, isotope, and radioisotope.**

All matter is composed of **elements**, unique substances that cannot be broken down into simpler substances by ordinary chemical methods. Among the well-known elements are oxygen, carbon, gold, silver, copper, and iron.

At present, 118 elements are recognized. Of these, 92 occur in nature. The rest are made artificially in particle accelerator devices.

Four elements—carbon, oxygen, hydrogen, and nitrogen—make up about 96% of body weight, and 20 others are present in the body, some in trace amounts. **Table 2.1** on p. 58 lists those of importance to the body. An oddly shaped checkerboard called the **periodic table** (see Appendix E) provides a listing of the known elements and helps to explain the properties of each element.

Each element is composed of essentially identical particles or building blocks, called **atoms**. The smallest atoms are less than 0.1 nanometer (nm) in diameter, and the largest are only about five times as large. [1 nm = 0.000000001 (or 10^{-9}) meter (m), or 40 billionths of an inch!]

Every element's atoms differ from those of all other elements and give the element its unique physical and chemical properties. *Physical properties* are those we can detect with our senses (such as color and texture) or measure (such as boiling point and freezing point). *Chemical properties* describe the way atoms interact with other atoms (bonding behavior) and account for the facts that iron rusts, animals can digest their food, and so on.

We designate each element by a one- or two-letter chemical shorthand called an **atomic symbol**, usually the first letter(s) of the element's name. For example, C stands for carbon, O for oxygen, and Ca for calcium. In a few cases, the atomic symbol is taken from the Latin name for the element. For example, sodium is indicated by Na, from the Latin word *natrium*.

Structure of Atoms

The word *atom* comes from the Greek word meaning "indivisible." However, we now know that atoms are clusters of even smaller particles called protons, neutrons, and electrons and that even those subatomic particles can be subdivided. Still, the old idea of atomic indivisibility is useful because an atom loses the unique properties of its element when it is split into its subatomic particles.

An atom's subatomic particles differ in mass, electrical charge, and position in the atom. An atom has a central **nucleus** containing protons and neutrons tightly bound together. The nucleus, in turn, is surrounded by orbiting electrons (**Figure 2.1**). **Protons** (p^+) bear a positive electrical charge, and **neutrons** (n^0) are neutral, so the nucleus is positively charged overall. Protons and neutrons are heavy particles and have approximately the same mass, arbitrarily designated as 1 **atomic mass unit** (1 amu). Since all of the heavy subatomic

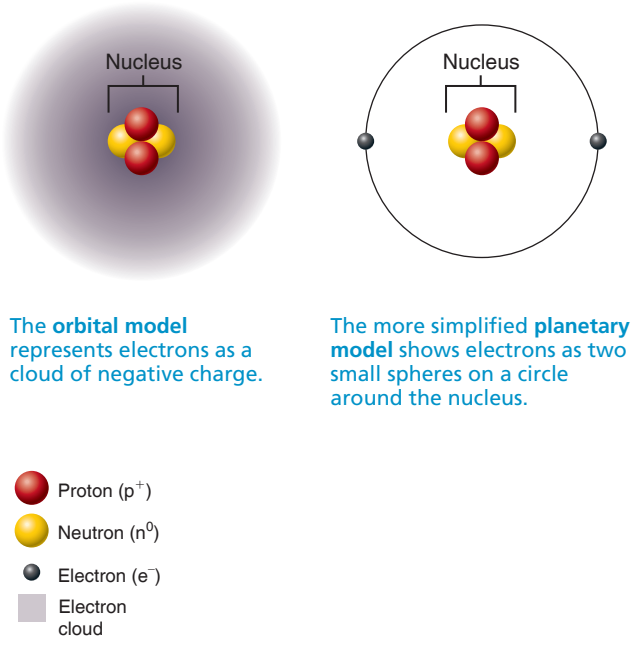


Figure 2.1 Two models of the structure of a helium atom. Helium has 2 protons, 2 neutrons, and 2 electrons ($2p^+$; $2n^0$; $2e^-$).

Table 2.1 Common Elements Composing the Human Body*

ELEMENT	ATOMIC SYMBOL	APPROX. % BODY MASS†	FUNCTIONS
Major (96.1%)			
Oxygen	O	65.0	A component of both organic (carbon-containing) and inorganic (non-carbon-containing) molecules. As a gas, it is needed for the production of cellular energy (ATP).
Carbon	C	18.5	A component of all organic molecules, which include carbohydrates, lipids (fats and oils), proteins, and nucleic acids.
Hydrogen	H	9.5	A component of all organic molecules. As an ion (proton), it influences the pH of body fluids.
Nitrogen	N	3.2	A component of proteins and nucleic acids (genetic material).
Lesser (3.9%)			
Calcium	Ca	1.5	Found as a salt in bones and teeth. Its ionic (Ca^{2+}) form is required for muscle contraction, conduction of nerve impulses, and blood clotting.
Phosphorus	P	1.0	Part of calcium phosphate salts in bones and teeth. Also present in nucleic acids, and as part of ATP and phospholipids.
Potassium	K	0.4	Its ion (K^+) is the major positive ion (cation) in cells. Necessary for conduction of nerve impulses and muscle contraction.
Sulfur	S	0.3	Component of proteins, particularly muscle proteins.
Sodium	Na	0.2	As an ion (Na^+), sodium is the major positive ion found in extracellular fluids (fluids outside of cells). Important for water balance, conduction of nerve impulses, and muscle contraction.
Chlorine	Cl	0.2	Its ion (chloride, Cl^-) is the most abundant negative ion (anion) in extracellular fluids.
Magnesium	Mg	0.1	Present in bone. Also an important cofactor in a number of metabolic reactions.
Iodine	I	0.1	Needed to make functional thyroid hormones.
Iron	Fe	0.1	Component of hemoglobin (which transports oxygen within red blood cells) and some enzymes.
Trace (less than 0.01%)			
Chromium (Cr); cobalt (Co); copper (Cu); fluorine (F); manganese (Mn); molybdenum (Mo); selenium (Se); silicon (Si); tin (Sn); vanadium (V); zinc (Zn)			
These elements are referred to as *trace elements* because they are required in very minute amounts; many are found as part of enzymes or are required for enzyme activation.			

*A listing of the elements by ascending order of atomic number appears in the periodic table (Appendix E).
†Percentage of "wet" body mass; includes water.

particles are concentrated in the nucleus, the nucleus is fantastically dense, accounting for nearly the entire mass (99.9%) of the atom.

The tiny **electrons** (e^-) bear a negative charge equal in strength to the positive charge of the proton. However, an electron has only about 1/2000 the mass of a proton, and the mass of an electron is usually designated as 0 amu.

All atoms are electrically neutral because the number of protons in an atom is precisely balanced by its number of electrons (the + and − charges will then cancel the effect of each other). For example, hydrogen has one proton and one electron, and iron has 26 protons and 26 electrons. For any atom, the number of protons and electrons is always equal.

The **planetary model** of the atom is a simplified model of atomic structure (Figure 2.1, right). As you can see, it depicts electrons moving around the nucleus in fixed, generally circular orbits. But we can never determine the exact location of electrons at a particular time because they jump around following unknown trajectories. So, instead of speaking of specific orbits, chemists talk about **orbitals**—regions around the nucleus in which a given electron or electron pair is likely to be found most of the time. This more modern **orbital model** is more useful for predicting the chemical behavior of atoms (Figure 2.1, left). The orbital model depicts *probable* regions of greatest electron density by denser shading (this haze is called the *electron cloud*). However, the planetary model is simpler to depict, so we will use that model in most illustrations of atomic structure in this text.

Hydrogen, with just one proton and one electron, is the simplest atom. You can visualize the spatial relationships in the hydrogen atom by imagining it as a sphere enlarged until its diameter equals the length of a football field. In that case, the nucleus could be represented by a lead ball the size of a gumdrop in the exact center of the sphere. Its lone electron could be pictured as a fly buzzing about unpredictably within the sphere. Though not completely accurate, this mental image demonstrates that most of the volume of an atom is empty space, and nearly all of its mass is concentrated in the central nucleus.

Identifying Elements

All protons are alike, regardless of the atom considered. The same is true of all neutrons and all electrons. So what determines the unique properties of each element? The answer is that atoms of different elements are composed of *different numbers* of protons, neutrons, and electrons and this determines the chemical and physical properties of each element.

The simplest and smallest atom, hydrogen, has 1 proton, 1 orbiting electron, and no neutrons (**Figure 2.2**). Next in size is the helium atom, with 2 protons, 2 neutrons, and 2 electrons. Lithium follows with 3 protons, 4 neutrons, and 3 electrons. If we continued this step-by-step progression, we would get a graded series of atoms containing from 1 to 118 protons, an equal number of electrons, and a slightly larger number of neutrons at each step.

All we really need to know about a particular element, however, are its atomic number, mass number, and atomic weight. Taken together, these provide a fairly complete picture of each element.

Atomic Number

The **atomic number** of any atom is equal to the number of protons in its nucleus and is written as a subscript to the left of its atomic symbol. Hydrogen, with one proton, has an atomic number of 1 ($_1$H). Helium, with two protons, has an atomic number of 2 ($_2$He), and so on. The number of protons is always equal to the number of electrons in an atom, so the atomic number *indirectly* tells us the number of electrons in the atom as well. As we will see shortly, this information is important indeed, because electrons determine the chemical behavior of atoms.

Mass Number and Isotopes

The **mass number** of an atom is the sum of the masses of its protons and neutrons. The mass of the electrons is so small that it is ignored. Recall that protons and neutrons have a mass of 1 amu. Hydrogen has only one proton in its nucleus, so its atomic and mass numbers are the same: 1. Helium, with 2 protons and 2 neutrons, has a mass number of 4.

The mass number is usually indicated by a superscript to the left of the atomic symbol. For example, helium is $^4_2$He. This simple notation allows us to deduce the total number and kinds of subatomic particles in any atom because it indicates the number of protons (the atomic number), the number of electrons (equal to the atomic number), and the number of neutrons (mass number minus atomic number). In our example, we can do the subtraction to find that $^4_2$He has two neutrons.

From what we have said so far, it may appear as if each element has one, and only one, type of atom representing it. This is not the case. Nearly all known elements have two or more structural variations called **isotopes** (i′so-tōps; *iso* = same; *topos* = place). Isotopes of an element have the same number of protons and electrons (and so have the same chemical properties), but they differ in the number of neutrons they contain. Earlier, when we said that hydrogen has a mass number of 1, we were speaking of ^{1}H, its most abundant isotope. A few hydrogen atoms have a mass of 2 or 3 amu (atomic mass units),

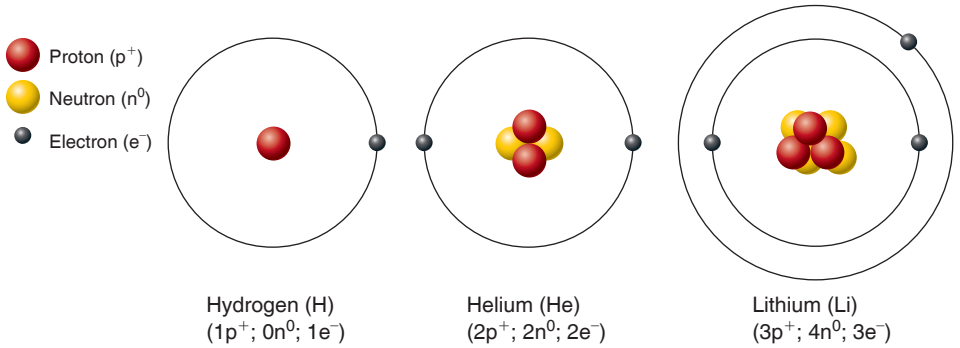


Figure 2.2 **Atomic structure of the three smallest atoms.**

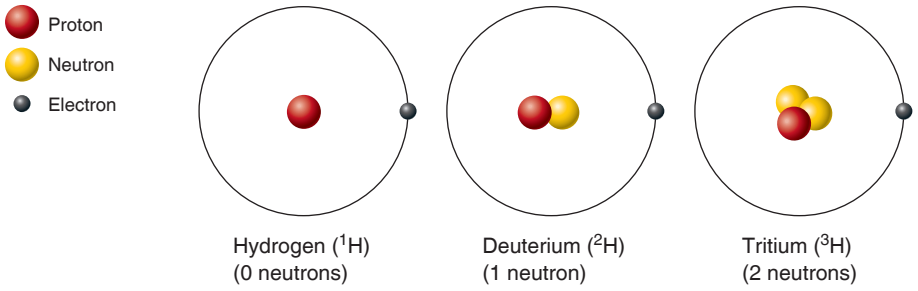


Figure 2.3 **Isotopes of hydrogen.**

which means that they have 1 proton and, respectively, 1 or 2 neutrons (**Figure 2.3**).

Carbon has several isotopes. The most abundant of these are ^{12}C, ^{13}C, and ^{14}C. Each of the carbon isotopes has six protons (otherwise it would not be carbon), but ^{12}C has six neutrons, ^{13}C has seven, and ^{14}C has eight. Isotopes can also be written with the mass number following the symbol: C-14, for example.

Atomic Weight

You might think that atomic weight should be the same as atomic mass, and this would be so if atomic weight referred to the weight of a single atom. However, **atomic weight** is an average of the weights (mass numbers) of *all* the isotopes of an element, taking into account their relative abundance in nature. As a rule, the atomic weight of an element is approximately equal to the mass number of its most abundant isotope. For example, the atomic weight of hydrogen is 1.008, which reveals that its lightest isotope (^{1}H) is present in much greater amounts in our world than its ^{2}H or ^{3}H forms.

Radioisotopes

The heavier isotopes of many elements are unstable, and their atoms decompose spontaneously into more stable forms. This process of atomic decay is called *radioactivity*, and isotopes that exhibit this behavior are called **radioisotopes** (ra″de-o-i′so-tōps). The disintegration of a radioactive nucleus may be compared to a tiny explosion. It occurs when subatomic *alpha* (α) *particles* (packets of 2p + 2n), *beta* (β) *particles* (electron-like particles), or *gamma* (γ) *rays* (electromagnetic energy) are ejected from the atomic nucleus.

Why does this happen? The answer is complex, but for our purposes, the important point is that the dense nuclear particles are composed of even smaller particles called *quarks* that associate in one way to form protons and in another way to form neutrons. The "glue" that holds these nuclear particles together is weaker in the heavier isotopes. When radioisotopes disintegrate, the element usually transforms to a different element.

Because we can detect radioactivity with scanners, and radioactive isotopes share the same chemistry as their more stable isotopes, radioisotopes are valuable tools for biological research and medicine. Most radioisotopes used in the clinical setting are used for diagnosis, that is, to localize and illuminate damaged or cancerous tissues. For example, iodine-123 is used to determine the size and activity of the thyroid gland and to detect thyroid cancer. PET scans (described in *A Closer Look* in Chapter 1, pp. 48–49) use radioisotopes to probe the workings of molecules deep within our bodies. All radioisotopes, regardless of the purpose for which they are used, damage living tissue, and they all gradually lose their radioactive behavior. The time required for a radioisotope to lose one-half of its activity is called its *half-life*. The half-lives of radioisotopes vary dramatically from hours to thousands of years.

Alpha emission is easily blocked outside the body, but if absorbed, it causes considerable damage. For this reason, alpha particles from decaying inhaled radon gas are second only to smoking as a cause of lung cancer. (Radon, a gas, results naturally from decay of uranium in the ground.) Gamma emission has the greatest penetrating power. Radium-226, cobalt-60, and certain other radioisotopes that decay by gamma emission are used to destroy localized cancers.

Contrary to what some believe, ionizing radiation does not damage organic molecules directly. Instead, it knocks electrons out of other atoms and sends them flying, like bowling balls smashing through pins all along their path. It is the electron's energy and the unstable molecules left behind that do the damage.

Check Your Understanding

4. What two elements besides H and N make up the bulk of living matter?
5. DRAW Draw a planetary model of an atom with a mass number of 7 and an atomic number of 3.
6. WHAT IF Look at the function of iron in Table 2.1 on p. 58. What would be the effect of an iron deficiency on blood?

For answers, see Answers Appendix.

2.3 Atoms bound together form molecules; different molecules can make mixtures

Learning Outcomes

- **Define molecule, and distinguish between a compound and a mixture.**
- **Compare solutions, colloids, and suspensions.**

Molecules and Compounds

Most atoms do not exist in the free state, but instead are chemically combined with other atoms. Such a combination of two or more atoms held together by chemical bonds is called a **molecule**.

If two or more atoms of the *same* element combine, the resulting substance is called a *molecule of that element*. When two hydrogen atoms bond, the product is a molecule of hydrogen gas and is written as H_2. Similarly, when two oxygen atoms combine, a molecule of oxygen gas (O_2) is formed. Sulfur

atoms commonly combine to form sulfur molecules containing eight sulfur atoms (S_8).

When two or more *different* kinds of atoms bind, they form molecules of a **compound**. Two hydrogen atoms combine with one oxygen atom to form the compound water (H_2O). Four hydrogen atoms combine with one carbon atom to form the compound methane (CH_4). Notice again that molecules of methane and water are compounds, but molecules of hydrogen gas are not, because compounds always contain atoms of at least two different elements.

Compounds are chemically pure, and all of their molecules are identical. So, just as an atom is the smallest particle of an element that still has the properties of the element, a molecule is the smallest particle of a compound that still has the specific characteristics of the compound. This concept is important because the properties of compounds are usually very different from those of the atoms they contain. Water, for example, is very different from the elements hydrogen and oxygen. Indeed, it is next to impossible to tell what atoms are in a compound without analyzing it chemically.

Mixtures

Mixtures are substances composed of two or more components *physically intermixed*. Most matter in nature exists in the form of mixtures, but there are only three basic types: *solutions*, *colloids*, and *suspensions* (**Figure 2.4**).

Solutions

Solutions are homogeneous mixtures of components that may be gases, liquids, or solids. *Homogeneous* means that the mixture has exactly the same composition or makeup throughout—a sample taken from any part of the mixture has the same composition (in terms of the atoms or molecules it contains) as a sample taken from any other part of the mixture. Examples include the air we breathe (a mixture of gases) and seawater (a mixture of salts, which are solids, and water). The substance present in the greatest amount is called the **solvent** (or dissolving medium). Solvents are usually liquids. Substances present in smaller amounts (dissolved in the solvent) are called **solutes**.

Water is the body's chief solvent. Most solutions in the body are *true solutions* containing gases, liquids, or solids dissolved in water. True solutions are usually transparent. Examples are saline solution [table salt (NaCl) and water], a mixture of glucose and water, and mineral water. The solutes of true solutions are very small, usually in the form of individual atoms and molecules. Consequently, they are not visible to the naked eye, do not settle out, and do not scatter light. In other words, if a beam of light is passed through a true solution, you will not see the path of light.

Concentration of Solutions We describe true solutions in terms of their *concentration*, which may be indicated in various ways. Solutions used in a college laboratory or a hospital are often described in terms of the **percent** (parts per 100 parts) of

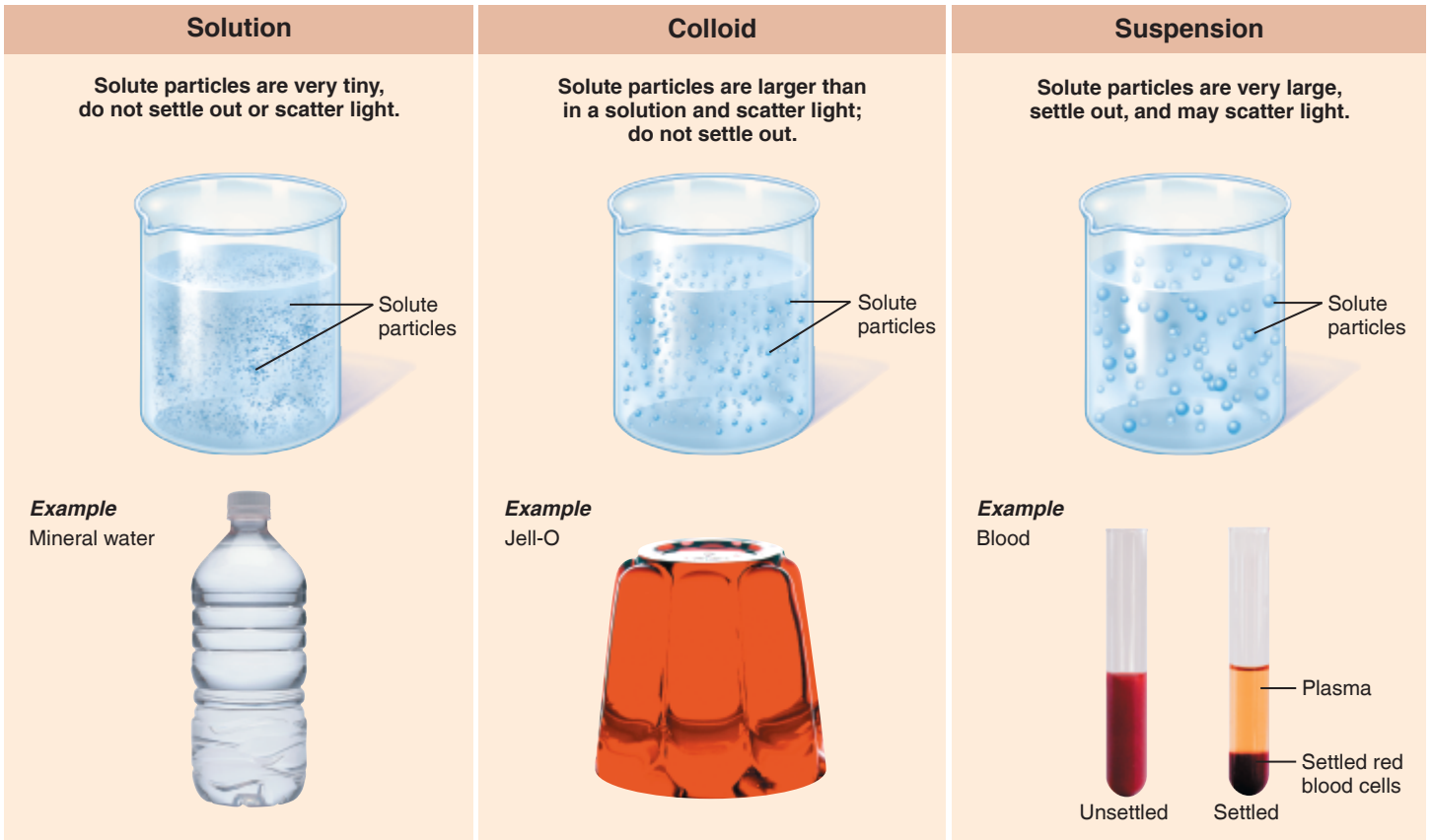


Figure 2.4 **The three basic types of mixtures.**

the solute in the total solution. This designation always refers to the solute percentage, and unless otherwise noted, water is assumed to be the solvent.

Milligrams per deciliter (*mg/dl*) is a concentration measurement commonly used to measure the blood concentration of glucose, cholesterol, and so on. (A deciliter is 100 milliliters or 0.1 liter.)

Still another way to express the concentration of a solution is in terms of its **molarity** (mo-lar′ĭ-te), or moles per liter, indicated by *M*. This method is more complicated but much more useful. To understand molarity, you must understand what a mole is. A **mole** of any element or compound is equal to its atomic weight or **molecular weight** (sum of the atomic weights) in grams. This concept is easier than it seems, as illustrated by the following example.

Glucose is $C_6H_{12}O_6$, which indicates that it has 6 carbon atoms, 12 hydrogen atoms, and 6 oxygen atoms. To compute the molecular weight of glucose, you would look up the atomic weight of each of its atoms in the periodic table (see Appendix E) and compute its molecular weight as follows:

Atom	Number of Atoms		Atomic Weight		Total Atomic Weight
C	6	×	12.011	=	72.066
H	12	×	1.008	=	12.096
O	6	×	15.999	=	95.994
					180.156

Then, to make a *one-molar* solution of glucose, you would weigh out 180.156 grams (g) of glucose and add enough water to make 1 liter (L) of solution. In short, a one-molar solution (abbreviated 1.0 *M*) of a chemical substance is the molecular weight of the substance in grams in 1 L (1000 milliliters) of solution.

The beauty of using the mole as the basis of preparing solutions is its precision. One mole of any substance always contains exactly the same number of solute particles, that is, 6.02×10^{23}. This number is called **Avogadro's number** (av″o-gad′rō). So whether you weigh out 1 mole of glucose (180 g) or 1 mole of water (18 g) or 1 mole of methane (16 g), in each case you will have 6.02×10^{23} molecules of that substance.* This allows almost mind-boggling precision to be achieved.

Because solute concentrations in body fluids tend to be quite low, those values are usually reported in terms of millimoles (m*M*; 1/1000 mole).

Colloids

Colloids (kol′oidz), also called *emulsions*, are *heterogeneous* mixtures, which means that their composition is dissimilar in different areas of the mixture. Colloids often appear translucent or milky and although the solute particles are larger than those in true solutions, they still do not settle out. However, they do scatter light, so the path of a light beam shining through a colloidal mixture is visible.

Colloids have many unique properties, including the ability of some to undergo **sol-gel transformations**, that is, to change reversibly from a fluid (sol) state to a more solid (gel) state. Jell-O, or any gelatin product (Figure 2.4), is a familiar example of a nonliving colloid that changes from a sol to a gel when refrigerated (and that gel will liquefy again if placed in the sun). Cytosol, the semifluid material in living cells, is also a colloid, largely because of its dispersed proteins. Its sol-gel transformations underlie many important cell activities, such as cell division and changes in cell shape.

Suspensions

Suspensions are *heterogeneous* mixtures with large, often visible solutes that tend to settle out. An example of a suspension is a mixture of sand and water. So is blood, in which the living blood cells are suspended in the fluid portion of blood (blood plasma). If left to stand, the suspended cells will settle out unless some means—mixing, shaking, or circulation in the body—keeps them in suspension.

All three types of mixtures are found in both living and nonliving systems. In fact, living material is the most complex mixture of all, since it contains all three kinds of mixtures interacting with one another.

Distinguishing Mixtures from Compounds

Now let's zero in on how to distinguish mixtures and compounds from one another. Mixtures differ from compounds in several important ways:

- The chief difference between mixtures and compounds is that no chemical bonding occurs between the components of a mixture. The properties of atoms and molecules are not changed when they become part of a mixture. Remember they are only physically intermixed.
- Depending on the mixture, its components can be separated by physical means—straining, filtering, evaporation, and so on. Compounds, by contrast, can be separated into their constituent atoms only by chemical means (breaking bonds).
- Some mixtures are homogeneous, whereas others are heterogeneous. A bar of brass is a homogeneous mixture of copper and zinc. However, when brass shavings are swept up from the workshop floor, what you have collected is a heterogeneous mixture of dirt, dust, and metal.

Check Your Understanding

7. What is the meaning of the term "molecule"?
8. Why is carbon dioxide (CO_2) considered a compound, but nitrogen gas (N_2) is not?
9. Blood contains a liquid component and living cells. Would it be classified as a compound or a mixture? Why?

For answers, see Answers Appendix.

* The important exception to this rule concerns molecules that ionize and break up into charged particles (ions) in water, such as salts, acids, and bases (see p. 71). For example, simple table salt (sodium chloride) breaks up into two types of charged particles. Therefore, in a 1.0 *M* solution of sodium chloride, 2 *moles* of solute particles are actually in solution.

2.4 Three types of chemical bonds are ionic, covalent, and hydrogen

Learning Outcomes

- **Explain the role of electrons in chemical bonding and in relation to the octet rule.**
- **Differentiate among ionic, covalent, and hydrogen bonds.**
- **Compare and contrast polar and nonpolar compounds.**

As noted earlier, when atoms combine with other atoms, they are held together by **chemical bonds**. A chemical bond is not a physical structure like a pair of handcuffs linking two people together. Instead, it is an energy relationship between the electrons of the reacting atoms, and it is made or broken in less than a trillionth of a second.

The Role of Electrons in Chemical Bonding

Electrons forming the electron cloud around the nucleus of an atom occupy regions of space called **electron shells** that consecutively surround the atomic nucleus. The atoms known so far can have electrons in seven shells (numbered 1 to 7 from the nucleus outward), but the actual number of electron shells occupied in a given atom depends on the number of electrons the atom has. Each electron shell contains one or more orbitals. (Recall that *orbitals* are regions around the nucleus in which a given electron is likely to be found most of the time.)

It is important to understand that each electron shell represents a different **energy level**, because this prompts you to think of electrons as particles with a certain amount of potential energy. In general, the terms *electron shell* and *energy level* are used interchangeably.

How much potential energy does an electron have? The answer depends on the energy level that it occupies. The attraction between the positively charged nucleus and negatively charged electrons is greatest when electrons are closest to the nucleus and falls off with increasing distance. This statement explains why electrons farthest from the nucleus (1) have the greatest potential energy (the energy they absorbed to overcome the nuclear attraction and reach the more distant energy levels) and (2) are most likely to interact chemically with other atoms. (They are the least tightly held by their own nucleus and the most easily influenced by other atoms and molecules.)

Each electron shell can hold a specific number of electrons. Shell 1, the shell immediately surrounding the nucleus, accommodates only 2 electrons. Shell 2 holds a maximum of 8, and shell 3 has room for 18. Subsequent shells hold larger and larger numbers of electrons, and the shells tend to be filled with electrons consecutively. For example, shell 1 fills completely before any electrons appear in shell 2.

Which electrons are involved in chemical bonding? When we consider bonding behavior, the only electrons that are important are those in the atom's outermost energy level. Inner electrons usually do not take part in bonding because they are more tightly held by the nucleus.

When the outermost energy level of an atom is filled to capacity or contains 8 electrons, the atom is stable. Such atoms are *chemically inert*, that is, unreactive. A group of elements called the *noble gases*, which include helium and neon, typify this condition (**Figure 2.5a**). On the other hand, atoms in which the outermost energy level contains fewer than 8 electrons tend to gain, lose, or share electrons with other atoms to achieve stability (Figure 2.5b).

What about atoms that have more than 20 electrons, in which the energy levels beyond shell 2 can contain *more* than 8 electrons? The number of electrons that can participate in bonding is still limited to a total of 8. The term **valence shell** (va′lens) refers to an atom's outermost energy level *or that portion of it* containing the electrons that are chemically reactive. The key to chemical reactivity is the **octet rule** (ok-tet′), or **rule of eights**. Except for shell 1, which is full when it has 2 electrons, atoms

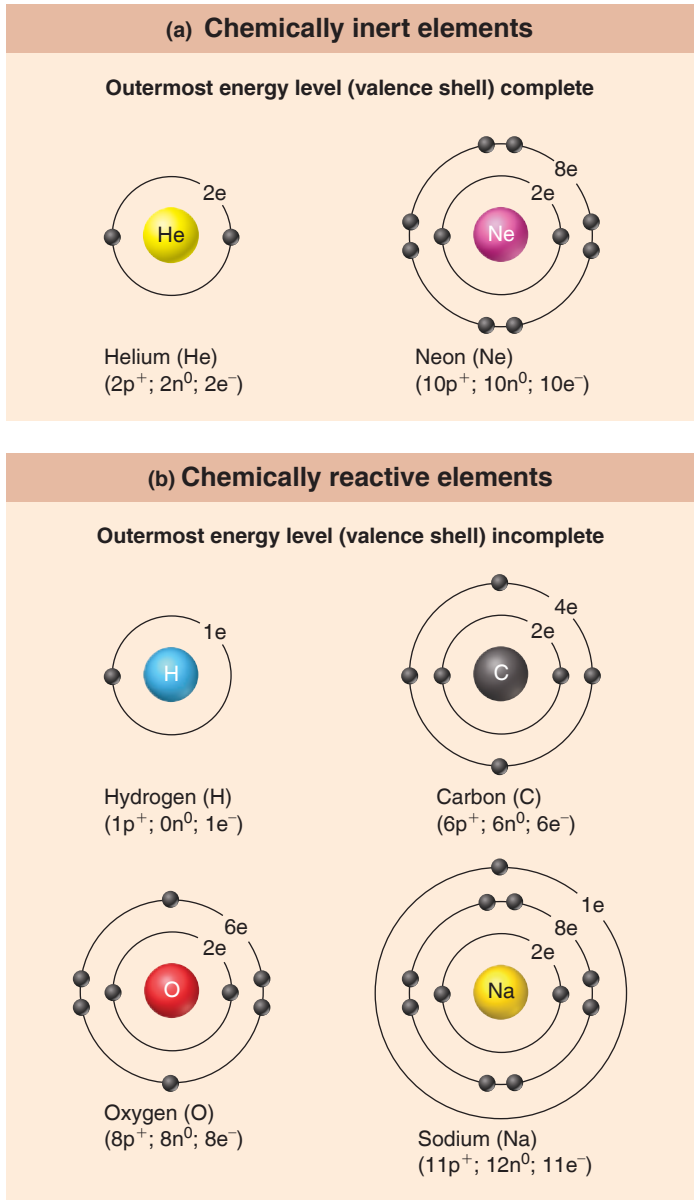
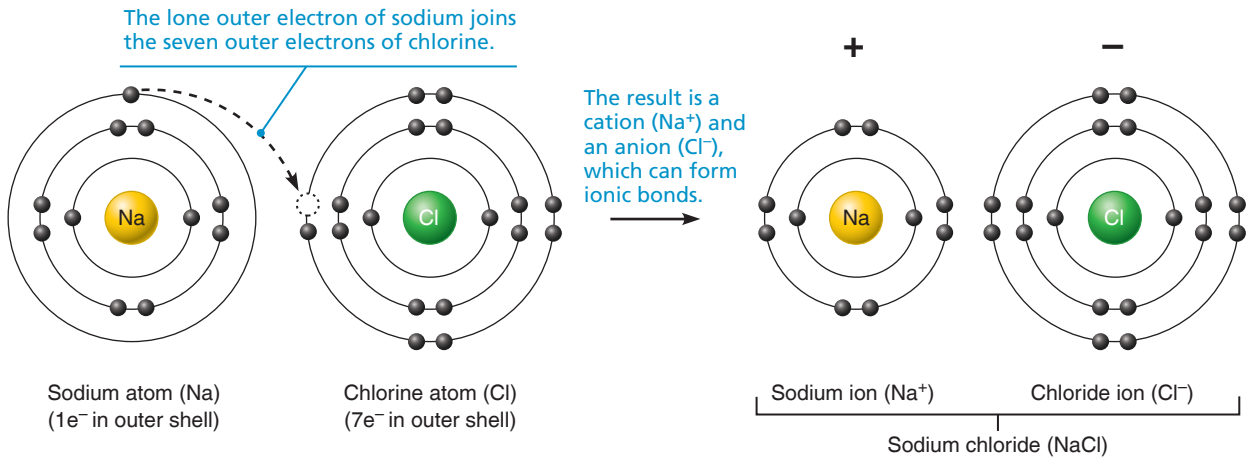
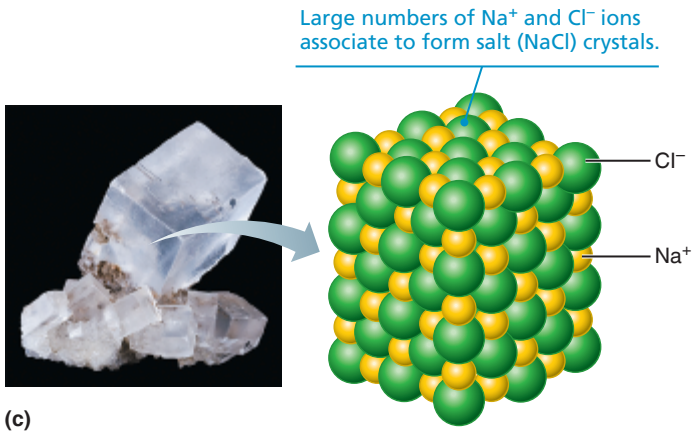


Figure 2.5 Chemically inert and reactive elements. (*Note*: For simplicity, each atomic nucleus is shown as a sphere with the atom's symbol; individual protons and neutrons are not shown.)



(a) (b)



(c)

Figure 2.6 Formation of ionic bonds.

tend to interact in such a way that they end up having *8 electrons in their valence shell*.

Types of Chemical Bonds

Three major types of chemical bonds—*ionic*, *covalent*, and *hydrogen bonds*—result from attractive forces between atoms. The key features of these three bond types are summarized in **Table 2.2** on p. 67.

Ionic Bonds

Recall that atoms are electrically neutral. However, electrons can be transferred from one atom to another, and when this happens, the precise balance of + and − charges is lost so that charged particles called **ions** are formed. An **ionic bond** (i-on′ik) is a chemical bond between atoms formed by the transfer of one or more electrons from one atom to the other. The atom that gains one or more electrons is the *electron acceptor*. It acquires a net negative charge and is called an **anion** (an′i-on). The atom that loses electrons is the *electron donor*. It acquires a net positive charge and is called a **cation** (kat′i-on). (To remember this term, think of the "t" in "cation" as a + sign.) Both anions and cations are formed whenever electron transfer between atoms occurs. Because opposite charges attract, these ions tend to stay close together, resulting in an ionic bond.

One example of ionic bonding is the formation of table salt, or sodium chloride (NaCl), by interaction of sodium and chlorine atoms (**Figure 2.6**). Sodium, with an atomic number of 11, has only 1 electron in its valence shell. It would be very difficult to attempt to fill this shell by adding 7 more. However, if this single electron is lost, shell 2 with 8 electrons becomes the valence shell (outermost energy level containing electrons) and is full. By losing the lone electron in its third energy level, sodium achieves stability and becomes a cation (Na^+). On the other hand, chlorine (atomic number 17) needs only 1 electron to fill its valence shell. By accepting an electron, chlorine achieves stability and becomes an anion.

When sodium and chlorine atoms interact, this is exactly what happens. Sodium donates an electron to chlorine (Figure 2.6a), and the oppositely charged ions created in this exchange attract each other, forming sodium chloride (Figure 2.6b). Ionic bonds are commonly formed between atoms with 1 or 2 valence shell electrons (the metallic elements, such as sodium, calcium, and potassium) and atoms with 7 valence shell electrons (such as chlorine, fluorine, and iodine).

Most ionic compounds fall in the chemical category called *salts*. In the dry state, salts such as sodium chloride do not exist as individual molecules. Instead, they form **crystals**, large arrays of cations and anions held together by ionic bonds (Figure 2.6c).

Sodium chloride is an excellent example of the difference in properties between a compound and its constituent atoms. Sodium is a silvery white metal, and chlorine in its molecular state is a poisonous green gas used to make bleach. However, sodium chloride is a white crystalline solid that we sprinkle on our food.

Covalent Bonds

Electrons do not have to be completely transferred for atoms to achieve stability. Instead, they may be *shared* so that each atom is able to fill its outer electron shell at least part of the time. Electron sharing produces molecules in which the shared electrons occupy a single orbital common to both atoms, which constitutes a **covalent bond** (ko-va′lent).

Hydrogen with its single electron can fill its only shell (shell 1) by sharing a pair of electrons with another atom. When it shares with another hydrogen atom, a molecule of hydrogen

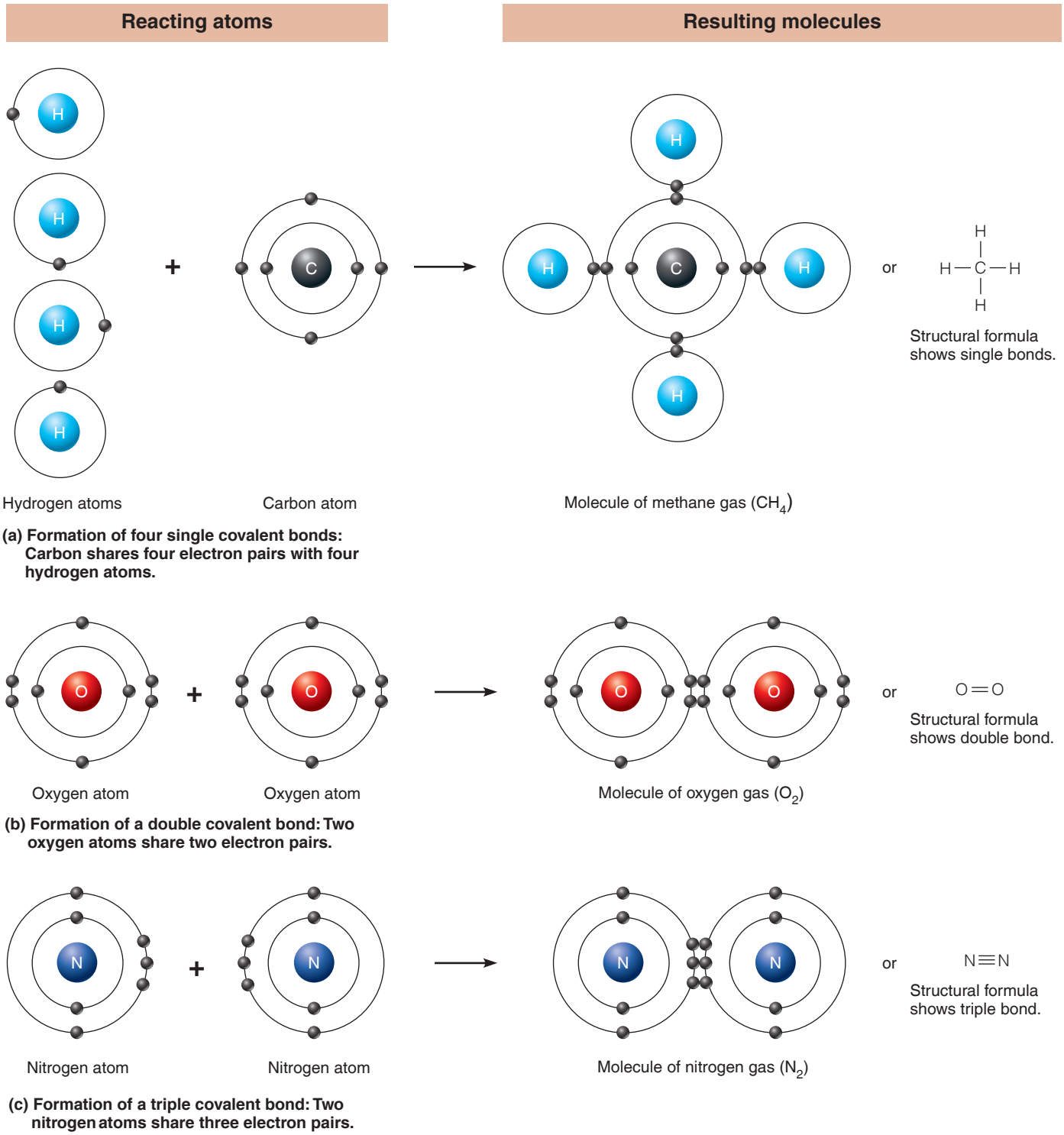


Figure 2.7 Formation of covalent bonds.

gas is formed. The shared electron pair orbits around the molecule as a whole, satisfying the stability needs of each atom.

Hydrogen can also share an electron pair with different kinds of atoms to form a compound (**Figure 2.7a**). Carbon has 4 electrons in its outermost shell, but needs 8 to achieve stability. Hydrogen has 1 electron, but needs 2. When a methane molecule (CH_4) is formed, carbon shares 4 pairs of electrons with 4 hydrogen atoms (1 pair with each hydrogen). Again, the shared electrons orbit and "belong to" the whole molecule, ensuring the stability of each atom.

When 2 atoms share 1 pair of electrons, a single covalent bond is formed (indicated by a single line connecting the atoms, such as H—H). In some cases, atoms share two or three electron pairs, resulting in *double* or *triple covalent bonds* (Figure 2.7b and c). (These bonds are indicated by double or triple connecting lines such as O=O or N≡N.)

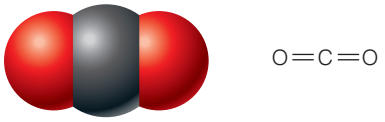
Polar and Nonpolar Molecules In the covalent bonds we have discussed, the shared electrons are shared equally between the atoms of the molecule for the most part. The molecules formed are electrically balanced and are called **nonpolar molecules** (because they do not have separate + and − poles of charge).

Such electrical balance is not always the case. When covalent bonds are formed, the resulting molecule always has a specific three-dimensional shape, with the bonds formed at definite angles. A molecule's shape helps determine what other molecules or atoms it can interact with. It may also result in unequal electron pair sharing, creating a **polar molecule**, especially in nonsymmetrical molecules containing atoms with different electron-attracting abilities.

