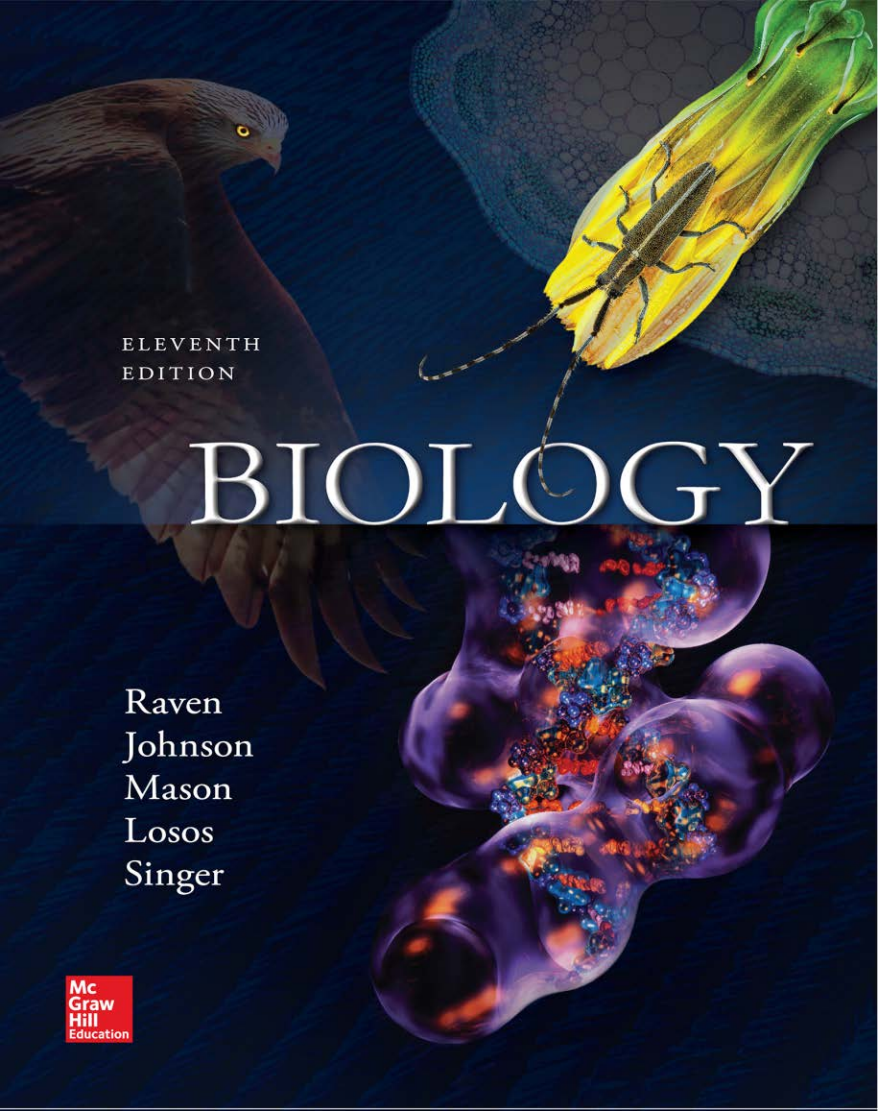
ELEVENTH
EDITION
BIOLOGY
Raven
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Education

Eleventh Edition

Biology

Kenneth A. Mason

University of Iowa

Jonathan B. Losos

Harvard University

Susan R. Singer

Carleton College

Contributors:

Shelley Jansky

University of Wisconsin – Madison

Tod Duncan

University of Colorado Denver

Based on the work of

Peter H. Raven

President Emeritus, Missouri Botanical Garden; George Engelmann Professor of Botany Emeritus, Washington University

George B. Johnson

Professor Emeritus of Biology, Washington University

Mc Graw Hill Education

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Brief Contents

About the Authors

Pictured left to right: Susan Rundell Singer, Jonathan Losos, Kenneth Mason

Kenneth Mason is currently associated with the University of Iowa, Department of Biology. His academic positions, as a teacher and researcher, include the faculty of the University of Kansas, where he designed and established the genetics lab, and taught and published on the genetics of pigmentation in amphibians. At Purdue University, he successfully developed and grew large introductory biology courses and collaborated with other faculty in an innovative biology, chemistry, and physics course supported by the National Science Foundation. At the University of Iowa, where his wife served as president of the university, he taught introductory biology and human genetics for eight years. His honor society memberships include Phi Sigma, Alpha Lambda Delta, and, by vote of Purdue pharmacy students, Phi Eta Sigma Freshman Honors Society.

Jonathan Losos is the Monique and Philip Lehner Professor for the Study of Latin America in the Department of Organismic and Evolutionary Biology and curator of herpetology at the Museum of Comparative Zoology at Harvard University. Losos's research has focused on studying patterns of adaptive radiation and evolutionary diversification in lizards. He is the recipient of several awards, including the prestigious Theodosius Dobzhanksy and David Starr Jordan Prizes, the Edward Osborne Wilson Naturalist Award, and the Daniel Giraud Elliot Medal from the National Academy of Sciences. Losos has published more than 150 scientific articles.

Susan Rundell Singer is the Laurence McKinley Gould Professor of Natural Sciences in the Department of Biology at Carleton College in Northfield, Minnesota, where she has taught introductory biology, plant biology, genetics, and plant development for nearly 30 years. Her research focuses on the development and evolution of flowering plants and genomics learning. Singer has authored numerous scientific publications on plant development and coauthored education reports including *Vision and Change* and "America's Lab Report." A fellow of the American Association for the Advancement of Science (AAAS), she has received the American Society of Plant Biology's Excellence in Teaching Award and the Botanical Society's Bessey Award, served on the National Academies Board on Science Education, and chaired several National Research Council study committees including the committee that produced *Discipline-Based Education Research*.

Lead Digital Author

Ian Quitadamo is a Professor with a dual appointment in Biological Sciences and Science Education at Central Washington University in Ellensburg, WA. He teaches introductory and majors biology courses and cell biology, genetics, and biotechnology as well as science teaching methods courses for future science teachers and interdisciplinary content courses in alternative energy and sustainability. Dr. Quitadamo was educated at Washington State University and holds a bachelor's degree in biology, master's degree in genetics and cell biology, and an interdisciplinary Ph.D. in science, education, and technology. Previously a researcher of tumor angiogenesis, he now investigates the behavioral and neurocognitive basis of critical thinking and has published numerous studies of factors that improve student critical-thinking performance. He has received the Crystal Apple award for teaching excellence and led multiple initiatives in critical thinking and assessment. He is active nationally in helping transform university faculty practices. He is a coauthor of *Biology*, 11th ed., by Mader and Windelspecht (2013), and is the lead digital author for *Biology*, 3rd and 4th ed., by Brooker (2014 and 2017), *Biology*, 10th ed., by Raven (2014), *Understanding Biology* by Mason (2015), and *Principles of Biology* by Brooker (2015), all published by McGraw-Hill. For fun, Dr. Quitadamo practices Kyokushin full contact karate and is a 5th degree blackbelt.

Committed to Excellence

With the new 11th edition, Raven and Johnson's *Biology* continues the momentum built over the last three editions. This edition provides an unmatched comprehensive text fully integrated with a continually evolving, state-of-the-art digital environment. We have used this digital environment in the revision of *Biology*. The McGraw-Hill SmartBook© for the 10th edition provided data on student responses, and thus identify material that students find difficult. This "heat-mapping" technology is unique in the industry, and allows us to direct editing to difficult areas, or problem areas for students. The text continues to be a leader with an organization that emphasizes important biological concepts, while keeping the student engaged with learning outcomes that allow assessment of progress in understanding these concepts. An inquiry-based approach with robust, adaptive tools for discovery and assessment in both text and digital resources provides the intellectual challenge needed to promote student critical thinking and ensure academic success. A major strength of both text and digital resources is assessment across multiple levels of Bloom's taxonomy that develops critical-thinking and problem-solving skills in addition to comprehensive factual knowledge. McGraw-Hill's Connect® platform offers a powerful suite of online tools that are linked to the text and now include new quantitative assessment tools. The adaptive learning system helps students learn faster, study efficiently, and retain more knowledge of key concepts.

The 11th edition continues our tradition of providing the student with clear learning paths that emphasize data analysis and quantitative reasoning. Additional embedded eBook resources link to asides that delve more deeply into quantitative aspects.

As a team, we continually strive to improve the text by integrating the latest cognitive and best practices research with methods that are known to positively affect learning. We have multiple features that are focused on scientific inquiry, including an increased quantitative emphasis in the Scientific Thinking figures. We continue to use the concise, accessible, and engaging writing style of past editions while maintaining the clear emphasis on evolution and scientific inquiry that have made this a leading textbook of choice for majors biology students. Our emphasis on evolution combined with integrated cell and molecular biology and genomics offers our readers a student-friendly text that is modern and well balanced.

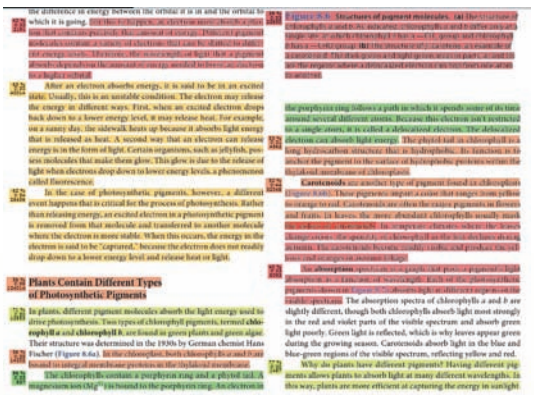
The 11th edition continues to employ the aesthetically stunning art program that the Raven and Johnson *Biology* text is known for. Complex topics are represented clearly and succinctly, helping students to build the mental models needed to understanding biology.

Insights into the diversity of life that are provided by molecular tools have led to a continued updating of these topics in the 11th edition. The diversity unit reflects the most current research on eukaryotic phylogenies, blending molecular, morphological, and development viewpoints. The biotechnology and genomics chapters have been completely revised to reflect changes in these fast-moving areas of modern biology. These are just a few examples of the many changes in the 11th edition of *Biology* that provide students with scientifically accurate context, historical perspective, and relevant supporting details essential to a modern understanding of life science.

As the pace of scientific discovery continues to provide new insights into the foundation of life on Earth, our author team will continue to use every means possible to ensure students are as prepared as possible to engage in biological topics. Our goal now, as it has always been, is to ensure student success. To that end, we approached this revision differently. To help guide our revision for this 11th edition, we were able to incorporate student usage data and input, derived from thousands of our SmartBook® users. SmartBook "heat maps" provided a quick visual snapshot of chapter usage data and the relative difficulty students experienced in mastering the content. With these data, we were able to hone not only our text content but also the SmartBook probes.

- If the data indicated that the subject was more difficult than other parts of the chapter, as evidenced by a high proportion of students responding incorrectly to the probes, we revised or reorganized the content to be as clear and illustrative as possible.
- In other cases, if one or more of the SmartBook probes for a section was not as clear as it might be or did not appropriately reflect the content, we edited the probe, rather than the text.

Below is an example of one of the heat maps from Chapter 8. The color-coding in highlighted sections indicate the various levels of difficulty students experienced in learning the material; topics highlighted in red being the most challenging for students.



We're excited about the 11th edition of this quality textbook providing a learning path for a new generation of students. All of us have extensive experience teaching undergraduate biology, and we've used this knowledge as a guide in producing a text that is up to date, beautifully illustrated, and pedagogically sound for the student. We've also worked to provide clear explicit learning outcomes, and more closely integrate the text with its media support materials to provide instructors with an excellent complement to their teaching.

Ken Mason, Jonathan Losos, Susan Rundell Singer

Cutting Edge Science

Changes to the 11th Edition

Part I: The Molecular Basis of Life

The revision for the 11th edition started with the end users—the students. As described earlier, the authors analyzed SmartBook student usage data collected over the life of the 10th edition. The data from SmartBook revealed content areas where students struggled and based on that information, the authors revised the text to improve clarity. All chapters were evaluated using the SmartBook heat-mapping data.

Other content-specific changes incude:

Part II: Biology of the Cell

Chapter 5—New information on how phospholipid composition differs in different membranes and how this can affect function was added. The chapter was reorganized and a new figure was added to highlight this material.

Chapter 6—Figures 6.4 and 6.5 were revised for clarity and accuracy.

Chapter 9—A new evolutionary aside on the Ras superfamily of small GTPases was added.

Part III: Genetic and Molecular Biology

The overall organization of this section remains the same. We have retained the split of transmission genetics into two chapters as it has proved successful for students.

Content changes in the molecular genetics portion of this section continue to update material that is the most rapidly changing in the entire book. We also continue to refine the idea that RNA plays a much greater role now than appreciated in the past.

Chapter 14—Extensive editing for clarity was done based on heat-map data.

Chapter 15—Extensive updating was done, including a rewritten section on eukaryotic transcription that emphasizes a more modern perspective. Extensive editing throughout the chapter for clarity was done based on heat-map data.

Chapter 16—Extensive updating was done, including a rewritten section on eukaryotic chromatin structure to emphasize a more modern view, taking new high-throughput data into account.

Chapter 17—The chapter was significantly revised to reflect advances in molecular biology techniques such as quantitative reverse-transcription PCR, the CRISPR/Cas9 and related gene-editing technologies, and genetic engineering approaches. Additional modifications include the revision or addition of relevant, engaging applications of biotechnology such as wastewater treatment, biofuel production, and disease detection and treatment.

Chapter 18—Changes to this chapter focus on updating content related to recent advances in sequencing technologies and include the addition of new comparative discussions on the human, wheat, and cancer genome projects. Also, a new analytical commentary on the ENCODE project helps students think critically about recent findings in the genomics field. The addition of a section on the applications of genomics helps students appreciate the social relevance of an often abstract subject area.

Part IV: Evolution

Chapter 20—The section on genetic variation was substantially revised to include recent genomic surveys quantifying the extent of genetic variation across the genome in humans. The text was clarified to say that "dominant" has no connotation of selective superiority. In addition, revisions were made to the information on the current cost in human lives of evolutionary change in microbes evolving resistance to antibiotics.

Chapter 21—The coverage of Darwin's finches and the peppered moth stories were revised to incorporate new information. A section on dating of fossils using radioactive decay was added.

Chapter 22—New additions include examples of geographic variation in the black rat snake incorporating recent phylogenetic analyses of DNA data; reproductive character displacement involving *Phlox* plants in Texas; and adaptive radiation in plants using the Hawaiian *Lobelia*. The phylogeny of Darwin's finches was modified based on current research. New data appear on the evolution of developmental regulation of beak shape in Darwin's finches, along with a new section on mass extinction.