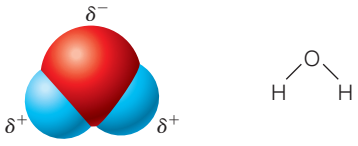
In general, *small* atoms with 6 or 7 valence shell electrons, such as oxygen, nitrogen, and chlorine, are electron-hungry and attract electrons very strongly, a capability called **electronegativity**. On the other hand, most atoms with only one or two valence shell electrons tend to be **electropositive**. In other words, their electron-attracting ability is so low that they usually lose *their* valence shell electrons to other atoms. Potassium and sodium, each with one valence shell electron, are good examples of electropositive atoms.

Carbon dioxide and water illustrate how molecular shape and the relative electron-attracting abilities of atoms determine whether a covalently bonded molecule is nonpolar or polar. In carbon dioxide (CO_2), carbon shares four electron pairs with two oxygen atoms (two pairs are shared with each oxygen). Oxygen is very electronegative and so attracts the shared electrons much more strongly than does carbon. However, because the carbon dioxide molecule is linear and symmetrical (**Figure 2.8a**), the electron-pulling ability of one oxygen atom offsets that of the other, like a standoff between equally strong teams in a game of tug-of-war. As a result, the shared electrons orbit the entire molecule and carbon dioxide is a nonpolar compound.

In contrast, a water molecule (H_2O) is bent, or V shaped (Figure 2.8b). The two electropositive hydrogen atoms are located at the same end of the molecule, and the very



(a) Carbon dioxide (CO_2) molecules are linear and symmetrical. They are nonpolar.



(b) V-shaped water (H_2O) molecules have two poles of charge—a slightly more negative oxygen end (δ^-) and a slightly more positive hydrogen end (δ^+).

Figure 2.8 Carbon dioxide and water molecules have different shapes, as illustrated by molecular models.

Ionic bond	Polar covalent bond	Nonpolar covalent bond
Complete transfer of electrons	Unequal sharing of electrons	Equal sharing of electrons
Separate ions (charged particles) form	Charge unbalanced among atoms [molecule has slightly positive (δ^+) and slightly negative (δ^-) ends]	Charge balanced among atoms
Na^+ Cl^-	δ^- O H H δ^+ δ^+	O=C=O
Sodium chloride	Water	Carbon dioxide

Figure 2.9 Ionic, polar covalent, and nonpolar covalent bonds compared along a continuum.

electronegative oxygen is at the opposite end. This arrangement allows oxygen to pull the shared electrons toward itself and away from the two hydrogen atoms. In this case, the electron pairs are *not* shared equally, but spend more time in the vicinity of oxygen. Because electrons are negatively charged, the oxygen end of the molecule is slightly more negative (the charge is indicated with a delta and minus as δ^-) and the hydrogen end slightly more positive (indicated by δ^+). Because water has two poles of charge, it is a *polar molecule*, or **dipole** (di′pōl).

Polar molecules orient themselves toward other dipoles or toward charged particles (such as ions and some proteins), and they play essential roles in chemical reactions in body cells. The polarity of water is particularly significant, as you will see later in this chapter.

Different molecules exhibit different degrees of polarity, and we can see a gradual change from ionic to nonpolar covalent bonding as summarized in **Figure 2.9**. Ionic bonds (complete electron transfer) and nonpolar covalent bonds (equal electron sharing) are the extremes of a continuum, with various degrees of unequal electron sharing in between.

Hydrogen Bonds

Unlike the stronger ionic and covalent bonds, hydrogen bonds are more like attractions than true bonds. Hydrogen bonds form when a hydrogen atom, already covalently linked to one electronegative atom (usually nitrogen or oxygen), is attracted by another electron-hungry atom, so that a "bridge" forms between them.

Hydrogen bonding is common between dipoles (such as water molecules) because the slightly negative oxygen atoms of one molecule attract the slightly positive hydrogen atoms of other

Table 2.2 Summary: Major Chemical Bond Types

TYPE	DESCRIPTION	STRENGTH
Covalent bonds	Sharing of pairs of electrons. May be polar (not equally shared) or nonpolar (equally shared).	Strongest
Ionic bonds	Attraction between two oppositely charged ions.	Intermediate
Hydrogen bonds	Attraction between a hydrogen atom carrying a partial positive charge (δ^+) and an electronegative atom with a slightly negative charge (δ^-).	Weakest

molecules (**Figure 2.10a**). Hydrogen bonding is responsible for the tendency of water molecules to cling together and form films, referred to as *surface tension*. This tendency helps explain why water beads up into spheres when it sits on a hard surface and why water striders can walk on a pond's surface (Figure 2.10b).

Although hydrogen bonds are too weak to bind atoms together to form molecules, they are important *intramolecular bonds* (literally, bonds within molecules), which hold different parts of a single large molecule in a specific three-dimensional shape. Some large biological molecules, such as proteins and DNA, have numerous hydrogen bonds that help maintain and stabilize their structures.

Check Your Understanding

10. What kinds of bonds form between water molecules?

11. How many electrons does magnesium ($_{12}$Mg) contain in its valence shell? If magnesium forms an ionic bond with another atom, will it lose or gain these electrons?

12. APPLY Hydrogen chloride (HCl) has a polar covalent bond. Consult the periodic table and explain what the charge distribution is between its two atoms.

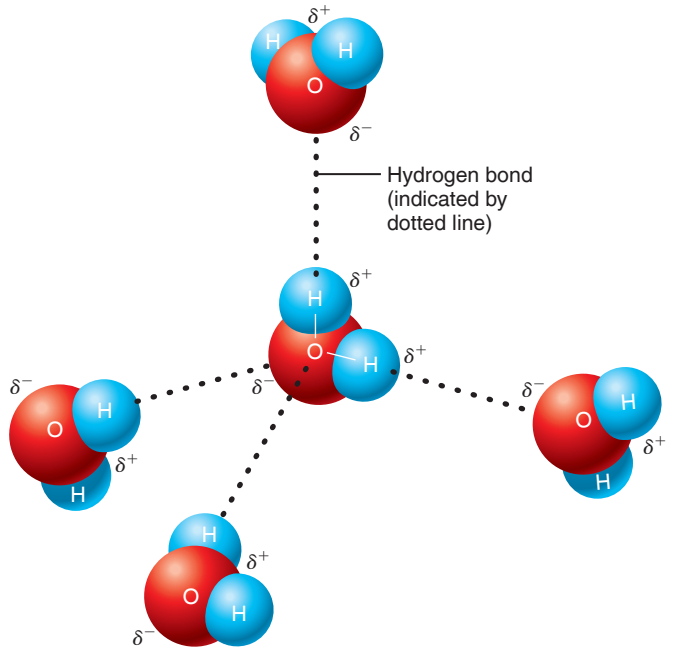
For answers, see Answers Appendix.

2.5 Chemical reactions occur when electrons are shared, gained, or lost

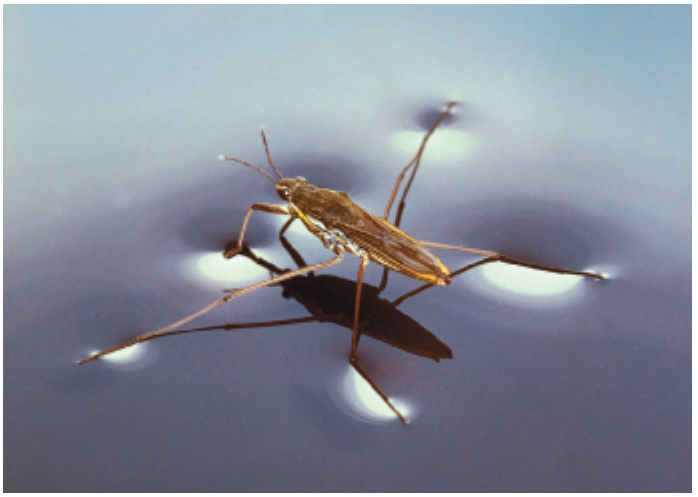
Learning Outcomes

- **Define the three major types of chemical reactions: synthesis, decomposition, and exchange. Comment on the nature of oxidation-reduction reactions and their importance.**
- **Explain why chemical reactions in the body are often irreversible.**
- **Describe factors that affect chemical reaction rates.**

As we noted earlier, all particles of matter are in constant motion because of their kinetic energy. Movement of atoms or molecules in a solid is usually limited to vibration because the particles are united by fairly rigid bonds. But in liquids or gases, particles dart about randomly, sometimes colliding with one another and interacting to undergo chemical reactions. A **chemical reaction** occurs whenever chemical bonds are formed, rearranged, or broken.



(a) The slightly positive ends (δ^+) of the water molecules become aligned with the slightly negative ends (δ^-) of other water molecules.



(b) A water strider can walk on a pond because of the high surface tension of water, a result of the combined strength of its hydrogen bonds.

Figure 2.10 Hydrogen bonds.

Chemical Equations

We can write chemical reactions in symbolic form as chemical equations. For example, we indicate the joining of two hydrogen atoms to form hydrogen gas as

$$\underset{\text{reactants}}{H + H} \rightarrow \underset{\text{product}}{H_2 \text{ (hydrogen gas)}}$$

and the combining of four hydrogen atoms and one carbon atom to form methane as

$$\underset{\text{reactants}}{4H + C} \rightarrow \underset{\text{product}}{CH_4 \text{ (methane)}}$$

Notice that in equations, a number written as a *subscript* indicates that the atoms are joined by chemical bonds. But a number written as a *prefix* denotes the number of *unjoined* atoms or molecules. For example, CH_4 reveals that four hydrogen atoms are bonded together with carbon to form the methane molecule, but 4H signifies four unjoined hydrogen atoms.

A chemical equation is like a sentence describing what happens in a reaction. It contains the following information:

- The **reactants**: The number and kinds of the interacting substances.
- The **products**: The chemical composition of the result of the reaction.
- The *relative proportions*: Balanced equations indicate the relative proportion of each reactant and product.

In the previous equations, the reactants are atoms, as indicated by their atomic symbols (H, C). The product in each case is a molecule, as represented by its **molecular formula** (H_2, CH_4). The equation for the formation of methane may be read in terms of molecules or moles—as *either* "four hydrogen atoms plus one carbon atom yield one molecule of methane" *or* "four moles of hydrogen atoms plus one mole of carbon yield one mole of methane." Using moles is more practical because it is impossible to measure out one atom or one molecule of anything!

Types of Chemical Reactions

Most chemical reactions can be categorized as one of three types: *synthesis*, *decomposition*, or *exchange reactions*.

When atoms or molecules combine to form a larger, more complex molecule, the process is a **synthesis**, or **combination**, **reaction**. A synthesis reaction always involves bond formation. It can be represented (using arbitrary letters) as

$$A + B \rightarrow AB$$

Synthesis reactions are the basis of constructive, or **anabolic**, activities in body cells, such as joining small molecules called amino acids into large protein molecules (**Figure 2.11a**). Synthesis reactions are conspicuous in rapidly growing tissues.

A **decomposition reaction** occurs when a molecule is broken down into smaller molecules or its constituent atoms:

$$AB \rightarrow A + B$$

Essentially, decomposition reactions are reverse synthesis reactions: Bonds are broken. Decomposition reactions underlie all degradative, or **catabolic**, processes in body cells. For example, the bonds of glycogen molecules are broken to release simpler molecules of glucose (Figure 2.11b).

Exchange, or **displacement**, **reactions** involve both synthesis and decomposition. Bonds are both made and broken. In an exchange reaction, parts of the reactant molecules change partners, so to speak, producing different product molecules:

$$AB + C \rightarrow AC + B \quad \text{and} \quad AB + CD \rightarrow AD + CB$$

An exchange reaction occurs when ATP reacts with glucose and transfers its end phosphate group (indicated by a circled P in Figure 2.11c) to glucose, forming glucose-phosphate. At the same time, the ATP becomes ADP. This important reaction occurs whenever glucose enters a body cell, and it effectively traps the glucose fuel molecule inside the cell.

Another group of important chemical reactions in living systems is **oxidation-reduction reactions**, called **redox reactions**

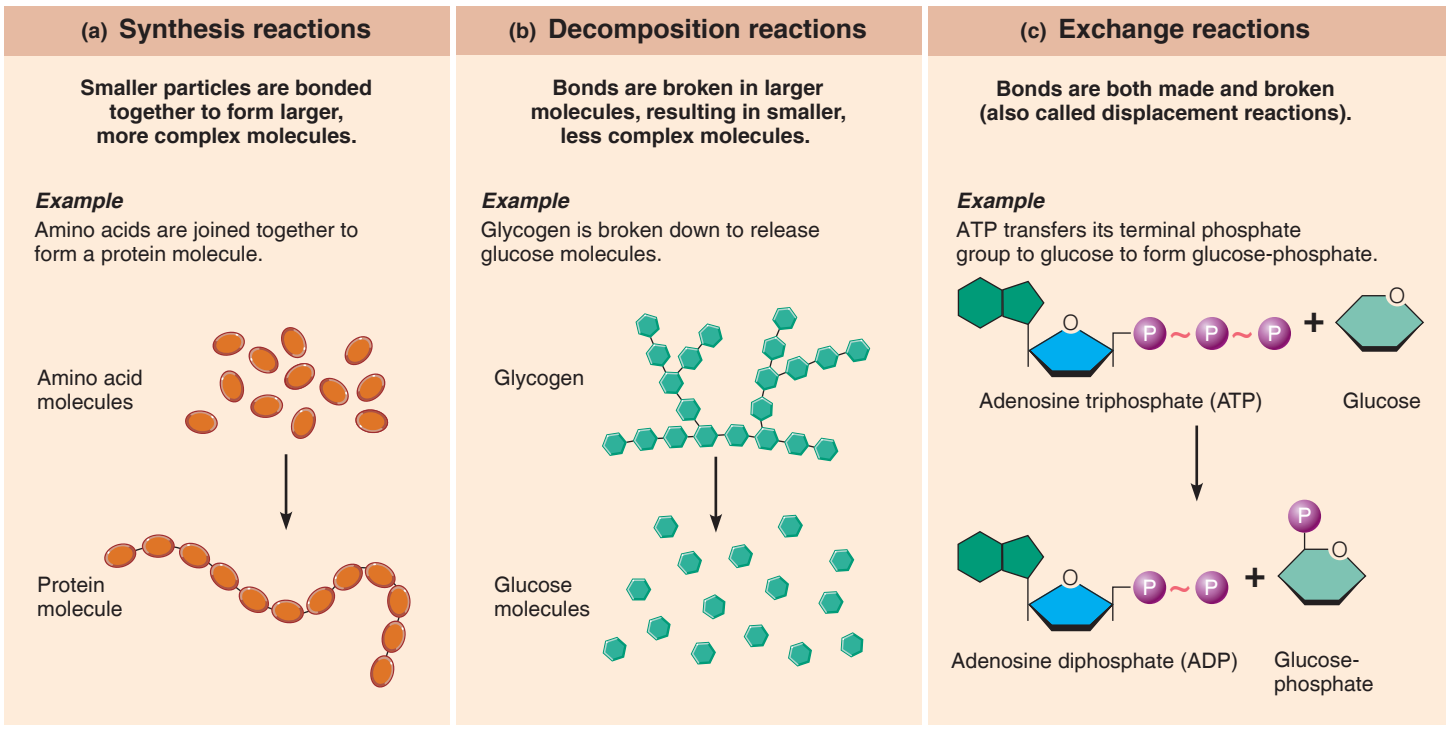


Figure 2.11 Types of chemical reactions.

for short. Oxidation-reduction reactions are decomposition reactions in that they are the basis of all reactions in which food fuels are broken down for energy (that is, in which ATP is produced). They are also a special type of exchange reaction because electrons are exchanged between the reactants. The reactant losing the electrons is the *electron donor* and is said to be **oxidized**. The reactant taking up the transferred electrons is the *electron acceptor* and is said to become **reduced**.

Redox reactions also occur when ionic compounds are formed. Recall that in the formation of NaCl (see Figure 2.6), sodium loses an electron to chlorine. Consequently, sodium is oxidized and becomes a sodium ion, and chlorine is reduced and becomes a chloride ion. However, not all oxidation-reduction reactions involve *complete transfer* of electrons—some simply change the pattern of electron sharing in covalent bonds. For example, a substance is oxidized either by losing hydrogen atoms or by combining with oxygen. The common factor in these events is that electrons that formerly "belonged" to the reactant molecule are lost. The electrons are lost either entirely (as when hydrogen is removed and takes its electron with it) or relatively (as the shared electrons spend more time in the vicinity of the very electronegative oxygen atom).

To understand the importance of oxidation-reduction reactions in living systems, take a look at the overall equation for *cellular respiration*, which represents the major pathway by which glucose is broken down for energy in body cells:

$$\underset{\text{glucose}}{C_6H_{12}O_6} + \underset{\text{oxygen}}{6O_2} \rightarrow \underset{\text{carbon dioxide}}{6CO_2} + \underset{\text{water}}{6H_2O} + \underset{\text{cellular energy}}{ATP}$$

As you can see, it is an oxidation-reduction reaction. Consider what happens to the hydrogen atoms (and their electrons). Glucose is oxidized to carbon dioxide as it loses hydrogen atoms, and oxygen is reduced to water as it accepts the hydrogen atoms. This reaction is covered in detail in Chapter 24.

Energy Flow in Chemical Reactions

Because all chemical bonds represent stored chemical energy, all chemical reactions ultimately result in net absorption or release of energy. Reactions that release energy are **exergonic reactions**. These reactions yield products with less energy than the initial reactants, along with energy that can be harvested for other uses. With a few exceptions, catabolic and oxidative reactions are exergonic.

In contrast, the products of energy-absorbing, or **endergonic**, reactions contain more potential energy in their chemical bonds than did the reactants. Anabolic reactions are typically endergonic reactions. In the body, endergonic reactions are usually coupled to exergonic reactions. For example, the energy released when fuel molecules are broken down (oxidized) is captured in ATP molecules and then used to synthesize the complex biological molecules the body needs to sustain life.

Reversibility of Chemical Reactions

All chemical reactions are potentially reversible. If chemical bonds can be made, they can be broken, and vice versa. Reversibility is indicated by a double arrow. When the arrows differ in length, the longer arrow indicates the major direction in which the reaction proceeds:

$$A + B \rightleftharpoons AB$$

In this example, the forward reaction (going to the right) predominates. Over time, the product (AB) accumulates and the reactants (A and B) decrease in amount.

When the arrows are of equal length, as in

$$A + B \rightleftharpoons AB$$

neither the forward reaction nor the reverse reaction is dominant. In other words, for each molecule of product (AB) formed, one product molecule breaks down, releasing the reactants A and B. Such a chemical reaction is said to be in a state of **chemical equilibrium**.

Once chemical equilibrium is reached, there is no further *net change* in the amounts of reactants and products unless more of either are added to the mix. Product molecules are still formed and broken down, but the balance established when equilibrium was reached (such as greater numbers of product molecules) remains unchanged.

Chemical equilibrium is analogous to the admission scheme used by many nightclubs that restrict the number of patrons admitted to comply with safety regulations. To stay within their allowed capacity (for example, 300), once 300 people are inside no one else is admitted until others leave. For instance, when 10 leave, 10 more may go in. So there is a constant turnover but the number of patrons in the club always stays at 300.

Although all chemical reactions are reversible, many biological reactions show so little tendency to go in the reverse direction that they are irreversible for all practical purposes. Chemical reactions that release energy will not go in the opposite direction unless energy is put back into the system. For example, when our cells break down glucose during cellular respiration to yield carbon dioxide and water, some of the energy released is trapped in the bonds of ATP. Because the cells then use ATP's energy for various functions (and more glucose will be along with the next meal), this particular reaction is never reversed in our cells. Furthermore, if a product of a reaction is continuously removed from the reaction site, it is unavailable to take part in the reverse reaction. This situation occurs when the carbon dioxide that is released during glucose breakdown leaves the cell, enters the blood, and is eventually removed from the body by the lungs.

Factors Influencing the Rate of Chemical Reactions

What influences the speed of chemical reactions? For atoms and molecules to react chemically in the first place, they must *collide* with enough force to overcome the repulsion between their electrons. Interactions between valence shell electrons—the basis of bond making and breaking—cannot occur long distance. The force of collisions depends on how fast the particles are moving. Solid, forceful collisions between rapidly moving particles in which valence shells overlap are much more likely to cause reactions than are collisions in which the particles graze each other lightly. The factors that affect the rate of chemical reactions are:

- **Temperature.** Higher temperatures increase the kinetic energy of particles and the force of their collisions, increasing the rate of chemical reactions.
- **Concentration.** High concentrations of reacting particles increase the chances of successful collisions, and reactions progress faster. Lowering concentrations slows reactions. Unless reactants are added or products removed, chemical equilibrium will eventually occur.
- **Particle size.** The smaller the reacting particles, the faster the chemical reaction. Smaller particles move faster than larger ones (at the same temperature) and so collide more frequently and forcefully.
- **Catalysts.** At normal body temperature, most chemical reactions would proceed far too slowly to maintain life were it not for the presence of catalysts. **Catalysts** (kat′ah-lists) are substances that increase the rate of chemical reactions without themselves becoming chemically changed or part of the product. Biological catalysts are called *enzymes* (en′zīmz). Later in this chapter we describe how enzymes work.

Check Your Understanding

13. Which reaction type—synthesis, decomposition, or exchange—occurs when fats are digested in your small intestine?

14. Why are many reactions that occur in living systems irreversible for all intents and purposes?

15. What specific name is given to decomposition reactions in which food fuels are broken down for energy?

For answers, see Answers Appendix.

PART 2
BIOCHEMISTRY

Biochemistry is the study of the chemical composition and reactions of living matter. Chemicals in the body fall into one of two major classes: organic or inorganic compounds. **Organic compounds** contain carbon and are made by living things. All organic compounds are covalently bonded molecules, and many are large.

All other chemicals in the body are considered **inorganic compounds**. These include water, salts, and many acids and bases. Inorganic compounds are generally defined as compounds that lack carbon. You should be aware of a few exceptions to this generalization: Carbon dioxide and carbon monoxide, for example, contain carbon but are considered to be inorganic compounds. Organic and inorganic compounds are equally essential for life.

2.6 Inorganic compounds include water, salts, and many acids and bases

Learning Outcomes

- **Explain the importance of water and salts to body homeostasis.**
- **Define acid and base, and explain the concept of pH.**

Water

Water is the most abundant and important inorganic compound in living material. It makes up 60–80% of the volume of most living cells. What makes water so vital to life? The answer lies in several properties:

- **High heat capacity.** Water has a high heat capacity. In other words, it absorbs and releases large amounts of heat before changing appreciably in temperature itself. This property of water prevents sudden changes in temperature caused by external factors, such as sun or wind exposure, or by internal conditions that release heat rapidly, such as vigorous muscle activity. As part of blood, water redistributes heat among body tissues, ensuring temperature homeostasis.
- **High heat of vaporization.** When water evaporates, or vaporizes, it changes from a liquid to a gas (water vapor). This transformation requires that large amounts of heat be absorbed to break the hydrogen bonds that hold water molecules together. This property is extremely beneficial when we sweat. As sweat (mostly water) evaporates from our skin, large amounts of heat are removed from the body, providing efficient cooling.
- **Polar solvent properties.** Water is an unparalleled solvent. Indeed, it is often called the **universal solvent**. Biochemistry is "wet chemistry." Biological molecules do not react chemically unless they are in solution, and virtually all chemical reactions in the body depend on water's solvent properties.

  Because water molecules are polar, they orient themselves with their slightly negative ends toward the positive ends of the solutes, and vice versa, first attracting the solute molecules, and then surrounding them. This polarity of water explains why ionic compounds and other small reactive molecules (such as acids and bases) *dissociate* in water, their ions separating from each other and becoming evenly scattered in the water, forming true solutions (**Figure 2.12**).

  Water also forms layers of water molecules, called **hydration layers**, around large charged molecules such as proteins, shielding them from the effects of other charged substances in the vicinity and preventing them from settling out of solution. Such protein-water mixtures are *biological colloids*. Blood plasma and cerebrospinal fluid (which surrounds the brain and spinal cord) are colloids.

  Water is the body's major transport medium because it is such an excellent solvent. Nutrients, respiratory gases, and metabolic wastes carried throughout the body are dissolved in blood plasma, and many metabolic wastes are excreted from the body in urine, another watery fluid. Lubricants (e.g., mucus) also use water as their dissolving medium.
- **Reactivity.** Water is an important *reactant* in many chemical reactions. For example, foods are broken down to their building blocks by adding a water molecule to each bond as it is broken. We will discuss such decomposition reactions (called *hydrolysis reactions*) in the next module.
- **Cushioning.** Water is not compressible, but it can flow. These properties allow water to form resilient cushions around certain body organs, helping to protect them from physical trauma. The cerebrospinal fluid surrounding the brain exemplifies water's cushioning role.

Salts

A **salt** is an ionic compound containing cations other than H^+ and anions other than the hydroxyl ion (OH^-). As already noted, when salts are dissolved in water, they dissociate into their component ions (Figure 2.12). For example, sodium sulfate (Na_2SO_4) dissociates into two Na^+ ions and one SO_4^{2-} ion. It dissociates easily because the ions are already formed. All that remains is for water to overcome the attraction between the oppositely charged ions.

All ions are **electrolytes** (e-lek′tro-līts), substances that conduct an electrical current in solution. [Note that groups of atoms that bear an overall charge, such as sulfate (SO_4^{2-}), are called *polyatomic ions*.]

Salts commonly found in the body include NaCl, $CaCO_3$ (calcium carbonate), and KCl (potassium chloride). However, the most plentiful salts are the calcium phosphates that make bones and teeth hard. In their ionized form, salts play vital roles in body function. For instance, the electrolyte properties of sodium and potassium ions are essential for nerve impulse transmission and muscle contraction. Ionic iron forms part of the hemoglobin molecules that transport oxygen within red blood cells, and zinc and copper ions are important to the activity of some enzymes. Other important functions of the elements found in body salts are summarized in Table 2.1 on p. 58.

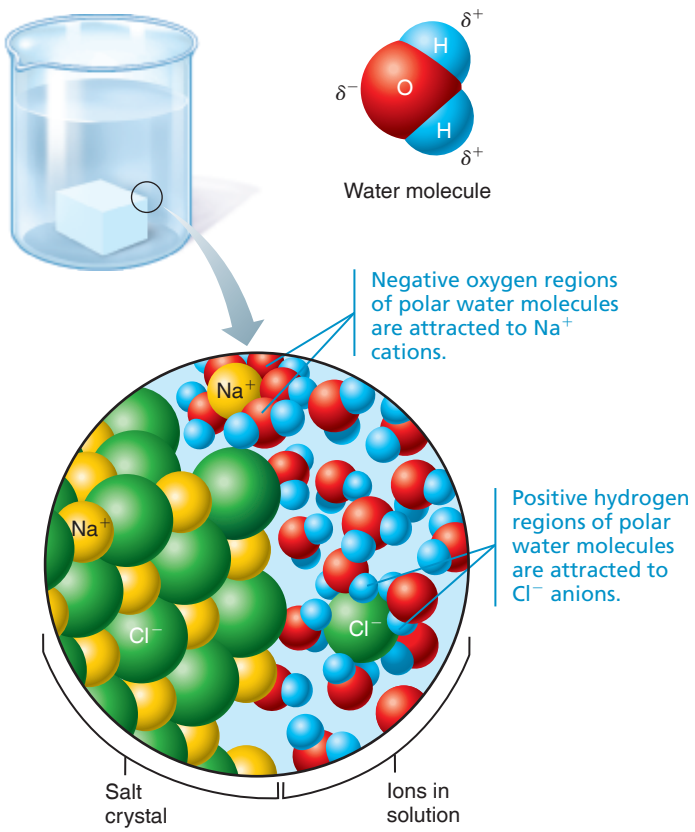


Figure 2.12 **Dissociation of salt in water.**

Acids and Bases

Like salts, acids and bases are electrolytes. They ionize and dissociate in water and can then conduct an electrical current.

Acids

Acids have a sour taste, can react with (dissolve) many metals, and "burn" a hole in your rug. But for our purposes the most useful definition of an acid is a substance that releases **hydrogen ions (H^+)** in detectable amounts. Because a hydrogen ion is just a hydrogen nucleus, which consists of a single "naked" proton, acids are also defined as **proton donors**.

When acids dissolve in water, they release hydrogen ions (protons) and anions. It is the concentration of protons that determines the acidity of a solution. For example, hydrochloric acid (HCl), an acid produced by stomach cells that aids digestion, dissociates into a proton and a chloride ion:

$$\underset{}{HCl} \rightarrow \underset{\text{proton}}{H^+} + \underset{\text{anion}}{Cl^-}$$

Other acids found or produced in the body include acetic acid ($HC_2H_3O_2$), which is the acidic portion of vinegar; and carbonic acid (H_2CO_3). The molecular formula for an acid is easy to recognize because the hydrogen is written first.

Bases

Bases have a bitter taste, feel slippery, and are **proton acceptors**—that is, they take up hydrogen ions (H^+) in detectable amounts. Common inorganic bases include the *hydroxides* (hi-drok′sīds), such as magnesium hydroxide (milk of magnesia) and sodium hydroxide (lye). Like acids, hydroxides dissociate when dissolved in water, but in this case **hydroxyl ions (OH^-)** (hi-drok′sil) and cations are liberated. For example, ionization of sodium hydroxide (NaOH) produces a hydroxyl ion and a sodium ion, and the hydroxyl ion then binds to (accepts) a proton present in the solution. This reaction produces water and simultaneously reduces the acidity (hydrogen ion concentration) of the solution:

$$\underset{}{NaOH} \rightarrow \underset{\text{cation}}{Na^+} + \underset{\text{hydroxyl ion}}{OH^-}$$

and then

$$OH^- + H^+ \rightarrow \underset{\text{water}}{H_2O}$$

Bicarbonate ion (HCO_3^-), an important base in the body, is particularly abundant in blood. **Ammonia (NH_3)**, a common waste product of protein breakdown in the body, is also a base. It has one pair of unshared electrons that strongly attracts protons. By accepting a proton, ammonia becomes an ammonium ion:

$$NH_3 + H^+ \rightarrow \underset{\text{ammonium ion}}{NH_4^+}$$

pH: Acid-Base Concentration

The more hydrogen ions in a solution, the more acidic the solution is. Conversely, the greater the concentration of hydroxyl ions (the lower the concentration of H^+), the more basic, or

alkaline (al′kuh-līn), the solution becomes. The relative concentration of hydrogen ions in various body fluids is measured in concentration units called **pH units** (pe-āch′).

The idea for a pH scale was devised by a Danish biochemist and beer brewer named Sören Sörensen in 1909. He was searching for a convenient means of checking the acidity of his alcoholic product to prevent its spoilage by bacterial action. (Acidic conditions inhibit many bacteria.) The pH scale that resulted is based on the concentration of hydrogen ions in a solution, expressed in terms of moles per liter, or molarity. The pH scale runs from 0 to 14 and is *logarithmic*. In other words, each successive change of one pH unit represents a tenfold change in hydrogen ion concentration (**Figure 2.13**). The pH of a solution is defined as the negative logarithm of the hydrogen ion concentration $[H^+]$ in moles per liter, or $-\log[H^+]$. (Note that brackets [ ] indicate concentration of a substance.)

At a pH of 7 (at which $[H^+]$ is 10^{-7} *M*), the solution is *neutral*—neither acidic nor basic. The number of hydrogen ions exactly equals the number of hydroxyl ions (pH = pOH). Absolutely pure (distilled) water has a pH of 7.

Solutions with a pH below 7 are acidic—the hydrogen ions outnumber the hydroxyl ions. The lower the pH, the more acidic the solution. A solution with a pH of 6 has ten times as many hydrogen ions as a solution with a pH of 7.

Solutions with a pH higher than 7 are alkaline, and the relative concentration of hydrogen ions decreases by a factor of 10 with each higher pH unit. So, solutions with pH values of 8 and 12 have, respectively, 1/10 and 1/100,000 (1/10 × 1/10 × 1/10 × 1/10 × 1/10) as many hydrogen ions as a solution of pH 7.

The approximate pH of several body fluids and of a number of common substances appears in Figure 2.13. Notice that as the hydrogen ion concentration decreases, the hydroxyl ion concentration rises, and vice versa.

HOMEOSTATIC IMBALANCE 2.1 — CLINICAL

Many of the life-preserving enzymes in your body work within a very narrow pH range. During cardiopulmonary resuscitation, an arterial pH of 7.0 predicts a poor outcome, and patients presenting with an arterial pH of less than 6.85 rarely survive.

Neutralization

What happens when acids and bases are mixed? They react with each other in displacement reactions to form water and a salt. For example, when hydrochloric acid and sodium hydroxide interact, sodium chloride (a salt) and water are formed.

$$\underset{\text{acid}}{HCl} + \underset{\text{base}}{NaOH} \rightarrow \underset{\text{salt}}{NaCl} + \underset{\text{water}}{H_2O}$$

This type of reaction is called a **neutralization reaction**, because the joining of H^+ and OH^- to form water neutralizes the solution. Although the salt produced is written in molecular form (NaCl), remember that it actually exists as dissociated sodium and chloride ions when dissolved in water.

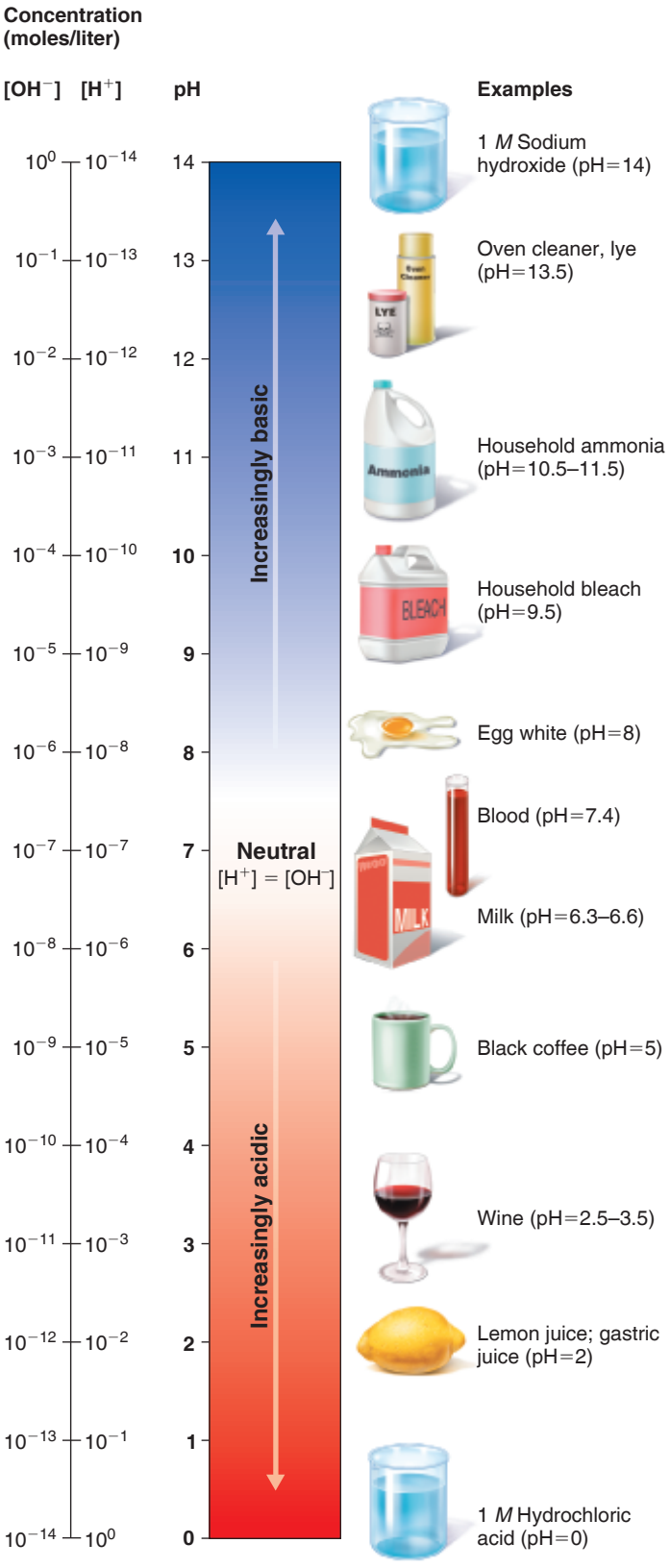


Figure 2.13 The pH scale and pH values of representative substances. The pH scale is based on the number of hydrogen ions in solution. The concentrations of hydrogen ions, $[H^+]$, and hydroxyl ions, $[OH^-]$, in moles per liter are indicated for each pH value noted. At a pH of 7, $[H^+] = [OH^-]$ and the solution is neutral.

Buffers

Living cells are extraordinarily sensitive to even slight changes in the pH of the environment. Imagine what would happen to all those hydrogen bonds in biological molecules with large numbers of free H^+ running around. (Can't you just hear those molecules saying, "Why share hydrogen when I can have my own?")

Homeostasis of acid-base balance is carefully regulated by the kidneys and lungs and by chemical systems (proteins and other types of molecules) called **buffers**. Buffers resist abrupt and large swings in the pH of body fluids by releasing hydrogen ions (acting as acids) when the pH begins to rise and by binding hydrogen ions (acting as bases) when the pH drops. Buffers can do this because they consist of a combination of a *weak acid* and a corresponding *weak base*. To comprehend how chemical buffer systems operate, you must thoroughly understand strong and weak acids and bases.

The first important concept is that the acidity of a solution reflects *only* the free hydrogen ions, not those still bound to anions. Consequently, acids that dissociate completely and irreversibly in water are called **strong acids**, because they dramatically change the pH of a solution. Examples are hydrochloric acid and sulfuric acid. If we could count out 100 molecules of hydrochloric acid and place them in 1 milliliter (ml) of water, we could expect to end up with 100 H^+, 100 Cl^-, and no undissociated hydrochloric acid molecules in that solution.

Acids that do not dissociate completely, like carbonic acid (H_2CO_3) and acetic acid (HAc), are **weak acids**. If we were to place 100 molecules of acetic acid in 1 ml of water, the reaction would be something like this:

$$100\ HAc \rightarrow 90\ HAc + 10\ H^+ + 10\ Ac^-$$

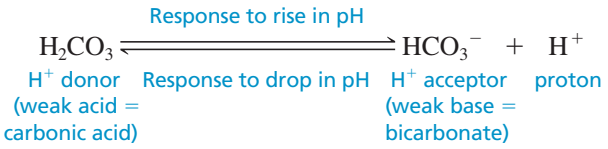
Because only free H^+ determines pH, you can see right away that the acetic acid solution with 10 H^+ is much less acidic than the HCl solution with 100 H^+. Weak acids dissociate in a predictable way, and molecules of the intact acid are in dynamic equilibrium with the dissociated ions. Consequently, the dissociation of acetic acid may also be written as

$$HAc \rightleftharpoons H^+ + Ac^-$$

This viewpoint allows us to see that if H^+ (released by a strong acid) is added to the acetic acid solution, the equilibrium will shift to the left and some H^+ and Ac^- will recombine to form HAc. On the other hand, if a strong base is added and the pH begins to rise, the equilibrium shifts to the right and more HAc molecules dissociate to release H^+. This characteristic of weak acids allows them to play important roles in the chemical buffer systems of the body.

The concept of strong and weak bases is more easily explained. Remember that bases are proton acceptors. **Strong bases** are those, like hydroxides, that dissociate easily in water and quickly tie up H^+. On the other hand, sodium bicarbonate (commonly known as baking soda) ionizes incompletely and reversibly. Because it accepts relatively few protons, its released bicarbonate ion is considered a **weak base**.

Now let's examine how one buffer system helps to maintain pH homeostasis of the blood. Normally, blood pH varies within a very narrow range (7.35 to 7.45). If the pH of blood varies from these limits by more than a few tenths of a unit, it may be fatal. Although there are other chemical blood buffers, the **bicarbonate buffer system** is a major one. In this buffer system, the weak acid is carbonic acid (H_2CO_3). It dissociates reversibly, releasing its corresponding weak base, bicarbonate ions (HCO_3^-), and protons (H^+):



The chemical equilibrium between carbonic acid and bicarbonate ion resists changes in blood pH by shifting to the right or left as H^+ ions are added to or removed from the blood. As blood pH rises (becomes more alkaline due to the addition of a strong base), the equilibrium shifts to the right, forcing more carbonic acid to dissociate. Similarly, as blood pH begins to drop (becomes more acidic due to the addition of a strong acid), the equilibrium shifts to the left as more bicarbonate ions begin to bind with protons. As you can see, strong bases are replaced by a weak base (bicarbonate ion) and protons released by strong acids are tied up in a weak one (carbonic acid). In either case, the blood pH changes much less than it would in the absence of the buffering system.We discuss acid-base balance and buffers in more detail in Chapter 26.

Check Your Understanding

16. Salts are electrolytes. What does that mean?

17. Which ion is responsible for increased acidity?

18. PREDICT Would you expect a small or large change in pH if you added a strong acid to a strong base? A strong acid to a weak base? Why?

19. MAKE CONNECTIONS We have learned about the complementarity of structure and function as it relates to anatomy and physiology (Chapter 1). See if you can extend your thinking about this principle to a simple molecule, and explain how the structure of a water molecule makes water an excellent solvent.

For answers, see Answers Appendix.

2.7 Organic compounds are made by dehydration synthesis and broken down by hydrolysis

Learning Outcome

- **Explain the role of dehydration synthesis and hydrolysis in forming and breaking down organic molecules.**

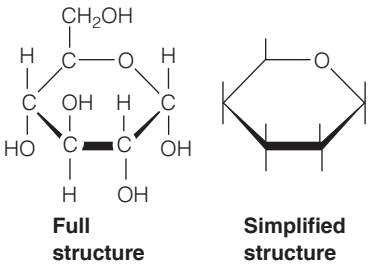
Molecules unique to living systems—carbohydrates, lipids (fats), proteins, and nucleic acids—all contain carbon. What makes carbon so special that "living" chemistry depends on its presence? To begin with, no other *small* atom is so precisely **electroneutral**. The consequence of its electroneutrality is that carbon never loses or gains electrons. Instead, it always shares

them. Furthermore, with four valence shell electrons, carbon forms four covalent bonds with other elements, as well as with other carbon atoms. As a result, carbon can help form long, chainlike molecules (common in fats), ring structures (typical of carbohydrates and steroids), and many other structures that are uniquely suited for specific roles in the body.

Many biological molecules (carbohydrates and proteins for example) are **macromolecules**—large complex molecules containing thousands of atoms. Most macromolecules are **polymers**, which are chainlike molecules made of many smaller, identical or similar subunits (**monomers**).

Monomers are joined together by a process called **dehydration synthesis** (Figure 2.14). During dehydration synthesis, a hydrogen atom is removed from one monomer and a hydroxyl group is removed from the monomer it is to be joined with. As a covalent bond unites the monomers, a water molecule is released. This removal of a water molecule at the bond site occurs each time a monomer is added to the growing polymer chain. The opposite reaction in which molecules are degraded is called **hydrolysis** (hi-drol′ĭ-sis; water splitting). In these reactions, a water molecule is added to each bond that is broken, thereby releasing its building blocks (smaller molecules).

Writing out all of the atoms in chemical structures is cumbersome, so everyone uses shortcuts. Here are two structures. The left structure shows all of the atoms. The structure on the right is the simplified version. It assumes that you know that each corner has a carbon. You will see these simplified structures throughout the chapter.



For the most part, organic molecules are very large molecules, but their interactions with other molecules typically

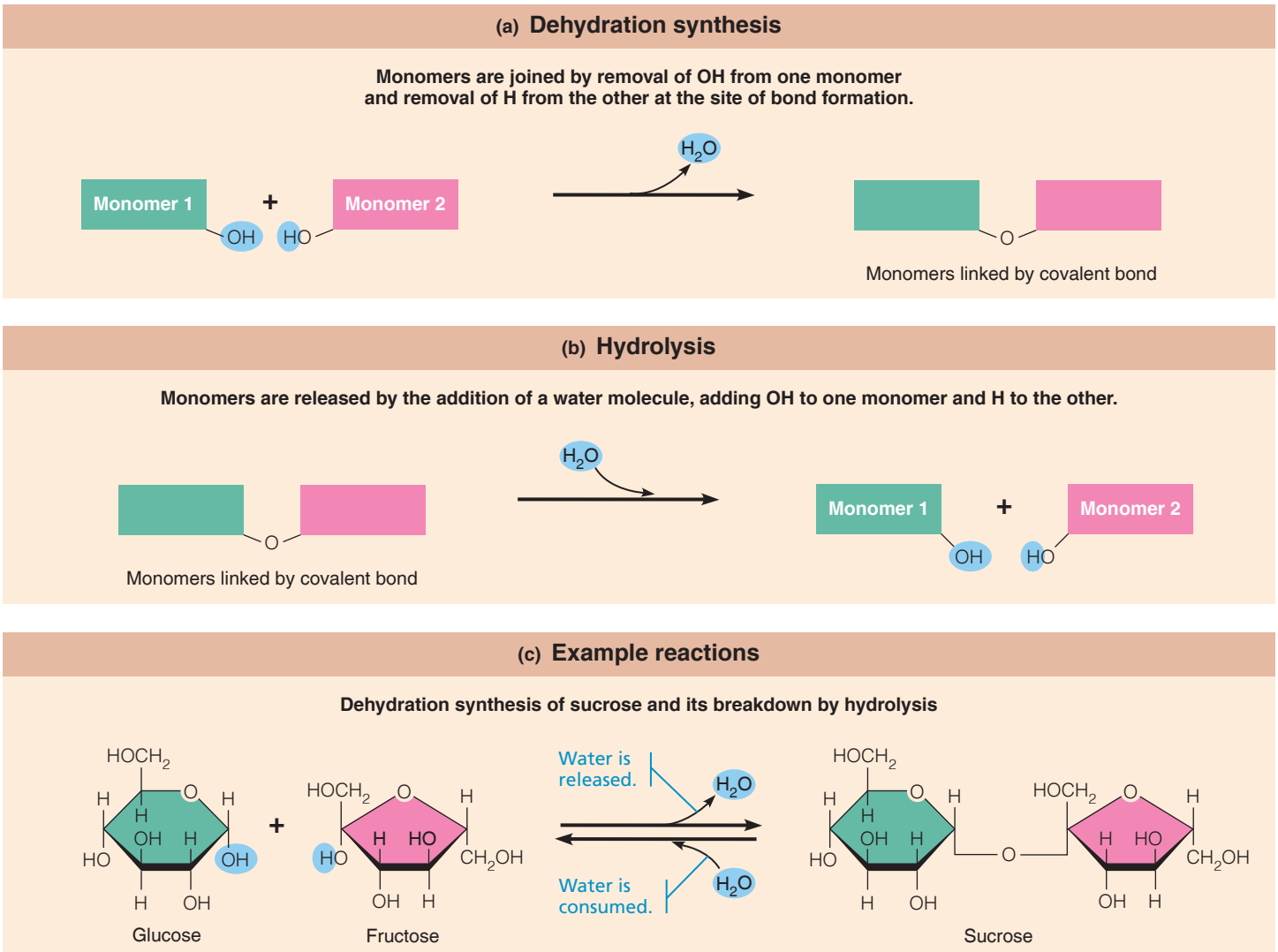


Figure 2.14 Dehydration synthesis and hydrolysis. Biological molecules are formed from their monomers, or subunits, by dehydration synthesis and broken down to the monomers by hydrolysis reactions. Note the use of simplified structures.

involve only small, reactive parts of their structure called *functional groups* (acid groups, amines, and others).The most important functional groups involved in biochemical reactions are illustrated in Appendix B.

We will explore the four types of macromolecules that form our cells in the next four modules.

Check Your Understanding

20. What is the result of hydrolysis reactions and how are these reactions accomplished?

For answers, see Answers Appendix.

2.8 Carbohydrates provide an easily used energy source for the body

Learning Outcome

▶ **Describe the building blocks, general structure, and biological functions of carbohydrates.**

Carbohydrates, a group of molecules that includes sugars and starches, represent 1–2% of cell mass. Carbohydrates contain carbon, hydrogen, and oxygen, and generally the hydrogen and oxygen atoms occur in the same 2:1 ratio as in water. This ratio is reflected in the word *carbohydrate* ("hydrated carbon").

A carbohydrate can be classified according to size and solubility as a monosaccharide ("one sugar"), disaccharide ("two sugars"), or polysaccharide ("many sugars"). Monosaccharides are the monomers, or building blocks, of the other carbohydrates. In general, the larger the carbohydrate molecule, the less soluble it is in water.

Monosaccharides

Monosaccharides (mon″o-sak′ah-rīdz), or *simple sugars*, are single-chain or single-ring structures containing from three to seven carbon atoms (**Figure 2.15a**). Usually the carbon, hydrogen, and oxygen atoms occur in the ratio 1:2:1, so a general formula for a monosaccharide is $(CH_2O)_n$, where n is the number of carbons in the sugar. Glucose, for example, has six carbon atoms, and its molecular formula is $C_6H_{12}O_6$. Ribose, with five carbons, is $C_5H_{10}O_5$.

Monosaccharides are named generically according to the number of carbon atoms they contain. Most important in the body are the pentose (five-carbon) and hexose (six-carbon) sugars. The pentose *deoxyribose* (de-ok″sĭ-ri′bōs) is part of DNA, and *glucose*, a hexose, is blood sugar.

Two other hexoses, *galactose* and *fructose*, are **isomers** (ī′so-mers) of glucose. That is, they have the same molecular

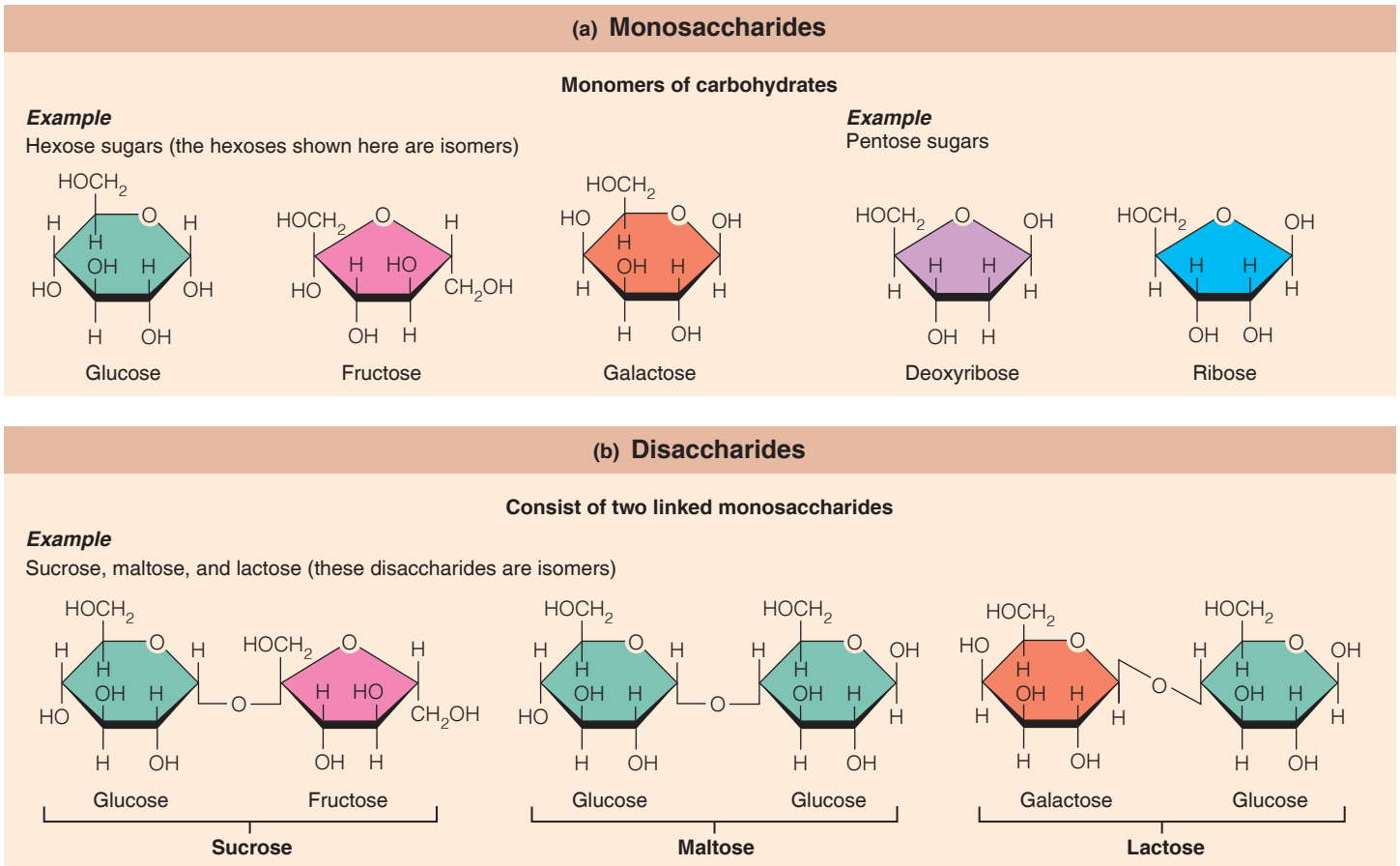


Figure 2.15 Carbohydrate molecules important to the body. *(Figure continues on p. 76 .)*

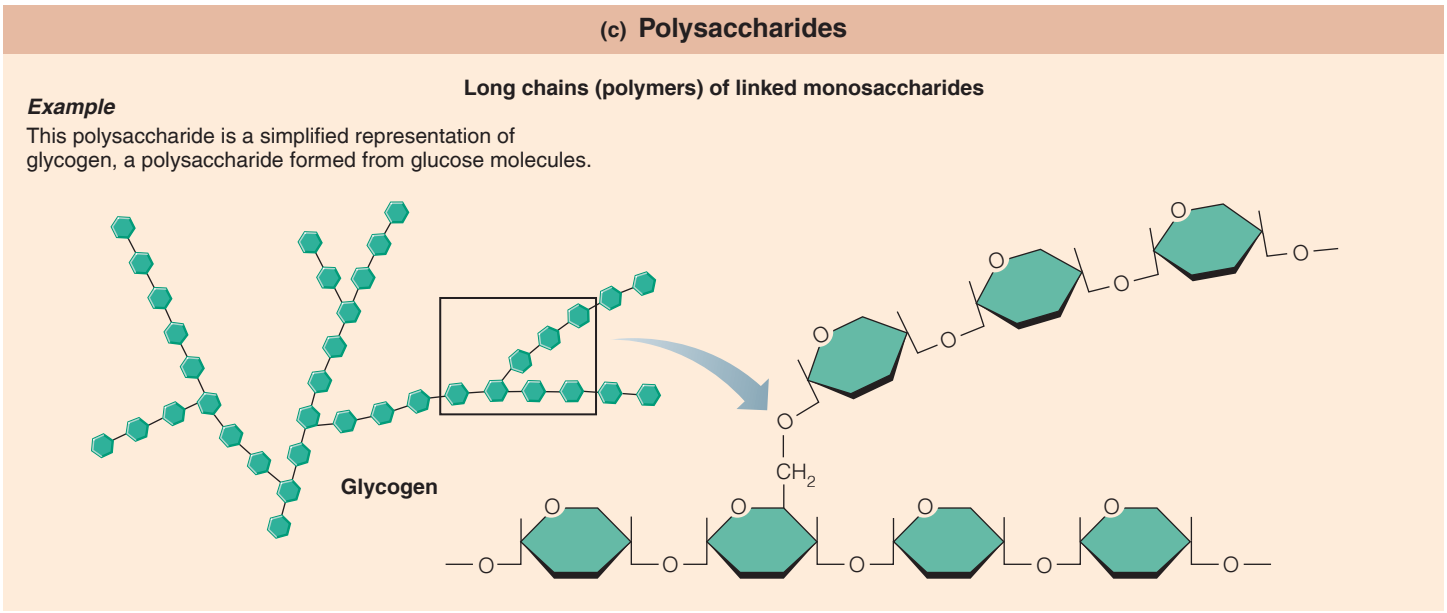


Figure 2.15 *(continued)* **Carbohydrate molecules important to the body.**

formula ($C_6H_{12}O_6$), but their atoms are arranged differently, giving them different chemical properties (Figure 2.15a).

Disaccharides

A **disaccharide** (di-sak′ah-rīd), or *double sugar*, is formed when two monosaccharides are joined by dehydration synthesis (Figure 2.14a, c). In this synthesis reaction, a water molecule is lost as the bond is made, as illustrated by the synthesis of sucrose (soo′krōs):

$$2C_6H_{12}O_6 \rightarrow C_{12}H_{22}O_{11} + H_2O$$

glucose + fructose → sucrose + water

Important disaccharides in the diet are *sucrose* (glucose + fructose), which is cane or table sugar; *lactose* (glucose + galactose), found in milk; and *maltose* (glucose + glucose), also called malt sugar (Figure 2.15b). Disaccharides are too large to be transported through cell membranes, so they must be hydrolyzed to monosaccharides (Figure 2.14b, c) before the digestive tract can absorb them. A water molecule is added as each bond is broken, releasing monosaccharides that can be absorbed from the digestive tract into the blood.

Polysaccharides

Polysaccharides (pol″e-sak′ah-rīdz) are polymers of simple sugars linked together by dehydration synthesis. Because polysaccharides are large, fairly insoluble molecules, they are ideal storage products. Another consequence of their large size is that they lack the sweetness of the simple and double sugars.

Only two polysaccharides are of major importance to the body: starch and glycogen. Both are polymers of glucose. Only their degree of branching differs.

Starch is the storage carbohydrate formed by plants. The number of glucose units composing a starch molecule is high and variable. When we eat starchy foods such as grain products and potatoes, the starch must be digested for its glucose units to be absorbed. We are unable to digest *cellulose*, another polysaccharide found in all plant products. However, it is important in providing the *bulk* (one form of fiber) that helps move feces through the colon.

Glycogen (gli′ko-jen), the storage carbohydrate of animal tissues, is stored primarily in skeletal muscle and liver cells. Like starch, it is highly branched and is a very large molecule (Figure 2.15c). Since each branch can be attacked by an enzyme, many glucose molecules can be released simultaneously when cells need glucose for fuel. Skeletal muscles use their glycogen for themselves, but liver cells use their stored glycogen to maintain blood sugar (glucose) levels. This allows the body's cells to get the fuel they need.

Carbohydrate Functions

The major function of carbohydrates in the body is to provide a ready, easily used source of cellular fuel. Most cells can use only a few types of simple sugars, and glucose is at the top of the cellular "menu." As described in our earlier discussion of oxidation-reduction reactions (p. 69), glucose is broken down and oxidized within cells. During these reactions, electrons are transferred, releasing the bond energy stored in glucose. This energy is used to synthesize ATP. When ATP supplies are sufficient, dietary carbohydrates are converted to glycogen or fat and stored. Those of us who have gained weight from eating too many carbohydrate-rich snacks have personal experience with this conversion process!

Only small amounts of carbohydrates are used for structural purposes. For example, some sugars are found in our genes. Others are attached to the external surfaces of cells where they act as identity molecules to guide cellular interactions.

Check Your Understanding

21. What are the monomers of carbohydrates called? Which monomer is blood sugar?

22. What is the animal form of stored carbohydrate called?

For answers, see Answers Appendix.

2.9 Lipids insulate body organs, build cell membranes, and provide stored energy

Learning Outcome

▶ **Describe the building blocks, general structure, and biological functions of lipids.**

Lipids are insoluble in water but dissolve readily in other lipids and in organic solvents such as alcohol and ether. Like carbohydrates, all lipids contain carbon, hydrogen, and oxygen, but the proportion of oxygen in lipids is much lower. In addition, phosphorus is found in some of the more complex lipids. Lipids include *triglycerides*, *phospholipids* (fos″fo-lip′idz), *steroids* (stē′roidz), and a number of other lipoid substances. **Table 2.3** on p. 79 gives the locations and functions of some lipids found in the body.

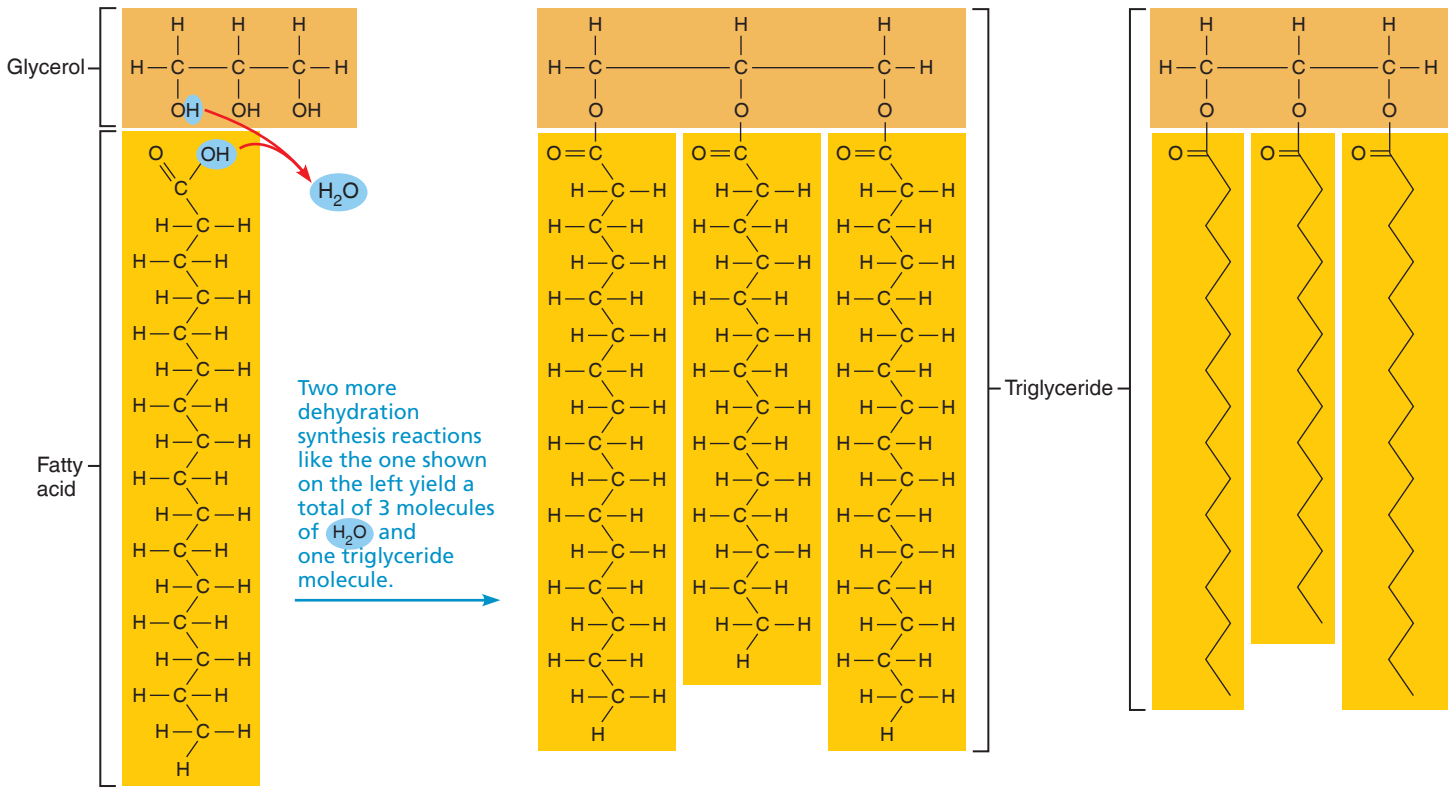
Triglycerides

Triglycerides (tri-glis′er-īdz) are commonly known as *fats* when solid or *oils* when liquid. Triglycerides are large molecules, often consisting of hundreds of atoms. They provide the body's most efficient and compact form of stored energy, and when they are oxidized, they yield large amounts of energy. A triglyceride is composed of two types of building blocks, **fatty acids** and **glycerol** (glis′er-ol), in a 3:1 ratio of fatty acids to glycerol (**Figure 2.16**). Fatty acids are linear chains of carbon and hydrogen atoms (hydrocarbon chains) with an organic acid group (—COOH) at one end. Glycerol is a modified simple sugar (a sugar alcohol).

Fat synthesis involves attaching three fatty acid chains to a single glycerol molecule by dehydration synthesis. The result is an E-shaped molecule. The glycerol backbone is the same in all triglycerides, but the fatty acid chains vary, resulting in different kinds of fats and oils.

Their hydrocarbon chains make triglycerides nonpolar molecules. Because polar and nonpolar molecules do not interact (oil and water do not mix), digestion and absorption of fats is complicated, and ingested fats and oils must be broken down to their building blocks.

Triglycerides are found mainly beneath the skin, where they insulate the deeper body tissues from heat loss and protect them



(a) One of three dehydration synthesis reactions in the synthesis of a triglyceride.

(b) One triglyceride molecule consists of a glycerol and three fatty acids bound together by dehydration synthesis.

(c) Simplified drawing of the same triglyceride.

Figure 2.16 Triglycerides consist of glycerol and three fatty acids. Simplified fatty acid structures are shown in **(c)**.

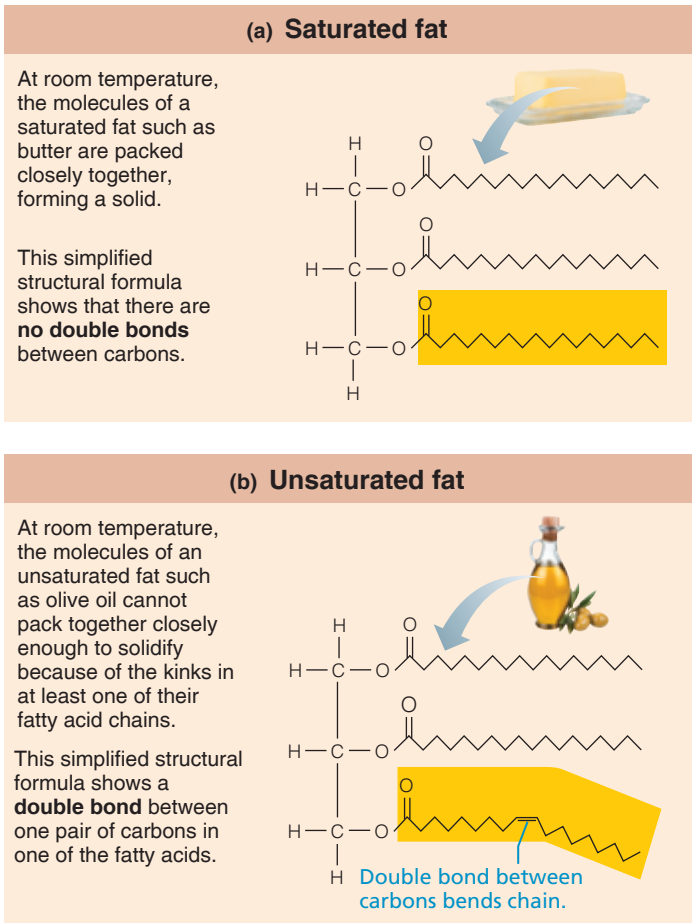


Figure 2.17 **Saturated and unsaturated fatty acids.**

from mechanical trauma. For example, women are usually more successful English Channel swimmers than men. Their success is due partly to their thicker subcutaneous fatty layer, which helps insulate them from the bitterly cold water of the Channel.

The length of a triglyceride's fatty acid chains and their degree of *saturation* with H atoms determine how solid the molecule is at a given temperature. Fatty acid chains with only single covalent bonds between carbon atoms are referred to as **saturated** (**Figure 2.17a**). Their fatty acid chains are straight and, at room temperature, the molecules of a saturated fat are packed closely together, forming a solid. Fatty acids that contain one or more double bonds between carbon atoms are said to be **unsaturated** (**monounsaturated** or **polyunsaturated**, respectively) (Figure 2.17b). The double bonds cause the fatty acid chains to kink so that they cannot be packed closely enough to solidify. As a result, triglycerides with short fatty acid chains or unsaturated fatty acids are oils (liquid at room temperature) and are typical of plant lipids. Examples include olive and peanut oils (rich in monounsaturated fats) and corn, soybean, and safflower oils, which contain a high percentage of polyunsaturated fatty acids. Longer fatty acid chains and more saturated fatty acids are common in animal fats such as butterfat and the fat of meats, which are solid at room temperature. Of the two types of fatty acids, the unsaturated variety, olive oil for example, is said to be more "heart healthy."

Trans fats, common in many margarines and baked products, are oils that have been solidified by addition of H atoms at sites of carbon double bonds. They increase the risk of heart disease even more than the solid animal fats. Conversely, the

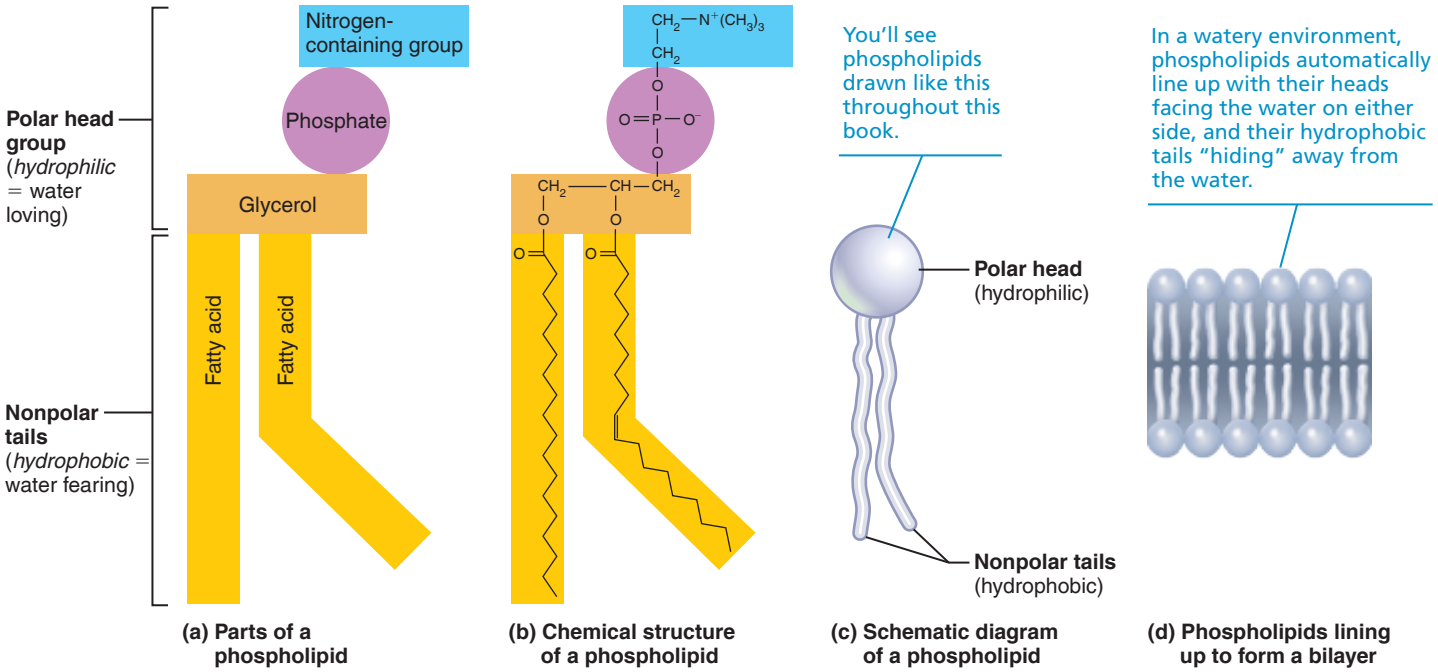


Figure 2.18 **Phospholipid structure.** A phospholipid consists of a glycerol backbone with two fatty acids, a phosphate group, and a nitrogen-containing group.

Table 2.3 Representative Lipids Found in the Body

LIPID TYPE	LOCATION/FUNCTION
Triglycerides	
	• Major form of stored energy in the body.
	• Fat deposits (in subcutaneous tissue and around organs) protect and insulate body organs.
Phospholipids	
	• Chief components of cell membranes.
	• Help transport lipids in blood (as part of *lipoproteins*; see below).
Steroids	
Cholesterol	• Component of cell membranes.
	• Starting molecule for synthesis of all body steroids.
Bile salts	• Breakdown products of cholesterol.
	• Released by the liver into the digestive tract, where they help with fat digestion and absorption.
Vitamin D	• Fat-soluble vitamin produced in the skin on exposure to UV radiation.
	• Necessary for normal bone growth and function.
Sex hormones	• Include estrogens and progesterone (female hormones) and testosterone (male hormone).
	• Produced in the gonads.
Corticosteroids (hormones from adrenal cortex)	• Cortisol is a metabolic hormone necessary for maintaining normal blood glucose levels.
	• Aldosterone helps to regulate salt and water balance of the body by targeting the kidneys.
Other Lipoid Substances	
Fat-soluble vitamins	• Vitamins A, D (a steroid, see above), E, and K are fat soluble. See Table 24.2 on p. 964 for details.
Eicosanoids (e.g.,prostaglandins, thromboxanes)	• Derived from fatty acids found in all cell membranes.
	• Prostaglandins have diverse effects, including promoting inflammation, stimulating uterine contractions, regulating blood pressure, and controlling gastrointestinal tract motility.
	• Thromboxanes are powerful vasoconstrictors.
Lipoproteins	• Lipoid and protein-based substances that transport fatty acids and cholesterol in the bloodstream.
	• Major varieties are high-density lipoproteins (HDLs) and low-density lipoproteins (LDLs).
Glycolipids	• Components of cell membranes.
	• Carbohydrates attached to lipids determine blood type and play roles in cell recognition and in recognition of foreign substances by immune cells.

omega-3 fatty acids, found naturally in cold-water fish, appear to decrease the risk of heart disease and some inflammatory diseases.

Phospholipids

Phospholipids are modified triglycerides. Specifically, they have two, rather than three, fatty acid chains. The third chain is replaced by a phosphate group (PO_4) with an attached nitrogen-containing group (**Figure 2.18**). The two fatty acid "tails" make one end of the phospholipid molecule nonpolar and **hydrophobic** (*hydro* = water; *phobia* = fear). These nonpolar tails interact only with other nonpolar molecules. The rest of the molecule, including the phosphate group, form the head—the polar, **hydrophilic** (*phil* = loving) region of the molecule. The head interacts with other polar or charged particles, such as water or ions. Having both hydrophilic and hydrophobic ends makes phospholipids ideally suited to be the chief building material for cellular membranes (Figure 2.18d).

Steroids

Structurally, steroids differ quite a bit from fats and oils. **Steroids** are basically flat molecules made of four interlocking hydrocarbon rings. Like triglycerides, steroids are fat soluble and contain little oxygen. The single most important

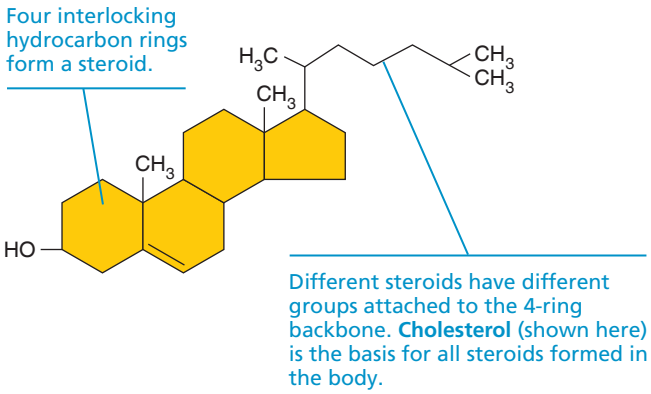


Figure 2.19 **Steroid structure.**

molecule in our steroid chemistry is *cholesterol* (ko-les′ter-ol) (**Figure 2.19**). We ingest cholesterol in animal products such as eggs, meat, and cheese, and our liver produces some.

Cholesterol has a bad reputation because of its role in atherosclerosis, but it is essential for human life. Cholesterol is found in cell membranes and is the raw material for synthesis of vitamin D, steroid hormones, and bile salts. Although steroid hormones are present in the body in only small quantities, they are vital to homeostasis. Without sex hormones, reproduction would be impossible, and a total lack of the corticosteroids produced by the adrenal glands is fatal.

Eicosanoids

The **eicosanoids** (i-ko′sah-noyds) are diverse lipids chiefly derived from a 20-carbon fatty acid (arachidonic acid) found in all cell membranes. Particularly important are the *prostaglandins*, which play roles in various body processes including blood clotting, regulation of blood pressure, inflammation, and labor contractions. Their synthesis and inflammatory actions are blocked by NSAIDs (nonsteroidal anti-inflammatory drugs; e.g., ibuprofen).

Check Your Understanding

23. How do triglycerides differ from phospholipids in body function and location?

For answers, see Answers Appendix.

2.10 Proteins are the body's basic structural material and have many vital functions

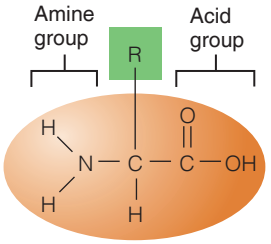
Learning Outcomes

- **Describe the four levels of protein structure.**
- **Describe enzyme action.**

Protein composes 10–30% of cell mass and is the basic structural material of the body. However, not all proteins are construction materials. Many play vital roles in cell function. Proteins, which include enzymes (biological catalysts), hemoglobin of the blood, and contractile proteins of muscle, have the most varied functions of any molecules in the body. These and other selected roles of proteins are shown in **Figure 2.20**.

Amino Acids and Peptide Bonds

The building blocks of proteins are molecules called **amino acids**, of which there are 20 common types (see Appendix C). As shown in the amino acid below, all amino acids have two important functional groups: a basic group called an *amine* (ah′mēn) *group* (—NH_2), and an organic *acid group* (—COOH).



An amino acid may therefore act either as a base (proton acceptor) or an acid (proton donor). All amino acids are identical except for a single group of atoms called their *R group*. It is differences in the R group that make each amino acid chemically unique. All amino acids contain carbon, oxygen, hydrogen, and nitrogen, and two contain sulfur as well.

Proteins are long chains of amino acids joined together by dehydration synthesis, with the acid end of one amino acid linked to the amine end of the next. The resulting bond produces a characteristic arrangement of linked atoms called a **peptide bond** (**Figure 2.21**). Two united amino acids form a *dipeptide*, three a *tripeptide*, and ten or more a **polypeptide**. Although polypeptides containing more than 50 amino acids are called proteins, most proteins are macromolecules containing from 100 to over 10,000 amino acids.

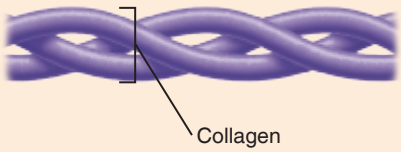
Because each type of amino acid has distinct properties, the sequence in which they are bound together produces proteins that vary widely in both structure and function. We can think of the 20 amino acids as a 20-letter "alphabet" used in specific combinations to form "words" (proteins). Just as a change in one letter can produce a word with an entirely different meaning (flour → floor) or that is nonsensical (flour → flocr), changes in the kinds or positions of amino acids can yield proteins with different functions or proteins that are nonfunctional. Nevertheless, there are thousands of different proteins in the body, each with distinct functional properties, and all constructed from different combinations of the 20 common amino acids.

Structural Levels of Proteins

Proteins can be described in terms of four structural levels: primary, secondary, tertiary, and quaternary. The linear sequence of amino acids composing the polypeptide chain is the *primary structure* of a protein. This structure, which resembles a strand

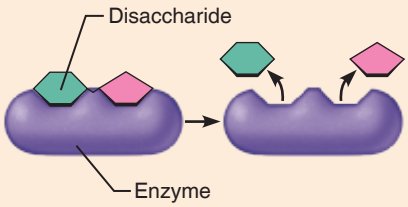
(a) Structural proteins

Function: Mechanical support.
Example: *Collagen*, found in all connective tissue, is the single most abundant protein in the body. It is responsible for the tensile strength of bones, tendons, and ligaments.



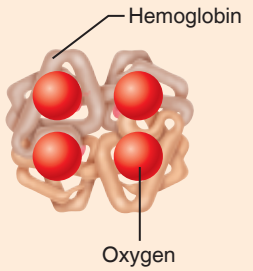
(b) Enzyme proteins

Function: Catalysis. Protein enzymes are essential for virtually every biochemical reaction in the body.
Examples: *Disaccharidases* hydrolyze disaccharides, *proteases* hydrolyze proteins, and *oxidases* oxidize food fuels.



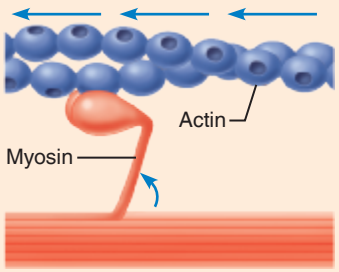
(c) Transport proteins

Function: Moving substances (in blood or across plasma membranes).
Example: *Hemoglobin* transports oxygen in blood. Some plasma membrane proteins transport substances (such as ions) across the plasma membrane.



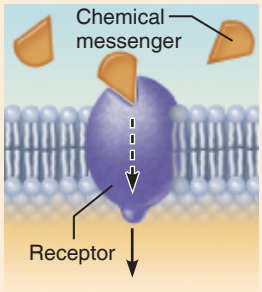
(d) Contractile proteins

Function: Movement.
Example: *Actin* and *myosin* cause muscle cell contraction and function in cell division in all cell types.



(e) Communication proteins

Function: Transmitting signals between cells. Can act as *chemical messengers* (e.g., hormones) or as *receptors* in the plasma membrane.
Example: *Insulin* (a protein) acts at its receptor to regulate blood sugar levels.



(f) Defensive proteins

Function: Protect against disease.
Example: *Antibodies* released by certain immune cells are specialized proteins that bind and inactivate foreign substances (e.g., bacteria, toxins, viruses).

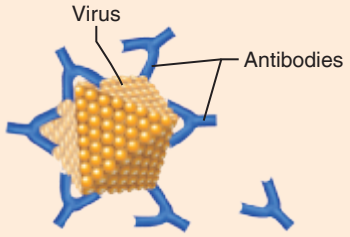


Figure 2.20 **Examples of protein functions.**

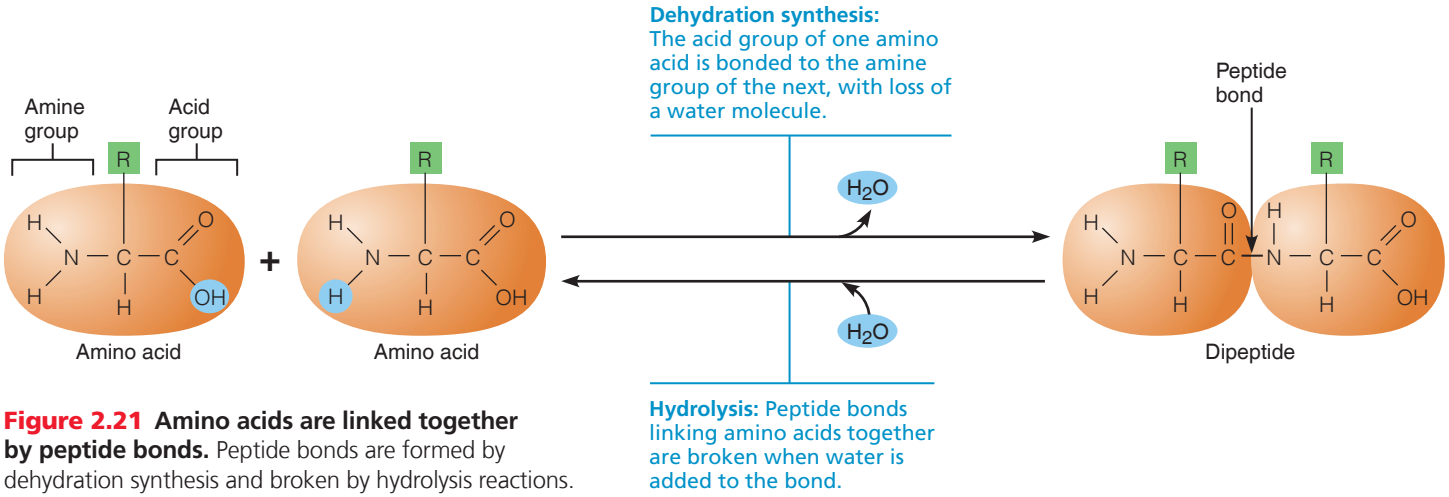


Figure 2.21 **Amino acids are linked together by peptide bonds.** Peptide bonds are formed by dehydration synthesis and broken by hydrolysis reactions.

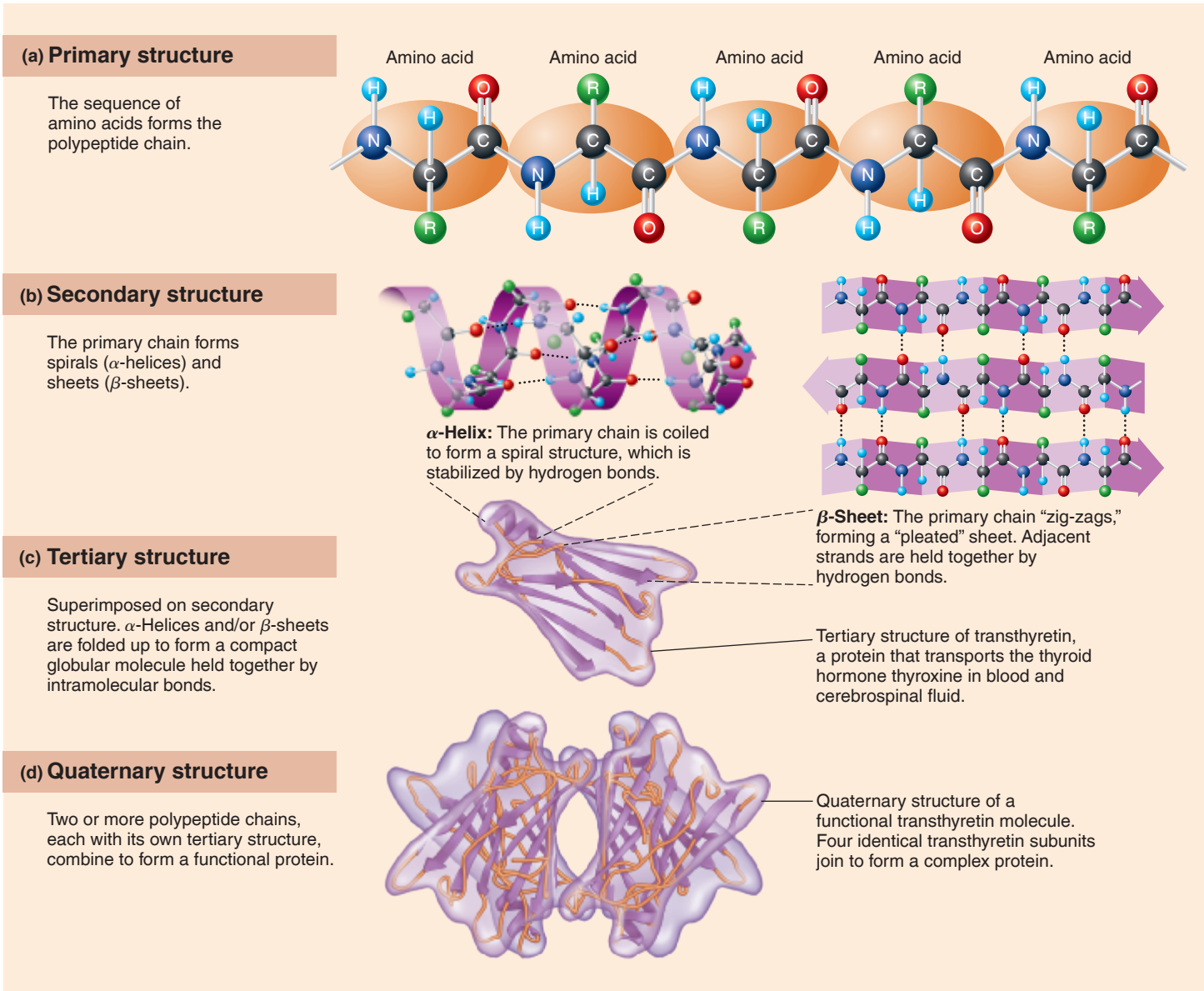


Figure 2.22 Levels of protein structure.

of amino acid "beads," is the backbone of the protein molecule (**Figure 2.22a**).