Chapter 23—A new section was added on the relationship between phylogenetics and taxonomic classifications. The figures illustrating how phylogenetics works and how character evolution is interpreted on an evolutionary tree were revised.

New data are included on the evolution of saber-teeth in mammals.

Chapter 24—Updates include new data on comparative genomics. Consideration of primate genomes is expanded, including human and Neanderthal.

Chapter 25—The introduction was rewritten. The cichlid and stickleback examples were updated with new information.

Part V: Diversity of Life on Earth

Chapter 26—The information on geological dating and taxonomic classification was moved to other chapters where the discussions were more relevant.

Chapter 27—This chapter was extensively revised and updated, including a new section on giant viruses and material on the recent Ebola outbreak in Africa.

Chapter 28—Extensive updates include a new section on CRISPR systems, which provide adaptive immunity in bacteria.

Chapter 29—Updated discussions appear on microfossils, malaria vaccines, micronucleus, and *Chlamydomonas genome*. Changes in section headings more clearly describe section contents. Numerous figures were updated to reflect changes in the text.

Chapters 30—The introduction has been modified to provide an overview of land plant evolution. Major trends in the evolution of land plants are now emphasized. The discussion on the effects of mutations on diploid versus haploid bodies has been clarified. The difference between animal and plant life cycles has been emphasized. Throughout the chapter, distinctions between sporophyte and gametophyte generations are clearly described. The significance of hornworts in land plant evolution is described. Section headings were changed to more clearly describe section contents.

Chapter 31—The reduction in the complexity of the gametophyte generation in the evolution of land plants is emphasized. Distinctions between gamete and gametophyte, male and female gametophyte, zygote and embryo, and gymnosperms and angiosperms have been clarified. A discussion of the hypothesis for the rapid expansion of the world's biomes by the angiosperms has been added. The development of the female gametophyte has been described in more detail. The significance of double fertilization has been described.

Chapter 32—The development of hyphae during the evolution of fungi is described. The significance of above-ground spore dispersal structures is emphasized. The characteristics of each fungus group are clearly and concisely described. The significance of fungi in rumen biology has been described. Section headings were changed to more clearly describe section contents. Numerous figures were updated to reflect changes in the text.

Chapters 33–35—These chapters have been streamlined, eliminating extraneous information that was outside the scope of the main topics in the chapters. Throughout, changes were made in the species used as illustrative examples. Information on number of species in different taxa was updated.

Chapter 34—The information on medical infection rates to various invertebrate groups was updated.

Chapter 35—The phylogeny of chordates was updated. A discussion of evolution of tortoises and new information on the sensory abilities of the platypus were added. The phylogeny of primates was updated. New information was added on the genome of Neanderthals and understanding of the evolution of modern humans.

Part VI: Plant Form and Function

Throughout the plant chapters, corrections have been made so that $2n$ and n refer to the sporophyte and gametophyte generations, respectively, and x refers to the number of sets of chromosomes.

Chapter 36—The anatomical positions of components of plant tissues are more clearly presented. Structural differences between angiosperms and gymnosperms are emphasized. Distinctions between similar structures in different tissues—for example, pits in xylem versus pores in phloem—are made.

Chapter 37—The significance of water potential gradients in water transport is clarified and emphasized. The association between anaerobic conditions and poor root growth is described.

Chapter 38—The mechanism of closing in the Venus flytrap leaf has been updated.

Chapter 41—The concept of alternation of generations has been clarified and emphasized.

Part VII: Animal Form and Function

Chapter 46—A new illustration of hinge joints was added.

Chapter 47—The section on pancreas function was revised.

Chapter 48—Information on cutaneous respiration in turtles was added. The discussion of gas exchange in the capillaries was revised.

Chapter 49—The illustration and explanation of components of blood cells were revised, along with the explanation of how blood clotting works.

Chapter 52—New information on facultative parthenogenesis in vertebrates was added. Information on birth control was updated.

Part VIII: Ecology and Behavior

Chapter 54—Information on the social behaviors and brains of prairie and montane voles was updated. The discussion of orientation and migration, plus the section on evolution of mate choice in frogs were revised. Extraneous examples were eliminated to streamline the chapter.

Chapter 55—The information on human population growth and population demographics for several countries was updated using current statistics.

Chapter 56— Extraneous material was removed to streamline the chapter.

Chapter 57—Figures and explanations of trophic cascades, how effects move from one level of the food web to the next, and the discussions of trophic levels and island biogeography were revised. New ideas are presented on why the tropics are so biologically rich.

Chapter 58—Up-to-date information appears on global warming and global ozone levels, with an illustration of how the Earth revolves around the sun. A section was added on new human diseases that come from animals (zoonotic diseases).

Chapter 59—Information on human population growth in biodiversity hot spots, human health toll of West Nile Virus, and the recovery of the peregrine falcon was updated.

A Note From the Authors

A revision of this scope relies on the talents and efforts of many people working behind the scenes and we have benefited greatly from their assistance.

Beatrice Sussman was the copyeditor for this edition. She has labored many hours and always improves the clarity and consistency of the text. She has made significant contributions to the quality of the final product.

We were fortunate to work again with MPS to update the art program and improve the layout of the pages. Our close collaboration resulted in a text that is pedagogically effective as well as more beautiful than any other biology text on the market.

We have the continued support of an excellent team at McGraw-Hill. Justin Wyatt, preceded by Rebecca Olson, the brand managers for *Biology* have been steady leaders during a time of change. Lead Product Developer Liz Sievers, provided support in so many ways it would be impossible to name them all. April Southwood, content project manager, and David Hash, designer, ensured our text was on time and elegantly designed. Patrick Reidy, executive marketing manager, is always a sounding board for more than just marketing, and many more people behind the scenes have all contributed to the success of our text. This includes the digital team, whom we owe a great deal for their efforts to continue improving our Connect assessment tools.

Throughout this edition we have had the support of spouses and children, who have seen less of us than they might have liked because of the pressures of getting this revision completed. They have adapted to the many hours this book draws us away from them, and, even more than us, looked forward to its completion.

In the end, the people we owe the most are the generations of students who have used the many editions of this text. They have taught us at least as much as we have taught them, and their questions and suggestions continue to improve the text and supplementary materials.

Finally, we need to thank instructors from across the country who are continually sharing their knowledge and experience with us through market feedback and symposia. The feedback we received shaped this edition. All of these people took time to share their ideas and opinions to help us build a better edition of *Biology* for the next generation of introductory biology students, and they have our heartfelt thanks.

Developing Critical Thinking with the Help of . . .

Detailed Feedback in Connect®

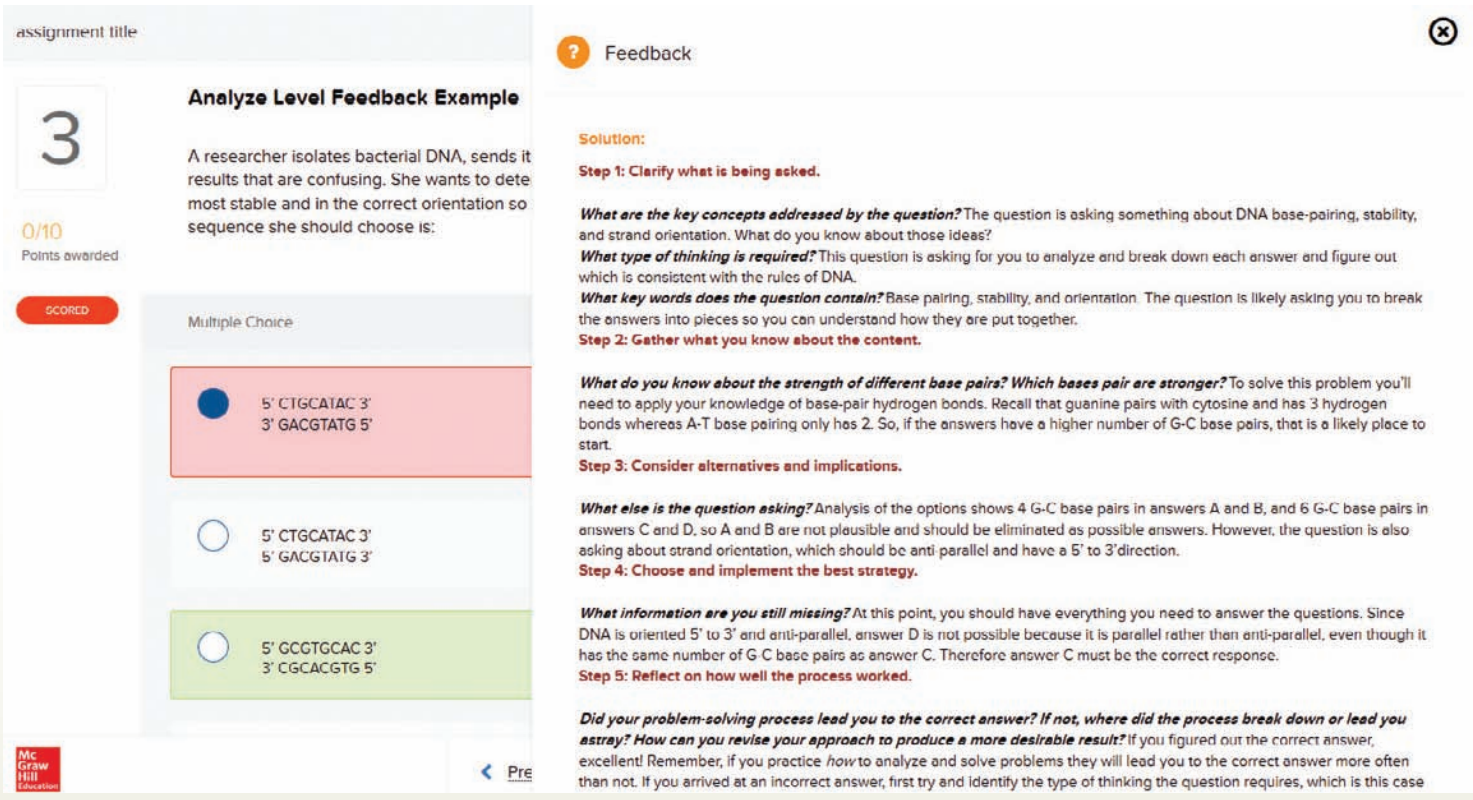
Learning is a process of iterative development, of making mistakes, reflecting, and adjusting over time. The question and test banks in Connect® for *Biology*, 11th edition, are more than direct assessments; they are self-contained learning experiences that systematically build student learning over time.

For many students, choosing the right answer is not necessarily based on applying content correctly; it is more a matter of increasing their statistical odds of guessing. A major fault with this approach is students don't learn how to process the questions correctly, mostly because they are repeating and reinforcing their mistakes rather than reflecting and learning from them. To help students develop problem-solving skills, all higher level Blooms questions in Connect are supported with hints, to help students focus on important information for answering the questions, and detailed feedback that walks students through the problem-solving process, using Socratic questions in a decision-tree-style framework to scaffold learning, where each step models and reinforces the learning process.

The feedback for each higher level Blooms question (Apply, Analyze, Evaluate) follows a similar process: Clarify Question, Gather Content, Choose Answer, Reflect on Process.

Unpacking the Concepts

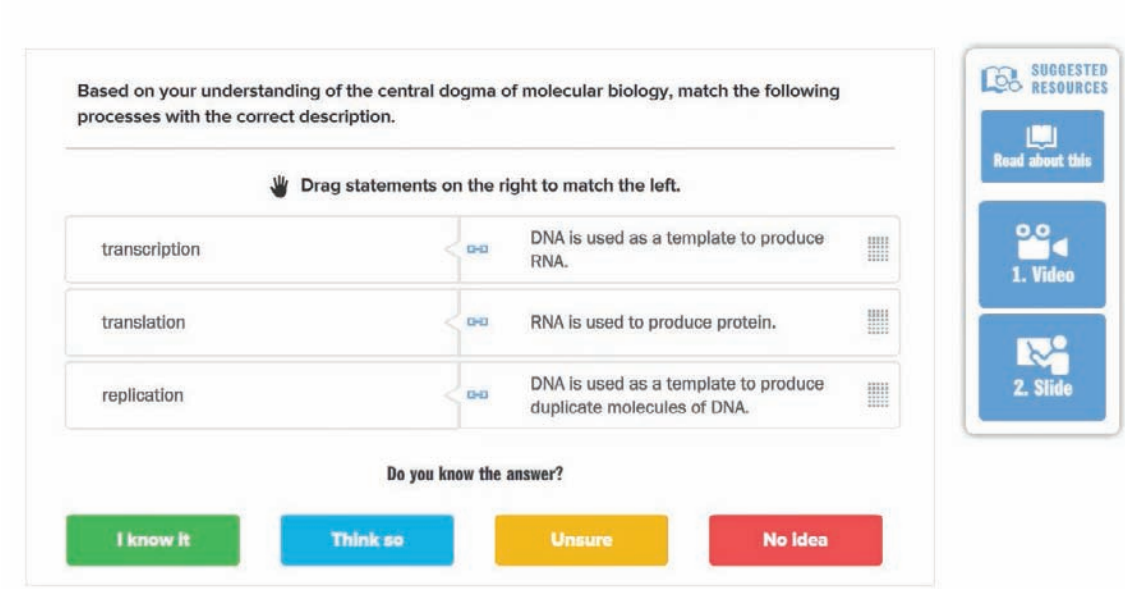
We've taken problem solving a step further. In each chapter, three to five higher level Blooms questions in the question and test banks are broken out by the steps of the detailed feedback. Rather than leaving it up to the student to work through the detailed feedback, a second version of the question is presented in a stepwise format. Following the problem-solving steps, students need to answer questions about earlier steps, such as "What is the key concept addressed by the question?" before proceeding to answer the question. A professor can choose which version of the question to include in the assignment based on the problem-solving skills of the students.

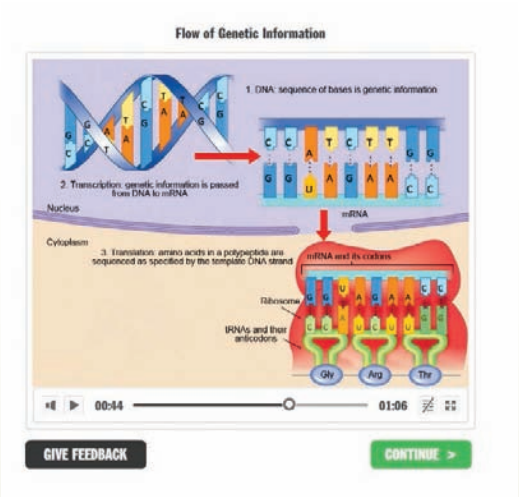


Strengthen Problem Solving Skills and Key Concept Development with Connect®

SmartBook with Learning Resources

To help students understand key concepts, SmartBook® for *Biology*, 11th edition, is enhanced with Learning Resources. Based on student usage data, derived from thousands of SmartBook users of the tenth edition, concepts that proved more challenging for students are supported with Learning Resources to enhance the textbook presentation. Learning Resources, such as animations or tutorials, are indicated in SmartBook adjacent to the textbook content. If a student is struggling with a concept based on his/her performance on the SmartBook questions, the student is given an option to review the Learning Resource or the student can click on the Learning Resources at any time.