Proteins do not normally exist as simple, linear chains of amino acids. Instead, they twist or bend upon themselves to form a more complex *secondary structure*. The most common type of secondary structure is the **alpha (α)-helix**, which resembles a Slinky® toy or a coiled spring (Figure 2.22b). The α-helix is formed by coiling the primary chain. It is stabilized by hydrogen bonds formed between NH and CO groups in amino acids in the primary chain that are about four amino acids apart. Hydrogen bonds in α-helices always link different parts of the *same* chain together.

In another type of secondary structure, the **beta (β)-pleated sheet**, the primary polypeptide chains do not coil, but are linked side by side by hydrogen bonds to form a pleated, ribbonlike structure that resembles an accordion's bellows (Figure 2.22b). Notice that in this type of secondary structure, the hydrogen bonds may link together *different polypeptide chains* as well as *different parts* of the same chain that has folded back on itself. A single polypeptide chain may exhibit both types of secondary structure at various places along its length.

Many proteins have *tertiary structure* (ter′she-a″re), the next higher level of complexity, which is superimposed on secondary structure and involves the amino acids' R-groups. Tertiary structure is achieved when α-helical or β-pleated regions of the polypeptide chain fold upon one another to produce a compact ball-like, or *globular*, molecule (Figure 2.22c). Hydrophobic R groups are on the inside of the molecule and hydrophilic R groups are on its outside. Their interactions plus those reinforced by covalent and hydrogen bonds help to maintain the unique tertiary shape.

When two or more polypeptide chains aggregate in a regular manner to form a complex protein, the protein has *quaternary structure* (kwah′ter-na″re). The transthyretin molecule with its four identical globular subunits represents this level of structure (Figure 2.22d). (Transthyretin transports thyroid hormone in the blood.)

How do these different levels of structure arise? Although a protein with tertiary or quaternary structure looks a bit like a clump of congealed pasta, the ultimate overall structure of any protein is very specific and is dictated by its primary structure. In other words, the types (hydrophilic versus hydrophobic) and relative positions of amino acids in the protein backbone determine the complex three-dimensional structure of the folded protein. Proteins fold so that hydrophilic amino acids are near the surface and hydrophobic amino acids are buried in the protein's core.

Fibrous and Globular Proteins

The overall structure of a protein determines its biological function. In general, proteins are classified according to their overall appearance and shape as either fibrous or globular.

Fibrous proteins, also known as **structural proteins**, form long strands. Some exhibit only secondary structure, but most have tertiary or even quaternary structure as well. For example, *collagen* (kol′ah-jen) is made of helical tropocollagen molecules packed together side by side to form a strong ropelike structure (Figure 2.20a on p. 81). Fibrous proteins are insoluble in water, and very stable—qualities ideal for providing mechanical support and tensile strength to the body's tissues. Besides structural proteins like collagen (the single most abundant protein in the body), the fibrous proteins include certain contractile proteins (see Figure 2.20d).

Globular proteins, also called **functional proteins**, are compact, spherical proteins that have at least tertiary structure. Some also exhibit quaternary structure. The globular proteins are water-soluble, chemically active molecules, and they play crucial roles in virtually all biological processes. Some (antibodies) help to provide immunity, others (protein-based hormones) regulate growth and development, some are transport proteins, and still others (enzymes) are catalysts that oversee just about every chemical reaction in the body (see Figure 2.20b, c, e, f).

Protein Denaturation

Fibrous proteins are stable, but globular proteins are quite the opposite. The activity of a protein depends on its specific three-dimensional structure. Intramolecular bonds, particularly hydrogen bonds, are important in maintaining that structure. However, hydrogen bonds are fragile and easily broken by many chemical and physical factors, such as excessive acidity or temperature. Although individual proteins vary in their sensitivity to environmental conditions, hydrogen bonds begin to break when the pH drops or the temperature rises above normal (physiological) levels. When this happens, proteins unfold and lose their specific three-dimensional shape. Such a protein is said to be **denatured**.

The disruption is reversible in most cases, and the "scrambled" protein regains its native structure when desirable conditions are restored. However, if the temperature or pH change is so extreme that protein structure is damaged beyond repair, the protein is *irreversibly denatured*. The coagulation of egg white (primarily albumin protein) that occurs when you boil or fry an egg is an example of irreversible protein denaturation. There is no way to restore the white, rubbery protein to its original translucent form.

When globular proteins are denatured, they can no longer perform their physiological roles. For example, an enzyme's function depends on the presence of specific arrangements of atoms where catalytic activity occurs, called **active sites**. Active sites are regions that fit and interact chemically with other molecules of complementary shape and charge. Because atoms contributing to an active site in the folded protein may actually be far apart in the primary chain, disruption of intramolecular bonds separates them and destroys the active site. The globular transport protein hemoglobin becomes totally unable to bind and transport oxygen when blood pH is too acidic, because the structure needed for its function has been destroyed.

We will describe most types of body proteins in conjunction with the organ systems or functional processes to which they are closely related. However, one group of proteins—*enzymes*—is intimately involved in the normal functioning of all cells, so we will consider these incredibly complex molecules here.

Enzymes and Enzyme Activity

Enzymes are globular proteins that act as biological catalysts. *Catalysts* are substances that regulate and accelerate the rate of biochemical reactions but are not used up or changed in those reactions. More specifically, enzymes can be thought of as chemical traffic cops that keep our metabolic pathways flowing. Enzymes cannot force chemical reactions to occur between molecules that would not otherwise react. They can only increase the speed of reaction, and they do so by staggering amounts—from 100,000 to over 1 billion times the rate of an uncatalyzed reaction. Without enzymes, biochemical reactions proceed so slowly that for practical purposes they do not occur at all.

Characteristics of Enzymes

Some enzymes are purely protein. In other cases, the functional enzyme consists of two parts: an **apoenzyme** (the protein portion) and a **cofactor**. Together, these two parts form a **holoenzyme**. Depending on the enzyme, the cofactor may be an ion of a metal element such as copper or iron, or an organic molecule needed to assist the reaction in some way. Most organic cofactors are derived from vitamins (especially the B complex vitamins). In this case the type of cofactor is more precisely called a **coenzyme**.

Each enzyme is chemically specific. Some enzymes control only a single chemical reaction. Others can regulate a small group of related reactions by binding with molecules that differ only slightly. The substance on which an enzyme acts is called a **substrate**. As mentioned earlier, catalytic activity occurs at the *active site*.

The presence of specific enzymes determines not only which reactions will be speeded up, but also which reactions will occur—no enzyme, no reaction. This also means that unwanted or unnecessary chemical reactions do not occur.

Most enzymes are named for the type of reaction they catalyze. *Hydrolases* (hi′druh-lās-es) add water during hydrolysis reactions and *oxidases* (ok′sĭ-dās-es) oxidize reactants by adding oxygen or removing hydrogen. You can recognize most enzyme names by the suffix *-ase*.

In many cases, enzymes are part of cellular membranes. They are often grouped together so that the product of one enzyme-catalyzed reaction becomes the substrate of the neighboring enzyme, and so on. Some enzymes are produced in an inactive form and must be activated in some way before they can function, often by a change in the pH of their surroundings. For example, digestive enzymes produced in the pancreas are activated in the small intestine, where they actually do their work. If they were produced in active form, the pancreas would digest itself.

Sometimes, enzymes are inactivated immediately after they have performed their catalytic function. This is true of enzymes that promote blood clot formation when the wall of a blood vessel is damaged. Once clotting is triggered, those enzymes are inactivated. Otherwise, you would have blood vessels full of solid blood instead of one protective clot. (Eek!)

Enzyme Action

How do enzymes perform their catalytic role? Every chemical reaction requires that a certain amount of energy, called **activation energy**, be absorbed to prime the reaction. The activation energy is needed to alter the bonds of the reactants so that they can be rearranged to become the product. It is present when kinetic energy pushes the reactants to an energy level where their random collisions are forceful enough to ensure interaction. Activation energy is needed regardless of whether the overall reaction is ultimately energy absorbing or energy releasing.

One way to increase kinetic energy is to increase the temperature, but this is not possible in the body because higher temperatures would denature proteins. Enzymes allow reactions to occur at normal body temperature by decreasing the amount of activation energy required (**Figure 2.23**). An enzyme speeds up a reaction by lowering the barrier. Think of a runner slowly climbing a 12-foot wall versus one that is running over hurdles.

Exactly how do enzymes accomplish this remarkable feat? The answer is not fully understood. However, we know that, due to structural and electrostatic factors, they decrease the randomness of reactions by binding to the reacting molecules temporarily and presenting them to each other in the proper position for chemical interaction (bond making or breaking) to occur.

Three basic steps are involved in enzyme action (**Figure 2.24**).

1. **Substrate(s) bind to the enzyme's active site, temporarily forming an enzyme-substrate complex.** Substrate binding causes the active site to change shape so that the substrate and the active site fit together precisely, and in an orientation that favors reaction. Although enzymes are specific for particular substrates, other (nonsubstrate) molecules may act as *enzyme inhibitors* if their structure is similar enough to occupy or block the enzyme's active site.
2. **The enzyme-substrate complex undergoes internal rearrangements that form the product(s).**
3. **The enzyme releases the product(s) of the reaction.** If the enzyme became part of the product, it would be a reactant and not a catalyst. The enzyme is not changed and returns to its original shape, available to catalyze another reaction.

Because enzymes are unchanged by their catalytic role and can act again and again, cells need only small amounts of each enzyme. Catalysis occurs with incredible speed. Most enzymes can catalyze millions of reactions per minute.

Check Your Understanding

24. What does the name "amino acid" tell you about the structure of this molecule?

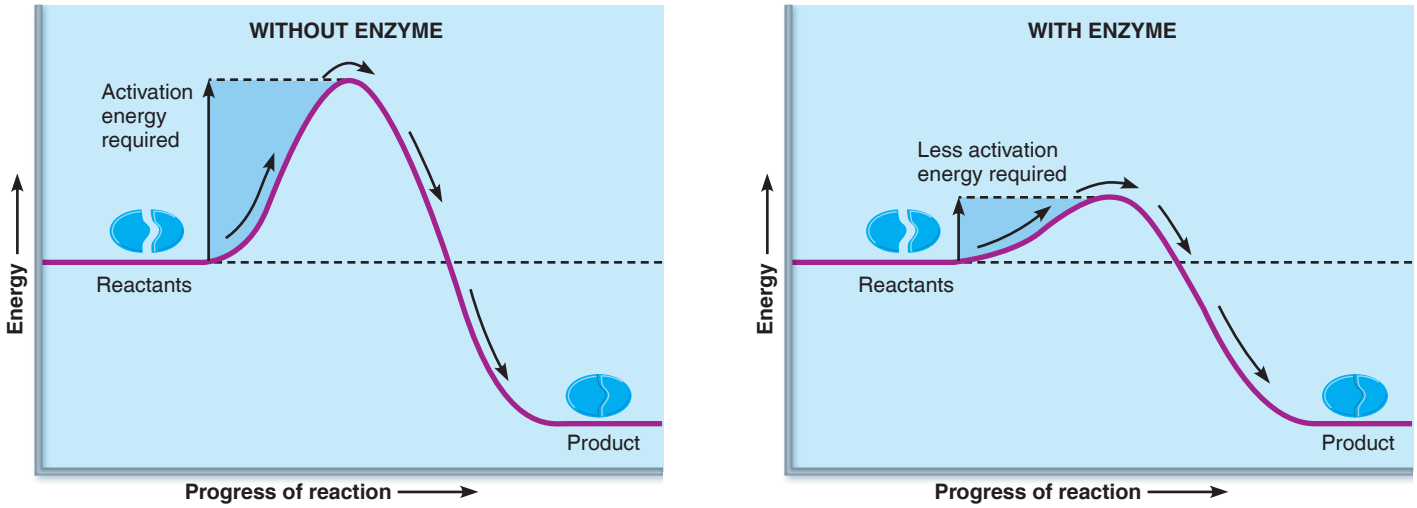


Figure 2.23 Enzymes lower the activation energy required for a reaction.

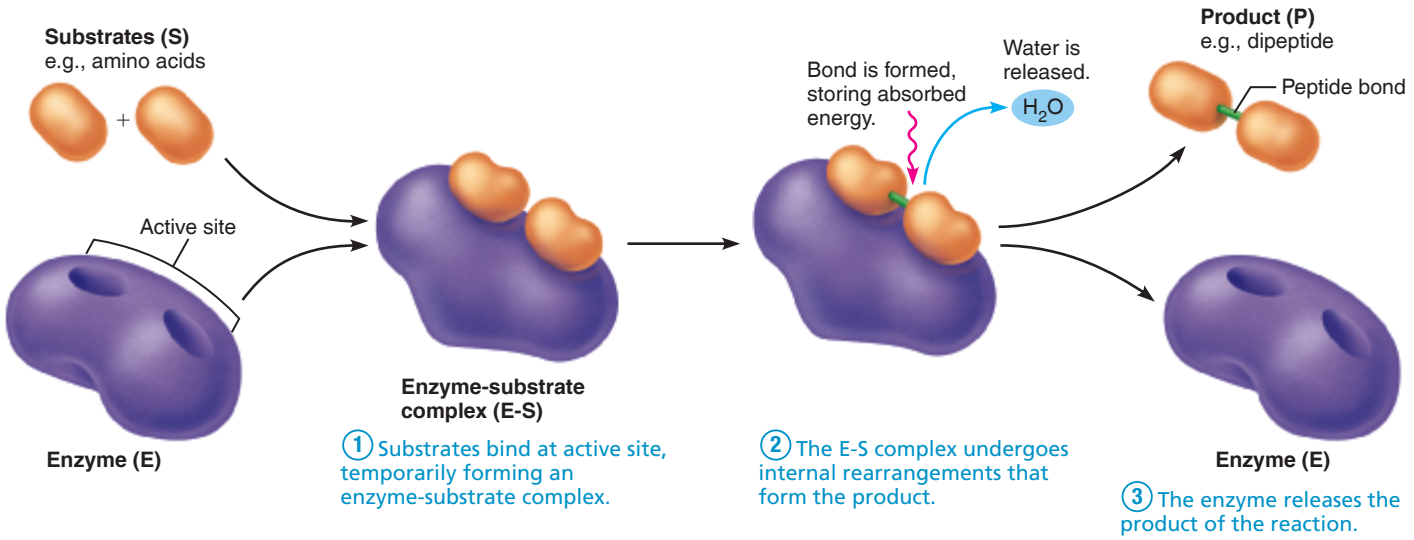


Figure 2.24 Mechanism of enzyme action. In this example, the enzyme catalyzes the formation of a dipeptide from specific amino acids. *Summary*: E + S → E-S → P + E

25. What is the primary structure of proteins?
26. What are the two types of secondary structure in proteins?
27. DRAW Figure 2.23 shows the effect of an enzyme on the activation energy of an exergonic reation. Draw two similar graphs showing the effect of an enzyme on an endergonic reaction (see p. 69 to refresh your memory on these terms).

For answers, see Answers Appendix.

2.11 DNA and RNA store, transmit, and help express genetic information

Learning Outcome

▶ **Compare and contrast DNA and RNA.**

The **nucleic acids** (nu-kle′ic), composed of carbon, oxygen, hydrogen, nitrogen, and phosphorus, are the largest molecules in the body. The nucleic acids include two major classes of molecules, **deoxyribonucleic acid (DNA)** (de-ok″sĭ-ri″bo-nu-kle′ik) and **ribonucleic acid (RNA)**.

Roles of DNA and RNA

DNA and RNA have different roles in the cell, as summarized in **Table 2.4**. Typically, DNA is found in the nucleus (control center) of the cell, where it constitutes the *genetic material*, also called the *genes*, or more recently the *genome*. DNA has two fundamental roles: It replicates (reproduces) itself before a cell divides, ensuring that the genetic information in the descendant cells is identical, and it provides the basic instructions for building every protein in the body. Although we have said that enzymes govern all chemical reactions, remember that enzymes, too, are proteins formed at the direction of DNA.

By providing the information for protein synthesis, DNA determines what type of organism you will be—frog, human, oak tree—and directs your growth and development. It also accounts for your uniqueness. DNA fingerprinting can help solve forensic mysteries (for example, verify one's presence at a crime scene), identify badly burned or mangled bodies after a disaster, and establish or disprove paternity. DNA fingerprinting analyzes tiny samples of DNA taken from blood, semen, or other body tissues and shows the results as a "genetic barcode" that distinguishes each of us from all others.

Table 2.4 Comparison of DNA and RNA

CHARACTERISTIC	DNA	RNA
Major cellular site	Nucleus	Cytoplasm (cell area outside the nucleus)
Major functions	Is the genetic material; directs protein synthesis; replicates itself before cell division	Carries out the genetic instructions for protein synthesis
Structure	Double strand coiled into a double helix	Single strand, straight or folded
Sugar	Deoxyribose	Ribose
Bases	Adenine (A), guanine (G), cytosine (C), thymine (T)	Adenine (A), guanine (G), cytosine (C), uracil (U)

RNA is located chiefly outside the nucleus and can be considered a "molecular slave" of DNA. That is, RNA carries out the orders for protein synthesis issued by DNA. [Viruses in which RNA (rather than DNA) is the genetic material are an exception to this generalization.]

There are three major varieties of RNA (messenger RNA, ribosomal RNA, and transfer RNA) that are distinguished by their relative size and shape. Each has a specific role to play in carrying out DNA's instructions for protein synthesis. In addition to these three RNAs, there are several types of small RNA molecules, including *microRNAs*.We will discuss DNA replication, the roles of DNA and RNA in protein synthesis, and these small RNA molecules in Chapter 3.

Structure of DNA and RNA

The structural units of nucleic acids, called **nucleotides**, are quite complex. Each nucleotide consists of three components (**Figure 2.25a**):

- A nitrogen-containing base
- A pentose sugar
- A phosphate group

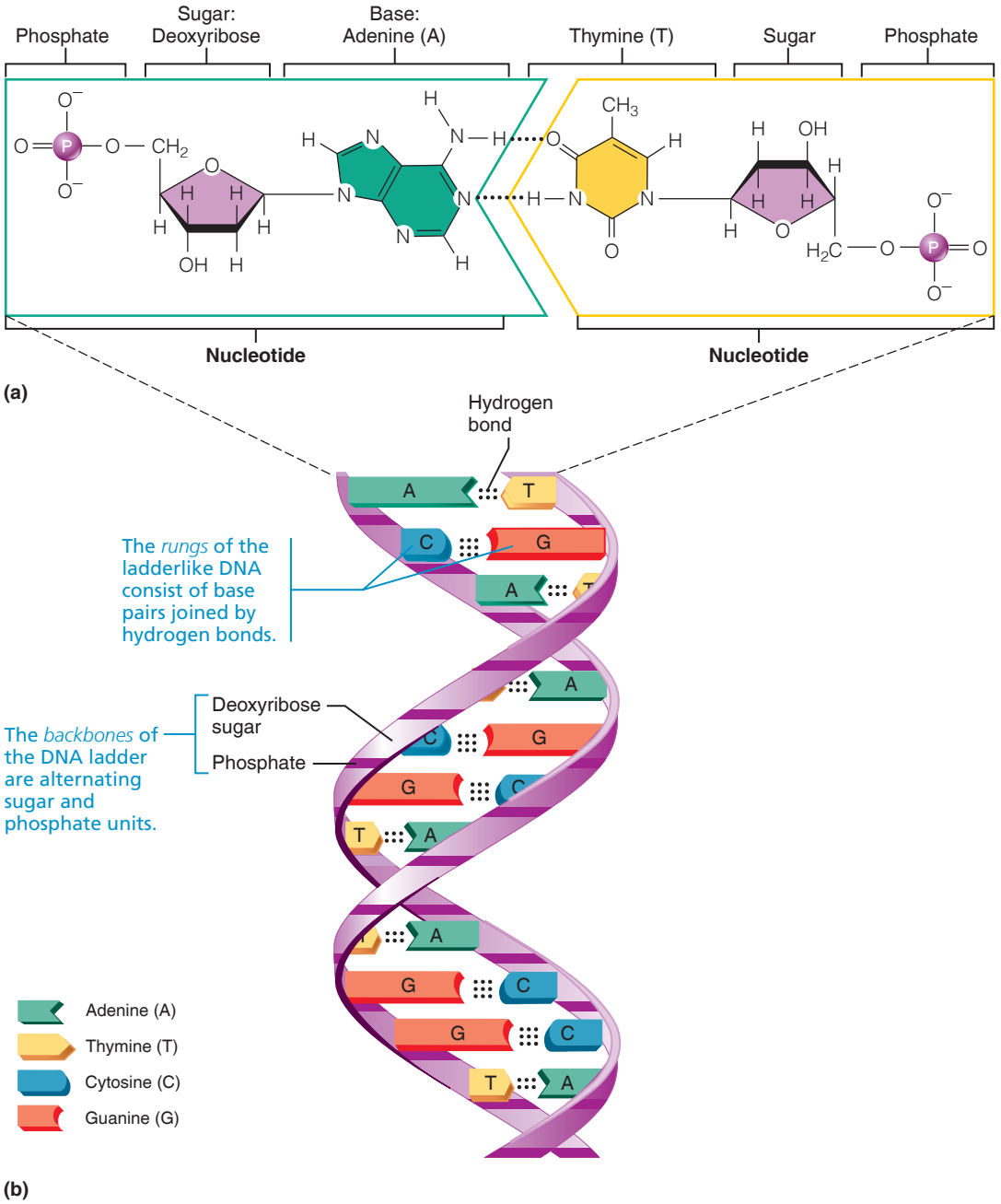


Figure 2.25 Structure of DNA. (a) Two nucleotides—the structural units of DNA. The nucleotides are linked by hydrogen bonds (shown by dotted lines) between their complementary bases. **(b)** DNA is a *double helix*—a coiled double polymer of nucleotides.

Table 2.5 Summary of Monomers and Polymers of Some Organic Molecules

CLASS OF ORGANIC MOLECULE*	MONOMERS (BUILDING BLOCKS)	POLYMER
Carbohydrates	Monosaccharides (e.g., glucose)	Polysaccharides
Proteins	Amino acids	Polypeptides or proteins
Nucleic acids	Nucleotides	DNA or RNA

*Lipids are not included in this table because they do not form polymers.

The synthesis of a nucleotide involves the attachment of a base and a phosphate group to the pentose sugar.

Five major varieties of nitrogen-containing bases can contribute to nucleotide structure: **adenine**, abbreviated **A** (ad′ĕ-nēn); **guanine**, **G** (gwah′nēn); **cytosine**, **C** (si′to-sēn); **thymine**, **T** (thi′mēn); and **uracil**, **U** (u′rah-sil). Adenine and guanine are large, two-ring bases (called purines), whereas cytosine, thymine, and uracil are smaller, single-ring bases (called pyrimidines).

DNA is a long, double-stranded polymer—a double chain of nucleotides (Figure 2.25b). The bases in DNA are A, G, C, and T, and its pentose sugar is *deoxyribose* (as reflected in its name). Its two nucleotide chains are held together by hydrogen bonds between the bases, so that a ladderlike molecule is formed. Alternating sugar and phosphate components of each chain form the *backbones* or "uprights" of the "ladder," and the joined bases form the "rungs." The whole molecule is coiled into a spiral staircase–like structure called a **double helix**.

Bonding of the bases is very specific: A always bonds to T, and G always bonds to C. A and T are therefore called **complementary bases**, as are C and G. According to these base-pairing rules, ATGA on one DNA nucleotide strand would necessarily be bonded to TACT (a complementary base sequence) on the other strand.

RNA molecules are single strands of nucleotides. RNA bases include A, G, C, and U (U replaces the T found in DNA), and its sugar is *ribose* instead of deoxyribose.

Table 2.5 offers a quick summary of the monomers and polymers of three types of macromolecules.

Check Your Understanding

28. How do DNA and RNA differ in the bases and sugars they contain?

29. PREDICT Look at Figure 2.25. Which base pair (A–T or C–G) do you think is less likely to come apart? Why?

For answers, see Answers Appendix.

2.12 ATP transfers energy to other compounds

Learning Outcome

▶ **Explain the role of ATP in cell metabolism.**

Glucose is the most important cellular fuel, but none of the chemical energy contained in its bonds is used directly to power cellular work. Instead, energy released during glucose catabolism is coupled to the synthesis of **adenosine triphosphate (ATP)**. In other words, some of this energy is captured and stored as small packets of energy in the bonds of ATP. ATP is the primary energy-transferring molecule in cells and it provides a form of energy that is immediately usable by all body cells. It is the dollar of the cell's metabolic economy.

Structurally, ATP is an adenine-containing RNA nucleotide to which two additional phosphate groups have been added (**Figure 2.26**). Chemically, the triphosphate tail of ATP can be compared to a tightly coiled spring ready to uncoil with tremendous energy when the catch is released. Actually, ATP can store energy because its three negatively charged phosphate groups are closely packed and repel each other. When its terminal (third) high-energy phosphate bond is broken (hydrolyzed), the chemical "spring" relaxes and the molecule as a whole becomes more stable.

Cells tap ATP's bond energy during coupled reactions. An enzyme transfers the terminal phosphate group from ATP to another molecule in a process called *phosphorylation*. These newly *phosphorylated* molecules temporarily become more energetic and capable of performing some type of cellular work. In the process of doing that work, they lose the phosphate

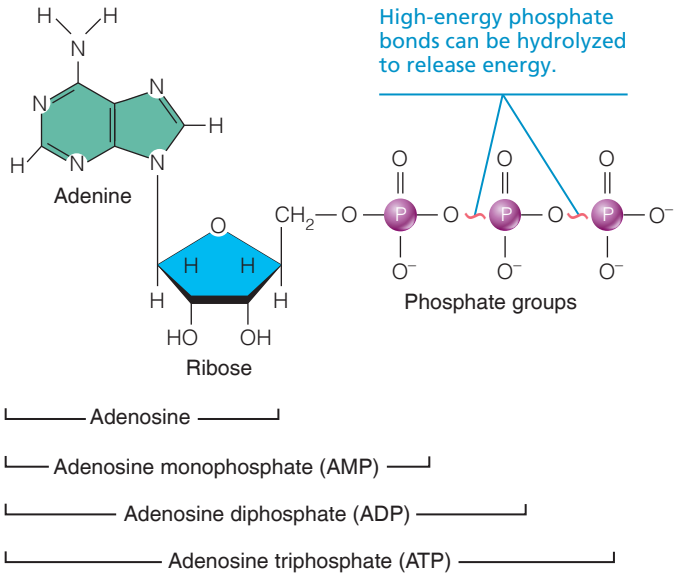
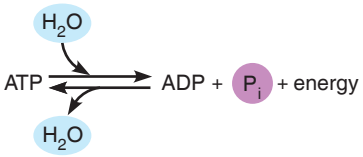


Figure 2.26 Structure of ATP (adenosine triphosphate). ATP is an adenine nucleotide to which two additional phosphate groups have been attached during breakdown of food fuels.

group. The amount of energy released and transferred during ATP hydrolysis corresponds closely to that needed to drive most biochemical reactions. As a result, cells are protected from excessive energy release that might be damaging, and energy squandering is kept to a minimum.

Breaking the terminal phosphate bond of ATP yields a molecule with two phosphate groups—*adenosine diphosphate* (*ADP*)—and an inorganic phosphate group, indicated by P_i, accompanied by a transfer of energy:



As ATP is hydrolyzed to provide energy for cellular needs, ADP accumulates. Breaking the terminal phosphate bond of ADP liberates a similar amount of energy and produces adenosine monophosphate (AMP) (see Figure 2.26).

The cell's ATP supplies are replenished as glucose and other fuel molecules are oxidized and their bond energy is released. The same amount of energy that is liberated when ATP's terminal phosphates are split off must be captured and used to reverse the reaction to reattach phosphates and re-form the energy-transferring phosphate bonds. Without ATP, molecules cannot be made or degraded, cells cannot transport substances across their membranes, muscles cannot shorten to tug on other structures, and life processes cease (**Figure 2.27**).

Check Your Understanding

30. Glucose is an energy-rich molecule. So why do body cells need ATP?

31. What change occurs in ATP when it releases energy?

For answers, see Answers Appendix.

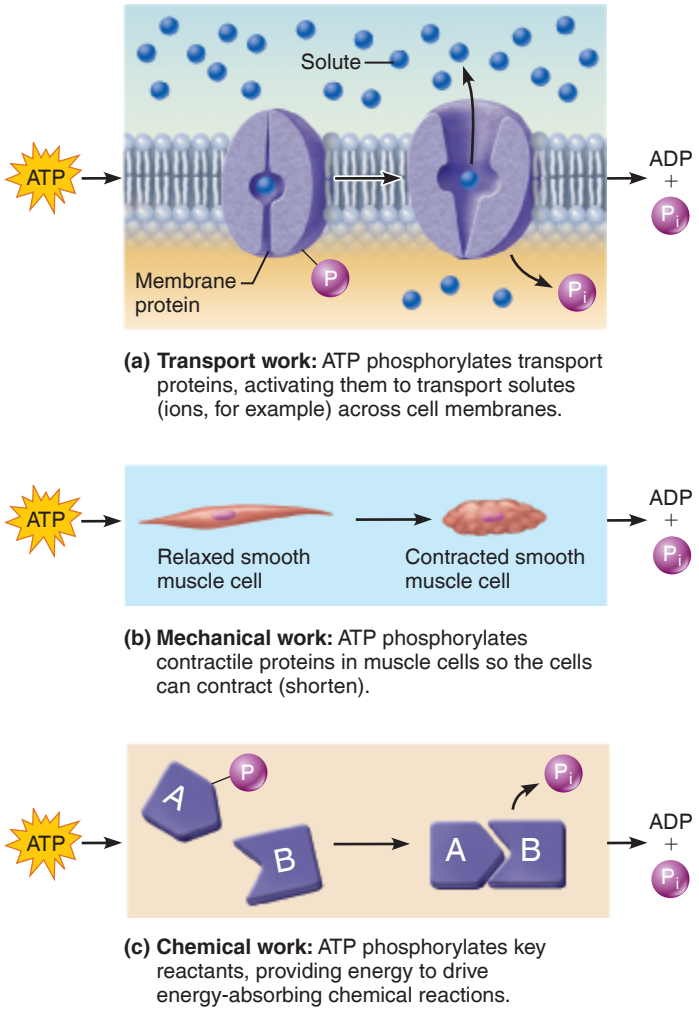


Figure 2.27 Three examples of cellular work driven by energy from ATP.

RELATED CLINICAL TERMS

Acidosis (as″ĭ-do′sis; *acid* = sour, sharp) A condition of acidity or low pH (below 7.35) of the blood; high hydrogen ion concentration.

Alkalosis (al″kah-lo′sis) A condition of basicity or high pH (above 7.45) of the blood; low hydrogen ion concentration.

Heavy metals Metals with toxic effects on the body, including arsenic, mercury, and lead. Iron, also included in this group, is toxic in high concentrations.

Ionizing radiation Radiation that causes atoms to ionize; for example, gamma rays and X rays.

Radiation sickness Disease resulting from exposure of the body to radioactivity; rapidly dividing cells are most affected—for example, blood-forming cells and the cells lining the digestive tract.

CHAPTER SUMMARY

PART 1
BASIC CHEMISTRY

2.1 Matter is the stuff of the universe and energy moves matter (pp. 56–57)

Matter (p. 56)

1. Matter is anything that takes up space and has mass.

Energy (pp. 56–57)

2. Energy is the capacity to do work or put matter into motion.
3. Energy exists as potential energy (stored energy) and kinetic energy (active or working energy).
4. Forms of energy involved in body functioning are chemical, electrical, radiant, and mechanical. Of these, chemical (bond) energy is most important.
5. Energy may be converted from one form to another, but some energy is always unusable (lost as heat) in such transformations.

2.2 The properties of an element depend on the structure of its atoms (pp. 57–60)

1. Elements are unique substances that cannot be decomposed into simpler substances by ordinary chemical methods. Four elements (carbon, hydrogen, oxygen, and nitrogen) make up 96% of body weight.
2. The building blocks of elements are atoms.

Structure of Atoms (pp. 57–59)

3. Atoms are composed of positively charged protons, negatively charged electrons, and uncharged neutrons. Protons and neutrons are located in the atomic nucleus, constituting essentially the atom's total mass. Electrons are outside the nucleus in the electron shells. In any atom, the number of electrons equals the number of protons.

Identifying Elements (pp. 59–60)

4. Atoms may be identified by their atomic number (p^+) and mass number ($p^+ + n^0$). The notation ${}^4_2He$ means that helium (He) has an atomic number of 2 and a mass number of 4.
5. Isotopes of an element differ in the number of neutrons they contain. The atomic weight of any element is approximately equal to the mass number of its most abundant isotope.

Radioisotopes (p. 60)

6. Many heavy isotopes are unstable (radioactive). These so-called radioisotopes decompose to more stable forms by emitting alpha or beta particles or gamma rays. Radioisotopes are useful in medical diagnosis and treatment and in biochemical research.

2.3 Atoms bound together form molecules; different molecules can make mixtures (pp. 60–62)

Molecules and Compounds (pp. 60–61)

1. A molecule is the smallest unit resulting from the chemical bonding of two or more atoms. If the atoms are different, they form a molecule of a compound.

Mixtures (pp. 61–62)

2. Mixtures are physical combinations of solutes in a solvent. Mixture components retain their individual properties.
3. The types of mixtures, in order of increasing solute size, are solutions, colloids, and suspensions.
4. Solution concentrations are typically designated in terms of percent or molarity.

Distinguishing Mixtures from Compounds (p. 62)

5. Compounds are homogeneous; their elements are chemically bonded. Mixtures may be homogeneous or heterogeneous; their components are physically combined and separable.

2.4 Three types of chemical bonds are ionic, covalent, and hydrogen (pp. 63–67)

The Role of Electrons in Chemical Bonding (pp. 63–64)

1. Electrons of an atom occupy areas of space called electron shells or energy levels. Electrons in the shell farthest from the nucleus (valence shell) are most energetic.
2. Chemical bonds are energy relationships between valence shell electrons of the reacting atoms. Atoms with a full valence shell or eight valence shell electrons are chemically unreactive (inert). Those with an incomplete valence shell interact with other atoms to achieve stability.

Types of Chemical Bonds (pp. 64–67)

3. Ionic bonds are formed when valence shell electrons are completely transferred from one atom to another.
4. Covalent bonds are formed when atoms share electron pairs. If the electron pairs are shared equally, the molecule is nonpolar. If they are shared unequally, it is polar (a dipole).
5. Hydrogen bonds are weak bonds formed between one hydrogen atom, already covalently linked to an electronegative atom, and another electronegative atom (such as nitrogen or oxygen). They bind together different molecules (e.g., water molecules) or different parts of the same molecule (as in protein molecules).

2.5 Chemical reactions occur when electrons are shared, gained, or lost (pp. 67–70)

Chemical Equations (pp. 67–68)

1. Chemical reactions involve the formation, breaking, or rearrangement of chemical bonds.

Types of Chemical Reactions (pp. 68–69)

2. Chemical reactions are either anabolic (constructive) or catabolic (destructive). They include synthesis, decomposition, and exchange reactions. Oxidation-reduction reactions may be considered a special type of exchange (or decomposition) reaction.

Energy Flow in Chemical Reactions (p. 69)

3. Bonds are energy relationships and there is a net loss or gain of energy in every chemical reaction.
4. In exergonic reactions, energy is liberated. In endergonic reactions, energy is absorbed.

Reversibility of Chemical Reactions (p. 69)

5. If reaction conditions remain unchanged, all chemical reactions eventually reach a state of chemical equilibrium in which the reaction proceeds in both directions at the same rate.
6. All chemical reactions are theoretically reversible, but many biological reactions go in only one direction because of energy requirements or the removal of reaction products.

Factors Influencing the Rate of Chemical Reactions (pp. 69–70)

7. Chemical reactions occur only when particles collide and valence shell electrons interact.
8. The smaller the reacting particles, the greater their kinetic energy and the faster the reaction rate. Higher temperature or reactant concentration, as well as the presence of catalysts, increases chemical reaction rates.

2

PART 2
BIOCHEMISTRY

2.6 Inorganic compounds include water, salts, and many acids and bases (pp. 70–73)

1. Most inorganic compounds do not contain carbon. Those found in the body include water, salts, and inorganic acids and bases.

Water (p. 70)

2. Water is the single most abundant compound in the body. It absorbs and releases heat slowly, acts as a universal solvent, participates in chemical reactions, and cushions body organs.

Salts (p. 71)

3. Salts are ionic compounds that dissolve in water and act as electrolytes. Calcium and phosphorus salts contribute to the hardness of bones and teeth. Ions of salts are involved in many physiological processes.

Acids and Bases (pp. 71–73)

4. Acids are proton donors; in water, they ionize and dissociate, releasing hydrogen ions (which account for their properties) and anions.
5. Bases are proton acceptors. The most common inorganic bases are the hydroxides; bicarbonate ion and ammonia are important bases in the body.
6. pH is a measure of hydrogen ion concentration of a solution (in moles per liter). A pH of 7 is neutral; a higher pH is alkaline, and a lower pH is acidic. Normal blood pH is 7.35–7.45. Buffers help to prevent excessive changes in the pH of body fluids.

2.7 Organic compounds are made by dehydration synthesis and broken down by hydrolysis (pp. 73–75)

1. Organic compounds contain carbon. Those found in the body include carbohydrates, lipids, proteins, and nucleic acids, all of which are synthesized by dehydration synthesis and digested by hydrolysis. All of these biological molecules contain C, H, and O. Proteins and nucleic acids also contain N.

2.8 Carbohydrates provide an easily used energy source for the body (pp. 75–77)

1. Carbohydrate building blocks are monosaccharides, the most important of which are hexoses (glucose, fructose, galactose) and pentoses (ribose, deoxyribose).
2. Disaccharides (sucrose, lactose, maltose) and polysaccharides (starch, glycogen) are composed of linked monosaccharide monomers.
3. Carbohydrates, particularly glucose, are the major energy fuel for forming ATP. Excess carbohydrates are stored as glycogen or converted to fat for storage.

2.9 Lipids insulate body organs, build cell membranes, and provide stored energy (pp. 77–80)

1. Lipids dissolve in fats or organic solvents, but not in water.
2. Triglycerides are composed of three fatty acid chains and glycerol. They are found chiefly in fatty tissue where they provide insulation and reserve body fuel. Unsaturated fatty acid chains produce oils. Saturated fatty acids produce solid fats typical of animal fats.
3. Phospholipids are modified phosphorus-containing triglycerides that have polar and nonpolar portions. They are found in all plasma membranes.
4. The steroid cholesterol is found in cell membranes and is the basis of steroid hormones, bile salts, and vitamin D.

2.10 Proteins are the body's basic structural material and have many vital functions (pp. 80–85)

1. The unit of proteins is the amino acid, and 20 common amino acids are found in the body.
2. Many amino acids joined by peptide bonds form a polypeptide. A protein (one or more polypeptides) is distinguished by the number and sequence of amino acids in its chain(s) and by the complexity of its three-dimensional structure.
3. Fibrous proteins, such as keratin and collagen, have secondary (α-helix or β-pleated sheet) and perhaps tertiary and quaternary structure. Fibrous proteins are used as structural materials.
4. Globular proteins achieve tertiary and sometimes quaternary structure and are generally spherical, soluble molecules. Globular proteins (e.g., enzymes, some hormones, antibodies, hemoglobin) perform special functional roles for the cell (e.g., catalysis, molecule transport).
5. Proteins are denatured by extremes of temperature or pH. Denatured globular proteins are unable to perform their usual function.
6. Enzymes are biological catalysts. They increase the rate of chemical reactions by decreasing the amount of activation energy needed. They do this by combining with the reactants and holding them in the proper position to interact. Many enzymes require cofactors to function.

2.11 DNA and RNA store, transmit, and help express genetic information (pp. 85–87)

1. Nucleic acids include deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). DNA specifies protein structure and replicates itself exactly before cell division. RNA is involved in carrying out DNA's instructions for protein synthesis and includes messenger, ribosomal, and transfer RNA.
2. The structural unit of nucleic acids is the nucleotide, which consists of a nitrogenous base (adenine, guanine, cytosine, thymine, or uracil), a sugar (ribose or deoxyribose), and a phosphate group.
3. DNA is a double-stranded helix. It contains deoxyribose and the bases A, G, C, and T.
4. RNA is single stranded. It contains ribose and the bases A, G, C, and U.

2.12 ATP transfers energy to other compounds (pp. 87–88)

1. ATP is the universal energy compound of body cells. Some of the energy liberated by the breakdown of glucose and other food fuels is captured in the bonds of ATP molecules and transferred via coupled reactions to energy-consuming reactions.

REVIEW QUESTIONS

To access additional practice questions using your smartphone, tablet, or computer: Mastering A&P® > Study Area > Practice Tests & Quizzes

(Some multiple choice questions have more than one correct answer. Select the best answer or answers from the choices given.)

Level 1 Remember/Understand

1. Which of the following elements is necessary for proper conduction of nervous impulses? **(a)** Fe, **(b)** I, **(c)** P, **(d)** Na.
2. All of the following are examples of the four major elements contributing to body mass except **(a)** hydrogen, **(b)** carbon, **(c)** nitrogen, **(d)** sodium, **(e)** oxygen.
3. The number of electrons in an electrically neutral element is equal to the **(a)** mass number, **(b)** number of isotopes, **(c)** number of neutrons, **(d)** atomic number.
4. Which of the following does *not* describe a mixture? **(a)** properties of its components are retained, **(b)** chemical bonds are formed, **(c)** components can be separated physically, **(d)** includes both heterogeneous and homogeneous examples.
5. In a beaker of water, the water-water bonds can properly be called **(a)** ionic bonds, **(b)** polar covalent bonds, **(c)** nonpolar covalent bonds, **(d)** hydrogen bonds.
6. When a pair of electrons is shared between two atoms, the bond formed is called **(a)** a single covalent bond, **(b)** a double covalent bond, **(c)** a triple covalent bond, **(d)** an ionic bond.
7. A synthesis reaction is characterized by all but **(a)** anabolic activities, **(b)** breaking of bonds, **(c)** formation of larger molecules, **(d)** formation of bonds.
8. Which of the following molecules is an inorganic molecule? **(a)** sucrose, **(b)** cholesterol, **(c)** collagen, **(d)** sodium chloride.
9. Bases **(a)** have a sour taste, **(b)** release hydrogen ions when dissolved in water, **(c)** are proton acceptors, **(d)** decrease the pH of a solution.
10. A phospholipid consists of **(a)** a long chain of hexose sugars, **(b)** a polar head and two nonpolar tails, **(c)** four interlocking hydrocarbon rings, **(d)** a glycerol and three fatty acids.
11. The lipid(s) used as the basis of vitamin D, sex hormones, and bile salts is/are **(a)** triglycerides, **(b)** cholesterol, **(c)** phospholipids, **(d)** prostaglandin.
12. Provide the atomic symbol for each of the following elements: **(a)** calcium, **(b)** carbon, **(c)** hydrogen, **(d)** iron, **(e)** nitrogen, **(f)** oxygen, **(g)** potassium, **(h)** sodium.

Level 2 Apply/Analyze

13. This element is needed in small amounts by the body to make functional thyroid hormones: **(a)** Ca, **(b)** Fe, **(c)** I, **(d)** Zn, **(e)** Mg.
14. Which of the following covalently bonded molecules are polar?

(a) **(b)** **(c)** **(d)**

15. Identify each reaction as one of the following: **(a)** a synthesis reaction, **(b)** a decomposition reaction, **(c)** an exchange reaction.

    _____ **(1)** $2Hg + O_2 \rightarrow 2HgO$

    _____ **(2)** $HCl + NaOH \rightarrow NaCl + H_2O$
16. A chemist, during the course of an analysis, runs across a chemical composed of carbon, hydrogen, and oxygen in the proportion 1:2:1 and having a six-sided molecular shape. It is probably **(a)** a pentose, **(b)** an amino acid, **(c)** a fatty acid, **(d)** a monosaccharide, **(e)** a nucleic acid.
17. If you require five moles of sodium bicarbonate ($NaHCO_3$) to make a buffer, how many grams do you need to weigh out? (*Note*: The approximate atomic weights of its atoms are Na = 23, H = 1, C = 12, and O = 16.)
18. The following equation, which represents the oxidative breakdown of glucose by body cells, is a reversible reaction.

    $$\text{Glucose} + \text{oxygen} \rightarrow \text{carbon dioxide} + \text{water} + \text{ATP}$$

    (a) How can you indicate that the reaction is reversible?
    (b) How can you indicate that the reaction is in chemical equilibrium?
    (c) Define chemical equilibrium.

Level 3 Evaluate/Synthesize

19. Consider the following information about three atoms:

    $^{12}_{6}C$ $^{13}_{6}C$ $^{14}_{6}C$

    (a) How are they similar to one another? **(b)** How do they differ from one another? **(c)** What are the members of such a group of atoms called? **(d)** Using the planetary model, draw the atomic configuration of $^{12}_{6}C$ showing the relative position and numbers of its subatomic particles.
20. What are hydrogen bonds and how are they important in the body?
21. Differentiate clearly between primary, secondary, and tertiary protein structure.
22. How are the physical characteristics of fibrous proteins suited for their function?
23. Explain why, if you pour water into a glass very carefully, you can "stack" the water slightly above the rim of the glass.
24. Some antibiotics act by binding to certain essential enzymes in the target bacteria. **(a)** How might these antibiotics influence the chemical reactions controlled by the enzymes? **(b)** What is the anticipated effect on the bacteria? On the person taking the antibiotic prescription?
25. Mrs. Roberts, in a diabetic coma, has just been admitted to Noble Hospital. Her blood pH indicates that she is in severe acidosis (low blood pH), and measures are quickly instituted to bring her blood pH back within normal limits. **(a)** Define pH and note the normal pH of blood. **(b)** Why is severe acidosis a problem?
26. Jason, a 12-year-old boy, was awakened suddenly by a loud crash. As he sat up in bed, straining to listen, his fright was revealed by his rapid breathing (hyperventilation), a breathing pattern effective in ridding the blood of CO_2. At this point, was his blood pH rising or falling?
27. Your lunch mainly consisted of carbohydrates in the form of starch, and you ate more than what your body required in terms of energy expenditure at that point in time. **(a)** Which chemical reactions would take place to digest the starch? **(b)** What would happen to the extra carbohydrates consumed?

3 Cells: The Living Units

In this chapter, you will learn that

3.1 Cells are the smallest unit of life

by exploring

- **Part 1 Plasma Membrane**
  - by asking
    - **3.2 What is the structure of the plasma membrane?**
    - **How do substances move across the plasma membrane?**
      - looking closer at
        - **3.3 Passive membrane transport**
        - **3.4 Active membrane transport**
    - **3.5 How does a cell generate a voltage across its plasma membrane?**
    - **3.6 How does the plasma membrane allow the cell to interact with its environment?**
- **Part 2 Cytoplasm**
  - looking closer at
    - **Cytosol**
    - **Inclusions**
    - **3.7 Cytoplasmic organelles**
      - exploring
        - **3.8 Cellular extensions**
- **Part 3 Nucleus**
  - by investigating
    - **3.9 The structure of the nucleus**
      - and asking
        - **3.10 How does a cell grow and divide?**
        - **3.11 What are the roles of DNA and RNA in protein synthesis?**
          - and further asking
            - **3.12 How are cells, organelles, and proteins destroyed?**

and finally, exploring

Developmental Aspects of Cells

CAREER CONNECTION

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Just as bricks and timbers are the structural units of a house, **cells** are the structural units of all living things, from one-celled "generalists" like amoebas to complex multicellular organisms such as humans, dogs, and trees. The human body has 50 to 100 trillion of these tiny building blocks.

This chapter focuses on structures and functions shared by all cells. We address specialized cells and their unique functions in later chapters.

3.1 Cells are the smallest unit of life

Learning Outcomes

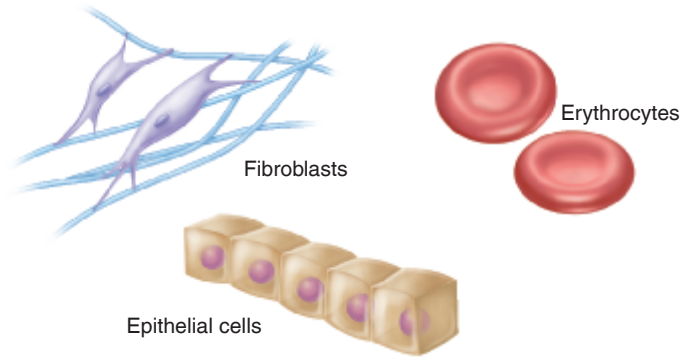
- **Define cell.**
- **Name and describe the composition of extracellular materials.**
- **List the three major regions of a generalized cell and their functions.**

Since the late 1800s, cell research has been exceptionally fruitful and has provided us with three concepts collectively known as the **cell theory**:

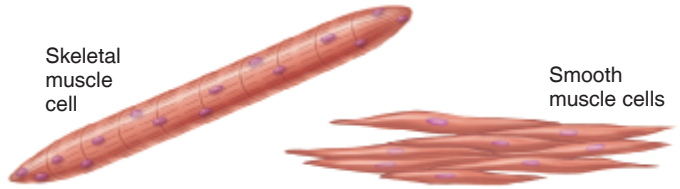
- **The cell is the smallest unit of life.** When you define the properties of cells, you define the properties of life.
- **All organisms are made of one or more cells.** Cells are the structural and functional building blocks of an organism. Different cell types have different functions within an organism, and the activity of an organism depends on the activities of individual cells and of all of the cells together. According to the *principle of complementarity of structure and function*, the activities of cells are dictated by their shapes, and by the types and relative numbers of the subcellular structures they contain.
- **Cells only arise from other cells.** Most body cells arise by *mitosis*, which we explore later in this chapter. Sperm and ovum (egg) cells arise by a related process called *meiosis* (mi-o′sis), which we describe in Chapter 27.

We will expand on all of these concepts as we progress. Let us begin with the idea that the cell is the smallest living unit. Whatever its form, however it behaves, the cell is the microscopic package that contains all the parts necessary to survive in an ever-changing world. It follows then that loss of homeostasis in cells underlies virtually every disease.

The trillions of cells in the human body include over 250 different cell types that vary greatly in shape, size, and function (**Figure 3.1**). The disc-shaped red blood cells, branching nerve cells, and cubelike cells of kidney tubules are just a few examples of the shapes cells take. Cells also vary in length—ranging from 2 micrometers (1/12,000 of an inch) in the smallest cells to over a meter in the nerve cells that cause you to wiggle your toes. A cell's shape reflects its function. For example, the flat, tilelike epithelial cells that line the inside of your cheek fit closely together, forming a living barrier that protects underlying tissues from bacterial invasion.



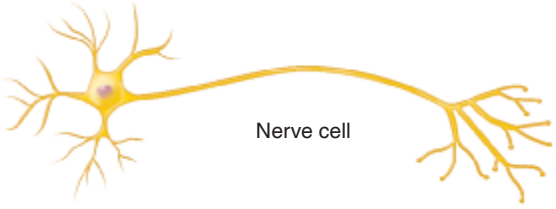
(a) Cells that connect body parts, form linings, or transport gases



(b) Cells that move organs and body parts

(c) Cell that stores nutrients

(d) Cell that fights disease



(e) Cell that gathers information and controls body functions

(f) Cell of reproduction

Figure 3.1 Cell diversity. (Note that cells are not drawn to the same scale.)

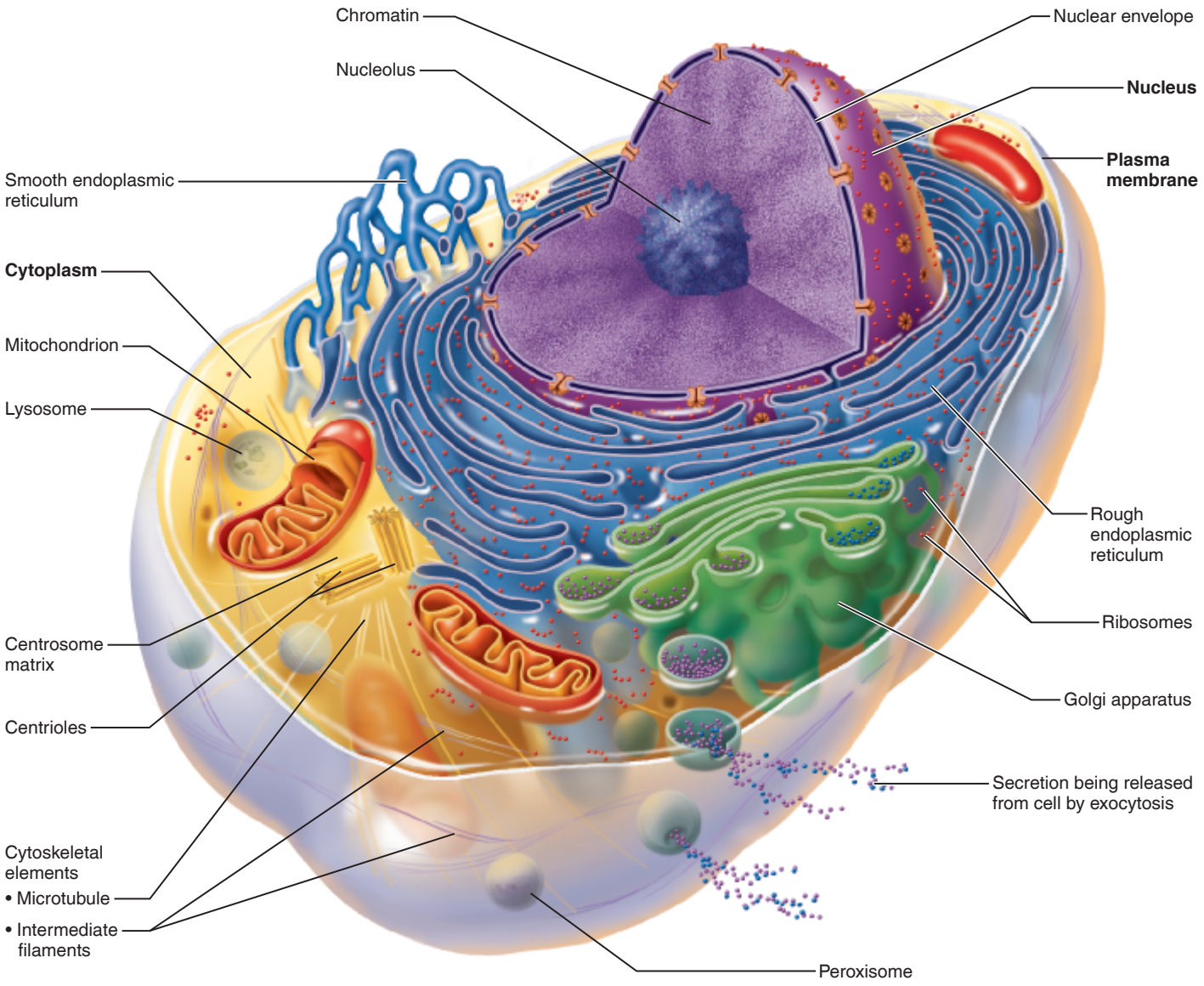


Figure 3.2 Structure of the generalized cell. No cell is exactly like this one, but this composite illustrates features common to many human cells. Note that not all of the organelles are drawn to the same scale in this illustration.

Regardless of these differences, all cells have the same basic parts and some common functions. For this reason, we will describe a *generalized*, or *composite*, *cell* (**Figure 3.2**).

A human cell has three main parts:

- The *plasma membrane*: the outer boundary of the cell, which acts as a selectively permeable barrier.
- The *cytoplasm* (si′to-plazm): the intracellular fluid packed with *organelles*, small structures that perform specific cell functions.
- The *nucleus* (nu′kle-us): an organelle that controls cellular activities. Typically the nucleus lies near the cell's center.

Extracellular Materials

Although we tend to think of the body as collections of cells—and it *is* that—it is impossible to discuss cells and their activities without saying something about extracellular materials. So—let's do that before going on to details about the generalized cell.

First of all, what are extracellular materials? **Extracellular materials** are substances contributing to body mass that are found outside the cells. The major classes of extracellular materials are:

- **Extracellular fluid. Extracellular fluid (ECF)** includes **interstitial fluid**, blood plasma, and cerebrospinal fluid. ECF dissolves and transports substances in the body. Interstitial fluid is the fluid in tissues that bathes all of our cells, and has endless major roles to play. Like a rich, nutritious "soup," interstitial fluid contains thousands of ingredients, including amino acids, sugars, fatty acids, regulatory substances, and wastes. To remain healthy, each cell must extract from this mix the exact amounts of the substances it needs depending on present conditions.

- **Cellular secretions.** These secretions include substances that aid in digestion (intestinal and gastric fluids) and some that act as lubricants (saliva, mucus, and serous fluids).
- **Extracellular matrix.** The **extracellular matrix** is the most abundant extracellular material. Most body cells are in contact with a jellylike substance composed of proteins and polysaccharides. Secreted by the cells, these molecules self-assemble into an organized mesh in the extracellular space, where they serve as a universal "cell glue" that helps bind body cells together. As described in Chapter 4, the extracellular matrix is particularly abundant in connective tissues—in some cases so abundant that it (rather than living cells) accounts for the bulk of that tissue type. Depending on the structure to be formed, the extracellular matrix in connective tissue ranges from soft to rock-hard.

Check Your Understanding

1. Summarize the three key points of the cell theory.
2. What are the three main parts of a human cell?

For answers, see Answers Appendix.

PART 1

PLASMA MEMBRANE

The flexible **plasma membrane** separates two of the body's major fluid compartments—the **intracellular fluid** within cells and the *extracellular fluid* outside cells. The term *cell membrane* is commonly used as a synonym for plasma membrane, but because nearly all cellular organelles are enclosed in a membrane, in this book we will always refer to the cell's surface, or outer limiting membrane, as the plasma membrane. The plasma membrane is much more than a passive envelope. As you will see, its unique structure allows it to play a dynamic role in cellular activities.

3.2 The plasma membrane is a double layer of phospholipids with embedded proteins

Learning Outcomes

- **Describe the chemical composition of the plasma membrane and relate it to membrane functions.**
- **Compare the structure and function of tight junctions, desmosomes, and gap junctions.**

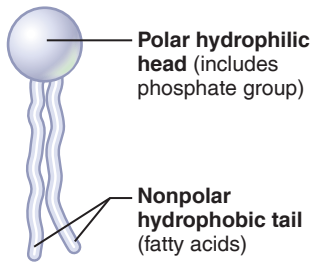
The **fluid mosaic model** of membrane structure depicts the plasma membrane as an exceedingly thin (7–10 nm) structure composed of a double layer, or bilayer, of lipid molecules with protein molecules "plugged into" or dispersed in it. The proteins, many of which float in the fluid *lipid bilayer*, form a constantly changing mosaic pattern. The model is named for this characteristic. In *Focus on the Plasma Membrane* (**Focus Figure 3.1** on pp. 96–97) we build a plasma membrane one key player at a time. Study this figure carefully before you read about the key players in more detail next.

Membrane Lipids

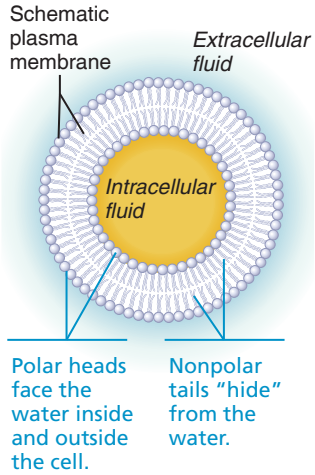
The lipid bilayer forms the basic "fabric" of the membrane. It is constructed largely of *phospholipids*, with smaller amounts of *cholesterol.*

Phospholipids

Recall from Chapter 2 (◀ **pp. 78–79**) that the polar *hydrophilic* heads of phospholipids (shown schematically at right) are attracted to water—the main constituent of both the intracellular and extracellular fluids. As a result they lie on both the inner and outer surfaces of the membrane. The nonpolar tails of phospholipids, being *hydrophobic*, avoid water and line up in the center of the membrane.



The result is that all plasma membranes, indeed all biological membranes, share a sandwich-like structure: They consist of two parallel sheets of phospholipid molecules lying tail to tail, with their polar heads bathed in water on either side of the membrane. This self-orienting property of phospholipids encourages biological membranes to self-assemble into generally spherical structures (as shown at right) and to reseal themselves when torn.



With a consistency similar to olive oil, the plasma membrane is a dynamic fluid structure in constant flux. Its phospholipids move freely from side to side, parallel to the membrane surface, but because of their self-orienting properties, they rarely flip-flop or move from one half of the bilayer to the other half. The inward-facing and outward-facing surfaces of the plasma membrane differ in the kinds and amounts of lipids they contain, and these variations help to determine local membrane structure and function.

Cholesterol

Some 20% of membrane lipid is cholesterol. Like phospholipids, cholesterol has a polar region (its hydroxyl group) and a nonpolar region (its fused ring system). It wedges its platelike hydrocarbon rings between the phospholipid tails, which stiffens the membrane.

Membrane Proteins

A cell's plasma membrane bristles with proteins that allow it to communicate with its environment. Proteins make up about half of the plasma membrane by mass and are responsible for

The Plasma Membrane

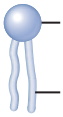
The plasma membrane is a phospholipid bilayer with embedded proteins arranged as a fluid mosaic.

Let's build a membrane by adding one key player at a time:

Lipids

Phospholipids

- Form basic structure of the membrane
- Hydrophobic tails prevent water-soluble substances from crossing, forming a boundary



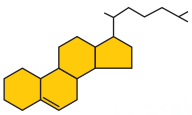
Polar hydrophilic head

Nonpolar, hydrophobic tail

Cholesterol

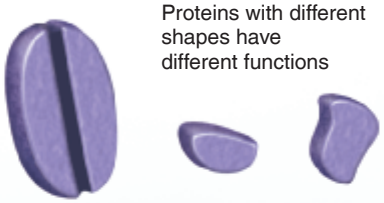
- Stiffens membrane
- Further decreases water solubility of membrane

Typical 4-ring steroid structure (see Figure 2.19)



Proteins

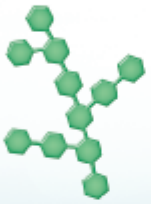
- Determine what functions the membrane can perform
- Many roles, e.g., transport, communication (acting as receptors for signal molecules), and joining cells to each other and to the extracellular matrix



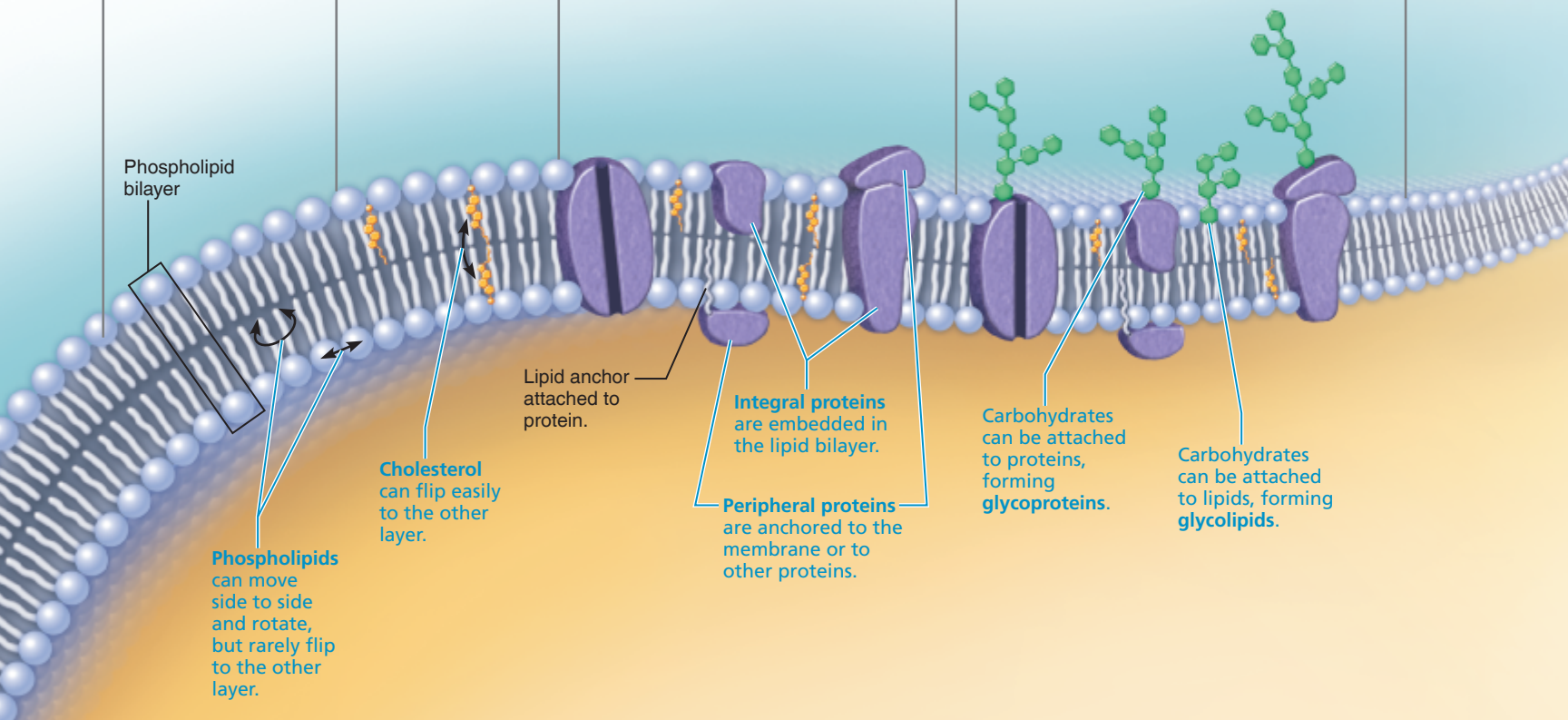
Proteins with different shapes have different functions

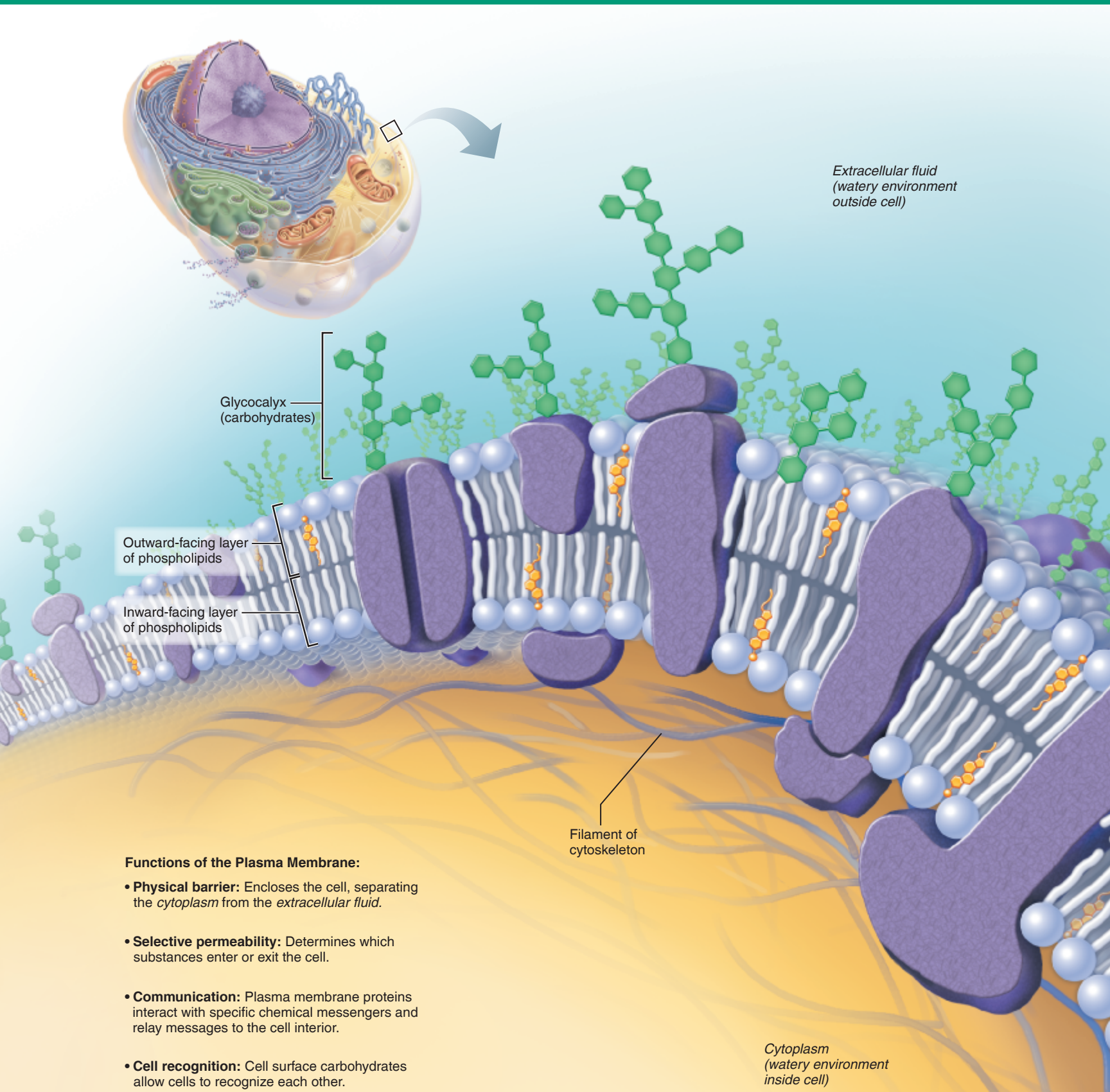
Carbohydrates

- Act as identity molecules
  - Allow cells to recognize "who is who," e.g., during development so cells can sort themselves into tissues and organs
  - Allow immune cells to recognize "friend" (our own cells) or "foe" (a pathogen)
- Are found only on the outer surface of the membrane, like the sugar-coating on breakfast cereal. Together, the carbohydrates on the outside of the cell form a coating called the **glycocalyx**



Short chains of linked monosaccharides (sugars)





Functions of the Plasma Membrane:

- **Physical barrier:** Encloses the cell, separating the *cytoplasm* from the *extracellular fluid.*
- **Selective permeability:** Determines which substances enter or exit the cell.
- **Communication:** Plasma membrane proteins interact with specific chemical messengers and relay messages to the cell interior.
- **Cell recognition:** Cell surface carbohydrates allow cells to recognize each other.

most of the specialized membrane functions (**Figure 3.3**). Some membrane proteins drift freely along the membrane surface. Others are "tethered" to intracellular or extracellular structures and are restricted in their movement.

There are two distinct populations of membrane proteins, integral and peripheral (Focus Figure 3.1, pp. 96–97).

Integral Proteins

Integral proteins are firmly inserted into the lipid bilayer. Some protrude from one membrane face only, but most are *transmembrane proteins* that span the entire membrane and protrude on both sides. Whether transmembrane or not, all integral proteins have both hydrophobic and hydrophilic regions. This structural feature allows them to interact with both the nonpolar lipid tails buried in the membrane and the water inside and outside the cell.

Some transmembrane proteins are involved in transport, and form *channels*, or pores. Small, water-soluble molecules or ions can move through these pores, bypassing the lipid part of the membrane. Others act as *carriers* that bind to a substance and then move it through the membrane (Figure 3.3a). Some transmembrane proteins are enzymes (Figure 3.3c). Still others are receptors for hormones or other chemical messengers and relay messages to the cell interior—a process called *signal transduction* (Figure 3.3b).

Peripheral Proteins

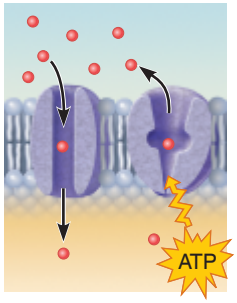
Unlike integral proteins, **peripheral proteins** are not embedded in the lipid bilayer. Instead, they either attach loosely to integral proteins or have a hydrophobic region that anchors them into the membrane. Peripheral proteins include a network of filaments that helps support the membrane from its cytoplasmic side (Figure 3.3e). Some peripheral proteins are enzymes. Others are motor proteins involved in mechanical functions, such as changing cell shape during cell division and muscle cell contraction. Still others link cells together.

Membrane Carbohydrates and the Glycocalyx

The extracellular surface (but not the intracellular surface) of the membrane is decorated with short branching carbohydrates. These are attached to most of the membrane's proteins and some of the membrane's lipids that are exposed on the exterior surface. Lipids and proteins with sugars attached are called **glycolipids** (gli″ko-lip′idz) and **glycoproteins**, respectively. Glycolipids have two fatty acid tails (like phospholipids), but a carbohydrate replaces the phosphate head group.

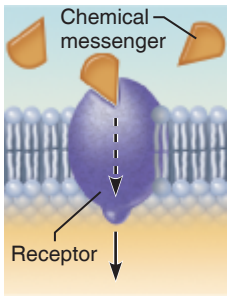
The **glycocalyx** (gli″ko-ka′liks; "sugar covering") consists of the fuzzy, sticky, carbohydrate-rich area at the cell surface created by the sugars of glycoproteins and glycolipids. Your cells are sugar-coated like breakfast cereal. The glycocalyx is further enriched by glycoproteins secreted by the cell.

Because every cell type has a different pattern of sugars in its glycocalyx, the glycocalyx provides identity molecules—highly



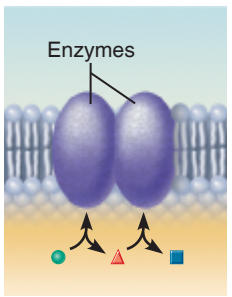
(a) Transport

- A protein (left) that spans the membrane may provide a hydrophilic channel across the membrane that is selective for a particular solute.
- Some transport proteins (right) hydrolyze ATP as an energy source to actively pump substances across the membrane.



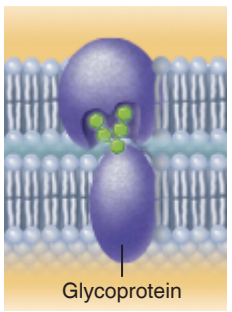
(b) Receptors for signal transduction

- A membrane protein exposed to the outside of the cell may have a binding site that fits the shape of a specific chemical messenger, such as a hormone.
- When bound, the chemical messenger may cause a change in shape in the protein that initiates a chain of chemical reactions in the cell.



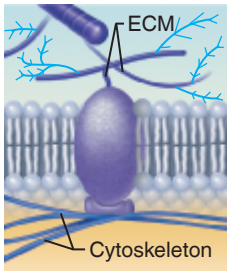
(c) Enzymatic activity

- A membrane protein may be an enzyme with its active site exposed to substances in the adjacent solution.
- A team of several enzymes in a membrane may catalyze sequential steps of a metabolic pathway as indicated (left to right) here.



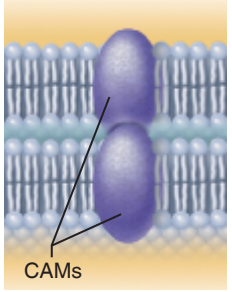
(d) Cell-cell recognition

- Some glycoproteins (proteins bonded to short chains of sugars which help to make up the glycocalyx) serve as identification tags that are specifically recognized by other cells.



(e) Attachment to the cytoskeleton and extracellular matrix (ECM)

- Elements of the cytoskeleton (cell's internal framework) and the extracellular matrix (fibers and other substances outside the cell) may anchor to membrane proteins.
- Helps maintain cell shape, fixes the location of certain membrane proteins, and plays a role in cell movement.



(f) Cell-to-cell joining

- Membrane proteins of adjacent cells may be hooked together in various kinds of intercellular junctions.
- Some membrane proteins (cell adhesion molecules or CAMs) of this group provide temporary binding sites that guide cell migration and other cell-to-cell interactions.

Figure 3.3 Membrane proteins perform many tasks. A single protein may perform a combination of these functions.

specific biological markers by which approaching cells recognize each other (Figure 3.3d). For example, immune system cells use these markers to determine which cells belong in the body and which are foreign.

HOMEOSTATIC IMBALANCE 3.1 CLINICAL

Definite changes occur in the glycocalyx of a cell that is becoming cancerous. In fact, a cancer cell's glycocalyx may change almost continuously, allowing it to keep ahead of immune system recognition mechanisms and avoid destruction. (Cancer is discussed on pp. 176–177.)

Cell Junctions

In many cases, the plasma membranes of adjacent cells are joined together by specialized cell junctions that allow neighboring cells to adhere and sometimes to communicate. These junctions may aid or inhibit movement of molecules between or past cells and also serve to tie cells together into tightly knit communities (**Figure 3.4**).

Let's look at each of the three types of cell junctions.

Tight Junctions

In a **tight junction**, a series of integral protein molecules in the plasma membranes of adjacent cells fuse together like the

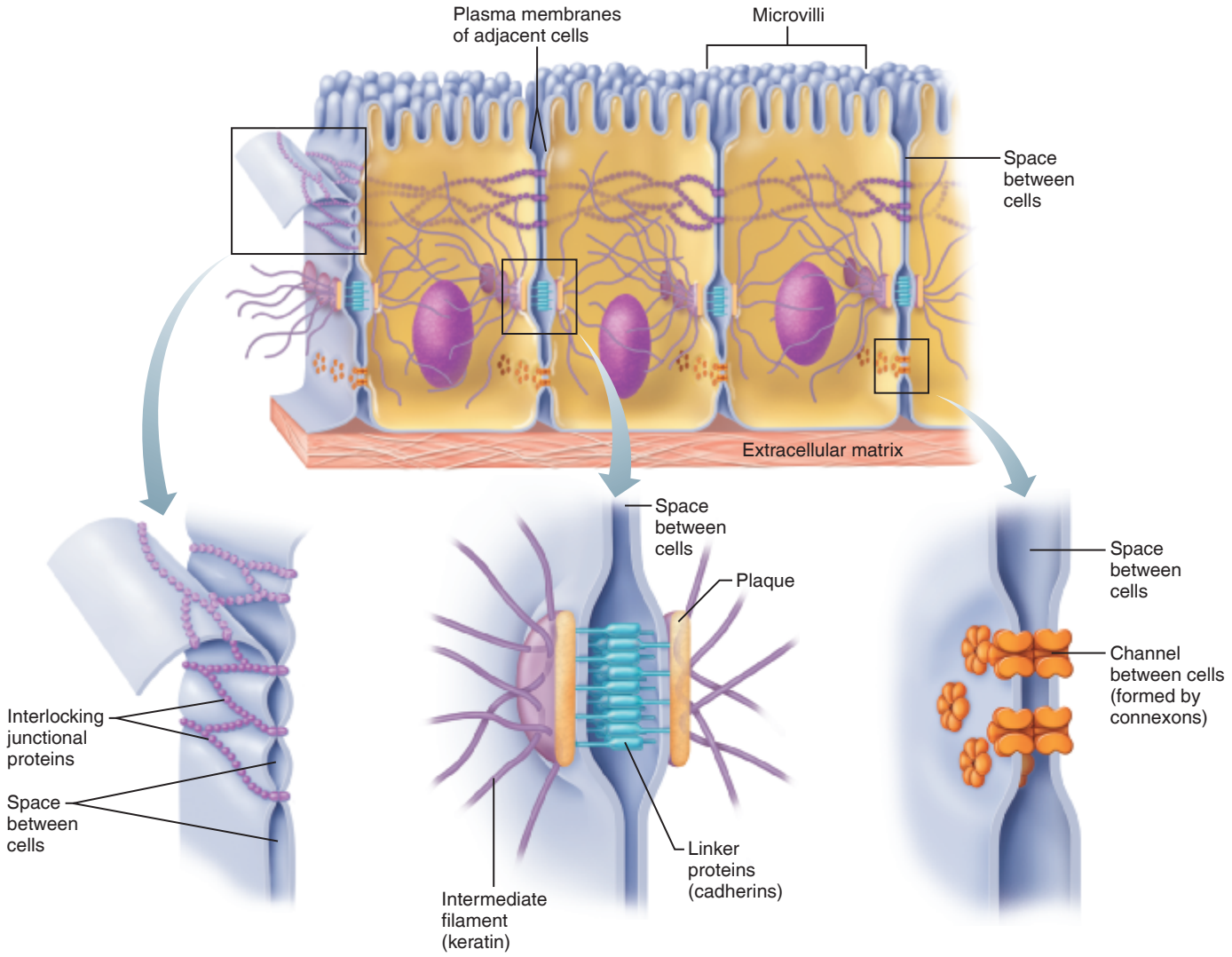


Figure 3.4 Cell junctions. An epithelial cell is shown joined to adjacent cells by three common types of cell junctions. (Note: Except for epithelia, it is unlikely that a single cell will have all three junction types.)

zipper of a Ziploc® bag. This forms an *impermeable junction* that encircles the cell and separates one fluid-filled compartment from another (Figure 3.4a). Tight junctions help prevent molecules from passing through the extracellular space between adjacent cells and restrict the movements of membrane proteins. For example, tight junctions between epithelial cells lining the digestive tract keep digestive enzymes and microorganisms in the intestine from seeping into the bloodstream. (Although called "impermeable" junctions, some tight junctions are leaky and may allow certain ions to pass.)

Desmosomes

Desmosomes (dez′muh-sōmz; "binding bodies") serve as *anchoring junctions*—mechanical couplings scattered like rivets along the sides of adjacent cells to prevent their separation (Figure 3.4b). On the cytoplasmic face of each plasma membrane is a buttonlike thickening called a *plaque*. Adjacent cells are held together by thin linker protein filaments (cadherins) that extend from the plaques and fit together like Velcro® in the intercellular (between cells) space. Thicker keratin filaments (intermediate filaments, which form part of the cytoskeleton) extend from the cytoplasmic side of the plaque across the width of the cell to anchor to the plaque on the cell's opposite side.

In this way, desmosomes bind neighboring cells together into sheets and also contribute to a continuous internal network of strong fibers that act as "guy-wires." These guy-wires distribute tension throughout a cellular sheet and reduce the chance of the sheet tearing when it is subjected to pulling forces. Desmosomes are abundant in tissues subjected to great mechanical stress, such as skin and heart muscle.

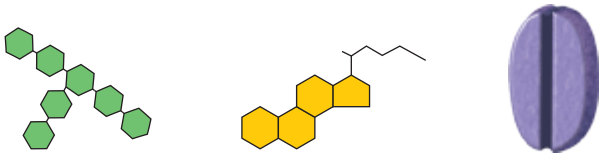
Gap Junctions

A **gap junction** is a *communicating junction* between adjacent cells. At gap junctions the adjacent plasma membranes are very close, and the cells are connected by hollow cylinders (called *connexons*) composed of transmembrane proteins. Different types of gap junctions are composed of different transmembrane proteins, and they determine what can pass through them from one cell to its neighbor. Ions, simple sugars, and other small molecules pass through these water-filled channels (Figure 3.4c).

Gap junctions are present in electrically excitable tissues, such as the heart and smooth muscle, where ion passage from cell to cell helps synchronize their electrical activity and contraction.

Check Your Understanding

3. What basic structure do all cellular membranes share?
4. Name the type of each of these molecules and state its role in the plasma membrane.



(a) (b) (c)

Table 3.1 Active versus Passive Tranport

PASSIVE TRANSPORT	ACTIVE TRANSPORT
No added energy required (uses kinetic energy)	Requires added energy (e.g., ATP)
Substances move from high to low concentration (i.e., "down" their concentration gradient)	Substances can move from low to high concentration (i.e., against their concentration gradient)

5. Which two types of cell junctions would you expect to find between muscle cells of the heart?
6. MAKE CONNECTIONS Phospholipid tails can be saturated or unsaturated (Chapter 2). This is true of phospholipids in plasma membranes as well. Which type—saturated or unsaturated—would make the membrane more fluid? Why?

For answers, see Answers Appendix.

Substances move through the plasma membrane in essentially two ways—passively or actively. In **passive processes**, substances cross the membrane without any energy input from the cell. In **active processes**, the cell provides the metabolic energy (usually ATP) needed to move substances across the membrane. Active and passive transport processes are the topics of the next two modules and are summarized in **Table 3.1**, Table 3.2 on p. 105, and Table 3.3 on p. 110.

3.3 Passive membrane transport is diffusion of molecules down their concentration gradient

Learning Outcomes

- **Relate plasma membrane structure to passive transport processes.**
- **Compare and contrast simple diffusion, facilitated diffusion, and osmosis relative to substances transported, direction, and mechanism.**

The three types of passive transport across the plasma membrane are *simple diffusion*, *facilitated diffusion*, and *osmosis*.* All of these are various types of diffusion. **Diffusion** (dĭ-fu′zhun) is the movement of molecules or ions from an area where they are in higher concentration to an area where they are in lower concentration. Movement from high to low concentration is also called movement down or along a **concentration gradient**.

The driving force for diffusion is the intrinsic kinetic energy of the molecules themselves. The constant random and high-speed motion of molecules and ions (a result of their intrinsic kinetic energy) results in collisions. With each collision, the particles ricochet off one another and change direction. The overall effect of this erratic movement is to scatter or disperse the particles throughout the environment (**Figure 3.5**).

*Some consider filtration as a fourth form of passive transport. However, filtration occurs across capillary walls, not plasma membranes, so we will discuss it in Chapter 19 together with capillary transport.

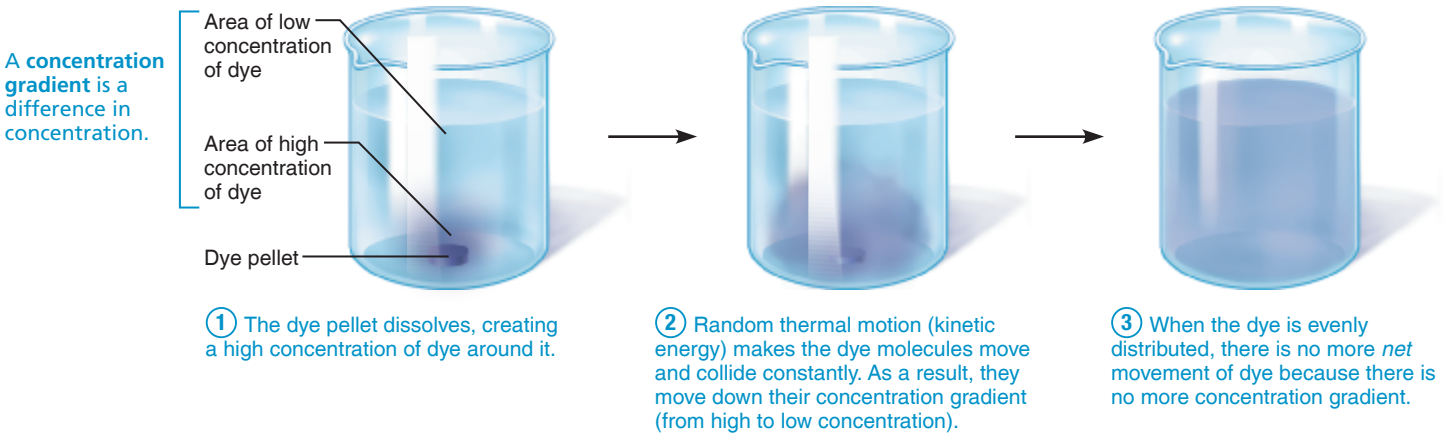


Figure 3.5 Diffusion.

The speed of diffusion is influenced by three factors:

- **Concentration.** The greater the difference in concentration of the diffusing molecules or ions between the two areas, the more collisions occur and the faster the particles diffuse.
- **Molecular size.** Smaller molecules diffuse more rapidly.
- **Temperature.** Higher temperature (more kinetic energy) increases the speed of molecular movement and means more rapid diffusion.

In a closed container, diffusion eventually produces a uniform mixture of molecules. In other words, the system reaches equilibrium, with molecules moving equally in all directions (no *net* movement).

Diffusion is immensely important in physiological systems and it occurs rapidly because the distances molecules are moving are very short, perhaps 1/1000 (or less) the thickness of this page! Examples include the movement of ions across cell membranes and the movement of neurotransmitters between two nerve cells.

The plasma membrane is a physical barrier to diffusion because of its hydrophobic core. That is, the membrane is a **selectively**, or **differentially**, **permeable** barrier: It allows some substances to pass while excluding others. For example, it allows nutrients to enter the cell, but keeps many undesirable substances out. At the same time, it keeps valuable cell proteins and other necessary substances in the cell, but allows wastes to exit.