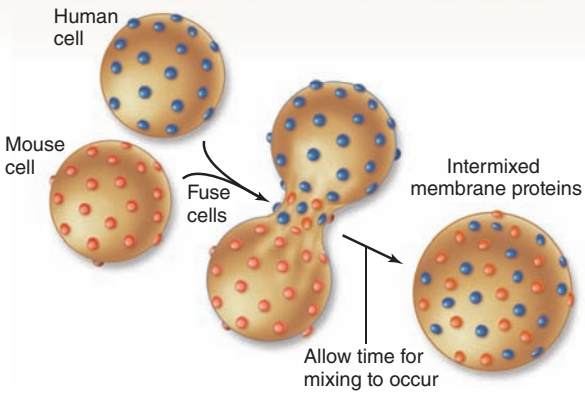


Scientific Thinking Art

Key illustrations in every chapter highlight how the frontiers of knowledge are pushed forward by a combination of hypothesis and experimentation. These figures begin with a hypothesis, then show how it makes explicit predictions, tests these by experiment and finally demonstrates what conclusions can be drawn, and where this leads. Scientific Thinking figures provide a consistent framework to guide the student in the logic of scientific inquiry. Each illustration concludes with open-ended questions to promote scientific inquiry.

SCIENTIFIC THINKING

Hypothesis: *The plasma membrane is fluid, not rigid.*
Prediction: *If the membrane is fluid, membrane proteins may diffuse laterally.*
Test: *Fuse mouse and human cells, then observe the distribution of membrane proteins over time by labeling specific mouse and human proteins.*



Result: *Over time, hybrid cells show increasingly intermixed proteins.*
Conclusion: *At least some membrane proteins can diffuse laterally in the membrane.*
Further Experiments: *Can you think of any other explanation for these observations? What if newly synthesized proteins were inserted into the membrane during the experiment? How could you use this basic experimental design to rule out this or other possible explanations?*

Figure 5.5 **Test of membrane fluidity.**

Data Analysis Questions

It's not enough that students learn concepts and memorize scientific facts, a biologist needs to analyze data and apply that knowledge. Data Analysis questions inserted throughout the text challenge students to analyze data and Interpret experimental results, which shows a deeper level of understanding.

Supporting Material Provided Online

Evolutionary Asides are inserted at relevant places in the book. The student links to this online content through the Evolutionary Aside icon found in the eBook. Evolutionary Asides provide additional examples or discussions of evolutionary topics related to the textual discussion.

Quantitative Asides are inserted at relevant places in the book. The student links to this online content through the Quantitative Aside icon found in the eBook. Quantitative Asides provide additional examples or expanded discussions of a quantitative aspect of the topic under discussion.

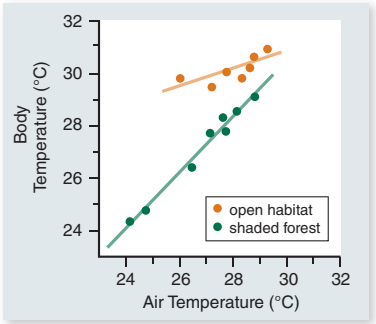


Figure 55.3 **Behavioral adaptation.** In open habitats, the Puerto Rican crested lizard, *Anolis cristatellus,* maintains a relatively constant temperature by seeking out and basking in patches of sunlight; as a result, it can maintain a relatively high temperature even when the air is cool. In contrast, in shaded forests, this behavior is not possible, and the lizard's body temperature conforms to that of its surroundings.

Inquiry question When given the opportunity, lizards regulate their body temperature to maintain a temperature optimal for physiological functioning. Would lizards in open habitats exhibit different escape behaviors from lizards in shaded forest?

Data analysis Can the slope of the line tell us something about the behavior of the lizard?

Inquiry Questions

Questions that challenge students to think about and engage in what they are reading at a more sophisticated level.

Using Connect® and *Biology*, 11th edition

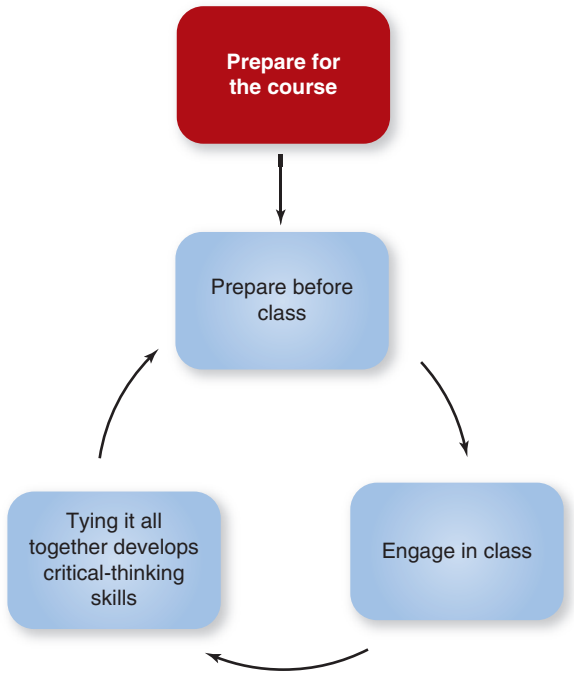
Biology 11th edition and its online assets have been carefully crafted to help professors and students work efficiently and effectively through the material in the course, making the most of instructional and study time.

Prepare for the Course

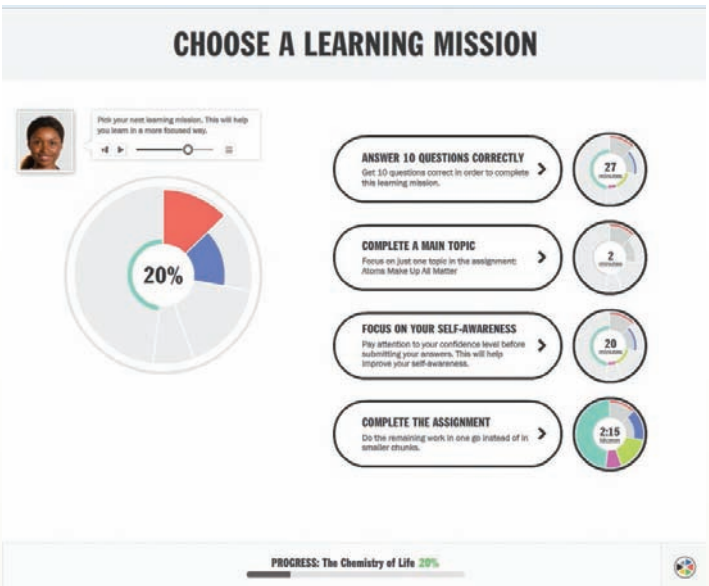
Many biology students struggle the first few weeks of class. Many institutions expect students to start majors biology having a working knowledge of basic chemistry and cellular biology. *LearnSmart Prep* is now available in Connect. Professors can assign modules in LearnSmart Prep to help students get up to speed on core concepts, or students can access LearnSmart Prep directly through the LearnSmart Prep link.

LEARNSMART PREP®

LearnSmart Prep is an adaptive learning tool designed to increase student success and aid retention through the first few weeks of class. Using this digital tool, Majors Biology students can master some of the most fundamental and challenging principles of biology before they begin to struggle in the first few weeks of class.



1. A diagnostic establishes your baseline comprehension and knowledge; then the program generates a learning plan tailored to your academic needs and schedule.



2. As you work through the learning plan, the program asks you questions and tracks your mastery of concepts. If you answer questions about a particular concept incorrectly, the program will provide a learning resource (ex. animation or tutorial) on that concept, then ensure that you understand the concept by asking you more questions. Didn't get it the first time? Don't worry—*LearnSmart Prep* will keep working with you!
3. Using *LearnSmart Prep*, you can identify the content you don't understand, focus your time on content you need to know but don't, and therefore improve your chances of success in your majors biology course.

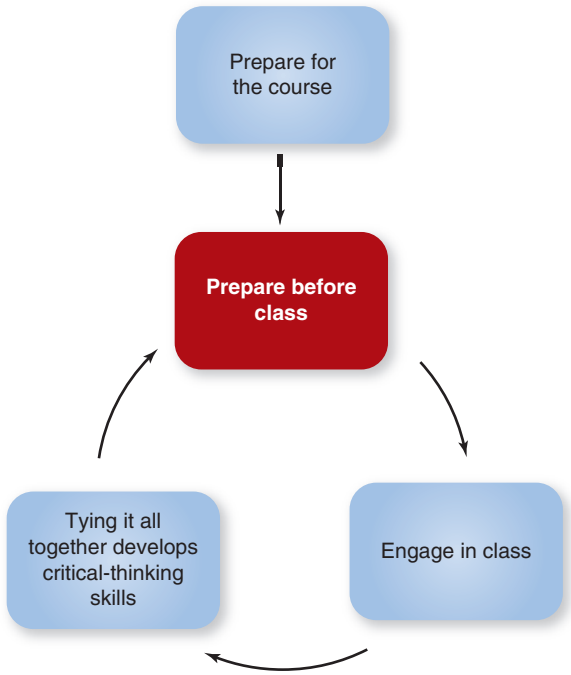
Prepare Before Class

Students who are most successful in college are those who have developed effective study skills and who use those skills before, during, and after class.

Students can maximize time in class by previewing the material before stepping into the lecture hall. *Biology*, 11th edition, is available in two formats: the printed text as well as the online SmartBook. Student can use either of these options to preview the material before lecture. Becoming familiar with terminology and basic concepts will allow students to follow along in class and engage in the content in a way that allows for better retention.

Professors can help students prepare for class by making preclass assignments. SmartBook assignments are effective for introducing terminology and general concepts.

SmartBook provides a personalized, adaptive reading experience.



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Powered by an intelligent diagnostic and adaptive engine, **SmartBook** facilitates the reading process by identifying what content a student knows and doesn't know through adaptive assessments.

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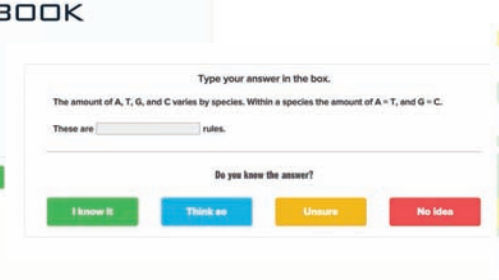
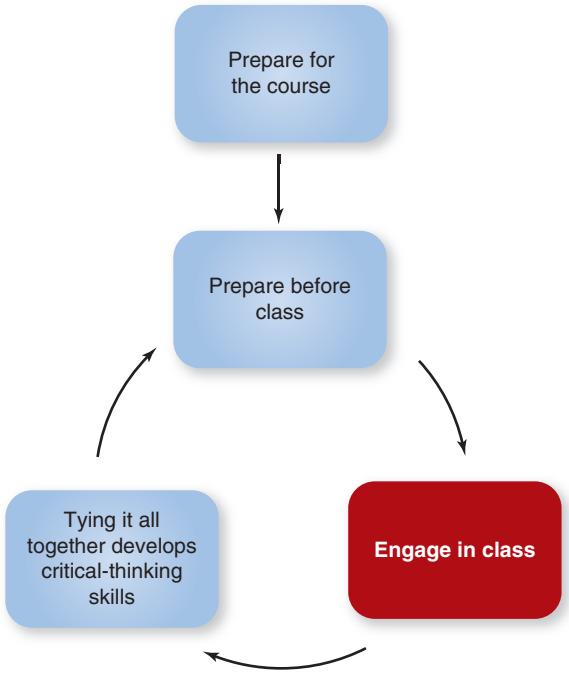


SmartBook asks you questions that identify gaps in your knowledge. The reading experience then continuously adapts in response to the assessments—highlighting the material you need to review based on what you don't know.

The reports in SmartBook help identify topics where you need more work.

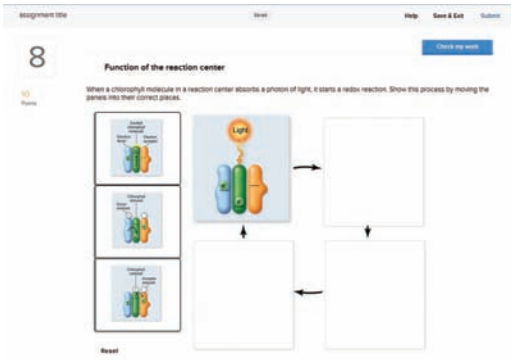
Engage in Class

McGraw-Hill Connect® provides online presentation, assignment, and assessment solutions. It connects students with the tools and resources they'll need to achieve success. A robust set of questions and activities is presented in the Question Bank and a separate set of questions to use for exams is presented in the Test Bank. Instructors can edit existing questions and author entirely new problems. They can track individual student performance—by question, assignment, or in relation to the class overall—with detailed grade reports.



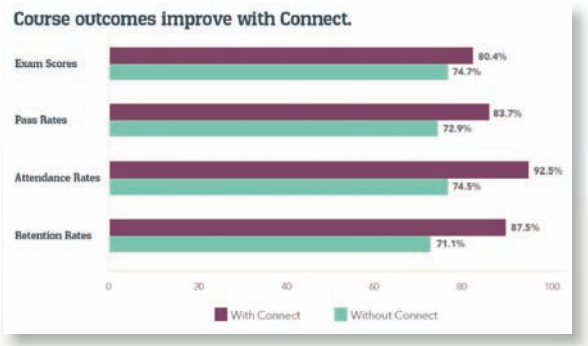
1 Preclass assignments to help students engage in the content during class.

Assignments are accessed through Connect and could include homework assignments, quizzes, SmartBook assignments, and other resources.

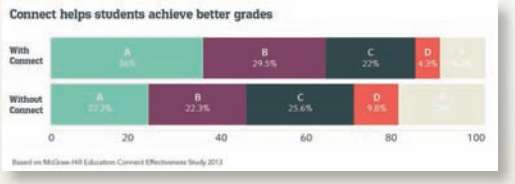


Interactive and traditional questions help assess students' knowledge of the material.

2 Connect Insight is Connect's visual analytics dashboard for instructors and students.



Provides at-a-glance student performance on assignments. Instructors can use the information for a just-in-time approach to teaching.



Presents data that empower students to improve performance that is efficient and effective.