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HOMEOSTATIC IMBALANCE 3.2 — CLINICAL

Selective permeability is a characteristic of healthy, intact cells. When a cell (or its plasma membrane) is severely damaged, the membrane becomes permeable to virtually everything, and substances flow into and out of the cell freely. This phenomenon is evident in patients with severe burns. Precious fluids, proteins, and ions "weep" from the damaged cells.

What determines whether a given substance can cross the plasma membrane? The following characteristics are key:

- *Lipid solubility*. The more lipid soluble, the more readily it will diffuse across.
- *Size*. The smaller the molecule, the more readily it will diffuse across.

In addition, molecules that are not sufficiently small or lipid soluble can still diffuse across if they are assisted by a carrier molecule such as an ion channel or transport protein. The unassisted diffusion of lipid-soluble or very small particles is called *simple diffusion*. Assisted diffusion is known as *facilitated diffusion*. A special name, *osmosis*, is given to the diffusion of a solvent (usually water) through a membrane.

Simple Diffusion

In **simple diffusion**, substances diffuse directly through the lipid bilayer (**Figure 3.6a**). Such substances are usually small nonpolar molecules that readily dissolve in lipids (are lipid soluble). These include gases (such as oxygen and carbon dioxide), steroid hormones, and fatty acids. To reiterate, the two criteria that determine how easily a substance will pass by simple diffusion through a plasma membrane are (1) lipid solubility and (2) size. Simple diffusion is not an all-or-none thing. Some substances diffuse readily and others hardly at all. For example, water is not lipid soluble and you would expect it to be repelled by the hydrophobic lipid tails of the membrane's core. However, its very small size allows very small amounts to move across the lipid bilayer by simple diffusion.

Facilitated Diffusion

Certain molecules, notably glucose and other sugars, some amino acids, and ions are transported passively even though they are unable to pass through the lipid bilayer. Instead they move through the membrane by a passive transport process called **facilitated diffusion** in which the transported substance either (1) binds to *carrier proteins* in the membrane and is ferried across or (2) moves through water-filled *channel proteins*.

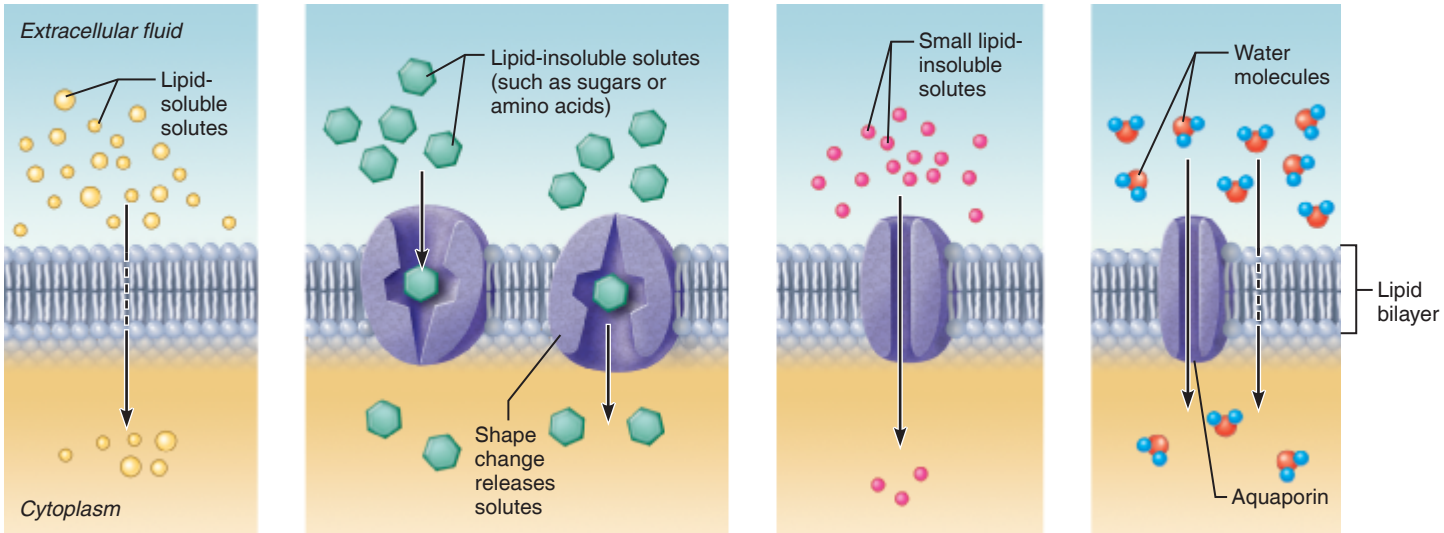
- **Carrier-mediated facilitated diffusion. Carriers** are transmembrane proteins that are specific for transporting certain polar molecules or classes of molecules, such as sugars and amino acids, that are too large to pass through membrane channels. Alterations in the shape of the carrier allow it to first envelop and then release the transported substance, allowing it to bypass the nonpolar regions of the membrane. Essentially, the carrier protein changes shape to move the binding site from one face of the membrane to the other (Figure 3.6b).

  Notice that a substance transported by carrier-mediated facilitated diffusion, such as glucose, moves down its concentration gradient (from high concentration to low), just as in simple diffusion. Glucose is normally in higher concentrations in the blood than in the cells, where it is rapidly used for ATP synthesis. So, glucose transport within the body is *typically* unidirectional—into the cells.

  Carrier-mediated transport is limited by the number of protein carriers that are available. For example, when all the glucose carriers are "engaged," they are said to be *saturated*, and glucose transport is occurring at its maximum rate.

- **Channel-mediated facilitated diffusion. Channels** are transmembrane proteins that transport substances, usually ions or water, through aqueous channels from one side of the membrane to the other (Figure 3.6c and d). Channels are selective due to pore size and the charges of the amino acids lining the pore. *Leakage channels* are always open and simply allow ions or water to move according to concentration gradients. *Gated channels* are controlled (opened or closed), usually by chemical or electrical signals. Like carriers, many channels can be inhibited by certain molecules, show saturation, and tend to be specific. Substances moving through them also follow the concentration gradient (always moving down the gradient).

Oxygen, water, glucose, and various ions are vitally important to cellular homeostasis. Their passive transport by diffusion



(a) Simple diffusion of lipid-soluble molecules directly through the phospholipid bilayer

(b) Carrier-mediated facilitated diffusion via protein carrier specific for one chemical; binding of solute causes transport protein to change shape

(c) Channel-mediated facilitated diffusion through a channel protein; mostly ions selected on basis of size and charge

(d) Osmosis, diffusion of a solvent such as water through a specific channel protein (aquaporin) or through the lipid bilayer

Figure 3.6 Diffusion through the plasma membrane.

(either simple or facilitated) represents a tremendous saving of cellular energy. Indeed, if these substances had to be transported actively, cell expenditures of ATP would be enormous!

Osmosis

The diffusion of a solvent, such as water, through a selectively permeable membrane is **osmosis** (oz-mo′sis; *osmos* = pushing). Osmosis is extremely important in determining the distribution of water in the various fluid-containing compartments of the body (cells, blood, and so on). In the clinic, you will encounter patients with swelling due to the abnormal accumulation of fluid in their tissues (*edema*, see Figure 19.20 on p. 766). In order to understand the causes and treatments of this condition, you will need to understand osmosis.

As we mentioned earlier, even though water is highly polar, a small amount of it can "sneak through" the plasma membrane by osmosis because of its small size. Water also moves freely and reversibly through water-specific channels constructed by transmembrane proteins called **aquaporins (AQPs)**, which allow single-file diffusion of water molecules. The water-filled aquaporin channels are particularly abundant in red blood cells and in cells involved in water balance such as kidney tubule cells.

Osmosis occurs whenever the water concentration differs on the two sides of a membrane. If distilled water is present on both sides of a selectively permeable membrane, no *net* osmosis occurs, even though water molecules move in both directions through the membrane. If the solute concentration on the two sides of the membrane differs, water concentration differs as well (as solute concentration increases, water concentration decreases).

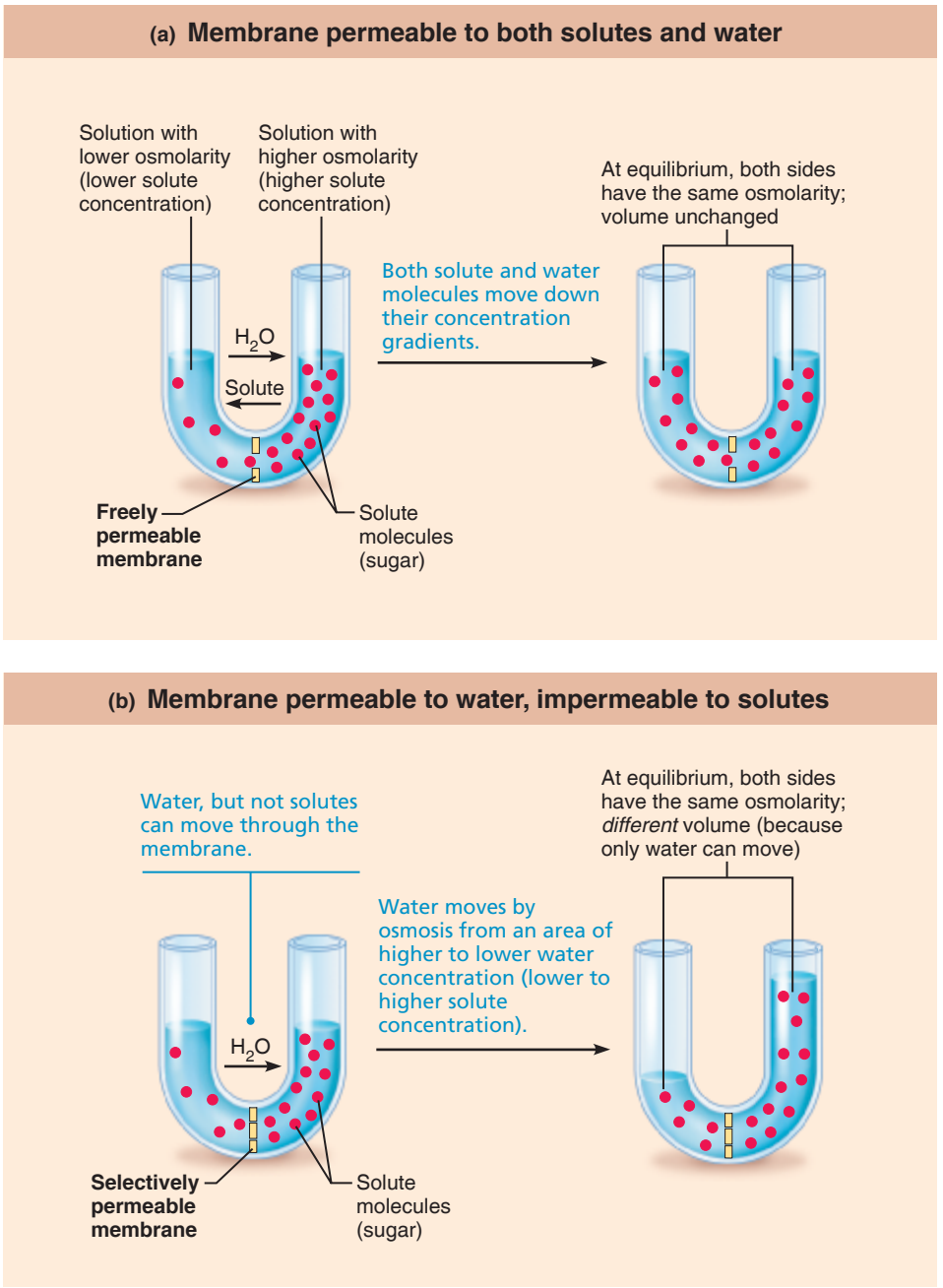


Figure 3.7 **Influence of membrane permeability on diffusion and osmosis.**

The extent to which solutes decrease water's concentration depends on the *number*—not the *type*—of solute particles, because one molecule or one ion of solute (typically) displaces one water molecule. The total concentration of all solute particles in a solution is referred to as the solution's **osmolarity** (oz″mo-lar′ĭ-te). When equal volumes of aqueous solutions of different osmolarity are separated by a membrane that is *permeable to all molecules* in the system, net diffusion of both solute and water occurs, each moving down its own concentration gradient. Equilibrium is reached when the water (and solute) concentration on both sides of the membrane is the same (**Figure 3.7a**).

If we consider the same system, but make the membrane *impermeable to solute particles*, we see quite a different result: Water moves and the volume changes (Figure 3.7b).

The latter situation mimics osmosis across plasma membranes of living cells, with one major difference. In our examples, the volumes of the compartments are infinitely expandable and the effect of pressure exerted by the added weight of the higher fluid column is not considered. What happens in a real cell? That depends on whether the cell is a plant cell (with a rigid cell wall) or an animal cell (with no cell wall).

As water diffuses into living plant cells, the point is finally reached where the **hydrostatic pressure** (the back pressure

exerted by water against the cell wall) within the cell is equal to its **osmotic pressure** (the tendency of water to move into the cell by osmosis). At this point, there is no further (net) water entry. As a rule, the higher the amount of nondiffusible, or *nonpenetrating*, solutes in a cell, the higher the osmotic pressure and the greater the hydrostatic pressure must be to resist further net water entry. In our plant cell, hydrostatic pressure is pushing water out, and osmotic pressure is pulling water in; therefore, you could think of the osmotic pressure as an osmotic "suck."

In living animal cells, such major changes in hydrostatic (and osmotic) pressures cannot occur because they lack rigid cell walls. Osmotic imbalances cause animal cells to swell or shrink (due to net water gain or loss) until either (1) the solute concentration is the same on both sides of the plasma membrane, or (2) the membrane stretches to its breaking point.

Tonicity

We have just learned that many solutes, particularly intracellular proteins and selected ions, cannot diffuse through the plasma membrane. Consequently, any change in their concentration alters the water concentration on the two sides of the membrane and results in a net loss or gain of water by the cell.

Tonicity (to-nis′ĭ-te) refers to the ability of a solution to change the shape (or plasma membrane tension) of cells by altering the cells' internal water volume (*tono* = tension).

- **Isotonic** ("the same tonicity") **solutions** have the same concentrations of nonpenetrating solutes as those found in cells (0.9% saline or 5% glucose). Cells exposed to isotonic solutions retain their normal shape, and exhibit no net loss or gain of water (**Figure 3.8a**). As you might expect, the body's extracellular fluids and most intravenous solutions (solutions infused into the body via a vein) are isotonic.
- **Hypertonic solutions** have a higher concentration of nonpenetrating solutes than seen in the cell (for example, a strong saline solution). Cells immersed in hypertonic solutions lose water and shrivel, or *crenate* (kre′nāt) (Figure 3.8b).
- **Hypotonic solutions** are more dilute (contain a lower concentration of nonpenetrating solutes) than cells. Cells placed in a hypotonic solution plump up rapidly as water rushes into them (Figure 3.8c). Distilled water represents the most extreme example of hypotonicity. Because it contains *no* solutes, water continues to enter cells until they finally burst, or *lyse*.

Notice that osmolarity and tonicity are not the same. A solution's osmolarity is based solely on its total solute concentration.* In contrast, its tonicity is based on how the solution affects cell volume, which depends on (1) solute concentration and (2) solute permeability of the plasma membrane.

*Osmolarity (Osm) is determined by multiplying molarity (moles per liter, or *M*) by the number of particles resulting from ionization. For example, since NaCl ionizes to $Na^+ + Cl^-$, a 1 *M* solution of NaCl is a 2 Osm solution. For substances that do not ionize (e.g., glucose), molarity and osmolarity are the same. More precisely, the term *osmolality* is used, which is equal to the number of particles mixed into a kilogram of water.

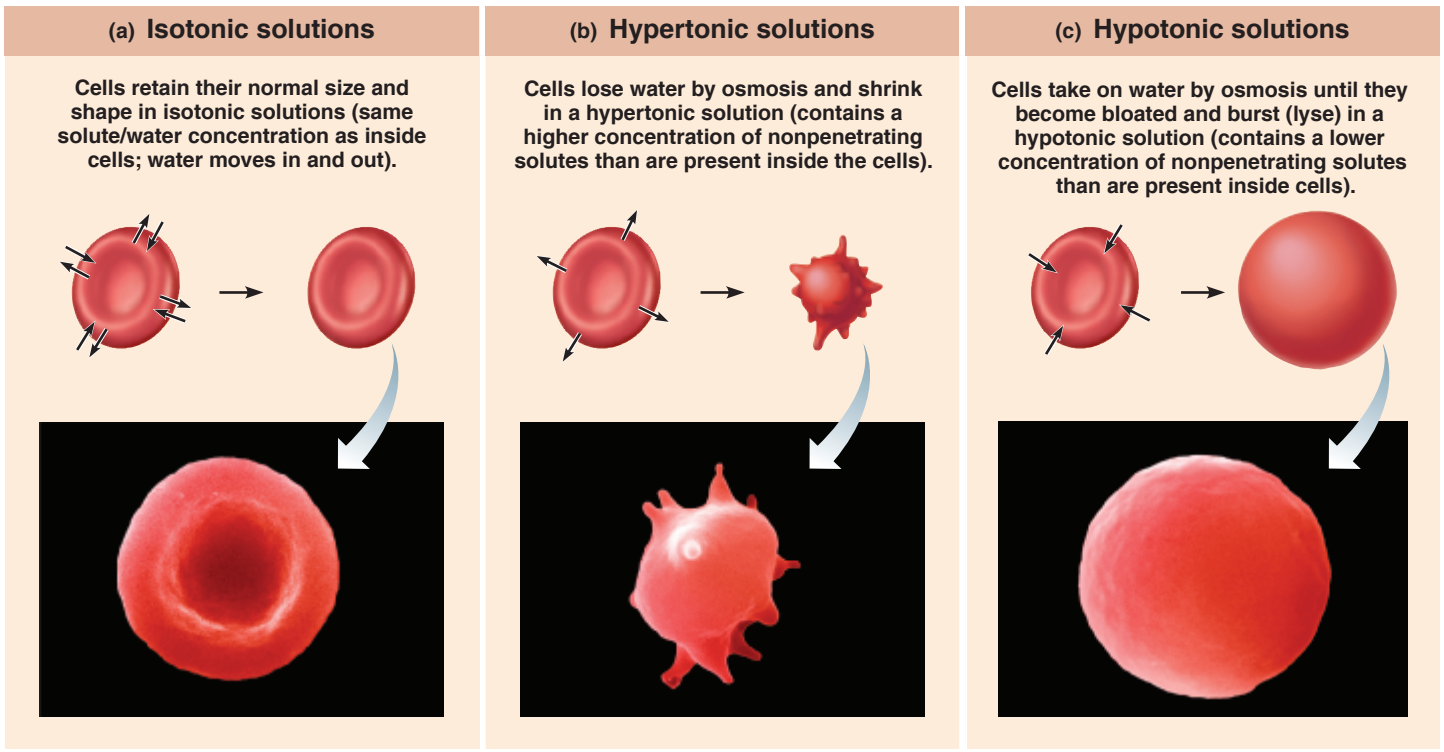


Figure 3.8 The effect of solutions of varying tonicities on living red blood cells.

Table 3.2 Passive Membrane Transport Processes: Diffusion

PROCESS	ENERGY SOURCE	DESCRIPTION	MEMBRANE TRANSPORT PROTEIN REQUIRED	SPECIFIC AND SATURABLE	EXAMPLES
Simple diffusion	Kinetic energy	Net movement of molecules down their concentration gradient (from higher concentration to lower concentration)	No	No (passage depends only on small size and lipid solubility)	Lipids, oxygen, and carbon dioxide
Facilitated diffusion	Kinetic energy	Same as simple diffusion, but the diffusing substance is attached to a membrane carrier protein or moves through a channel protein	Yes	Yes (specificity depends on shape inside transport protein)	Glucose, Na^+, K^+
Osmosis	Kinetic energy	Diffusion of water through a selectively permeable membrane; can occur directly through the lipid bilayer or via membrane channels (aquaporins)	No, except for movement through aquaporins	No, except for movement through aquaporins	Water is the only example

Osmolarity is expressed as osmoles per liter (osmol/L) where 1 osmol is equal to 1 mole of nonionizing molecules. A 0.3 osmol/L solution of NaCl is isotonic because sodium ions are usually prevented from diffusing through the plasma membrane. But if the cell is immersed in a 0.3 osmol/L solution of a penetrating solute, both water and solute will enter the cell. The cell will swell and burst, just as if it had been placed in pure water.

Summary of Passive Membrane Transport

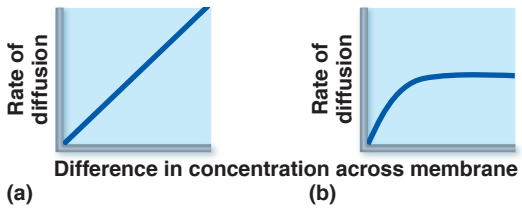
There are two important characteristics of any transport process: *specificity* and *saturability*. Any transport process that depends on a transport protein (such as a carrier or channel) will be *saturable*. This means that there is a *maximum rate* of transport because there are only a limited number of these proteins in the membrane. Like enzymes, transport proteins exhibit a high degree of *specificity*. For example, the carrier for glucose combines specifically with glucose in much the same way that an enzyme binds to its specific substrate.

Simple diffusion and osmosis occurring directly through the plasma membrane are not specific or saturable processes. They are not specific because they don't depend on the shape of the molecule. As long as the molecule can diffuse through the lipid barrier of the membrane, it will pass. Because no proteins are involved, these processes are not saturable. The rate of transport depends only on the size of the concentration gradient—the larger the gradient, the greater the movement.

Table 3.2 summarizes the processes of passive membrane transport.

Check Your Understanding

7. What is the energy source for all types of diffusion?
8. How do the two types of facilitated diffusion differ?
9. PREDICT Usually, Na^+ and Cl^- cannot cross the plasma membranes of cells. What would happen to a cell if it suddenly became permeable to both Na^+ and Cl^-?
10. APPLY For the two graphs below, which one represents simple diffusion and which represents facilitated diffusion? What is the name of the transport property illustrated by these graphs?



For answers, see Answers Appendix.

3.4 Active membrane transport directly or indirectly uses ATP

Learning Outcomes

- **Differentiate between primary and secondary active transport.**
- **Compare and contrast endocytosis and exocytosis in terms of function and direction.**
- **Compare and contrast pinocytosis, phagocytosis, and receptor-mediated endocytosis.**

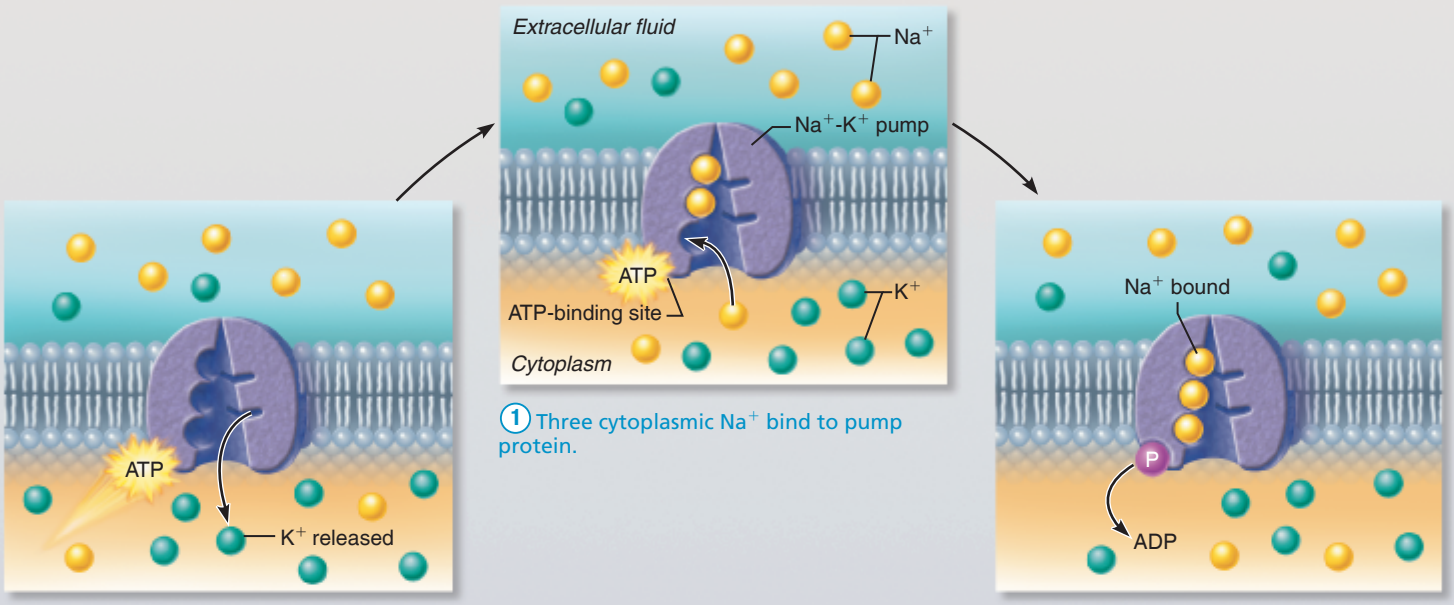
An *active process* occurs whenever a cell uses energy to move solutes across the membrane. Substances moved actively across the plasma membrane are usually unable to pass in the necessary direction by passive transport processes. The substance may be too large to pass through the channels, incapable of dissolving in the lipid bilayer, or moving against its concentration gradient.

There are two major means of active membrane transport: active transport and vesicular transport.

Primary Active Transport: The Na^+-K^+ Pump

Primary active transport is the process in which solutes are moved across cell membranes against electrochemical gradients using energy supplied directly by ATP. The action of the Na^+-K^+ pump is an important example of primary active transport.

Watch a 3-D animation of this process: Mastering A&P® > Study Area > Animations & Videos > A&P Flix



1 Three cytoplasmic Na^+ bind to pump protein.

2 Na^+ binding promotes hydrolysis of ATP. The energy released during this reaction phosphorylates the pump.

3 Phosphorylation causes the pump to change shape, expelling Na^+ to the outside.

4 Two extracellular K^+ bind to pump.

5 K^+ binding triggers release of the phosphate. The dephosphorylated pump resumes its original conformation.

6 The pump protein binds ATP and releases K^+ to the inside, and Na^+ sites are ready to bind Na^+ again. The cycle repeats.

Active Transport

Like carrier-mediated facilitated diffusion, **active transport** requires transport proteins that combine *specifically* and *reversibly* with the transported substances. However, facilitated diffusion always follows concentration gradients because its driving force is kinetic energy. In contrast, active transporters move solutes, most importantly ions, "uphill" *against* a concentration gradient. To do this work, cells must expend energy.

Active transport processes are distinguished according to their source of energy:

- In *primary active transport*, the energy to do work comes *directly from hydrolysis of ATP* by transport proteins called **pumps**.
- In *secondary active transport*, transport is driven *by energy stored in concentration gradients of ions* created by primary active transport pumps. Secondary active transport systems always move more than one substance at a time using a **cotransport protein**.

Regardless of whether the energy is provided directly (primary active transport) or indirectly (secondary active transport), each membrane pump or cotransporter transports only specific substances. Active transport systems provide a way for the cell to be very specific in cases where substances cannot pass by diffusion. No transporter—no transport.

Primary Active Transport

In **primary active transport**, hydrolysis of ATP results in the *phosphorylation* of the pump. (In other words, the transport protein is energized by the transfer of a phosphate group from ATP.) This step causes the protein to change its shape in such a manner that it pumps the bound solute across the membrane.

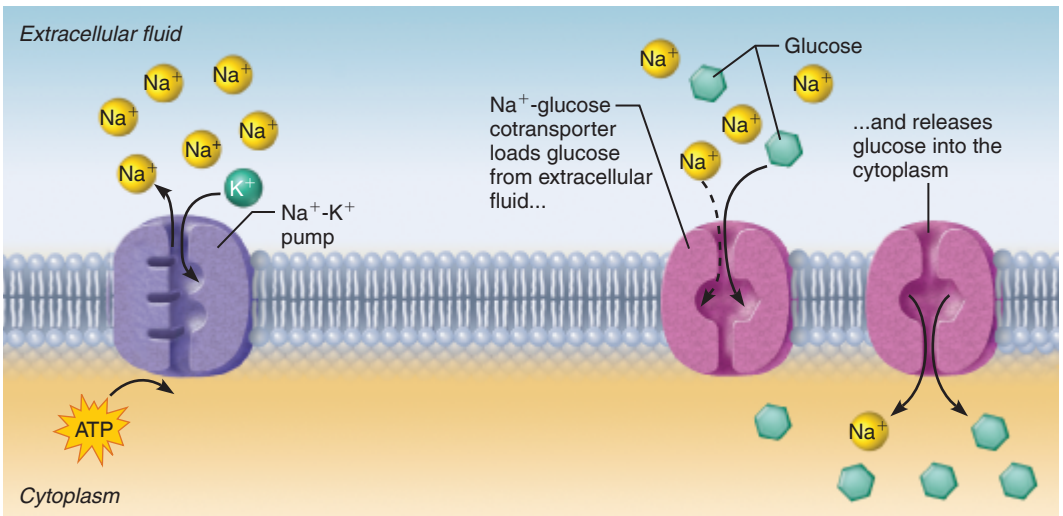
Primary active transport systems include calcium and hydrogen pumps, but the most important example of a primary active transport system is the **sodium-potassium pump**, for which the pump protein is an enzyme called **Na^+-K^+ ATPase**. **Focus Figure 3.2**, *Focus on Primary Active Transport: The Na^+-K^+ Pump*, describes the operation of this pump. For each molecule of ATP used, the Na^+-K^+ pump drives three Na^+ out of the cell and pumps two K^+ back in. As a result the concentration of K^+ inside the cell is some 10 times higher than that outside, and the reverse is true of Na^+. These ionic concentration differences are essential for excitable cells like muscle and nerve cells to function normally and for all body cells to maintain their normal fluid volume. Because Na^+ and K^+ leak slowly but continuously through leakage channels in the plasma membrane down their concentration gradient (and cross more rapidly in stimulated muscle and nerve cells), the Na^+-K^+ pump operates almost continuously.

Earlier we said that solutes diffuse down their concentration gradients. This is true for uncharged solutes, but ions are more complicated. The negatively and positively charged faces of the plasma membrane can help or hinder diffusion of ions driven by a concentration gradient. It is more correct to say that ions diffuse according to **electrochemical gradients**. This recognizes the effect of both electrical and concentration (chemical) forces. The electrochemical gradients maintained by the Na^+-K^+ pump are crucial for cardiac, skeletal muscle, and neuron function. They also underlie most secondary active transport as we shall see next.

Secondary Active Transport (Cotransport)

Secondary active transport (also called **cotransport**) uses a cotransport protein to couple the "downhill" (down its concentration gradient) movement of one solute to the "uphill" (against its concentration gradient) movement of another solute. The concentration gradient that is the source of energy for secondary active transport is created by primary active transport—in many cases by the Na^+-K^+ pump. By moving sodium across the plasma membrane against its concentration gradient, the pump stores energy (in the gradient). Then, just as water held back by a dam can do work as it flows downward (to generate electricity, for instance), a substance pumped across a membrane can do work as it leaks back, propelled "downhill" along its concentration gradient.

For example, as sodium moves back into the cell, other substances are "dragged along," or cotransported, by the same protein (**Figure 3.9**). Some sugars, amino acids, and many ions are cotransported via secondary active transport into cells lining the small intestine. Because the



① **Primary active transport**
The ATP-driven Na^+-K^+ pump stores energy by creating a steep concentration gradient for Na^+ entry into the cell.

② **Secondary active transport**
As Na^+ diffuses back across the membrane through a membrane cotransporter protein, it drives glucose against its concentration gradient into the cell.

Figure 3.9 Secondary active transport is driven by the concentration gradient created by primary active transport.

energy for this type of transport is the concentration gradient of the ion (in this case Na^+), Na^+ has to be pumped back out of the cell to maintain its concentration gradient.

In a **symport system**, such as the one we just described, the two transported substances move in the same direction (*sym* = same). In an **antiport system** (*anti* = opposite, against), the transported substances "wave to each other" as they cross the membrane in opposite directions. An example of an antiport system is a cotransporter that cells use to regulate their intracellular pH. This cotransporter uses the Na^+ concentration gradient to pump H^+ ions out of the cell.

Vesicular Transport

In **vesicular transport**, fluids containing large particles and macromolecules are transported across cellular membranes inside bubble-like, membranous sacs called *vesicles*. Like active transport, vesicular transport moves substances into the cell (endocytosis) and out of the cell (exocytosis). It is also used for combination processes such as *transcytosis* and *vesicular trafficking*. **Transcytosis** moves substances into, across, and then out of the cell. Transcytosis is common in the endothelial cells lining blood vessels because it provides a quick means to get substances from the blood to the interstitial fluid. **Vesicular trafficking** moves substances from one area (or membranous organelle) in the cell to another. The fleet of vesicles involved in vesicular transport can be thought of as the FedEx® of the cell. Vesicular transport processes are energized by ATP (or in some cases another energy-rich compound, *GTP*—guanosine triphosphate).

Endocytosis

Vesicles provide the main route for bringing bulk solids, most macromolecules, and fluids into a cell (or transporting them across a cell via transcytosis). Many types of endocytosis rely

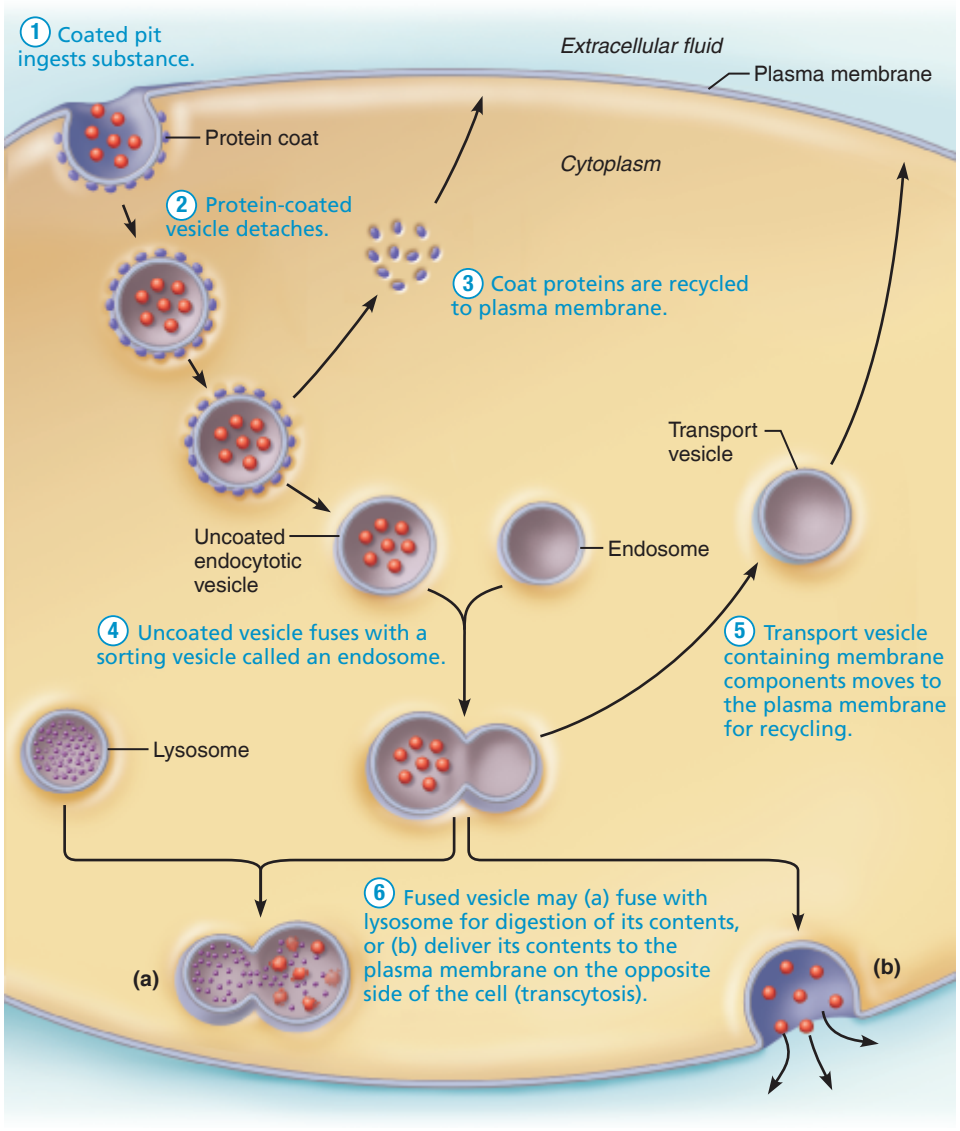


Figure 3.10 Events of endocytosis. Note the three possible fates for a vesicle and its contents, shown in (5) and (6).

on receptors in the membrane to determine the substances to be transported.

Endocytosis begins with a *coated pit*—an infolding of the membrane. Coated pits have a protein coating on the cytoplasmic face that deforms the membrane to produce the vesicle. **Figure 3.10** shows the basic steps in endocytosis and transcytosis.

Three types of endocytosis differ in the type and amount of material taken up and the means of uptake. These are phagocytosis, pinocytosis, and receptor-mediated endocytosis.

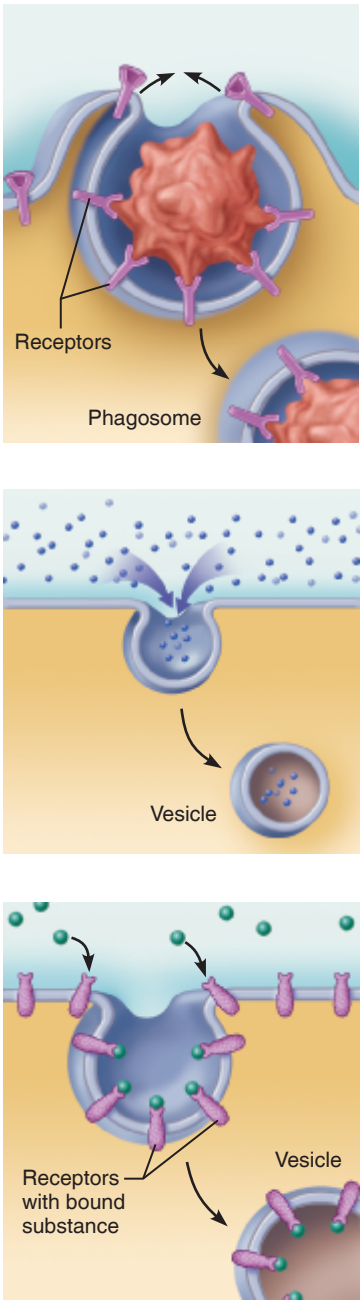
- **Phagocytosis.** In **phagocytosis** (fag″o-si-to′sis; "cell eating"), the cell engulfs some relatively large or solid material, such as a clump of bacteria, cell debris, or inanimate particles (asbestos fibers or glass, for example) (**Figure 3.11a**). When a particle binds to receptors on the cell's surface, cytoplasmic extensions called pseudopods (soo′do-pahdz; *pseudo* = false, *pod* = foot) form and flow around the particle. This forms an endocytotic vesicle called a **phagosome** (fag′o-sōm; "eaten body"). In most cases, the phagosome then fuses with a lysosome and its contents are digested.

  In the human body, only cells called *macrophages* and certain white blood cells are "experts" at phagocytosis. Commonly referred to as *phagocytes*, these cells help protect the body by ingesting and disposing of bacteria, other foreign substances, and dead tissue cells. The disposal of dying cells is crucial, because dead cell remnants trigger inflammation in the surrounding area. Most phagocytes move about by **amoeboid motion** (ah-me′boyd; "changing shape"); that is, their cytoplasm flows into temporary extensions that allow them to creep along.

- **Pinocytosis.** In **pinocytosis** ("cell drinking"), also called **fluid-phase endocytosis**, a bit of infolding plasma membrane surrounds a very small volume of extracellular fluid containing dissolved molecules (Figure 3.11b). This droplet enters the cell and fuses with a sorting vesicle called an endosome. Unlike phagocytosis, pinocytosis is a routine activity of most cells, affording them a nonselective way of sampling the extracellular fluid. It is particularly important in cells that absorb nutrients, such as cells that line the intestines.

  As mentioned, bits of the plasma membrane are removed when the membranous sacs are internalized. However, these membranes are recycled back to the plasma membrane by exocytosis as described shortly, so the surface area of the plasma membrane remains remarkably constant.

- **Receptor-mediated endocytosis.** The main mechanism for the *specific* endocytosis and transcytosis of most macromolecules by body cells is **receptor-mediated endocytosis** (Figure 3.11c). This exquisitely selective mechanism allows cells to concentrate material that is present only in small amounts in the extracellular fluid. The receptors for this process are plasma membrane proteins that bind only certain substances. Both the receptors and attached molecules are internalized and then dealt with in one of the ways discussed above. Substances taken up by receptor-mediated endocytosis include enzymes, insulin (and some other hormones), low-density lipoproteins (such as cholesterol attached to a transport protein), and iron. Unfortunately, flu viruses, diphtheria, and cholera toxins hijack this route to enter our cells.



(a) Phagocytosis
The cell engulfs a large particle by forming a projecting pseudopod ("false foot") around it and enclosing it within a membranous sac called a phagosome. The phagosome combines with a lysosome and its contents are digested. The vesicle has receptors capable of binding to microorganisms or solid particles.

(b) Pinocytosis
The cell "gulps" a drop of extracellular fluid containing solutes into tiny vesicles. No receptors are used, so the process is nonspecific.

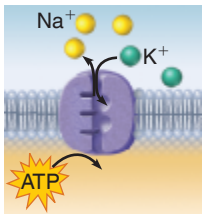
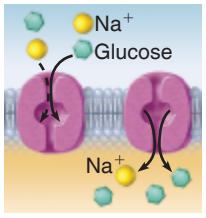
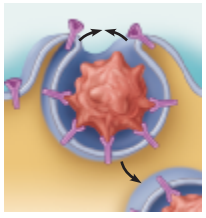
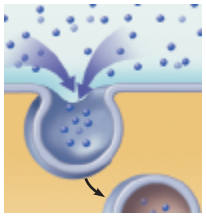
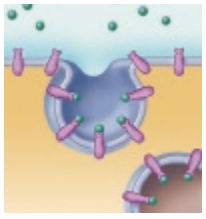
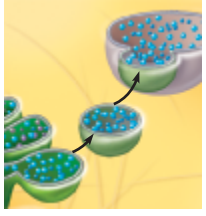
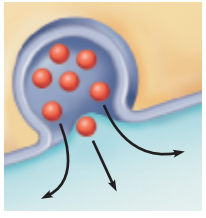
(c) Receptor-mediated endocytosis
Extracellular substances bind to specific receptor proteins, enabling the cell to ingest and concentrate specific substances in protein-coated vesicles. Substances may be released inside the cell or digested in a lysosome.

Figure 3.11 Comparison of three types of endocytosis.

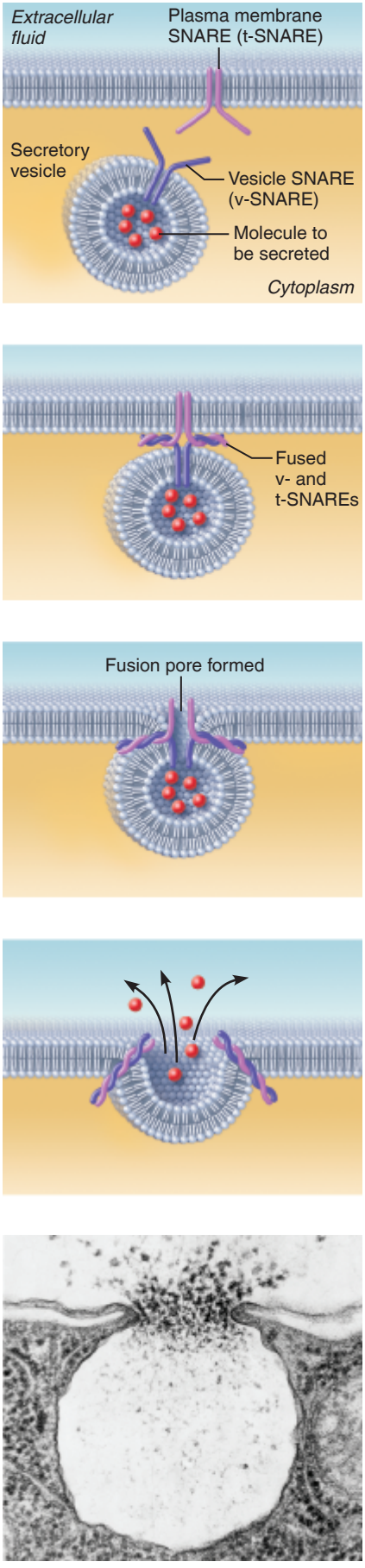
Exocytosis

Vesicular transport processes that eject substances from the cell interior into the extracellular fluid are called **exocytosis** (ek″so-si-to′sis; "out of the cell"). Exocytosis is typically stimulated by a cell-surface signal such as binding of a hormone to a membrane receptor or a change in membrane voltage. Exocytosis accounts for hormone secretion, neurotransmitter release, mucus secretion, and in some cases, ejection of wastes. The

Table 3.3 Active Membrane Transport Processes

PROCESS	ILLUSTRATION	ENERGY SOURCE	DESCRIPTION	EXAMPLES
Active Transport				
Primary active transport*		ATP	• Transport of substances against a concentration (or electrochemical) gradient. • A pump protein moves substances across the plasma membrane. • Directly uses energy of ATP hydrolysis.	Ions (Na^+, K^+, H^+, Ca^{2+}, and others)
Secondary active transport*		Ion concentration gradient maintained with ATP	• Cotransport (coupled transport) of two solutes across the membrane. • Energy is supplied by the concentration gradient created by primary active transport. • *Symporters* move the transported substances in the same direction; *antiporters* move transported substances in opposite directions across the membrane.	Movement of polar or charged solutes, e.g., amino acids (into cell by symporters); Ca^{2+}, H^+ (out of cells via antiporters)
Vesicular Transport				
Endocytosis				
Phagocytosis		ATP	• A large external particle (proteins, bacteria, dead cell debris) is surrounded by a pseudopod ("false foot") and becomes enclosed in a vesicle (phagosome).	Occurs primarily in phagocytes (some white blood cells and macrophages)
Pinocytosis (fluid-phase endocytosis)		ATP	• Plasma membrane sinks beneath an external fluid droplet containing small solutes. Membrane edges fuse, forming a fluid-filled vesicle.	Occurs in most cells; important for taking in dissolved solutes by absorptive cells of the kidney and intestine
Receptor-mediated endocytosis		ATP	• External substance binds to membrane receptors. • Selective endocytosis and transcytosis.	Means of intake of some hormones, cholesterol, iron, and most macromolecules
Vesicular trafficking		ATP	• Vesicles pinch off from organelles and travel to other organelles to deliver their cargo.	Intracellular trafficking between certain organelles, e.g., endoplasmic reticulum and Golgi apparatus
Exocytosis		ATP	• Secretion or ejection of substances from a cell. • The substance is enclosed in a membranous vesicle, which fuses with the plasma membrane and ruptures, releasing the substance to the exterior.	Secretion of neurotransmitters, hormones, mucus, etc.

*Like facilitated diffusion, primary and secondary active transport require a transport protein in the membrane. For this reason, they are both specific and saturable.



(a) The process of exocytosis

① The membrane-bound vesicle migrates to the plasma membrane.

② Proteins at the vesicle surface (v-SNAREs) bind with t-SNAREs (plasma membrane proteins).

③ The vesicle and plasma membrane fuse and a pore opens up.

④ Vesicle contents are released to the cell exterior.

(b) Photomicrograph of a secretory vesicle releasing its contents by exocytosis (100,000×)

Figure 3.12 Exocytosis.

substance to be removed from the cell is first enclosed in a protein-coated membranous sac called a *secretory vesicle*. In most cases, the vesicle migrates to the plasma membrane, fuses with it, and then ruptures, spilling the sac contents out of the cell (**Figure 3.12**).

Exocytosis, like other mechanisms in which vesicles are targeted to their destinations, involves a "docking" process in which transmembrane proteins on the vesicles, fancifully called v-SNAREs (*v* for vesicle), recognize certain plasma membrane proteins, called t-SNAREs (*t* for target), and bind with them. This binding causes the membranes to "corkscrew" together and fuse, rearranging the lipid monolayers without mixing them (Figure 3.12a). As described, membrane material added by exocytosis is removed by endocytosis—the reverse process.

Table 3.3 summarizes active membrane transport processes.

Check Your Understanding

11. Does the Na^+-K^+ ATPase pump K^+ into or out of the cell? What is the ratio of Na^+ to K^+ it pumps?

12. As a cell grows, its plasma membrane expands. Does this membrane expansion involve endocytosis or exocytosis?

13. Phagocytic cells gather in the lungs, particularly in the lungs of smokers. What is the connection?

14. Which vesicular transport process allows a cell to take in cholesterol from the extracellular fluid?

For answers, see Answers Appendix.

3.5 Selective diffusion establishes the membrane potential

Learning Outcome

Define membrane potential and explain how the resting membrane potential is established and maintained.

As you're now aware, the selective permeability of the plasma membrane can lead to dramatic osmotic flows, but that is not its only consequence. An equally important result is the generation of a **membrane potential**, or voltage, across the membrane. While all body cells have a membrane potential, it is especially important for nerve and muscle cells because they use changes in membrane potential as a form of communication.

A *voltage* is electrical potential energy resulting from the separation of oppositely charged particles. In cells, the oppositely charged particles are ions, and the barrier that keeps them apart is the plasma membrane.

In their resting state, plasma membranes of all body cells exhibit a **resting membrane potential** that typically ranges from −50 to −90 millivolts (mV), depending on cell type. For this reason, all cells are said to be **electrically polarized**. The minus sign before the voltage indicates that the *inside* of the cell is negative compared to its outside. This voltage (or charge separation) exists *only at the membrane*. If we

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added up all the negative and positive charges in the cytoplasm, we would find that the cell interior is electrically neutral. Likewise, the positive and negative charges in the extracellular fluid balance each other exactly.

So how does the resting membrane potential come about, and how is it maintained? The short answer is that diffusion causes ionic imbalances that polarize the membrane, and active transport processes *maintain* that membrane potential. First, let's look at how diffusion polarizes the membrane.

K^+ Is the Key Player

Many kinds of ions are found both inside cells and in the extracellular fluid, but the resting membrane potential is determined mainly by the concentration gradient of potassium (K^+) and by the differential permeability of the plasma membrane to K^+ and other ions (**Figure 3.13**). K^+ and protein anions predominate inside body cells, and the extracellular fluid contains relatively more Na^+, which is largely balanced by Cl^-. The plasma membrane is somewhat permeable to K^+ because of leakage channels, but it is impermeable to the protein anions. Consequently, as shown in Figure 3.13 (1), K^+ diffuses out of the cell along its concentration gradient but the protein anions are unable to follow, and this loss of positive charges makes the cytoplasmic side of the membrane more negative.

(2) As more and more K^+ leaves the cell, the negativity of the inner membrane face becomes great enough to attract K^+ back toward and even into the cell. (3) At a membrane voltage of −90 mV, potassium's concentration gradient is exactly balanced by the electrical gradient (membrane potential), and one K^+ enters the cell as one leaves.

In many cells, sodium (Na^+) also contributes to the resting membrane potential. Sodium is strongly attracted to the cell interior by its concentration gradient, bringing the resting membrane potential to −70 mV. However, K^+ still largely determines the resting membrane potential because the membrane is much more permeable to K^+ than to Na^+. Even though the membrane is permeable to Cl^-, in most cells Cl^- does not contribute to the resting membrane potential, because its concentration and electrical gradients exactly balance each other.

We may be tempted to believe that massive flows of K^+ ions are needed to generate the resting potential, but this is not the case. Surprisingly, the number of ions producing the membrane potential is so small that it does not change ion concentrations in any significant way.

In a cell at rest, very few ions cross its plasma membrane. However, Na^+ and K^+ are not at equilibrium and there is some net movement of K^+ out of the cell and of Na^+ into the cell. Na^+ is strongly pulled into the cell by both its concentration gradient and the interior negative charge. If only passive forces were at work, these ion concentrations would eventually become equal inside and outside the cell.

Active Transport Maintains Electrochemical Gradients

Diffusion establishes the membrane potential. Now let's look at how active transport processes maintain the membrane potential to keep the cell in a *steady state*. This requires that the rate of active transport of Na^+ out of the cell is equal to, and depends on, the rate of Na^+ diffusion into the cell. If more Na^+ enters, more is pumped out. (This is like being in a leaky boat. The more water that comes in, the faster you bail!) The Na^+-K^+ pump couples sodium and potassium transport (see Focus Figure 3.2 on p. 106). The pump maintains both the membrane potential (the charge separation) and the osmotic balance. Indeed, if Na^+ was not continuously removed from cells, so much would accumulate intracellularly that the osmotic gradient would draw water into the cells, causing them to burst.

As we described on p. 107, diffusion of charged particles across the membrane is affected not only by concentration gradients, but by the electrical charge on the inner and outer faces of the membrane. Together these gradients make up the *electrochemical gradient.* The diffusion of K^+ across the plasma membrane is aided by the membrane's greater permeability to it and by the ion's concentration gradient, but the negative charges on the cell interior resist K^+ diffusion. In contrast, a

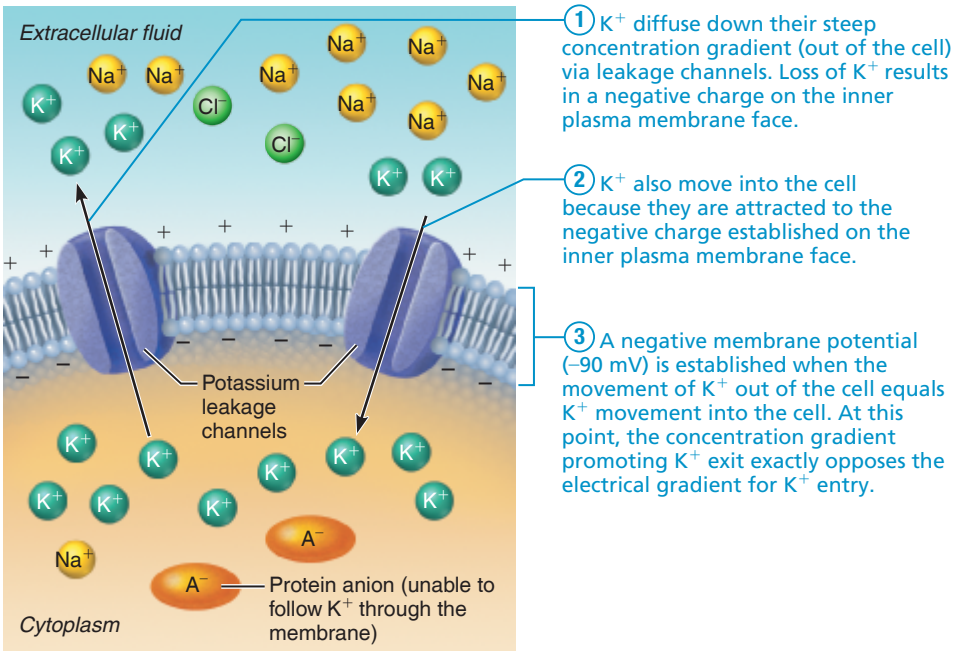


Figure 3.13 The key role of K^+ in generating the resting membrane potential. The resting membrane potential is largely determined by K^+ because at rest, the membrane is much more permeable to K^+ than Na^+. The active transport of sodium and potassium ions by the Na^+-K^+ pump maintains the Na^+ and K^+ concentration gradients.

steep electrochemical gradient draws Na^+ into the cell, but the membrane's relative impermeability to it limits Na^+ diffusion.

The transient opening of gated Na^+ and K^+ channels in the plasma membrane "upsets" the resting membrane potential. As we describe in later chapters, this is a normal means of activating neurons and muscle cells. We will revisit the resting membrane potential and have a closer look at how it is established in *Focus on the Resting Membrane Potential*, Focus Figure 11.1 on p. 434.

Check Your Understanding

15. What process establishes the resting membrane potential?

16. Is the inside of the plasma membrane negative or positive relative to its outside in a polarized membrane of a resting cell?

For answers, see Answers Appendix.

3.6 Cell adhesion molecules and membrane receptors allow the cell to interact with its environment

Learning Outcomes

- **Describe the role of cell adhesion molecules in allowing cells to interact with their environment.**
- **List several roles of membrane receptors and that of G protein–coupled receptors.**

Cells are biological minifactories and, like other factories, they receive and send orders from and to the outside community. But *how* does a cell interact with its environment, and *what* activates it to carry out its homeostatic functions?

Sometimes cells interact directly with other cells. However, in many cases cells respond to extracellular chemicals, such as hormones and neurotransmitters distributed in body fluids. Cells also interact with extracellular molecules that act as signposts to guide cell migration during development and repair. The most important molecules cells use to interact with their environment fall into two large families—cell adhesion molecules and plasma membrane receptors (see Figure 3.3).

Roles of Cell Adhesion Molecules (CAMs)

Thousands of **cell adhesion molecules (CAMs)** are found on almost every cell in the body. CAMs play key roles in embryonic development and wound repair (situations where cell mobility is important) and in immunity. These sticky glycoproteins (*cadherins* and *integrins*) act as:

- The molecular Velcro® that cells use to anchor themselves to molecules in the extracellular space (see Figure 3.3e on p. 98) and to each other (see Figure 3.3f)
- The "arms" that migrating cells use to haul themselves past one another
- SOS signals sticking out from the blood vessel lining that rally protective white blood cells to a nearby infected or injured area
- Mechanical sensors that transmit information about changes in the extracellular matrix into the cell, bringing about a variety of cellular responses such as cell migration, proliferation (growth by cell division), and specialization

Roles of Plasma Membrane Receptors

A huge and diverse group of integral proteins that serve as binding sites are collectively known as **membrane receptors**. Some function in contact signaling, and others in chemical signaling. Most are glycoproteins. Let's take a look.

Contact Signaling

Contact signaling, in which cells come together and touch, is the means by which cells recognize one another. It is particularly important for normal development and immunity. Some bacteria and other infectious agents use contact signaling to identify their "preferred" target tissues.

Chemical Signaling

Many signals originating outside of the cell are in the form of chemical messengers. *Chemical signaling* is the process in which a **ligand**, the chemical messenger, binds a specific receptor and initiates a response. Ligands include most *neurotransmitters* (nervous system signals), *hormones* (endocrine system signals), and *paracrines* (chemicals that act locally and are rapidly destroyed).

Different cells respond in different ways to the same ligand. Acetylcholine, for instance, stimulates skeletal muscle cells to contract, but inhibits heart muscle. Why do different cells respond so differently? The reason is that a target cell's response depends on the internal machinery that the receptor is linked to, not the specific ligand that binds to it.

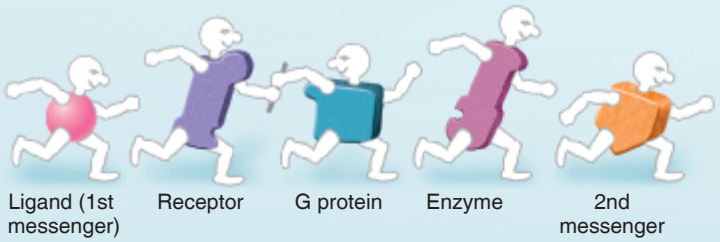
Though cell responses to receptor binding vary widely, there is a fundamental similarity: When a ligand binds to a membrane receptor, the receptor's structure changes, and cell proteins are altered in some way. For example, some membrane proteins respond to ligands by becoming activated enzymes, while others common in muscle and nerve cells respond by transiently opening or closing ion channels, which in turn changes the membrane potential of the cell.

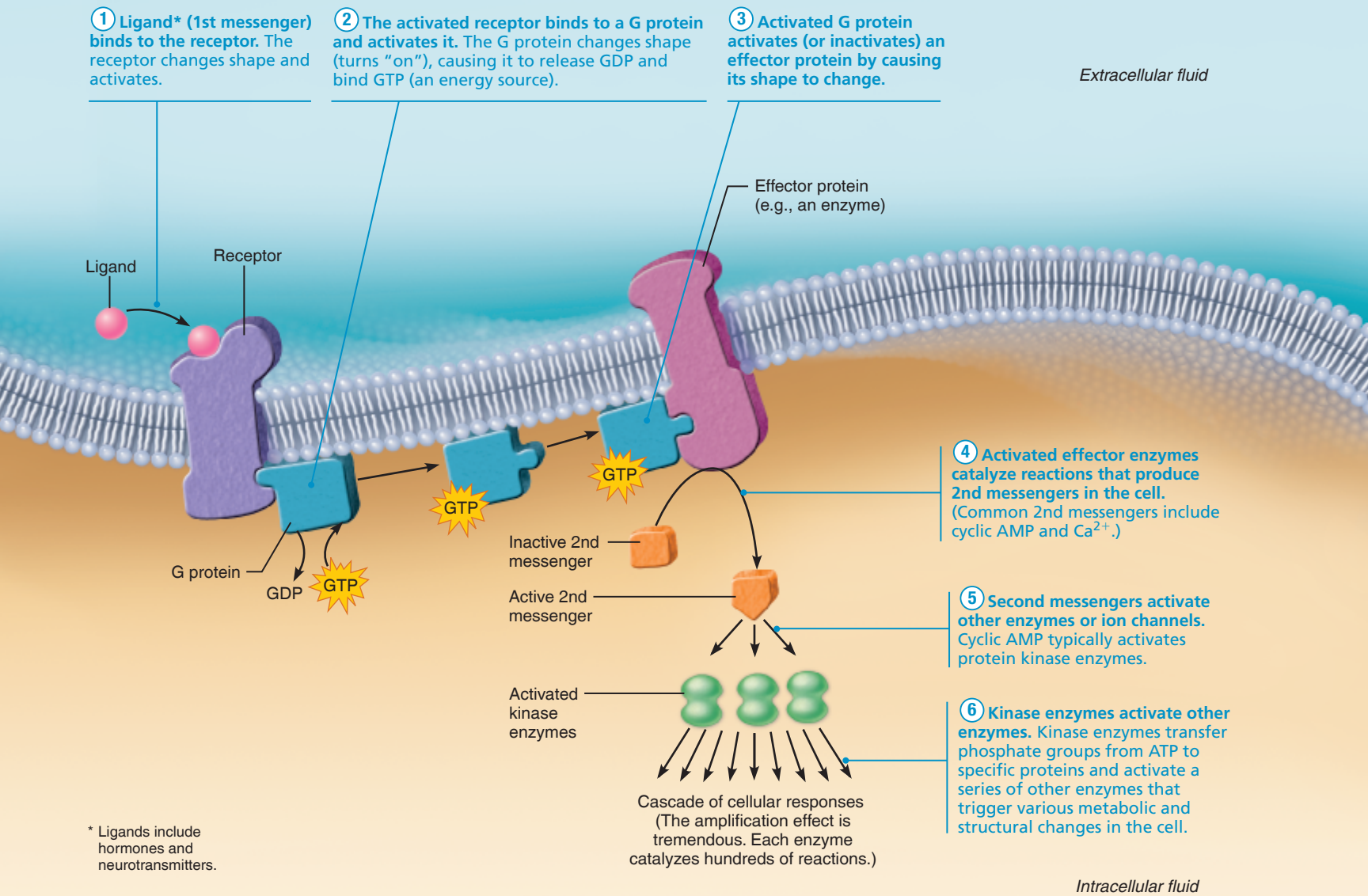
G protein–coupled receptors exert their effect *indirectly* through a **G protein**, a regulatory molecule that acts as a middleman or relay to activate (or inactivate) a membrane-bound enzyme or ion channel. This in turn generates one or more intracellular chemical signals, commonly called **second messengers**, which connect plasma membrane events to the internal metabolic machinery of the cell. Two important second messengers are **cyclic AMP** and ionic calcium, both of which typically activate *protein kinase enzymes*. These enzymes transfer phosphate groups from ATP to other proteins, activating a whole series of enzymes that bring about the desired cellular activity. Because a single enzyme can catalyze hundreds of reactions, the amplification effect of such a chain of events is tremendous, much like a video "going viral." *Focus on G Proteins* (**Focus Figure 3.3**, p. 114) describes a G protein signaling system. Take a moment to study this figure carefully because this key signaling pathway is involved in neurotransmission, smell, vision, and hormone action (Chapters 11, 15, and 16).

G Proteins

G proteins act as middlemen or relays between extracellular first messengers and intracellular second messengers that cause responses within the cell.

The sequence described here is like a molecular relay race. Instead of a baton passed from runner to runner, the message (a shape change) is passed from molecule to molecule as it makes its way across the plasma membrane from outside to inside the cell.





* Ligands include hormones and neurotransmitters.

Check Your Understanding

17. What do you call signaling chemicals that bind to membrane receptors? Which type of membrane receptor is most important in directing intracellular events by promoting formation of second messengers?

For answers, see Answers Appendix.

PART 2
THE CYTOPLASM

Learning Outcome

- **Describe the composition of the cytosol.**

Cytoplasm ("cell-forming material"), the cellular material between the plasma membrane and the nucleus, is the site of most cellular activities. Although early microscopists thought that the cytoplasm was a structureless gel, the electron microscope reveals that it consists of three major elements: the *cytosol*, *organelles*, and *inclusions*.

The **cytosol** (si′to-sol) is the viscous, semitransparent fluid in which the other cytoplasmic elements are suspended. It is a complex mixture with properties of both a colloid and a true solution. Dissolved in the cytosol, which is largely water, are proteins, salts, sugars, and a variety of other solutes.

Inclusions are chemical substances that may or may not be present, depending on cell type. Examples include stored nutrients, such as the glycogen granules in liver and muscle cells; lipid droplets in fat cells; and pigment (melanin) granules in certain skin and hair cells.

The **organelles** are the metabolic machinery of the cell. Each type of organelle carries out a specific function for the cell—some synthesize proteins, others generate ATP, and so on.

3.7 Cytoplasmic organelles each perform a specialized task

Learning Outcomes

- **Discuss the structure and function of mitochondria.**
- **Discuss the structure and function of ribosomes, the endoplasmic reticulum, and the Golgi apparatus, including functional interrelationships among these organelles.**
- **Compare the functions of lysosomes and peroxisomes.**
- **Name and describe the structure and function of cytoskeletal elements.**

The organelles ("little organs") are specialized cellular compartments or structures, each performing its own job to maintain the life of the cell.

Although certain organelles such as ribosomes and centrioles lack a membrane (are nonmembranous), most organelles are bounded by a membrane similar in composition to the plasma membrane. These membranes enable the *membranous organelles* to maintain an internal environment different from that of the surrounding cytosol. This compartmentalization is crucial to cell functioning. Without it, biochemical activity would be chaotic. Now let's consider what goes on in each of the workshops of our cellular factory.

Mitochondria

Mitochondria (mi″to-kon′dre-ah) are typically threadlike (*mitos* = thread) or lozenge-shaped membranous organelles. In living cells they squirm, elongate, and change shape almost continuously. They are the power plants of a cell, providing most of its ATP supply. The density of mitochondria in a particular cell reflects that cell's energy requirements, and mitochondria generally cluster where the action is. Busy cells like kidney and liver cells have hundreds of mitochondria, whereas relatively inactive cells (such as certain lymphocytes) have just a few.

A mitochondrion is enclosed by *two* membranes, each with the general structure of the plasma membrane (**Figure 3.14**). The *outer membrane* is smooth and featureless, but the *inner membrane* folds inward, forming shelflike **cristae** (krĭ′ste; "crests") that protrude into the *matrix*, the gel-like substance

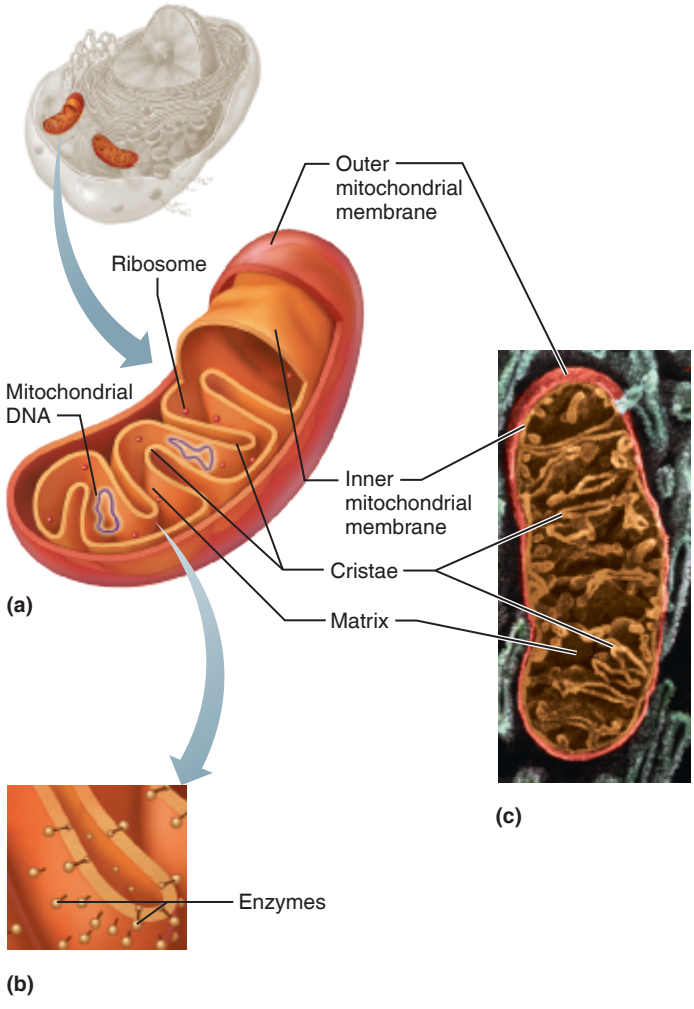


Figure 3.14 Mitochondrion. (a) Diagram of a longitudinally sectioned mitochondrion. **(b)** Close-up of a crista showing enzymes (stalked particles). **(c)** Electron micrograph of a mitochondrion (50,000×).

within the mitochondrion. Teams of enzymes, some dissolved in the mitochondrial matrix and others forming part of the crista membrane, break down intermediate products of food fuels (glucose and others) to water and carbon dioxide.

As the metabolites are broken down and oxidized, some of the energy released is captured and used to attach phosphate groups to ADP molecules to form ATP. This multistep mitochondrial process (described in Chapter 24) is called *aerobic cellular respiration* (a-er-o′bik) because it requires oxygen.

Mitochondria are complex organelles: They contain their own DNA, RNA, and ribosomes and are able to reproduce themselves. Mitochondrial genes (some 37 of them) direct the synthesis of 1% of the proteins required for mitochondrial function, and the DNA of the cell's nucleus encodes the other 99%. When cellular requirements for ATP increase, the mitochondria synthesize more cristae or simply pinch in half (a process called *fission*) to increase their number, then grow to their former size.

Intriguingly, mitochondria are similar to bacteria in the purple bacteria phylum, and mitochondrial DNA is bacteria-like. It is widely believed that mitochondria arose from bacteria that invaded the ancient ancestors of plant and animal cells, and that this unique merger gave rise to all complex cells.

Ribosomes

Ribosomes (ri′bo-sōmz) are small, dark-staining granules composed of proteins and a variety of RNAs called *ribosomal RNAs*. Each ribosome has two globular subunits that fit together like the body and cap of an acorn. Ribosomes are sites of protein synthesis, a function we discuss in detail later in this chapter.

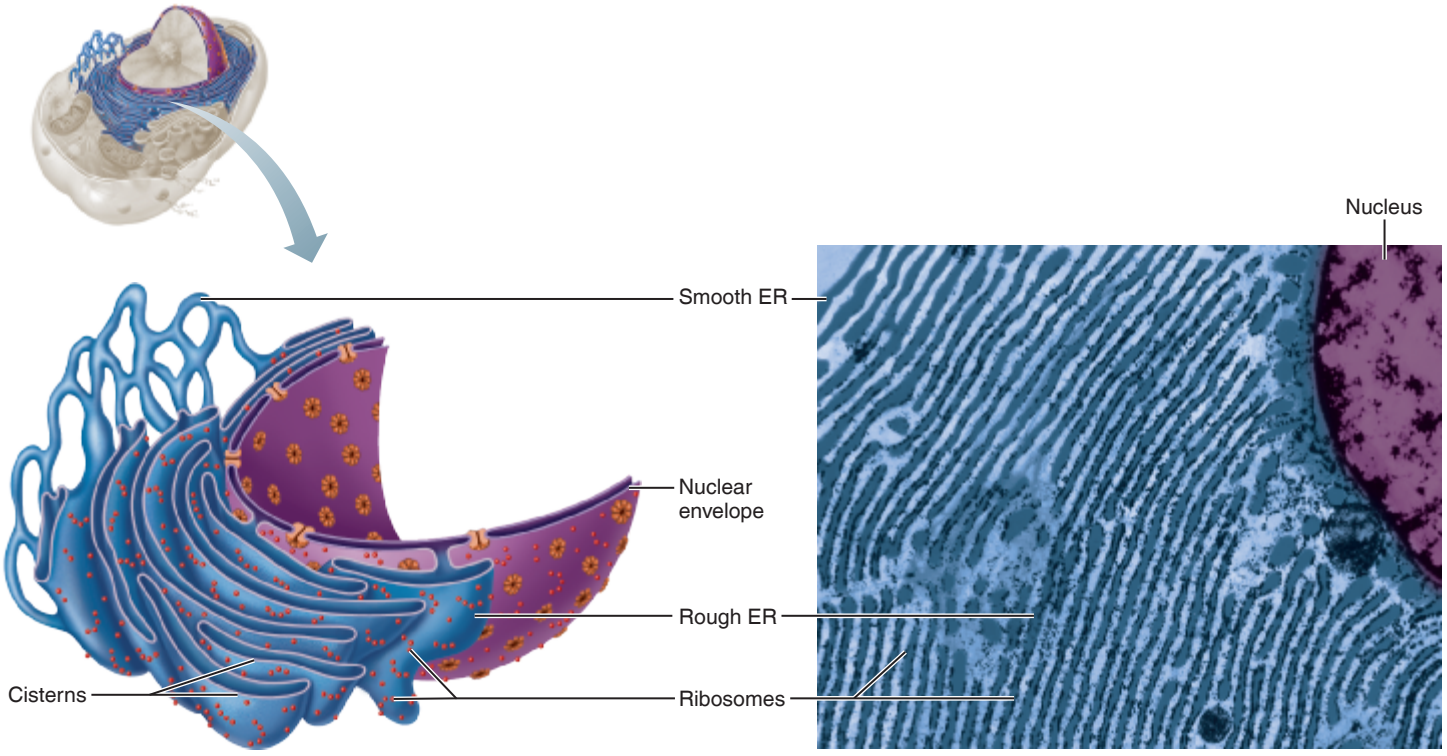
Two ribosomal populations divide the chore of protein synthesis:

- *Free ribosomes* float freely in the cytosol. They make soluble proteins that function in the cytosol, as well as those imported into mitochondria and some other organelles.
- *Membrane-bound ribosomes* are attached to membranes, forming a complex called the *rough endoplasmic reticulum* (**Figure 3.15**). They synthesize proteins destined either for incorporation into cell membranes or lysosomes, or for export from the cell.

Ribosomes can switch back and forth between these two functions, attaching to and detaching from the membranes of the endoplasmic reticulum, according to the type of protein they are making at a given time.

Endoplasmic Reticulum (ER)

The **endoplasmic reticulum (ER)** (en″do-plaz′mik rĕ-tik′u-lum; "network within the cytoplasm") is an extensive system of interconnected tubes and parallel sacs called **cisterns** (sis′ternz) (Figure 3.15). The cavities of cisterns are filled with fluid. Coiling and twisting through the cytosol, the ER is continuous with the outer nuclear membrane and accounts for about half of the cell's membranes. There are two distinct varieties: rough ER and smooth ER.



(a) Diagrammatic view of smooth and rough ER

(b) Electron micrograph of smooth and rough ER (25,000×)

Figure 3.15 The endoplasmic reticulum.

Rough Endoplasmic Reticulum

The external surface of the **rough ER** is studded with ribosomes, which is why it is called "rough" (see Figures 3.2 and 3.15a, b). Proteins assembled on these ribosomes thread their way into the fluid-filled interior of the ER cisterns (as described on p. 137). When complete, the newly made proteins are enclosed in vesicles for their journey to the Golgi apparatus where they undergo further processing.

The rough ER has several functions:

- Its ribosomes manufacture all proteins secreted from cells. For this reason, the rough ER is particularly abundant and well developed in most secretory cells, antibody-producing immune cells, and liver cells, which produce most blood proteins.
- It is also the cell's "membrane factory" where integral proteins and phospholipids that form part of all cellular membranes are manufactured. Within the cisterns, sugar groups are attached to those proteins that will eventually face the extracellular environment. The enzymes that catalyze lipid synthesis have their active sites on the external (cytosolic) face of the ER membrane, where the needed substrates are readily available.

Smooth Endoplasmic Reticulum

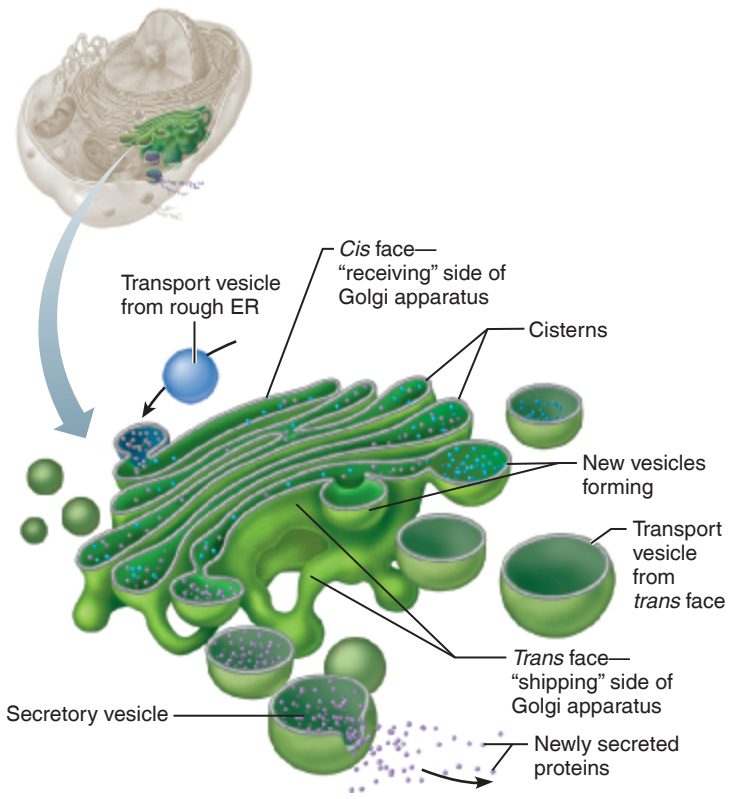
The **smooth ER** (see Figures 3.2 and 3.15) is continuous with the rough ER and consists of tubules arranged in a looping network. Its enzymes (all integral proteins integrated into its membranes) play no role in protein synthesis. Instead, the enzymes catalyze reactions involved with the following tasks:

- Metabolize lipids, synthesize cholesterol and phospholipids, and synthesize the lipid components of lipoproteins (in liver cells)
- Synthesize steroid-based hormones such as sex hormones (for example, testosterone-synthesizing cells of the testes are full of smooth ER)
- Detoxify drugs, certain pesticides, and cancer-causing chemicals (in liver and kidneys)
- Break down stored glycogen to form free glucose (in liver cells especially)
- Store calcium ions in most cell types [skeletal and cardiac muscle cells have an elaborate smooth ER (called the sarcoplasmic reticulum) that stores calcium and releases it as a trigger for contraction]

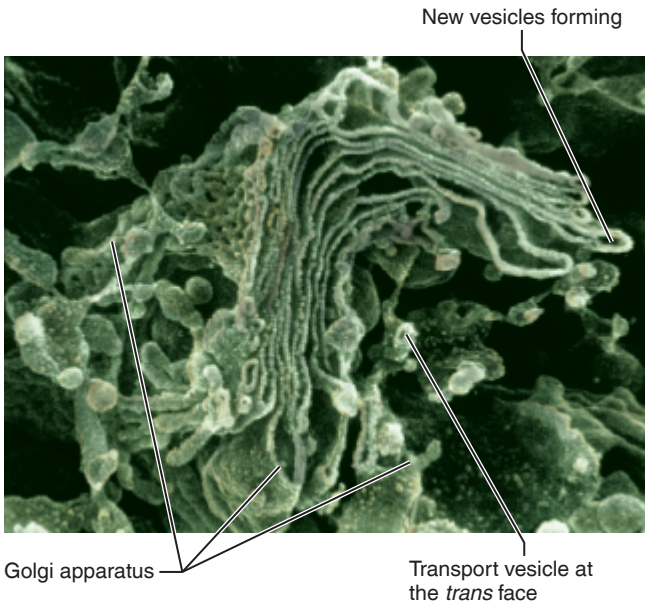
The amount of smooth ER varies widely between different types of cells. As you can see from the list above, it plays a role in diverse cellular processes, depending on the type of cell.

Golgi Apparatus

The **Golgi apparatus** (gol′je) consists of stacked and flattened membranous sacs, shaped like hollow dinner plates, associated with swarms of tiny membranous vesicles (**Figure 3.16**). The



(a) Many vesicles in the process of pinching off from the Golgi apparatus



(b) Electron micrograph of the Golgi apparatus (90,000×)

Figure 3.16 Golgi apparatus.

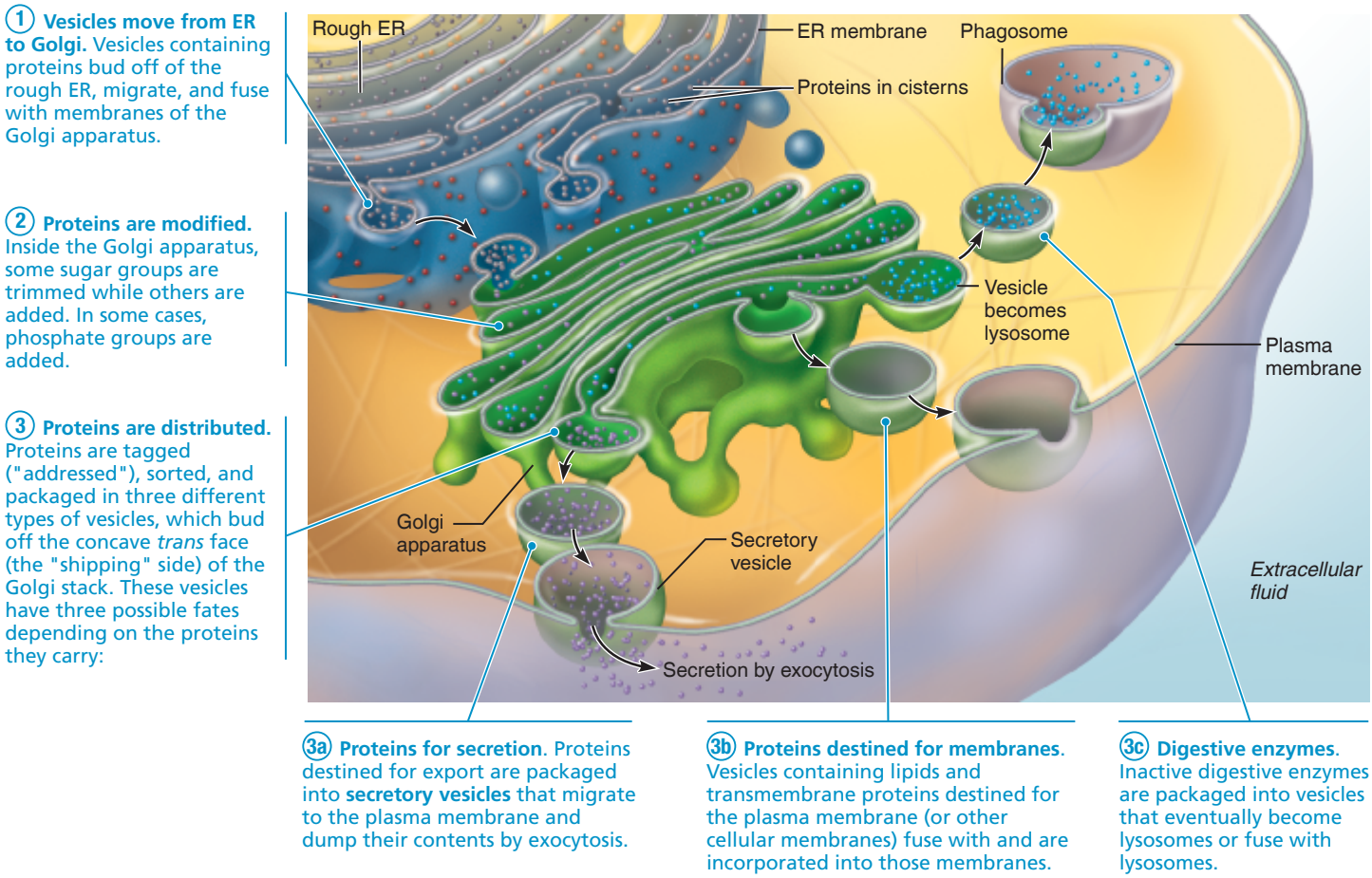


Figure 3.17 Processing and distribution of newly synthesized proteins.

Golgi apparatus is the principal "traffic director" for cellular proteins. Its major function is to modify, concentrate, and package the proteins and lipids made at the rough ER and destined for export from the cell.

This process is shown in **Figure 3.17**.

Peroxisomes

Resembling small lysosomes, **peroxisomes** (pĕ-roks′ĭ-sōmz; "peroxide bodies") are spherical membranous sacs containing a variety of powerful enzymes, the most important of which are oxidases and catalases.

Oxidases use molecular oxygen (O_2) to detoxify harmful substances, including alcohol and formaldehyde. Their most important function is to neutralize **free radicals**, highly reactive chemicals with unpaired electrons that can scramble the structure of biological molecules. Oxidases convert free radicals to hydrogen peroxide, which is also reactive and dangerous but which the catalases quickly convert to water. Free radicals and hydrogen peroxide are normal by-products of cellular metabolism, but they have devastating effects on cells if allowed to accumulate.

Peroxisomes are especially numerous in liver and kidney cells, which are very active in detoxification. They also play a role in energy metabolism by breaking down and synthesizing fatty acids.

Some peroxisomes are formed when existing peroxisomes simply pinch in half. However, most new peroxisomes form by budding off of the endoplasmic reticulum via a special ER machinery that differs from that used for vesicles destined for modification in the Golgi apparatus.

Lysosomes

Lysosomes ("disintegrator bodies") are spherical membranous organelles containing activated hydrolytic (digestive) enzymes (**Figure 3.18**). As you might guess, lysosomes are large and abundant in phagocytes, the cells that dispose of invading bacteria and cell debris. Lysosomal enzymes can digest almost all kinds of biological molecules. They work best in acidic conditions and so are called *acid hydrolases*.