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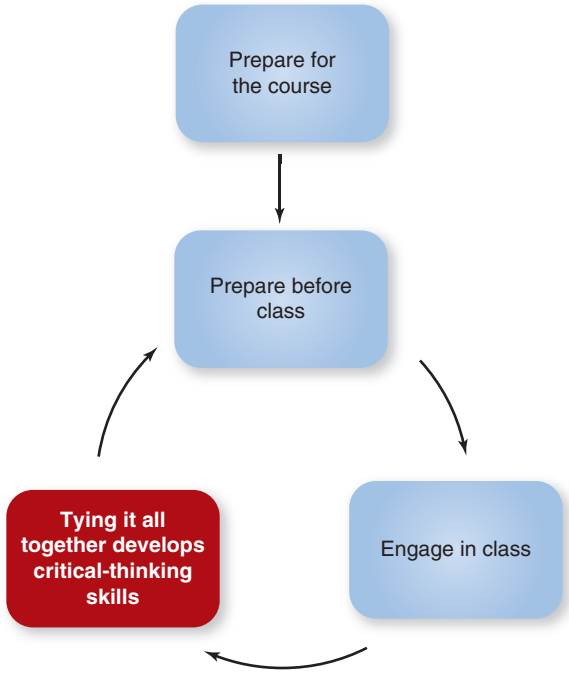
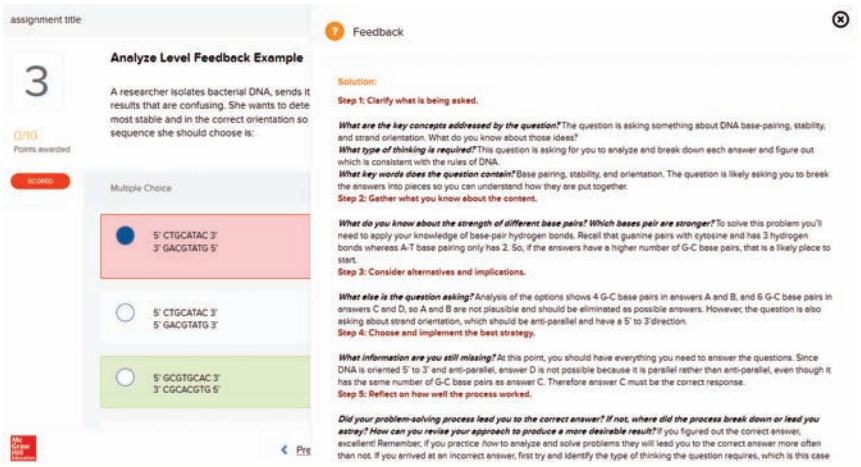
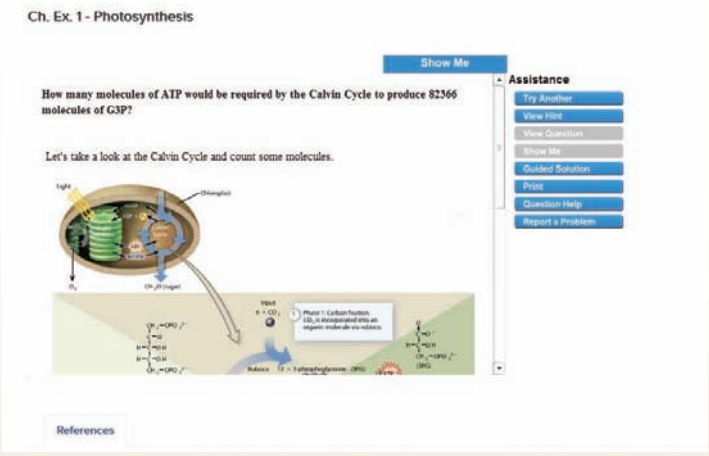




Detailed Feedback All higher level Bloom's questions that involve problem solving contain detailed feedback in Connect. The feedback walks students through the steps of the problem-solving process and helps them evaluate their scientific-thinking skills.

Many chapters also contain a **Quantitative Question Bank**. These are more challenging algorithmic questions, intended to help your students practice their quantitative reasoning skills. Hints and guided solution options step students through a problem.



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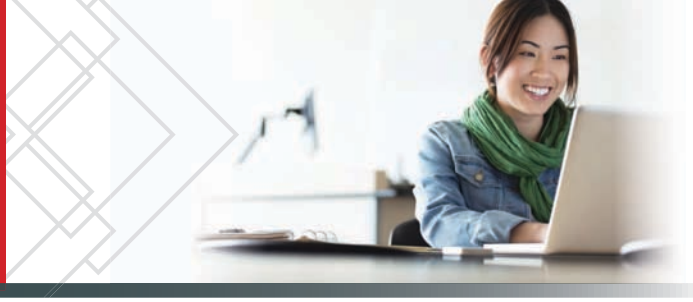

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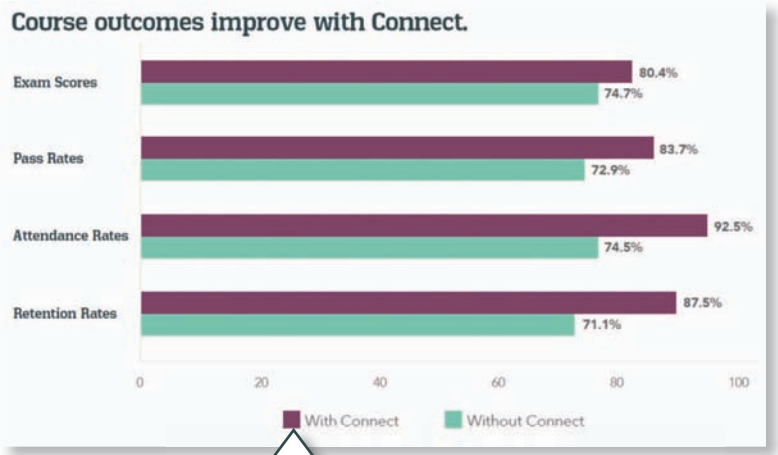

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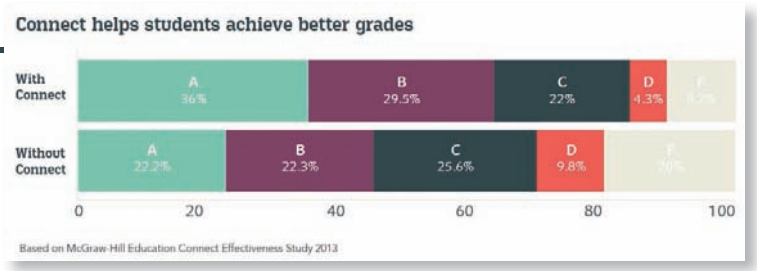

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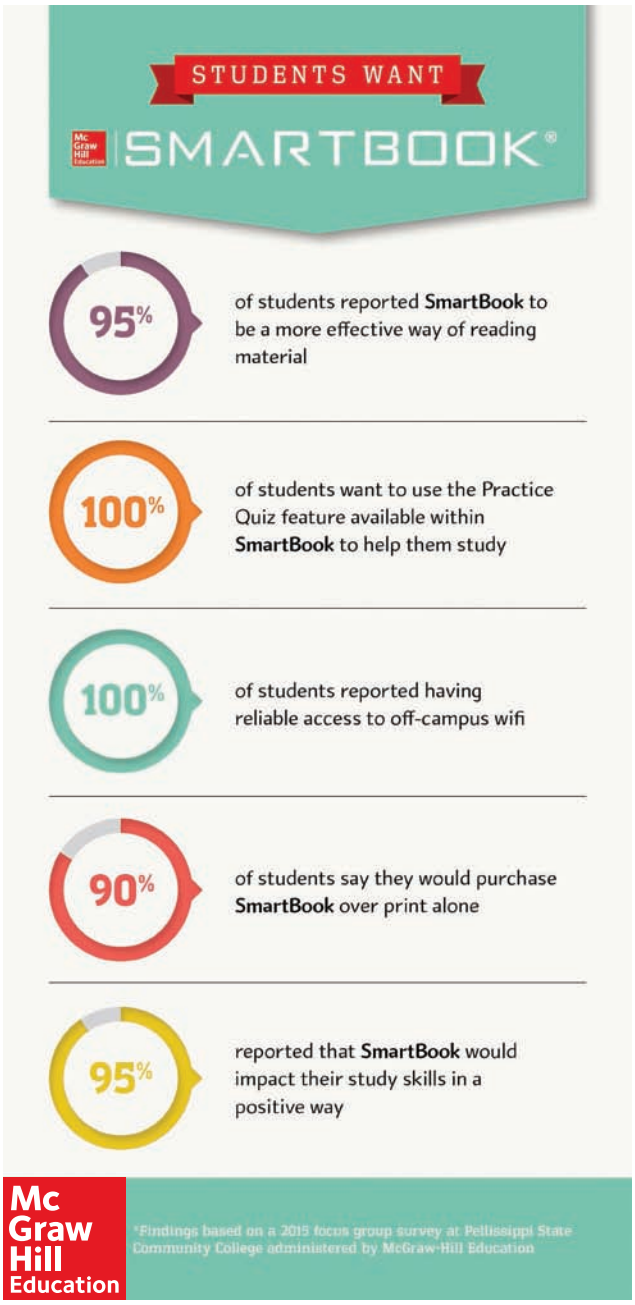

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CHAPTER 1

The Science of Biology

Chapter Contents

Introduction

You are about to embark on a journey—a journey of discovery about the nature of life. More than 180 years ago, a young English naturalist named Charles Darwin set sail on a similar journey on board H.M.S. *Beagle*; a replica of this ship is pictured here. What Darwin learned on his five-year voyage led directly to his development of the theory of evolution by natural selection, a theory that has become the core of the science of biology. Darwin's voyage seems a fitting place to begin our exploration of biology—the scientific study of living organisms and how they have evolved. Before we begin, however, let's take a moment to think about what biology is and why it's important.

1.1 The Science of Life

Learning Outcomes

1. *Compare biology to other natural sciences.*
2. *Describe the characteristics of living systems.*
3. *Characterize the hierarchical organization of living systems.*

This is the most exciting time to be studying biology in the history of the field. The amount of information available about the natural world has exploded in the last 42 years since the construction of the first recombinant DNA molecule. We are now in a position to ask and answer questions that previously were only dreamed of.

The 21st century began with the completion of the sequence of the human genome. The largest single project in the history of biology took about 20 years. Yet less than 15 years later, we can sequence an entire genome in a matter of days. This flood of sequence data and genomic analysis are altering the landscape of biology. These and other discoveries are also moving into the

clinic as never before with new tools for diagnostics and treatment. With robotics, advanced imaging, and analytical techniques, we have tools available that were formerly the stuff of science fiction.

In this text, we attempt to draw a contemporary picture of the science of biology, as well as provide some history and experimental perspective on this exciting time in the discipline. In this introductory chapter, we examine the nature of biology and the foundations of science in general to put into context the information presented in the rest of the text.

Biology unifies much of natural science

The study of biology is a point of convergence for the information and tools from all of the natural sciences. Biological systems are the most complex chemical systems on Earth, and their many functions are both determined and constrained by the principles of chemistry and physics. Put another way, no new laws of nature can be gleaned from the study of biology—but that study does illuminate and illustrate the workings of those natural laws.

The intricate chemical workings of cells can be understood using the tools and principles of chemistry. And every level of biological organization is governed by the nature of energy transactions first studied by thermodynamics. Biological systems do not represent any new forms of matter, and yet they are the most complex organization of matter known. The complexity of living systems is made possible by a constant source of energy—the Sun. The conversion of this radiant energy into organic molecules by photosynthesis is one of the most beautiful and complex reactions known in chemistry and physics.

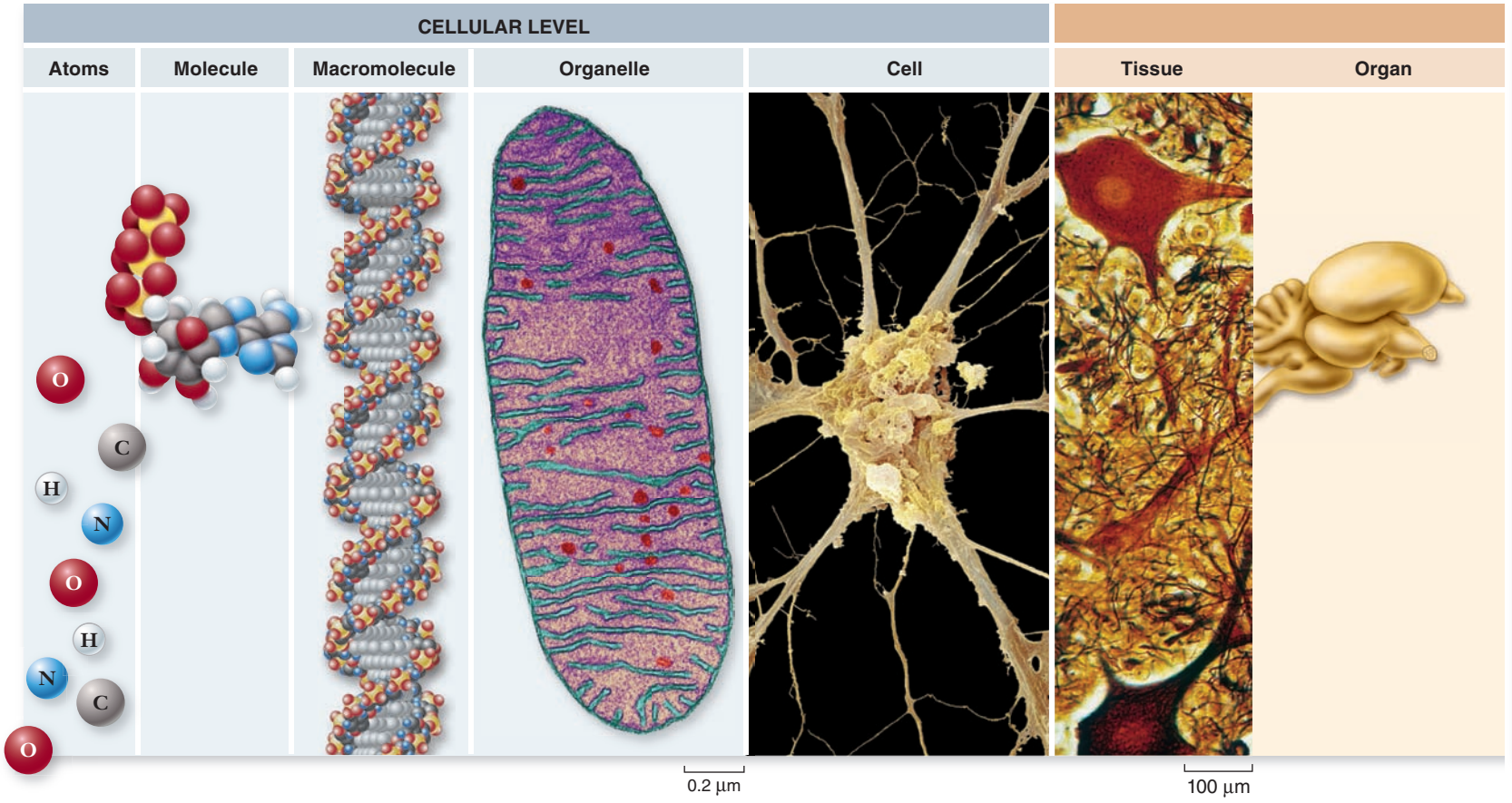
The way we do science is changing to grapple with increasingly difficult modern problems. Science is becoming more interdisciplinary, combining the expertise from a variety of traditional disciplines and emerging fields such as nanotechnology. Biology is at the heart of this multidisciplinary approach because biological problems often require many different approaches to arrive at solutions.

Life defies simple definition

In its broadest sense, biology is the study of living things—*the science of life.* Living things come in an astounding variety of shapes and forms, and biologists study life in many different ways. They live with gorillas, collect fossils, and listen to whales. They read the messages encoded in the long molecules of heredity and count how many times a hummingbird's wings beat each second.

What makes something "alive"? Anyone could deduce that a galloping horse is alive and a car is not, but why? We cannot say, "If it moves, it's alive," because a car can move, and gelatin can wiggle in a bowl. They certainly are not alive. Although we cannot define life with a single simple sentence, we can come up with a series of seven characteristics shared by living systems:

- **Cellular organization.** All organisms consist of one or more cells. Often too tiny to see, cells carry out the basic activities of living. Each cell is bounded by a membrane that separates it from its surroundings.
- **Ordered complexity.** All living things are both complex and highly ordered. Your body is composed of many different kinds of cells, each containing many complex molecular structures. Many nonliving things may also be



complex, but they do not exhibit this degree of ordered complexity.

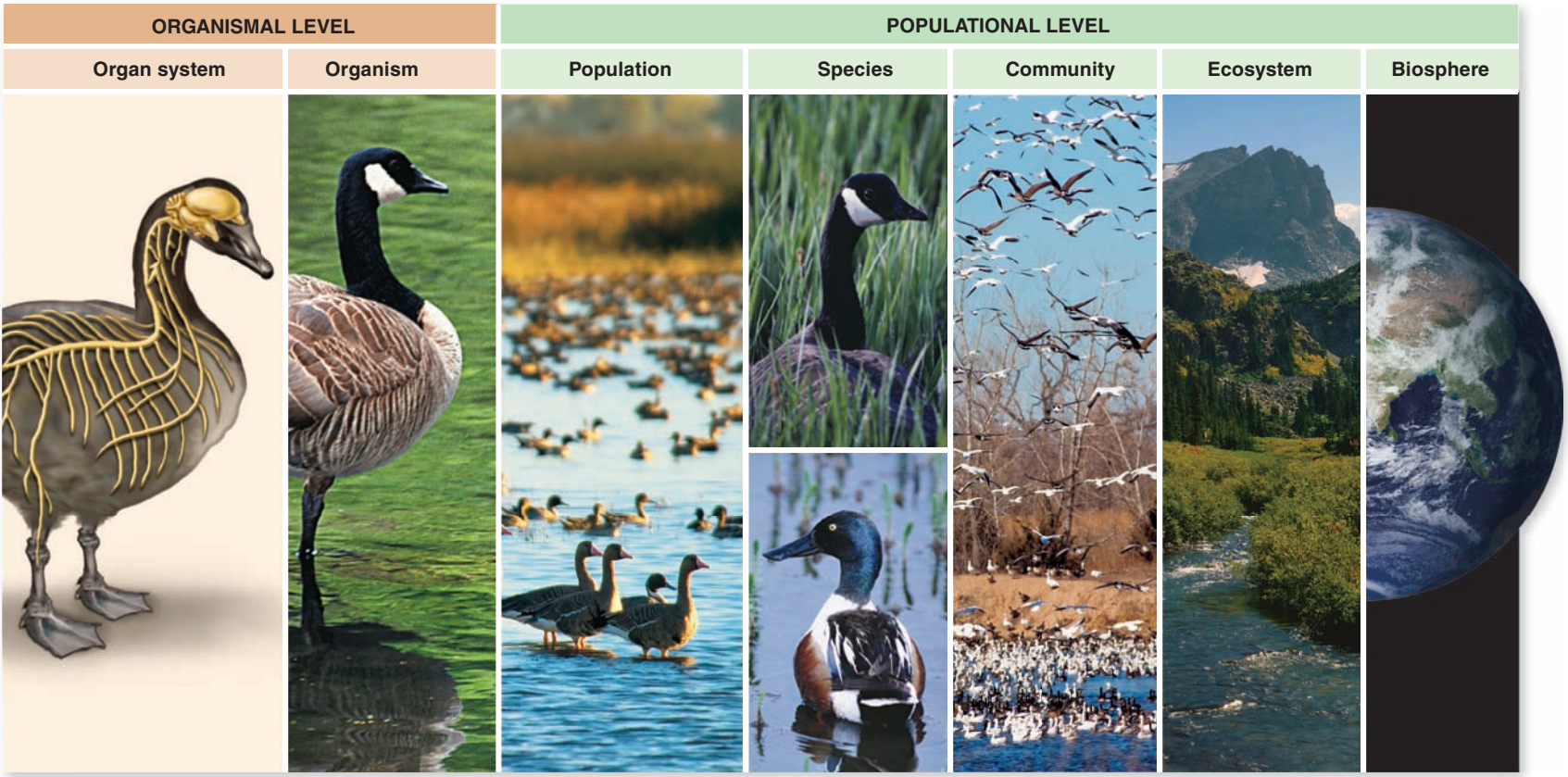
- **Sensitivity.** All organisms respond to stimuli. Plants grow toward a source of light, and the pupils of your eyes dilate when you walk into a dark room.
- **Growth, development, and reproduction.** All organisms are capable of growing and reproducing, and they all possess hereditary molecules that are passed to their offspring, ensuring that the offspring are of the same species.
- **Energy utilization.** All organisms take in energy and use it to perform many kinds of work. Every muscle in your body is powered with energy you obtain from your diet.
- **Homeostasis.** All organisms maintain relatively constant internal conditions that are different from their environment, a process called **homeostasis.** For example, your body temperature remains stable despite changes in outside temperatures.
- **Evolutionary adaptation.** All organisms interact with other organisms and the nonliving environment in ways that influence their survival, and as a consequence, organisms evolve adaptations to their environments.

Living systems show hierarchical organization

The organization of the biological world is hierarchical—that is, each level builds on the level below it:

1. **The cellular level.** At the cellular level (figure 1.1), **atoms,** the fundamental elements of matter, are joined together into clusters called **molecules.** Complex biological molecules are assembled into tiny structures called **organelles** within membrane-bounded units we call **cells.** The cell is the basic unit of life. Many independent organisms are composed only of single cells. Bacteria are single cells, for example. All animals and plants, as well as most fungi and algae, are multicellular—composed of more than one cell.
2. **The organismal level.** Cells in complex multicellular organisms exhibit three levels of organization. The most basic level is that of **tissues,** which are groups of similar cells that act as a functional unit. Tissues, in turn, are grouped into **organs—**body structures composed of several different tissues that act as a structural and functional unit. Your brain is an organ composed of nerve cells and a variety of associated tissues that form protective coverings and contribute blood. At the third level of organization, organs are grouped into **organ systems.** The nervous system, for example, consists of sensory organs, the brain and spinal cord, and neurons that convey signals.

Figure 1.1 Hierarchical organization of living systems. Life forms a hierarchy of organization from atoms to complex multicellular organisms. Atoms are joined together to form molecules, which are assembled into more complex structures such as organelles. These in turn form subsystems that provide different functions. Cells can be organized into tissues, then into organs and organ systems such as the goose's nervous system pictured. This organization then extends beyond individual organisms to populations, communities, ecosystems, and finally the biosphere.



3. **The populational level.** Individual organisms can be categorized into several hierarchical levels within the living world. The most basic of these is the **population—**a group of organisms of the same species living in the same place. All populations of a particular kind of organism together form a **species,** its members similar in appearance and able to interbreed. At a higher level of biological organization, a **biological community** consists of all the populations of different species living together in one place.
4. **The ecosystem level.** At the highest tier of biological organization, populations of organisms interact with each other and their physical environment. Together populations and their environment constitute an ecological system, or **ecosystem.** For example, the biological community of a mountain meadow interacts with the soil, water, and atmosphere of a mountain ecosystem in many important ways.
5. **The biosphere.** The entire planet can be thought of as an ecosystem that we call the biosphere.

As you move up this hierarchy, the many interactions occurring at lower levels can produce novel properties. These so-called **emergent properties** may not be predictable. Examining individual cells, for example, gives little hint about the whole animal. Many weather phenomena, such as hurricanes, are actually emergent properties of many interacting meteorological variables. It is because the living world exhibits many emergent properties that it is difficult to define "life."

The previous descriptions of the common features and organization of living systems begins to get at the nature of what it is to be alive. The rest of this book illustrates and expands on these basic ideas to try to provide a more complete account of living systems.

Learning Outcomes Review 1.1

Biology as a science brings together other natural sciences, such as chemistry and physics, to study living systems. Life does not have a simple definition, but living systems share a number of properties that together describe life. Living systems can be organized hierarchically, from the cellular level to the entire biosphere, with emergent properties that may exceed the sum of the parts.

- *Can you study biology without studying other sciences?*

1.2 The Nature of Science

Learning Outcomes

1. *Compare the different types of reasoning used by biologists.*
2. *Demonstrate how to formulate and test a hypothesis.*

Much like life itself, the nature of science defies simple description. For many years scientists have written about the "scientific method" as though there is a single way of doing science. This oversimplification has contributed to confusion on the part of nonscientists about the nature of science.

At its core, science is concerned with developing an increasingly accurate understanding of the world around us using observation and reasoning. To begin with, we assume that natural forces acting now have always acted, that the fundamental nature of the universe has not changed since its inception, and that it is not changing now. A number of complementary approaches allow understanding of natural phenomena—there is no one "scientific method."

Scientists also attempt to be as objective as possible in the interpretation of the data and observations they have collected. Because scientists themselves are human, this is not completely possible, but because science is a collective endeavor subject to scrutiny, it is self-correcting. One person's results are verified by others, and if the results cannot be repeated, they are rejected.

Much of science is descriptive

The classic vision of the scientific method is that observations lead to hypotheses that in turn make experimentally testable predictions. In this way, we dispassionately evaluate new ideas to arrive at an increasingly accurate view of nature. We discuss this way of doing science later in this section but it is important to understand that much of science is purely descriptive: In order to understand anything, the first step is to describe it completely. Much of biology is concerned with arriving at an increasingly accurate description of nature.

The study of biodiversity is an example of descriptive science that has implications for other aspects of biology in addition to societal implications. Efforts are currently under way to classify all life on Earth. This ambitious project is purely descriptive, but it will lead to a much greater understanding of biodiversity as well as the effect our species has on biodiversity.

One of the most important accomplishments of molecular biology at the dawn of the 21st century was the completion of the sequence of the human genome. Many new hypotheses about human biology will be generated by this knowledge, and many experiments will be needed to test these hypotheses, but the determination of the sequence itself was descriptive science.

Science uses both deductive and inductive reasoning

The study of logic recognizes two opposite ways of arriving at logical conclusions: deductive and inductive reasoning. Science makes use of both of these methods, although induction is the primary way of reasoning in hypothesis-driven science.

Deductive reasoning

Deductive reasoning applies general principles to predict specific results. More than 2200 years ago, the Greek scientist Eratosthenes used Euclidean geometry and deductive reasoning to accurately estimate the circumference of the Earth (figure 1.2). Deductive reasoning is the reasoning of mathematics and philosophy, and it is used to test the validity of general ideas in all branches of

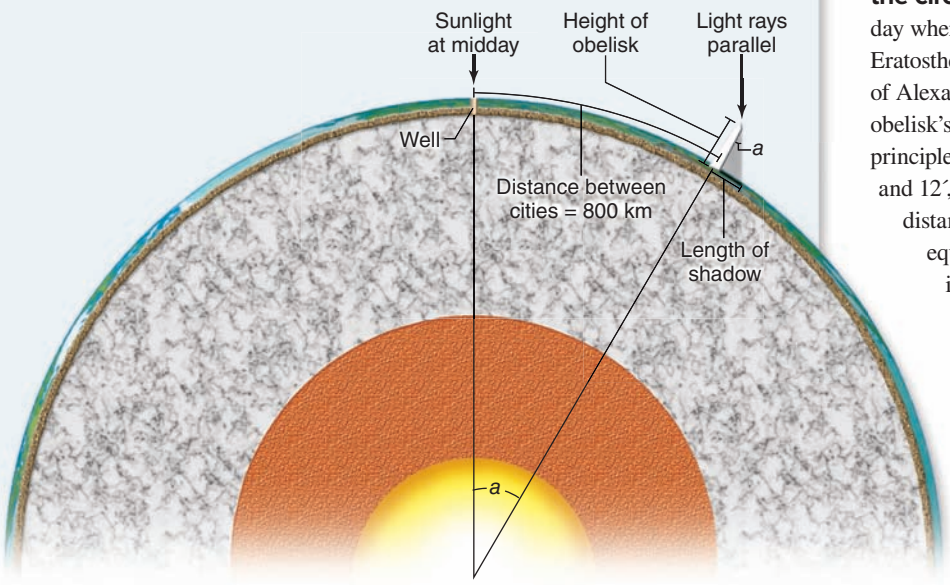


Figure 1.2 Deductive reasoning: How Eratosthenes estimated the circumference of the Earth using deductive reasoning. *1.* On a day when sunlight shone straight down a deep well at Syene in Egypt, Eratosthenes measured the length of the shadow cast by a tall obelisk in the city of Alexandria, about 800 kilometers (km) away. *2.* The shadow's length and the obelisk's height formed two sides of a triangle. Using the recently developed principles of Euclidean geometry, Eratosthenes calculated the angle, *a,* to be 7° and 12′, exactly 1/50 of a circle (360°). *3.* If angle *a* is 1/50 of a circle, then the distance between the obelisk (in Alexandria) and the well (in Syene) must be equal to 1/50 the circumference of the Earth. *4.* Eratosthenes had heard that it was a 50-day camel trip from Alexandria to Syene. Assuming a camel travels about 18.5 km per day, he estimated the distance between obelisk and well as 925 km (using different units of measure, of course). *5.* Eratosthenes thus deduced the circumference of the Earth to be $50 \times 925 = 46{,}250$ km. Modern measurements put the distance from the well to the obelisk at just over 800 km. Using this distance Eratosthenes's value would have been $50 \times 800 = 40{,}000$ km. The actual circumference is 40,075 km.

knowledge. For example, if all mammals by definition have hair, and you find an animal that does not have hair, then you may conclude that this animal is not a mammal. A biologist uses deductive reasoning to infer the species of a specimen from its characteristics.