The lysosomal membrane is adapted to serve lysosomal functions in two important ways. First, it contains H^+ (proton) "pumps," which are ATPases that gather hydrogen ions from the surrounding cytosol to maintain the organelle's acidic pH. Second, it retains the dangerous lysosomal enzymes (acid hydrolases) while permitting the final products of digestion to escape so that they can be used by the cell or excreted. In this

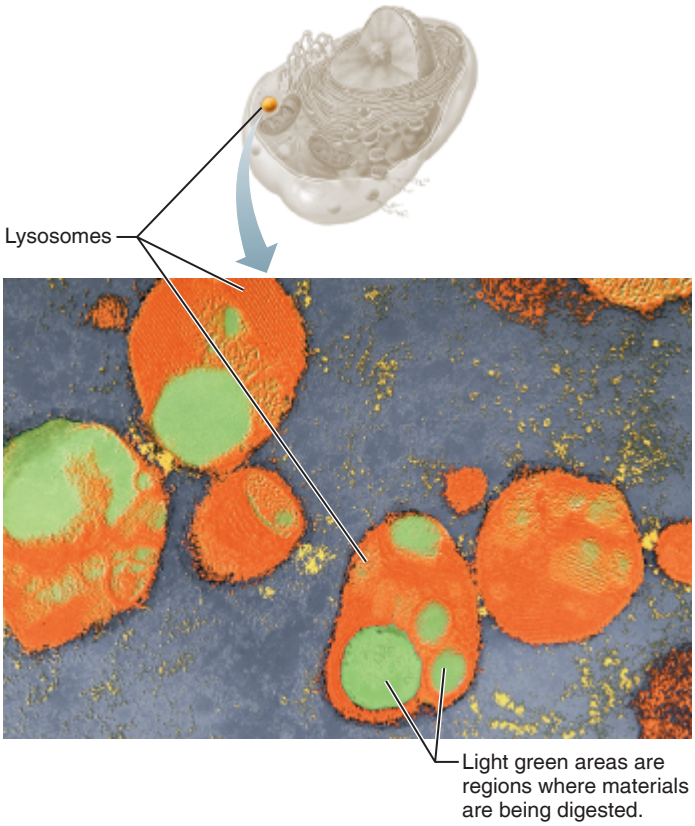


Figure 3.18 Electron micrograph of lysosomes (20,000×).

way, lysosomes provide sites where digestion can proceed *safely* within a cell.

Lysosomes function as a cell's "demolition crew" by:

- Digesting particles taken in by endocytosis, particularly ingested bacteria, viruses, and toxins
- Degrading stressed or dead cells and worn-out or nonfunctional organelles, a process more specifically called autophagy ("self-eating") (discussed further on p. 141)
- Performing metabolic functions, such as glycogen breakdown and release
- Breaking down bone to release calcium ions into the blood

The lysosomal membrane is ordinarily quite stable, but it becomes fragile when the cell is injured or deprived of oxygen and when excessive amounts of vitamin A are present. When lysosomes rupture, the cell digests itself, a process called **autolysis** (aw″tol′ĭ-sis).

HOMEOSTATIC IMBALANCE 3.3 CLINICAL

Lysosomes degrade glycogen and certain lipids in the brain at a relatively constant rate. In *Tay-Sachs disease*, a rare neurodegenerative disorder, the lysosomes lack an enzyme needed to break down a specific glycolipid in nerve cell membranes. These lysosomes swell with undigested lipids, interfering with nervous system functioning. Children with the disease begin to lose developmental milestones at 3 to 6 months. One physical finding is a "cherry red spot" on the macula of the retina at the back of the eye. No cure currently exists, and the disease progresses to blindness, deafness, seizures, and paralysis. Most children with Tay-Sachs die by age 5.

The Endomembrane System

The **endomembrane system** is a system of organelles (most described above) that work together mainly to (1) produce, degrade, store, and export biological molecules, and (2) degrade potentially harmful substances. It includes the ER, Golgi apparatus, secretory vesicles, and lysosomes, as well as the nuclear envelope—that is, all of the membranous elements that are either structurally connected or arise via forming or fusing transport vesicles (**Figure 3.19**). The nuclear envelope is directly connected to the rough and smooth ER (see Figure 3.15). The plasma membrane, though not actually an *endo*-membrane, is also functionally part of this system.

Besides these direct structural relationships, a wide variety of indirect interactions (indicated by arrows in Figure 3.19) occur among the members of the system. Some of the vesicles "born" in the ER migrate to and fuse with the Golgi apparatus or the plasma membrane, and vesicles arising from the Golgi apparatus can become part of the plasma membrane or lysosomes.

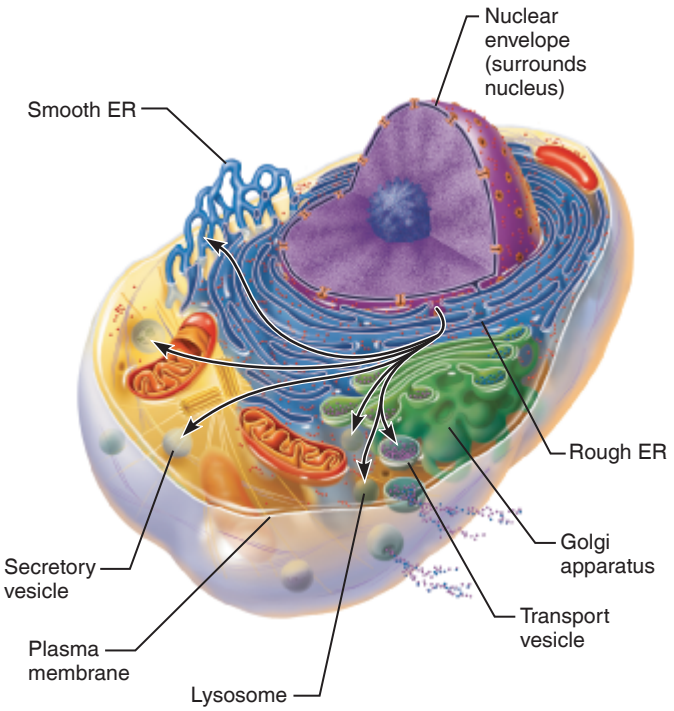


Figure 3.19 The endomembrane system.

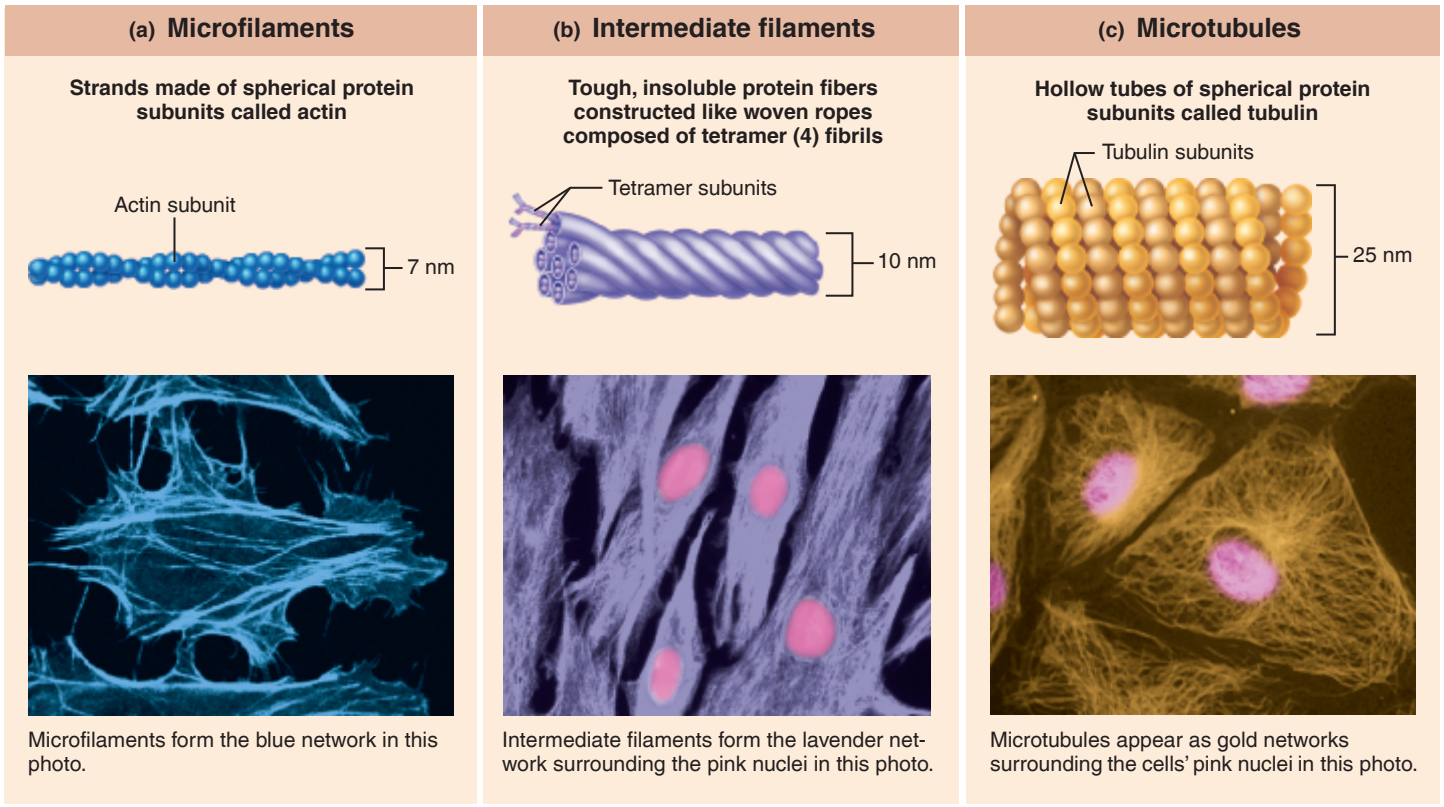


Figure 3.20 Cytoskeletal elements support the cell and help to generate movement.
The photos (bottom) are of fibroblasts treated with fluorescent tags for the structure of interest.

Cytoskeleton

The **cytoskeleton**, literally, "cell skeleton," is an elaborate network of rods running through the cytosol and hundreds of accessory proteins that link these rods to other cell structures. It acts as a cell's "bones," "muscles," and "ligaments" by supporting cellular structures and providing the machinery to generate various cell movements. The three types of rods in the cytoskeleton are *microfilaments*, *intermediate filaments*, and *microtubules*. None of these is membrane covered.

Microfilaments

The thinnest elements of the cytoskeleton, **microfilaments** (mi″kro-fil′ah-ments), are semiflexible strands of the protein *actin* ("ray") (**Figure 3.20a**). Most microfilaments are involved in cell motility (movement) or changes in cell shape. Except in muscle cells, where they are especially abundant and stable, actin filaments are constantly breaking down and re-forming from smaller subunits whenever and wherever their services are needed. As they break down and re-form, actin filaments push or pull on the plasma membrane, changing the cell's shape. You could say that cells move "when they get their act(in) together." For example:

- Actin forms the cleavage furrow that pinches one cell into two during cell division.
- Microfilaments attached to cell adhesion molecules (see Figure 3.3e, f) are responsible for the crawling movements of amoeboid motion, and for membrane changes that accompany endocytosis and exocytosis.
- In muscle cells, actin filaments interact with another protein, *myosin* (mi′o-sin), to generate contractile forces in a cell.

In nonmoving cells, actin filaments also help maintain cell shape and distribute tension throughout the cell.

Intermediate Filaments

Intermediate filaments are tough, insoluble protein fibers that resemble woven ropes. Made of twisted units of *tetramer* (4) *fibrils*, they have a diameter between those of microfilaments and microtubules (Figure 3.20b). Intermediate filaments are the most stable and permanent of the cytoskeletal elements and strongly resist tension. They attach to desmosomes, and their main job is to act as internal cables to resist pulling forces exerted on the cell. Because their protein composition varies in different cell types, there are numerous names for these cytoskeletal elements—for example, they are called neurofilaments in nerve cells and keratin filaments in epithelial cells.

Microtubules

The elements with the largest diameter, **microtubules** (mi″kro-tu′būlz), are hollow tubes made of spherical protein subunits called *tubulin* (Figure 3.20c). Most microtubules radiate from a small region of cytoplasm near the nucleus called the *centrosome* or *cell center* (see Figure 3.2 on p. 94).

Microtubules are remarkably dynamic organelles, constantly growing out from the centrosome, disassembling, and then reassembling at the same or different sites. The microtubules determine the overall shape of the cell, as well as the distribution of cellular organelles.

Mitochondria, lysosomes, and secretory vesicles attach to the microtubules like ornaments hanging from tree branches. Tiny protein machines called **motor proteins** (*kinesins*, *dyneins*, and others) continually move and reposition the organelles along the microtubules.

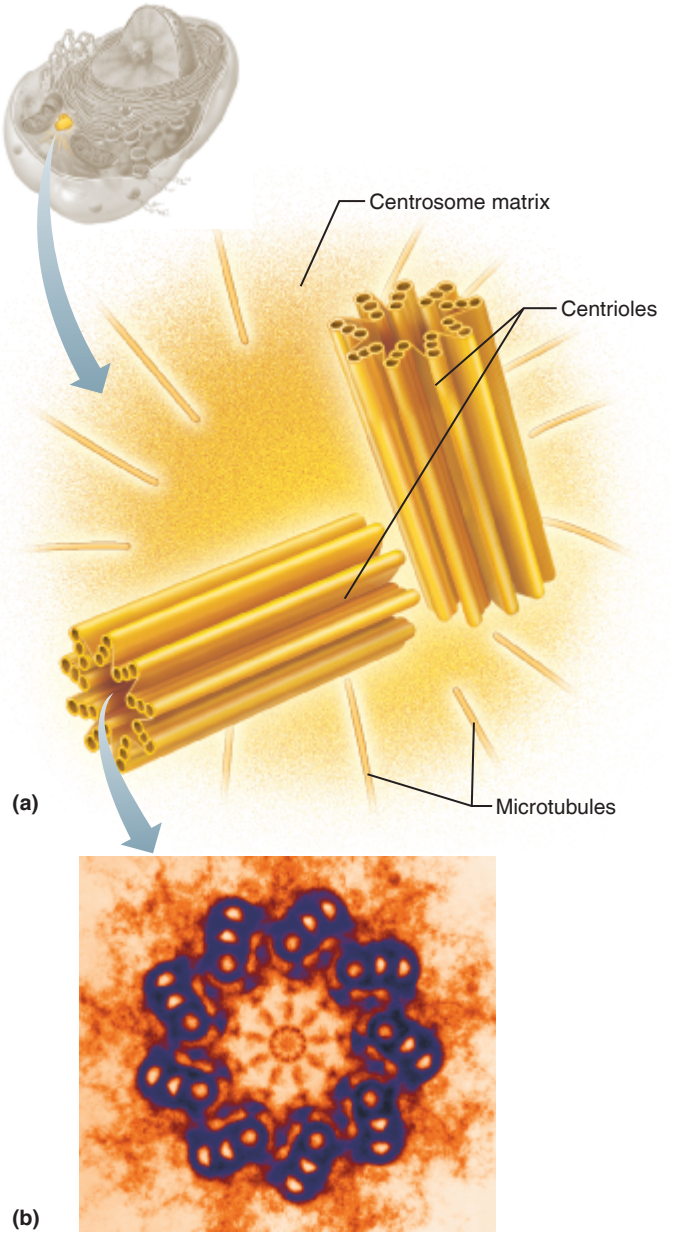


Figure 3.21 Centrioles. (a) Three-dimensional view of a centriole pair oriented at right angles, as they are usually seen in the cell. **(b)** An electron micrograph showing a cross section of a centriole (190,000×). Notice that it is composed of nine microtubule triplets.

Powered by ATP, motor proteins act like train engines moving substances along on the microtubular "railroad tracks." They move "hand over hand" somewhat like an orangutan—gripping, releasing, and then gripping again at a new site further along the microtubule.

Centrosome and Centrioles

As mentioned, microtubules are anchored at one end in an inconspicuous region near the nucleus called the **centrosome** or *cell center*. The centrosome acts as a *microtubule organizing center*. It has few distinguishing marks other than a granular-looking *matrix* that contains paired **centrioles**, small, barrel-shaped organelles oriented at right angles to each other (**Figure 3.21**). The centrosome matrix is best known for generating microtubules and organizing the mitotic spindle in cell division (see *Focus on Mitosis*, Focus Figure 3.4 on pp. 132–133). Each centriole consists of a pinwheel array of nine *triplets* of microtubules, each connected to the next by nontubulin proteins and arranged to form a hollow tube. Centrioles also form the bases of cilia and flagella, our next topics.

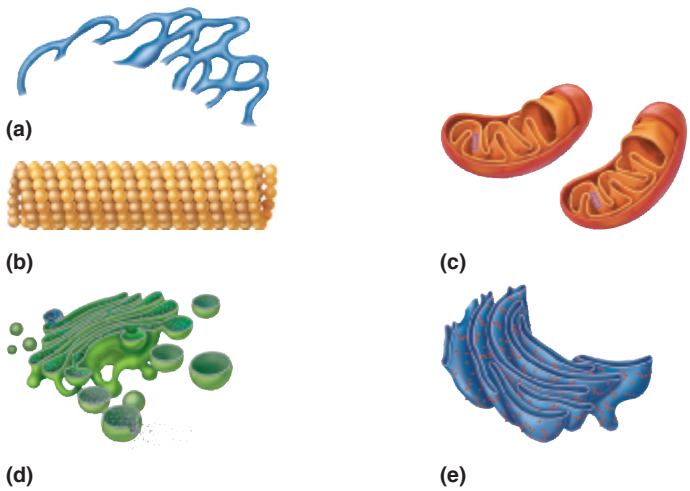
Check Your Understanding

18. Compare the functions of lysosomes and peroxisomes.

19. How are microtubules and microfilaments related functionally?

20. Name each of the organelles below. Match the organelle(s) with the applicable statement(s). Answers may be used more than once.

__ (1) Moves organelles within cell using motor proteins
__ (2) Contains its own DNA
__, __, __ (3) Has cisterns
__ (4) Major site of ATP synthesis
__ (5) Site of steroid hormone synthesis
__ (6) Has *cis* and *trans* faces



21. APPLY Consider a plasma membrane glycoprotein. Describe the protein's path through the cell to the plasma membrane starting with its synthesis on the ribosome.

For answers, see Answers Appendix.

3.8 Cilia and microvilli are two main types of cellular extensions

Learning Outcomes

- **Describe the role of centrioles in the formation of cilia and flagella.**
- **Describe how the two main types of cell extensions, cilia and microvilli, differ in structure and function.**

3

Cilia and Flagella

Cilia (sil′e-ah; "eyelashes") are whiplike, motile cellular extensions (**Figure 3.22**) that occur, typically in large numbers, on the exposed surfaces of certain cells. Ciliary action moves substances in one direction across cell surfaces. For example, ciliated cells that line the respiratory tract propel mucus laden with dust particles and bacteria upward away from the lungs.

When a cell is about to form cilia, the centrioles multiply and line up beneath the plasma membrane at the cell's free (exposed) surface. Microtubules then "sprout" from each centriole, forming the ciliary projections by exerting pressure on the plasma membrane.

Flagella (flah-jel′ah) are also projections formed by centrioles, but are substantially longer than cilia. The only flagellated cell in the human body is a sperm, which has one propulsive flagellum, commonly called a tail. Notice that cilia *propel other substances* across a cell's surface, whereas a flagellum *propels the cell itself.*

Centrioles forming the bases of cilia and flagella are referred to as **basal bodies** (ba′sal) (Figure 3.22). The "9 + 2" pattern of microtubules in the cilium or flagellum itself (nine *doublets*, or pairs, of microtubules encircling one central pair) differs slightly from that of a centriole (nine microtubule *triplets*). Additionally, the cilium has flexible "wagon wheels" of cross-linking proteins (purple in Figure 3.22).

Extending from the microtubule doublets are arms composed of the motor protein dynein (green dynein arms in Figure 3.22). The dynein arms produce the movement of the cilium or flagellum. Arms of one doublet grip the adjacent doublet and, powered by ATP, push it up, release, and then grip again. Because the doublets are physically restricted by other proteins, they are forced to bend. The collective bending action of all the doublets causes the cilium to bend.

As a cilium moves, it alternates rhythmically between a propulsive *power stroke*, when it is nearly straight and moves in an arc, and a *recovery stroke*, when it bends and returns to its initial position (**Figure 3.23a**). With these two strokes, the cilium

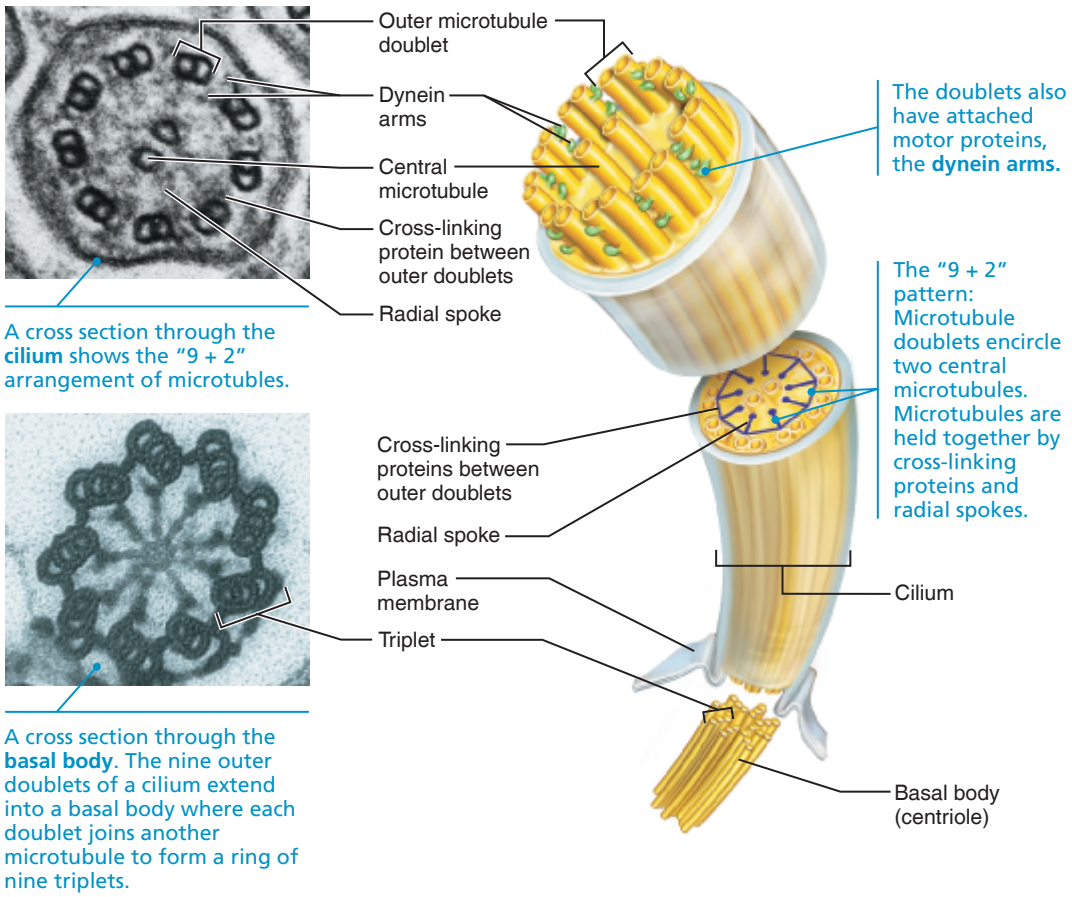
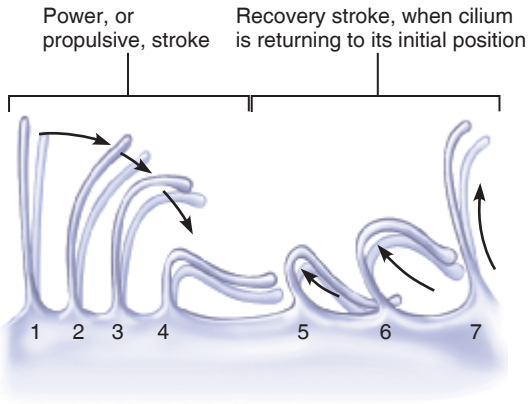
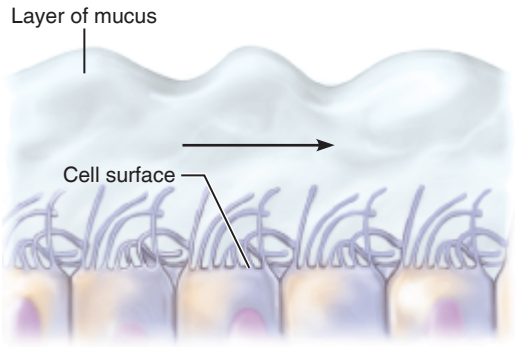


Figure 3.22 **Structure of a cilium.**



(a) Phases of ciliary motion.



(b) Traveling wave created by the activity of many cilia acting together propels mucus across cell surfaces.

Figure 3.23 Ciliary function.

produces a pushing motion in a single direction that repeats some 10 to 20 times per second. The bending of one cilium is quickly followed by the bending of the next and then the next, creating a current at the cell surface that resembles the traveling waves that pass across a field of grass on a windy day (Figure 3.23b).

Microvilli

Microvilli (mi″kro-vil′i; "little shaggy hairs") are tiny, finger-like extensions of the plasma membrane that project from an exposed cell surface (Figure 3.4 top and **Figure 3.24**). They increase the plasma membrane surface area tremendously and are most often found on the surface of absorptive cells such as intestinal and kidney tubule cells. Microvilli have a core of bundled actin filaments that extend into a mat of actin filaments, called the *terminal web*, near the surface of the cell. (Actin is often a contractile protein, but in microvilli and the terminal web it acts as a mechanical "stiffener" that shapes the cell.)

Check Your Understanding

22. The major function of cilia is to move substances across the free cell surface. What is the major role of microvilli?

For answers, see Answers Appendix.

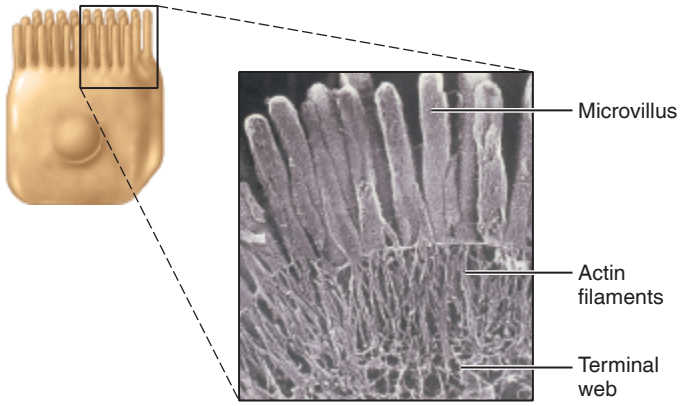


Figure 3.24 Microvilli.

Practice Histology questions: Mastering A&P® > Study Area > Lab Tools > PAL

3

PART 3 NUCLEUS

Anything that works, works best when it is controlled. For cells, the control center is the gene-containing **nucleus** (*nucle* = pit, kernel). The nucleus can be compared to a computer, design department, construction boss, and board of directors—all rolled into one. As the genetic library, it contains the instructions needed to build nearly all the body's proteins. Additionally, it dictates the kinds and amounts of proteins to be synthesized at any one time in response to signals acting on the cell.

Most cells have only one nucleus, but some, including skeletal muscle cells, bone destruction cells, and some liver cells, are **multinucleate** (mul″tĭ-nu′kle-āt), that is, they have many nuclei. The presence of more than one nucleus usually signifies that a larger-than-usual cytoplasmic mass must be regulated.

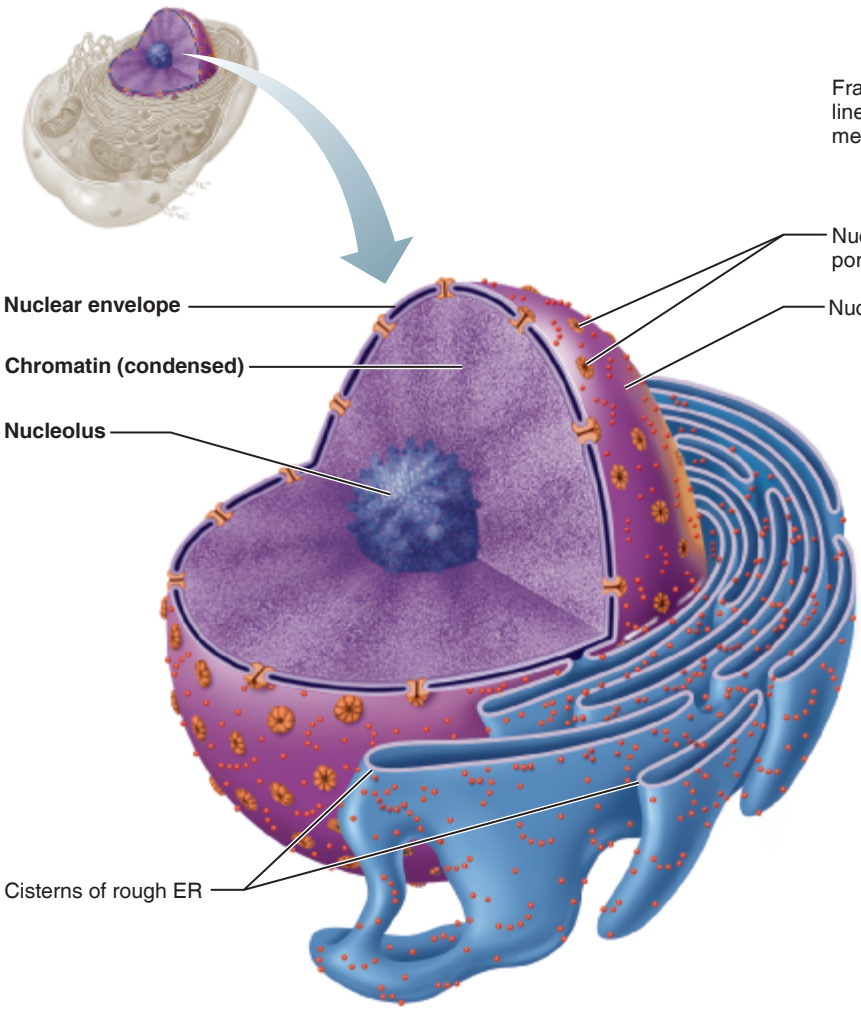
Except for mature red blood cells, whose nuclei are ejected before the cells enter the bloodstream, all of our body cells have nuclei. **Anucleate** (a-nu′kle-āt; *a* = without) cells cannot reproduce and therefore live in the bloodstream for only three to four months before they deteriorate. Without a nucleus, a cell cannot produce mRNA to make proteins, and when its enzymes and cell structures start to break down (as all eventually do), they cannot be replaced.

3.9 The nucleus includes the nuclear envelope, the nucleolus, and chromatin

Learning Outcome

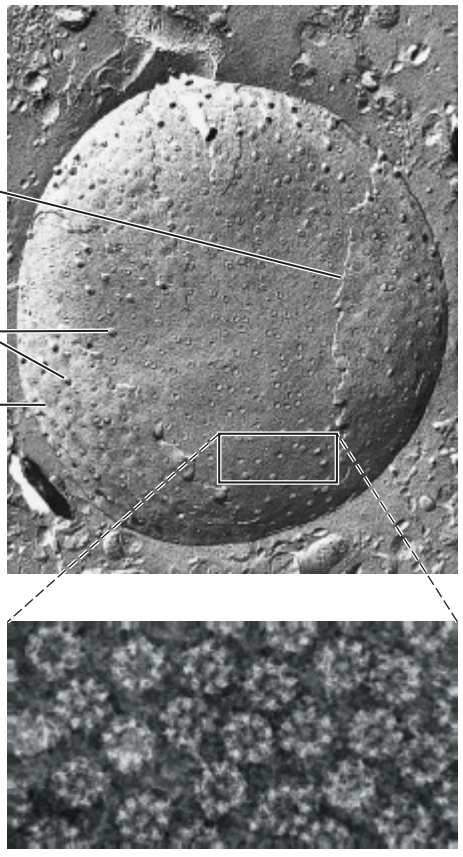
▶ **Outline the structure and function of the nuclear envelope, nucleolus, and chromatin.**

The nucleus, averaging 5 μm in diameter, is larger than any of the cytoplasmic organelles. Although most often spherical or oval, its shape usually conforms to the shape of the cell. The

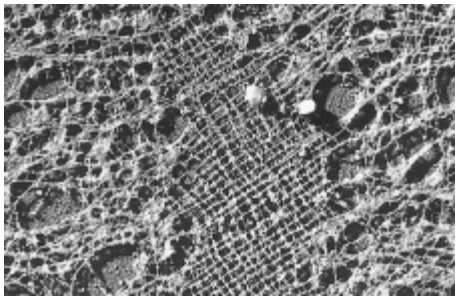


(a)

Surface of nuclear envelope.



Nuclear pore complexes. Each pore is ringed by protein particles.



Nuclear lamina. The netlike lamina composed of intermediate filaments formed by lamins lines the inner surface of the nuclear envelope.

(b)

Figure 3.25 The nucleus. (a) Three-dimensional diagram of the nucleus, showing the continuity of its double membrane with the ER. **(b)** Freeze-fracture transmission electron micrographs (TEMs).

nucleus has three recognizable regions or structures: the *nuclear envelope* (*membrane*), *nucleoli*, and *chromatin* (**Figure 3.25a**).

The Nuclear Envelope

The nucleus is bounded by the **nuclear envelope**, a *double* membrane barrier separated by a fluid-filled space (like the mitochondrial membrane). The outer nuclear membrane is continuous with the rough ER of the cytoplasm and is studded with ribosomes on its external face. The inner nuclear membrane is lined by the *nuclear lamina*, a network of *lamins* (rod-shaped proteins that assemble to form intermediate filaments) that maintains the shape of the nucleus and acts as a scaffold to organize DNA in the nucleus (Figure 3.25b, bottom).

At various points, the nuclear envelope is punctured by **nuclear pores**. An intricate complex of proteins, called a *nuclear pore complex*, lines each pore, forming an aqueous transport channel and regulating entry and exit of molecules (e.g., mRNAs) and large particles into and out of the nucleus (Figure 3.25b, middle).

Like other cell membranes, the nuclear envelope is selectively permeable, but here substances pass much more freely than elsewhere. Small molecules pass through the relatively large nuclear pore complexes unhindered. Protein molecules imported from the cytoplasm and RNA molecules exported from the nucleus move through the central channel of the pores. This process is energy dependent and guided by soluble transport proteins.

The nuclear envelope encloses a jellylike fluid called *nucleoplasm* (nu′kle-o-plazm) in which other nuclear elements are

suspended. Like the cytosol, the nucleoplasm contains dissolved salts, nutrients, and other essential solutes.

Nucleoli

Within the nucleus are **nucleoli** (nu-kle′o-li; "little nuclei"), dark-staining spherical bodies where the ribosomal subunits are assembled. Nucleoli are not membrane bounded. Typically, there are one or two per nucleus, but there may be more. Nucleoli are usually largest in growing cells that are making large amounts of tissue proteins.

Nucleoli are aggregations of all of the components needed to synthesize and assemble ribosomal subunits. They center around the DNA that codes for ribosomal RNA (rRNA). As rRNA molecules are synthesized, they combine with proteins to form the two kinds of ribosomal subunits. (The proteins are manufactured on ribosomes in the cytoplasm and imported into the nucleus.) The finished subunits leave the nucleus through the nuclear pores and enter the cytoplasm, where they join to form functional ribosomes.

Chromatin

Seen through a light microscope, **chromatin** (kro′mah-tin) appears as a fine, unevenly stained network, but special techniques reveal it as a system of bumpy threads weaving through the nucleoplasm. Chromatin is composed of approximately:

- 30% **DNA**, our genetic material
- 60% globular **histone proteins** (his′tōn), which package and regulate the DNA
- 10% RNA chains, newly formed or forming

The fundamental units of chromatin are **nucleosomes** (nu′kle-o-sōmz; "nuclear bodies"), which consist of flattened disc-shaped cores or clusters of eight histone proteins connected like beads on a string by a DNA molecule. The DNA winds (like a ribbon of Velcro®) twice around each nucleosome and continues on to the next cluster via *linker* DNA segments (**Figure 3.26** ① and ②).

Histones provide a physical means for packing the very long DNA molecules (some 2 meters' worth per cell) in a compact, orderly way, but they also play an important role in gene regulation. In a nondividing cell, for example, the presence of methyl groups on histone proteins shuts down the nearby DNA. As another example, addition of acetyl groups to histone exposes different DNA segments, or genes, so that they can dictate the specifications for synthesizing proteins or various RNA species. Such active chromatin segments, referred to as *extended chromatin*, are not usually visible under the light microscope. The generally inactive *condensed chromatin* segments are darker staining and more easily detected. Understandably, the most active body cells have much larger amounts of extended chromatin.

When a cell is preparing to divide, the chromatin threads coil and condense enormously to form short, barlike bodies called **chromosomes** ("colored bodies") (Figure 3.26 ④ and ⑤). Chromosome compactness prevents the delicate chromatin strands from tangling and breaking during the movements that occur during cell division. Next, we describe the events of cell division and the functions of DNA.

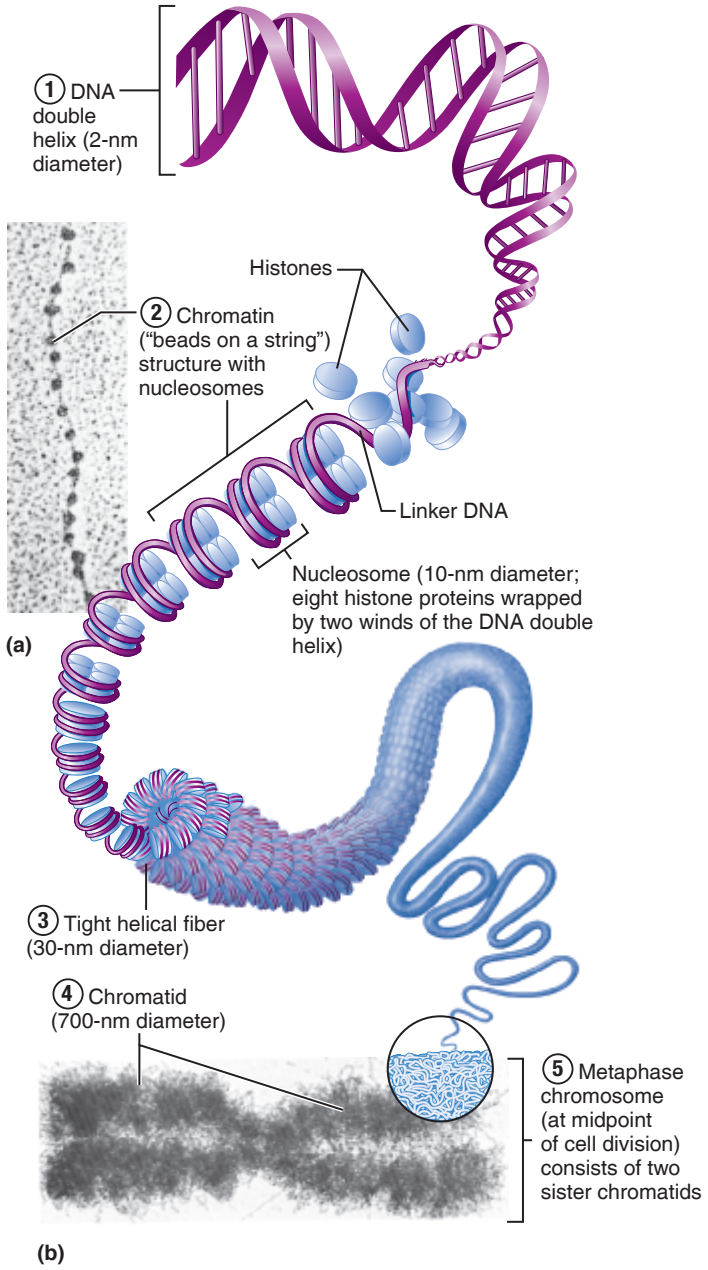


Figure 3.26 Chromatin and chromosome structure. **(a)** Electron micrograph of chromatin fiber (125,000×). **(b)** DNA packed in a chromosome. The levels of increasing structural complexity (coiling) are shown in order from the smallest (①–⑤).

Table 3.4 beginning on p. 126 summarizes the parts of the cell.

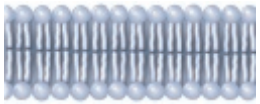
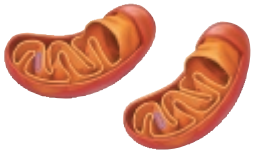
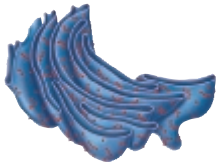
Check Your Understanding

23. If a cell ejects or loses its nucleus, what is its fate and why?
24. What is the role of nucleoli?
25. What is the importance of the histone proteins present in the nucleus?

For answers, see Answers Appendix.

(Text continues on p. 128.)

Table 3.4 Parts of the Cell: Structure and Function

CELL PART*	STRUCTURE	FUNCTIONS
Plasma Membrane (Focus Figure 3.1)		
	Membrane made of a double layer of phospholipids within which cholesterol and proteins are embedded. Proteins may extend entirely through the lipid bilayer or protrude on only one face. Most externally facing proteins and some lipids have attached sugar groups.	Serves as an external cell barrier. Transmembrane proteins act as receptors for chemical messengers (e.g., hormones, neurotransmitters), as transport proteins, and in cell-to-cell recognition. Maintains a resting potential that is essential for functioning of excitable cells.
Cytoplasm		
	Cellular region between the nuclear and plasma membranes. Consists of fluid **cytosol** containing dissolved solutes, **organelles** (the metabolic machinery of the cytoplasm), and **inclusions** (stored nutrients, secretory products, pigment granules).	
Organelles		
• Mitochondria (Figure 3.14) 	Rodlike, double-membrane structures; inner membrane folded into projections called cristae.	Site of ATP synthesis; powerhouse of the cell.
• Ribosomes (Figures 3.32, 3.33, Focus Figure 3.5) 	Dense particles consisting of two subunits, each composed of ribosomal RNA and protein. Free or attached to rough endoplasmic reticulum.	The sites of protein synthesis.
• Rough endoplasmic reticulum (Figures 3.15, 3.33) 	Membranous system enclosing a cavity, the cistern, and coiling through the cytoplasm. Externally studded with ribosomes.	Sugar groups are attached to proteins within the cisterns. Proteins are bound in vesicles for transport to the Golgi apparatus and other sites. External face synthesizes phospholipids.
• Smooth endoplasmic reticulum (Figure 3.15) 	Membranous system of sacs and tubules; free of ribosomes.	Site of lipid and steroid (cholesterol) synthesis, lipid metabolism, drug detoxification, and Ca^{2+} storage.
• Golgi apparatus (Figures 3.16, 3.17) 	A stack of flattened membranes and associated vesicles close to the nucleus.	Packages, modifies, and segregates proteins for secretion from the cell, inclusion in lysosomes, and incorporation into the plasma membrane. Modifies carbohydrates on proteins.
• Peroxisomes (Figure 3.2) 	Membranous sacs containing catalase and oxidase enzymes.	The enzymes detoxify a number of toxic substances. The most important enzyme, catalase, breaks down hydrogen peroxide.

*Individual cellular structures are not drawn to scale.

Table 3.4 *(continued)*

CELL PART*	STRUCTURE	FUNCTIONS
Cytoplasm		
• Lysosomes (Figure 3.18) 	Membranous sacs containing acid hydrolases.	Sites of intracellular digestion.
• Microtubules (Figures 3.20–3.22) 	Cylindrical structures made of tubulin proteins.	Support the cell and give it shape. Involved in intracellular and cellular movements. Form centrioles and cilia and flagella, if present.
• Intermediate filaments (Figure 3.20) 	Protein fibers; composition varies.	The stable cytoskeletal elements; resist mechanical forces acting on the cell.
• Microfilaments (Figure 3.20) 	Fine filaments composed of the protein actin.	Involved in muscle contraction and other types of intracellular movement; help form the cell's cytoskeleton.
• Centrioles (Figure 3.21) 	Paired cylindrical bodies, each composed of nine triplets of microtubules.	As part of the centrosome, organize the microtubule network. During mitosis (cell division), form the spindle and asters. As basal bodies, form the bases of cilia and flagella.
Inclusions	Varied; includes stored nutrients such as lipid droplets and glycogen granules, protein crystals, pigment granules.	Storage for nutrients, wastes, and cell products.
Cellular Extensions		
• Cilia (Figures 3.22, 3.23) 	Short cell-surface projections; each cilium contains nine pairs of microtubules surrounding a central pair.	Coordinated movement creates a unidirectional current that propels substances across cell surfaces.
• Flagellum 	Like a cilium, but longer; only example in humans is the sperm tail.	Propels the cell.
• Microvilli (Figure 3.24) 	Tubular extensions of the plasma membrane; contain a bundle of actin filaments.	Increase surface area for absorption.
Nucleus (Figures 3.2, 3.25)		
	Largest organelle. Surrounded by the nuclear envelope; contains fluid nucleoplasm, nucleoli, and chromatin.	Control center of the cell; responsible for transmitting genetic information and providing the instructions for protein synthesis.

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