Inductive reasoning

In **inductive reasoning,** the logic flows in the opposite direction, from the specific to the general. Inductive reasoning uses specific observations to construct general scientific principles. For example, if poodles have hair, and terriers have hair, and every dog that you observe has hair, then you may conclude that all dogs have hair. Inductive reasoning leads to generalizations that can then be tested. Inductive reasoning first became important to science in the 1600s in Europe, when Francis Bacon, Isaac Newton, and others began to use the results of particular experiments to infer general principles about how the world operates.

An example from modern biology is the role of homeobox genes in development. Studies in the fruit fly, *Drosophila melanogaster,* identified genes that could cause dramatic changes in developmental fate, such as a leg appearing in the place of an antenna. These genes have since been found in essentially all multicellular animals analyzed. This led to the general idea that homeobox genes control developmental fate in animals.

Hypothesis-driven science makes and tests predictions

Scientists establish which general principles are true from among the many that might be true through the process of systematically testing alternative proposals. If these proposals prove inconsistent with experimental observations, they are rejected as untrue. Figure 1.3 illustrates the process.

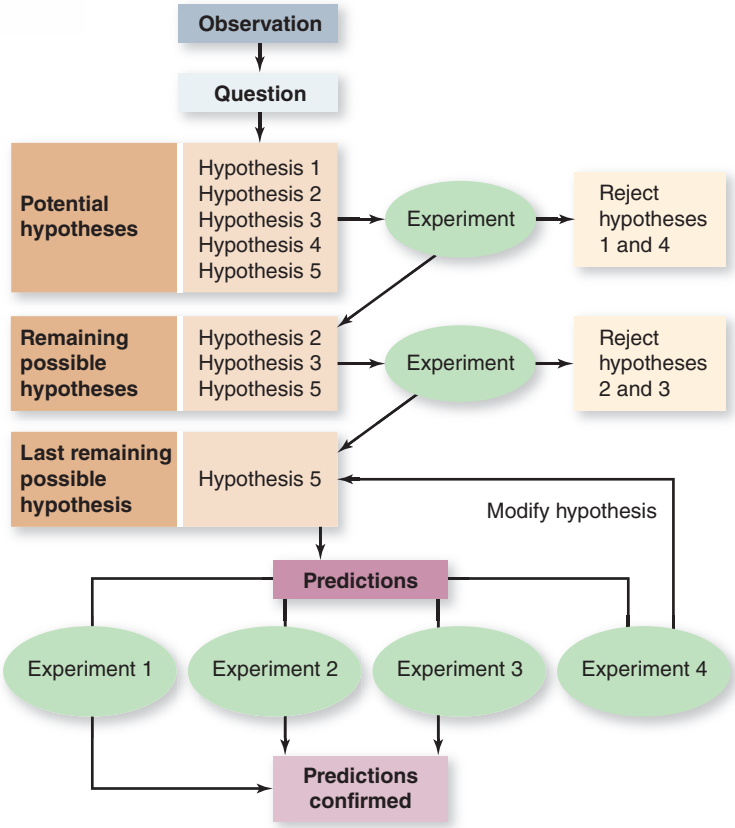


Figure 1.3 How science is done. This diagram illustrates how scientific investigations proceed. First, scientists make observations that raise a particular question. They develop a number of potential explanations (hypotheses) to answer the question. Next, they carry out experiments in an attempt to eliminate one or more of these hypotheses. Then, predictions are made based on the remaining hypotheses, and further experiments are carried out to test these predictions. The process can also be iterative. As experimental results are performed, the information can be used to modify the original hypothesis to fit each new observation.

After making careful observations, scientists construct a **hypothesis,** which is a suggested explanation that accounts for those observations. A hypothesis is a proposition that might be true. Those hypotheses that have not yet been disproved are retained. They are useful because they fit the known facts, but they are always subject to future rejection if, in the light of new information, they are found to be incorrect.

This is usually an ongoing process with a hypothesis changing and being refined with new data. For instance, geneticists George Beadle and Edward Tatum studied the nature of genetic information to arrive at their "one-gene/one-enzyme" hypothesis (see chapter 15). This hypothesis states that a gene represents the genetic information necessary to make a single enzyme. As investigators learned more about the molecular nature of genetic information, the hypothesis was refined to "one-gene/one-polypeptide" because enzymes can be made up of more than one polypeptide. With still more information about the nature of genetic information, other investigators found that a single gene can specify more than one polypeptide, and the hypothesis was refined again.

Testing hypotheses

We call the test of a hypothesis an **experiment.** Suppose you enter a dark room. To understand why it is dark, you propose several hypotheses. The first might be, "There is no light in the room because the light switch is turned off." An alternative hypothesis might be, "There is no light in the room because the lightbulb is burned out." And yet another hypothesis might be, "I am going blind." To evaluate these hypotheses, you would conduct an experiment designed to eliminate one or more of the hypotheses.

For example, you might test your hypotheses by flipping the light switch. If you do so and the room is still dark, you have disproved the first hypothesis: Something other than the setting of the light switch must be the reason for the darkness. Note that a test such as this does not prove that any of the other hypotheses are true; it merely demonstrates that the one being tested is not. A successful experiment is one in which one or more of the alternative hypotheses is demonstrated to be inconsistent with the results and is thus rejected.

As you proceed through this text, you will encounter many hypotheses that have withstood the test of experiment. Many will continue to do so; others will be revised as new observations are made by biologists. Biology, like all science, is in a constant state of change, with new ideas appearing and replacing or refining old ones.

Establishing controls

Often scientists are interested in learning about processes that are influenced by many factors, or **variables.** To evaluate alternative hypotheses about one variable, all other variables must be kept constant. This is done by carrying out two experiments in parallel: a test experiment and a control experiment. In the **test experiment,** one variable is altered in a known way to test a particular hypothesis. In the **control experiment,** that variable is left unaltered. In all other respects the two experiments are identical, so any difference in the outcomes of the two experiments must result from the influence of the variable that was changed.

Much of the challenge of experimental science lies in designing control experiments that isolate a particular variable from other factors that might influence a process.

Using predictions

A successful scientific hypothesis needs to be not only valid but also useful—it needs to tell us something we want to know. A hypothesis is most useful when it makes predictions because those predictions provide a way to test the validity of the hypothesis. If an experiment produces results inconsistent with the predictions, the hypothesis must be rejected or modified. In contrast, if the predictions are supported by experimental testing, the hypothesis is supported. The more experimentally supported predictions a hypothesis makes, the more valid the hypothesis is.

As an example, in the early history of microbiology it was known that nutrient broth left sitting exposed to air becomes contaminated. Two hypotheses were proposed to explain this observation: spontaneous generation and the germ hypothesis. Spontaneous generation held that there was an inherent property in organic molecules that could lead to the spontaneous generation of life. The germ hypothesis proposed that preexisting microorganisms that were present in the air could contaminate the nutrient broth.

These competing hypotheses were tested by a number of experiments that involved filtering air and boiling the broth to kill any contaminating germs. The definitive experiment was performed by Louis Pasteur, who constructed flasks with curved necks that could be exposed to air, but that would trap any contaminating germs. When such flasks were boiled to sterilize them, they remained sterile, but if the curved neck was broken off, they became contaminated (figure 1.4).

SCIENTIFIC THINKING

Question: *What is the source of contamination that occurs in a flask of nutrient broth left exposed to the air?*

Germ Hypothesis: *Preexisting microorganisms present in the air contaminate nutrient broth.*

Prediction: *Sterilized broth will remain sterile if microorganisms are prevented from entering flask.*

Spontaneous Generation Hypothesis: *Living organisms will spontaneously generate from nonliving organic molecules in broth.*

Prediction: *Organisms will spontaneously generate from organic molecules in broth after sterilization.*

Test: *Use swan-necked flasks to prevent entry of microorganisms. To ensure that broth can still support life, break swan-neck after sterilization.*

Flask is sterilized by boiling the broth.

Unbroken flask remains sterile.

Broken flask becomes contaminated after exposure to germ-laden air.

Result: *No growth occurs in sterile swan-necked flasks. When the neck is broken off, and the broth is exposed to air, growth occurs.*

Conclusion: *Growth in broth is of preexisting microorganisms.*

Figure 1.4 **Experiment to test spontaneous generation versus germ hypothesis.**

This result was predicted by the germ hypothesis—that when the sterile flask is exposed to air, airborne germs are deposited in the broth and grow. The spontaneous generation hypothesis predicted no difference in results with exposure to air. This experiment disproved the hypothesis of spontaneous generation and supported the hypothesis of airborne germs under the conditions tested.

Reductionism breaks larger systems into their component parts

Scientists use the philosophical approach of **reductionism** to understand a complex system by reducing it to its working parts. Reductionism has been the general approach of biochemistry, which has been enormously successful at unraveling the complexity of cellular metabolism by concentrating on individual pathways and specific enzymes. By analyzing all of the pathways and their components, scientists now have an overall picture of the metabolism of cells.

Reductionism has limits when applied to living systems, however—one of which is that enzymes do not always behave exactly the same in isolation as they do in their normal cellular context. A larger problem is that the complex interworking of many interconnected functions leads to emergent properties that cannot be predicted based on the workings of the parts. For example, ribosomes are the cellular factories that synthesize proteins, but this function could not be predicted based on analysis of the individual proteins and RNA that make up the structure. On a higher level, understanding the physiology of a single Canada goose would not lead to predictions about flocking behavior. The emerging field of systems biology uses mathematical and computational models to deal with the whole as well as understanding the interacting parts.

Biologists construct models to explain living systems

Biologists construct models in many different ways for a variety of uses. Geneticists construct models of interacting networks of proteins that control gene expression, often even drawing cartoon figures to represent that which we cannot see. Population biologists build models of how evolutionary change occurs. Cell biologists build models of signal transduction pathways and the events leading from an external signal to internal events. Structural biologists build actual models of the structure of proteins and macromolecular complexes in cells.

Models provide a way to organize how we think about a problem. Models can also get us closer to the larger picture and away from the extreme reductionist approach. The working parts are provided by the reductionist analysis, but the model shows how they fit together. Often these models suggest other experiments that can be performed to refine or test the model.

As researchers gain more knowledge about the actual flow of molecules in living systems, more sophisticated kinetic models can be used to apply information about isolated enzymes to their cellular context. In systems biology, this modeling is being applied on a large scale to regulatory networks during development, and even to modeling an entire bacterial cell.

The nature of scientific theories

Scientists use the word **theory** in two main ways. The first meaning of theory is a proposed explanation for some natural phenomenon, often based on some general principle. Thus, we speak of the principle first proposed by Newton as the "theory of gravity." Such theories often bring together concepts that were previously thought to be unrelated.

The second meaning of theory is the body of interconnected concepts, supported by scientific reasoning and experimental evidence, that explains the facts in some area of study. Such a theory provides an indispensable framework for organizing a body of knowledge. For example, quantum theory in physics brings together a set of ideas about the nature of the universe, explains experimental facts, and serves as a guide to further questions and experiments.

To a scientist, theories are the solid ground of science, expressing ideas of which we are most certain. In contrast, to the general public, the word theory usually implies the opposite—a *lack* of knowledge, or a guess. Not surprisingly, this difference often results in confusion. In this text, theory will always be used in its scientific sense, in reference to an accepted general principle or body of knowledge.

Some critics outside of science attempt to discredit evolution by saying it is "just a theory." The hypothesis that evolution has occurred, however, is an accepted scientific fact—it is supported by overwhelming evidence. Modern evolutionary theory is a complex body of ideas, the importance of which spreads far beyond explaining evolution. Its ramifications permeate all areas of biology, and it provides the conceptual framework that unifies biology as a science. Again, the key is how well a hypothesis fits the observations. Evolutionary theory fits the observations very well.

Research can be basic or applied

In the past it was fashionable to speak of the "scientific method" as consisting of an orderly sequence of logical, either–or steps. Each step would reject one of two mutually incompatible alternatives, as though trial-and-error testing would inevitably lead a researcher through the maze of uncertainty to the ultimate scientific answer. If this were the case, a computer would make a good scientist. But science is not done this way.

As the British philosopher Karl Popper has pointed out, successful scientists without exception design their experiments with a pretty fair idea of how the results are going to come out. They have what Popper calls an "imaginative preconception" of what the truth might be. Because insight and imagination play such a large role in scientific progress, some scientists are better at science than others—just as Bruce Springsteen stands out among songwriters or Claude Monet stands out among Impressionist painters.

Some scientists perform *basic research,* which is intended to extend the boundaries of what we know. These individuals typically work at universities, and their research is usually supported by grants from various agencies and foundations.

The information generated by basic research contributes to the growing body of scientific knowledge, and it provides the scientific foundation utilized by *applied research.* Scientists who

conduct applied research are often employed in some kind of industry. Their work may involve the manufacture of food additives, the creation of new drugs, or the testing of environmental quality.

Research results are written up and submitted for publication in scientific journals, where the experiments and conclusions are reviewed by other scientists. This process of careful evaluation, called *peer review,* lies at the heart of modern science. It helps to ensure that faulty research or false claims are not given the authority of scientific fact. It also provides other scientists with a starting point for testing the reproducibility of experimental results. Results that cannot be reproduced are not taken seriously for long.

Learning Outcomes Review 1.2

Much of science is descriptive, amassing observations to gain an accurate view. Both deductive reasoning and inductive reasoning are used in science. Scientific hypotheses are suggested explanations for observed phenomena. Hypotheses need to make predictions that can be tested by controlled experiments. Theories are coherent explanations of observed data, but they may be modified by new information.

- ***How does a scientific theory differ from a hypothesis?***

1.3 An Example of Scientific Inquiry: Darwin and Evolution

Learning Outcomes

1. *Examine Darwin's theory of evolution by natural selection as a scientific theory.*
2. *Describe the evidence that supports the theory of evolution.*

Darwin's theory of evolution explains and describes how organisms on Earth have changed over time and acquired a diversity of new forms. This famous theory provides a good example of how a scientist develops a hypothesis and how a scientific theory grows and wins acceptance.

Charles Robert Darwin (1809–1882; figure 1.5) was an English naturalist who, after 30 years of study and observation, wrote one of the most famous and influential books of all time. This book, *On the Origin of Species by Means of Natural Selection,* created a sensation when it was published, and the ideas Darwin expressed in it have played a central role in the development of human thought ever since.

The idea of evolution existed prior to Darwin

In Darwin's time, most people believed that the different kinds of organisms and their individual structures resulted from direct actions of a Creator (many people still believe this). Species were thought to have been specially created and to be unchangeable over the course of time.

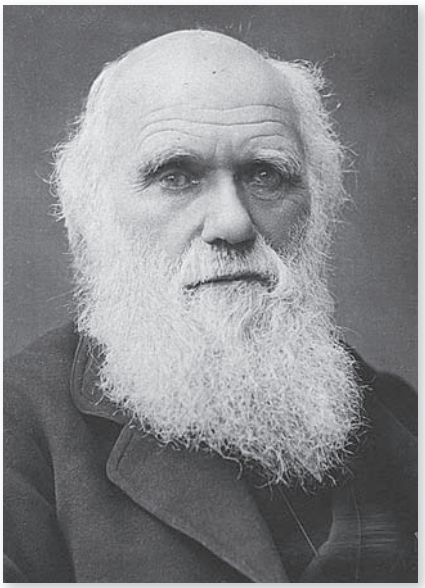


Figure 1.5 Charles Darwin. This newly rediscovered photograph taken in 1881, the year before Darwin died, appears to be the last ever taken of the great biologist.

In contrast to these ideas, a number of earlier naturalists and philosophers had presented the view that living things must have changed during the history of life on Earth. That is, **evolution** has occurred, and living things are now different from how they began. Darwin's contribution was a concept he called *natural selection,* which he proposed as a coherent, logical explanation for this process, and he brought his ideas to wide public attention.

Darwin observed differences in related organisms

The story of Darwin and his theory begins in 1831, when he was 22 years old. He was part of a five-year navigational mapping expedition around the coasts of South America (figure 1.6), aboard H.M.S. *Beagle.* During this long voyage, Darwin had the chance to study a wide variety of plants and animals on continents and islands and in distant seas. Darwin observed a number of phenomena that were of central importance to his reaching his ultimate conclusion.

Repeatedly, Darwin saw that the characteristics of similar species varied somewhat from place to place. These geographical patterns suggested to him that lineages change gradually as species migrate from one area to another. On the Galápagos Islands, 960 km (600 miles) off the coast of Ecuador, Darwin encountered a variety of different finches on the various islands. The 14 species, although related, differed slightly in appearance, particularly in their beaks (figure 1.7).

Darwin thought it was reasonable to assume that all these birds had descended from a common ancestor arriving from the South American mainland several million years ago. Eating different foods on different islands, the finches' beaks had changed during their descent—"descent with modification," or evolution. (These finches are discussed in more detail in chapters 21 and 22.)

Figure 1.6 The five-year voyage of H.M.S. *Beagle*. Most of the time was spent exploring the coasts and coastal islands of South America, such as the Galápagos Islands. Darwin's studies of the animals of the Galápagos Islands played a key role in his eventual development of the concept of evolution by means of natural selection.

In a more general sense, Darwin was struck by the fact that the plants and animals on these relatively young volcanic islands resembled those on the nearby coast of South America. If each one of these plants and animals had been created independently and simply placed on the Galápagos Islands, why didn't they resemble the plants and animals of islands with similar climates—such as those off the coast of Africa, for example? Why did they resemble those of the adjacent South American coast instead?

Darwin proposed natural selection as a mechanism for evolution

It is one thing to observe the results of evolution, but quite another to understand how it happens. Darwin's great achievement lies in his ability to move beyond all the individual observations to formulate the hypothesis that evolution occurs because of natural selection.

Figure 1.7 Three Galápagos finches and what they eat. On the Galápagos Islands, Darwin observed 14 different species of finches differing mainly in their beaks and feeding habits. These three finches eat very different food items, and Darwin surmised that the different shapes of their bills represented evolutionary adaptations that improved their ability to eat the foods available in their specific habitats.

Darwin and Malthus

Of key importance to the development of Darwin's insight was his study of Thomas Malthus's *An Essay on the Principle of Population* (1798). In this book, Malthus stated that populations of plants and animals (including humans) tend to increase geometrically, while humans are able to increase their food supply only arithmetically. Put another way, population increases by a multiplying factor—for example, in the series 2, 6, 18, 54, the starting number is multiplied by 3. Food supply increases by an additive factor—for example, the series 2, 4, 6, 8 adds 2 to each starting number. Figure 1.8 shows the difference that these two types of relationships produce over time.

Because populations increase geometrically, virtually any kind of animal or plant, if it could reproduce unchecked, would cover the entire surface of the world surprisingly quickly. Instead, populations of species remain fairly constant year after year, because death limits population numbers.

Sparked by Malthus's ideas, Darwin saw that although every organism has the potential to produce more offspring than can survive, only a limited number actually do survive and produce further offspring. Combining this observation with what he had seen on the voyage of the *Beagle,* as well as with his own experiences in breeding domestic animals, Darwin made an important association: Individuals possessing physical, behavioral, or other attributes that give them an advantage in their environment are more likely to survive and reproduce than those with less advantageous traits. By surviving, these individuals gain the opportunity to pass on their favorable characteristics to their offspring. As the frequency of these characteristics increases in the population, the nature of the population as a whole will gradually change. Darwin called this process *selection.*

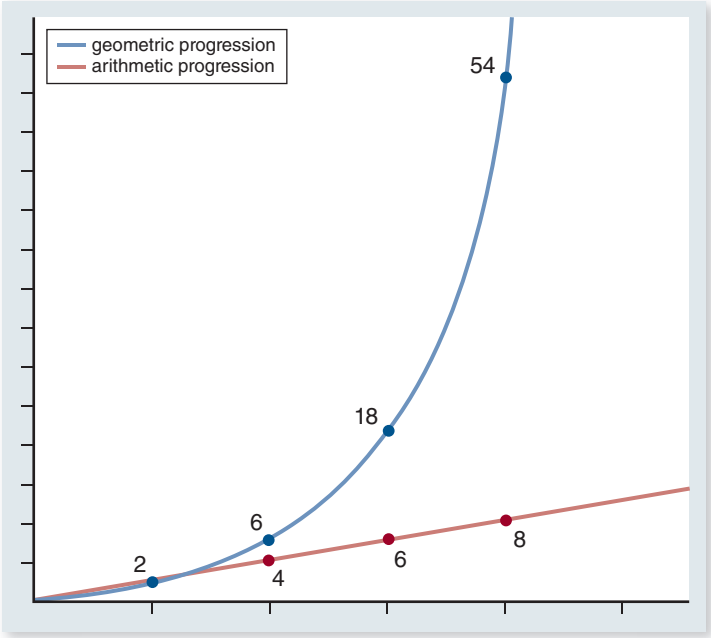


Figure 1.8 Geometric and arithmetic progressions. A geometric progression increases by a constant factor (for example, the curve shown increases ×3 for each step), whereas an arithmetic progression increases by a constant difference (for example, the line shown increases +2 for each step). Malthus contended that the human growth curve was geometric, but the human food production curve was only arithmetic.

Data analysis What is the effect of reducing the constant factor for a geometric progression? How would this change the curve in the figure?

Inquiry question Might this effect be achieved with humans? How?

Natural selection

Darwin was thoroughly familiar with variation in domesticated animals, and he began *On the Origin of Species* with a detailed discussion of pigeon breeding. He knew that animal breeders selected certain varieties of pigeons and other animals, such as dogs, to produce certain characteristics, a process Darwin called **artificial selection.**

Artificial selection often produces a great variation in traits. Domestic pigeon breeds, for example, show much greater variety than all of the wild species found throughout the world. Darwin thought that this type of change could occur in nature, too. Surely if pigeon breeders could foster variation by artificial selection, nature could do the same—a process Darwin called **natural selection.**

Darwin drafts his argument

Darwin drafted the overall argument for evolution by natural selection in a preliminary manuscript in 1842. After showing the manuscript to a few of his closest scientific friends, however, Darwin put it in a drawer, and for 16 years turned to other research. No one knows for sure why Darwin did not publish his initial manuscript—it is very thorough and outlines his ideas in detail.

The stimulus that finally brought Darwin's hypothesis into print was an essay he received in 1858. A young English naturalist named Alfred Russel Wallace (1823–1913) sent the essay to Darwin from Indonesia; it concisely set forth the hypothesis of evolution by means of natural selection, a hypothesis Wallace had developed independently of Darwin. After receiving Wallace's essay, friends of Darwin arranged for a joint presentation of their ideas at a seminar in London. Darwin then completed his own book, expanding the 1842 manuscript he had written so long ago, and submitted it for publication.

The predictions of natural selection have been tested

More than 130 years have elapsed since Darwin's death in 1882. During this period, the evidence supporting his theory has grown progressively stronger. We briefly explore some of this evidence here; in chapter 21, we will return to the theory of evolution by natural selection and examine the evidence in more detail.

The fossil record

Darwin predicted that the fossil record would yield intermediate links between the great groups of organisms—for example, between fishes and the amphibians thought to have arisen from them, and between reptiles and birds. Furthermore, natural selection predicts the relative positions in time of such transitional forms. We now know the fossil record to a degree that was unthinkable in the

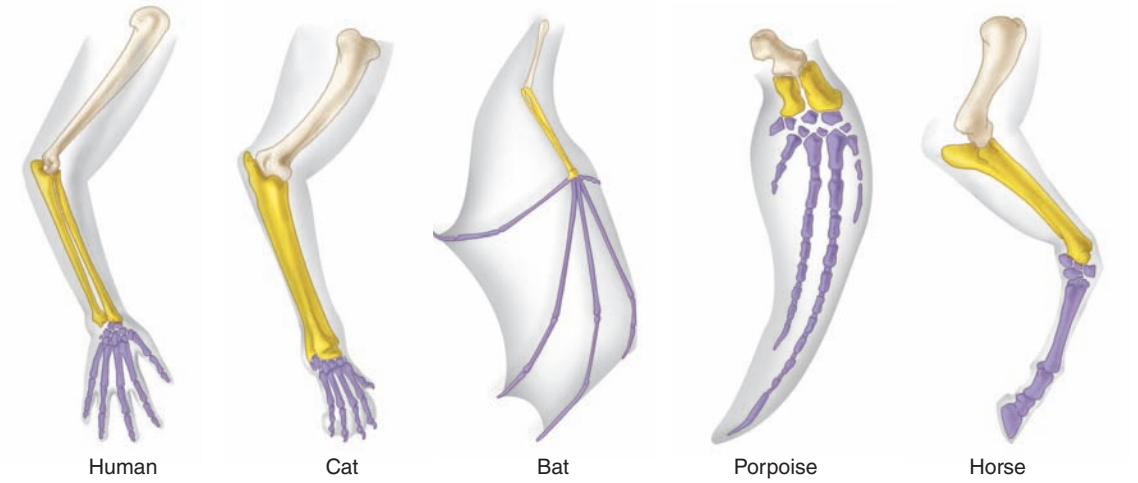


Figure 1.9 Homology among vertebrate limbs. The forelimbs of these five vertebrates show the ways in which the relative proportions of the forelimb bones have changed in relation to the particular way of life of each organism.

19th century, and although truly "intermediate" organisms are hard to determine, paleontologists have found what appear to be transitional forms and found them at the predicted positions in time.

Recent discoveries of microscopic fossils have extended the known history of life on Earth back to about 3.5 billion years ago (BYA). The discovery of other fossils has supported Darwin's predictions and has shed light on how organisms have, over this enormous time span, evolved from the simple to the complex. For vertebrate animals especially, the fossil record is rich and exhibits a graded series of changes in form, with the evolutionary sequence visible for all to see.

The age of the Earth

Darwin's theory predicted the Earth must be very old, but some physicists argued that the Earth was only a few thousand years old. This bothered Darwin, because the evolution of all living things from some single original ancestor would have required a great deal more time. Using evidence obtained by studying the rates of radioactive decay, we now know that the physicists of Darwin's time were very wrong: The Earth was formed about 4.5 BYA.

The mechanism of heredity

Darwin received some of his sharpest criticism in the area of heredity. At that time, no one had any concept of genes or how heredity works, so it was not possible for Darwin to explain completely how evolution occurs.

Even though Gregor Mendel was performing his experiments with pea plants in Brünn, Austria (now Brno, the Czech Republic), during roughly the same period, genetics was established as a science only at the start of the 20th century. When scientists began to understand the laws of inheritance (discussed in chapters 12 and 13), this problem with Darwin's theory vanished.

Comparative anatomy

Comparative studies of animals have provided strong evidence for Darwin's theory. In many different types of vertebrates, for example, the same bones are present, indicating their evolutionary past. Thus, the forelimbs shown in figure 1.9 are all constructed from the same basic array of bones, modified for different purposes.

These bones are said to be **homologous** in the different vertebrates—that is, they have the same evolutionary origin, but they now differ in structure and function. They are contrasted with **analogous** structures, such as the wings of birds and butterflies, which have similar function but different evolutionary origins.

Molecular evidence

Evolutionary patterns are also revealed at the molecular level. By comparing the genomes (that is, the sequences of all the genes) of different groups of animals or plants, we can more precisely specify the degree of relationship among the groups. A series of evolutionary changes over time should involve a continual accumulation of genetic changes in the DNA.

This difference can be seen clearly in the protein hemoglobin (figure 1.10). Rhesus monkeys, which like humans are primates, have fewer differences from humans in the 146-amino-acid

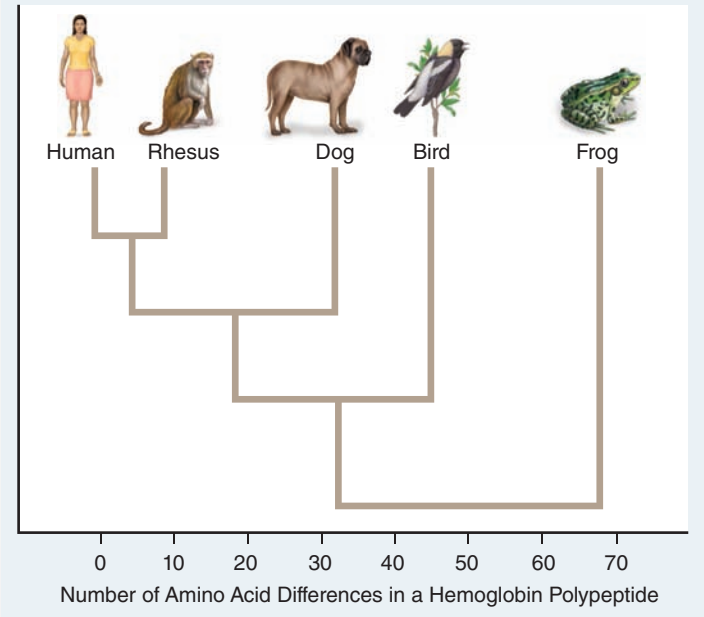


Figure 1.10 Molecules reflect evolutionary patterns. Vertebrates that are more distantly related to humans have a greater number of amino acid differences in the hemoglobin polypeptide.

Inquiry question Where do you imagine a snake might fall on the graph? Why?

hemoglobin β chain than do more distantly related mammals, such as dogs. Nonmammalian vertebrates, such as birds and frogs, differ even more.

The sequences of some genes, such as the ones specifying the hemoglobin proteins, have been determined in many organisms, and the entire time course of their evolution can be laid out with confidence by tracing the origins of particular nucleotide changes in the gene sequence. The pattern of descent obtained is called a **phylogenetic tree.** It represents the evolutionary history of the gene, its "family tree." Molecular phylogenetic trees agree well with those derived from the fossil record, which is strong direct evidence of evolution. The pattern of accumulating DNA changes represents, in a real sense, the footprints of evolutionary history.

Learning Outcomes Review 1.3

Darwin observed differences in related organisms and proposed the hypothesis of evolution by natural selection to explain these differences. The predictions generated by natural selection have been tested and continue to be tested by analysis of the fossil record, genetics, comparative anatomy, and even the DNA of living organisms.

- ***Does Darwin's theory of evolution by natural selection explain the origin of life?***

1.4 Unifying Themes in Biology

Learning Outcomes

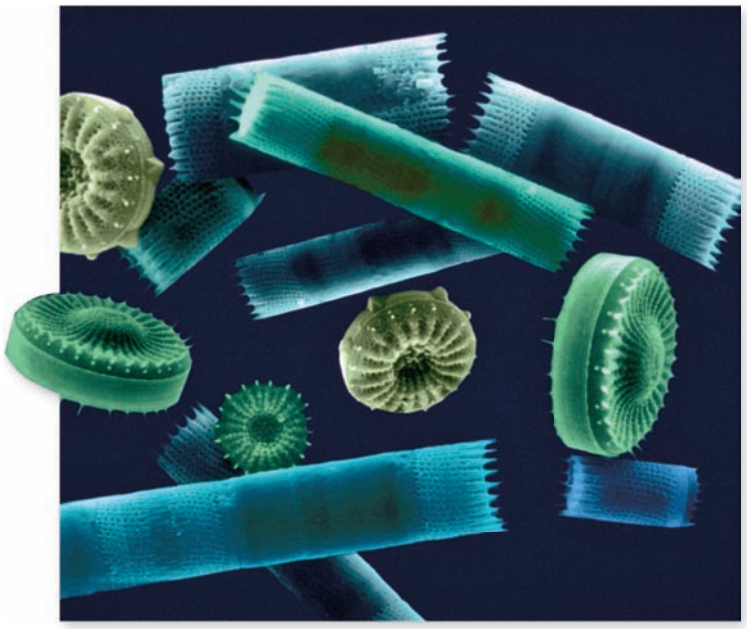
1. *Discuss the unifying themes in biology.*
2. *Contrast living and nonliving systems.*

The study of biology encompasses a large number of different subdisciplines, ranging from biochemistry to ecology. In all of these, however, unifying themes can be identified. Among these are cell theory, the molecular basis of inheritance, the relationship between structure and function, evolution, and the emergence of novel properties.

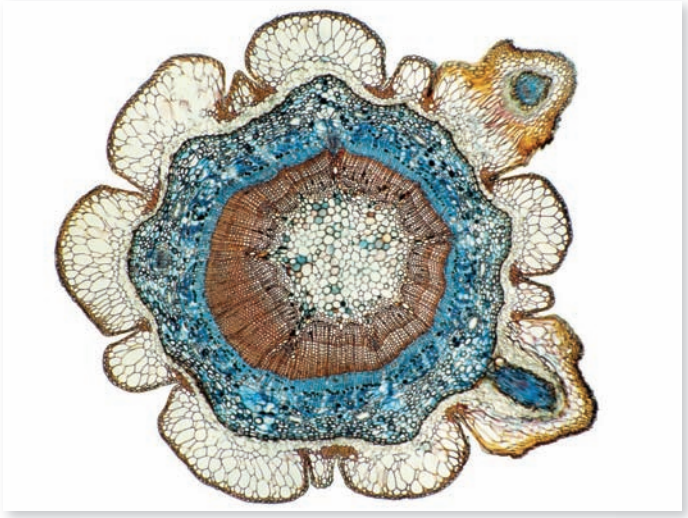
Living systems are organized into cells

As was stated at the beginning of this chapter, all organisms are composed of cells, life's basic units (figure 1.11). Cells were discovered by Robert Hooke in England in 1665, using one of the first microscopes, one that magnified 30 times. Not long after that, the Dutch scientist Anton van Leeuwenhoek used microscopes capable of magnifying 300 times and discovered an amazing world of single-celled life in a drop of pond water.

In 1839, the German biologists Matthias Schleiden and Theodor Schwann, summarizing a large number of observations by themselves and others, concluded that all living organisms consist of cells. Their conclusion has come to be known as the **cell theory.** Later, biologists added the idea that all cells come from preexisting cells. The cell theory, one of the basic ideas in biology, is the foundation for understanding the reproduction and growth of all organisms.



a.



b.

Figure 1.11 Cellular basis of life. All organisms are composed of cells. Some organisms, including the protists, shown in part ***(a)*** are single-celled. Others, such as the plant shown in cross section in part ***(b)*** consist of many cells.

The molecular basis of inheritance explains the continuity of life

Even the simplest cell is incredibly complex—more intricate than any computer. The information that specifies what a cell is like—its detailed plan—is encoded in **deoxyribonucleic acid (DNA),** a long, cablelike molecule. Each DNA molecule is formed from two long chains of building blocks, called nucleotides, wound around each other (see chapter 14). Four different nucleotides are found in DNA, and the sequence in which they occur encodes the cell's information. Specific sequences of several hundred to many thousand nucleotides make up a **gene,** a discrete unit of information.

The continuity of life from one generation to the next—heredity—depends on the faithful copying of a cell's DNA into daughter cells. The entire set of DNA instructions that specifies a cell is called its *genome*. The sequence of the human genome, 3 billion nucleotides long, was decoded in rough draft form in 2001, a triumph of scientific investigation.

The relationship between structure and function underlies living systems

One of the unifying themes of molecular biology is the relationship between structure and function. Function in molecules, and larger macromolecular complexes, is dependent on their structure.

Although this observation may seem trivial, it has far-reaching implications. We study the structure of molecules and macromolecular complexes to learn about their function. When we know the function of a particular structure, we can infer the function of similar structures found in different contexts, such as in different organisms.

Biologists study both aspects, looking for the relationships between structure and function. On the one hand, this allows similar structures to be used to infer possible similar functions. On the other hand, this knowledge also gives clues as to what kinds of structures may be involved in a process if we know about the functionality.

For example, suppose that we know the structure of a human cell's surface receptor for insulin, the hormone that controls uptake of glucose. We then find a similar molecule in the membrane of a cell from a different species—perhaps even a very different organism, such as a worm. We might conclude that this membrane molecule acts as a receptor for an insulin-like molecule produced by the worm. In this way, we might be able to discern the evolutionary relationship between glucose uptake in worms and in humans.

The diversity of life arises by evolutionary change

The unity of life that we see in certain key characteristics shared by many related life-forms contrasts with the incredible diversity of living things in the varied environments of Earth. The underlying unity of biochemistry and genetics argues that all life has evolved from the same origin event. The diversity of life arises by evolutionary change leading to the present biodiversity we see.

Biologists divide life's great diversity into three great groups, called domains: Bacteria, Archaea, and Eukarya (figure 1.12). The domains Bacteria and Archaea are composed of single-celled organisms *(prokaryotes)* with little internal structure, and the domain Eukarya is made up of organisms *(eukaryotes)* composed of a complex, organized cell or multiple complex cells.

Within Eukarya are four main groups called kingdoms (figure 1.12). Kingdom Protista consists of all the unicellular eukaryotes except yeasts (which are fungi), as well as the multicellular algae. Because of the great diversity among the protists, many biologists feel kingdom Protista should be split into several kingdoms.

Kingdom Plantae consists of organisms that have cell walls of cellulose and obtain energy by photosynthesis. Organisms in the kingdom Fungi have cell walls of chitin and obtain energy by secreting digestive enzymes and then absorbing the products they release from the external environment. Kingdom Animalia contains organisms that lack cell walls and obtain energy by first ingesting other organisms and then digesting them internally.

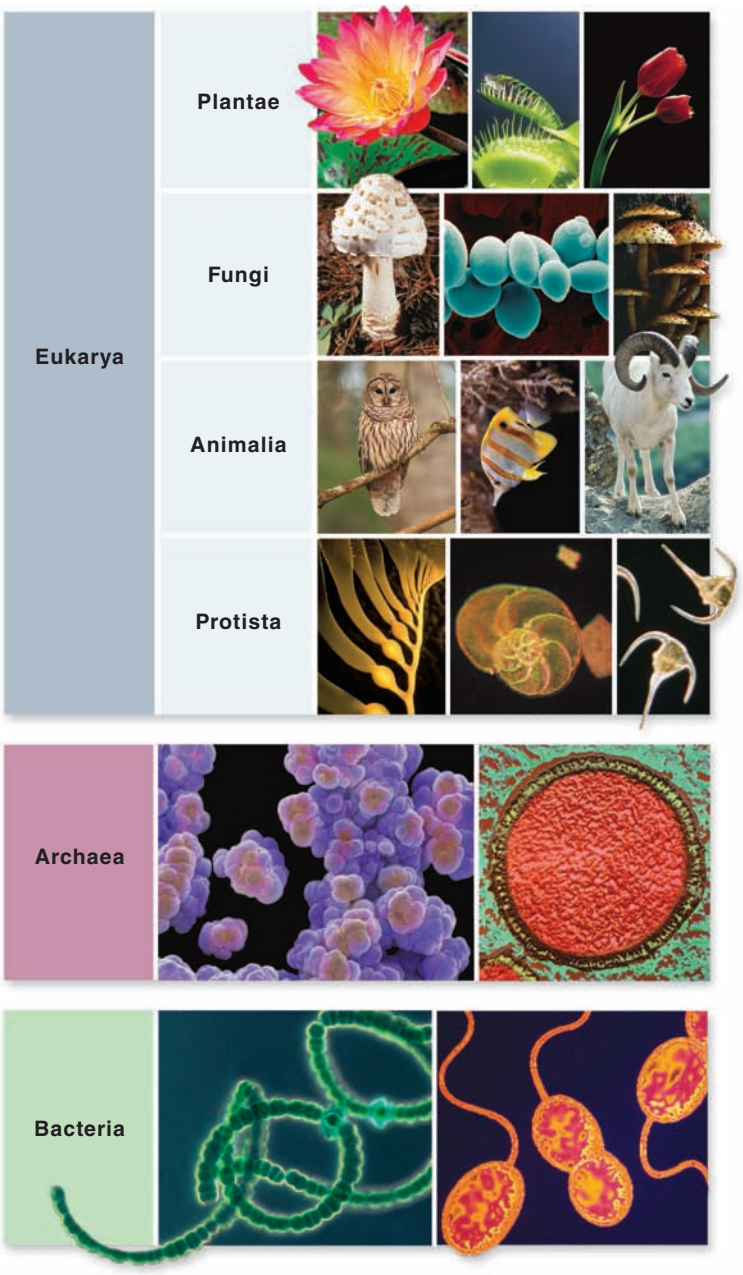


Figure 1.12 The diversity of life. Biologists categorize all living things into three overarching groups called domains: Bacteria, Archaea, and Eukarya. Domain Eukarya is composed of four kingdoms: Plantae, Fungi, Animalia, and Protista.

Evolutionary conservation explains the unity of living systems

Biologists agree that all organisms alive today have descended from some simple cellular creature that arose about 3.5 BYA. Some of the characteristics of that earliest organism have been preserved.

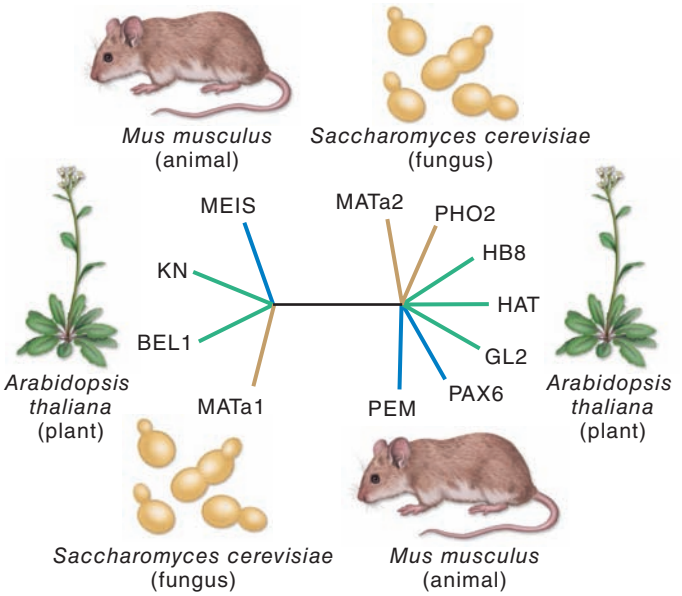


Figure 1.13 Tree of homeodomain proteins.
Homeodomain proteins are found in fungi *(brown),* plants *(green),* and animals *(blue).* Based on their sequence similarities, these 11 different homeodomain proteins (uppercase letters at the ends of branches) fall into two groups, with representatives from each kingdom in each group. That means, for example, the mouse homeodomain protein PAX6 is more closely related to fungal and flowering plant proteins, such as PHO2 and GL2, than it is to the mouse protein MEIS.

The storage of hereditary information in DNA, for example, is common to all living things.

Evolutionary conservation of characteristics through a long line of descent usually reflects that they have a fundamental role in the biology of the organism—one not easily changed once adopted. A good example is provided by the homeodomain proteins, which play critical roles in early development in eukaryotes. Conserved characteristics can be seen in approximately 1850 homeodomain proteins, distributed among three different kingdoms of organisms (figure 1.13). The homeodomain proteins are powerful developmental tools that evolved early, and for which no better alternative has arisen.

Cells are information-processing systems

One way to think about cells is as highly complex nanomachines that process information. The information stored in DNA is used to direct the synthesis of cellular components, and the particular set of components can differ from cell to cell. The way that proteins fold in space is a form of information that is three-dimensional, and interesting properties emerge from the interaction of these shapes in macromolecular complexes. The control of gene expression allows differentiation of cell types in time and space, leading to changes over developmental time into different tissue types—even though all cells in an organism carry the same genetic information.

Cells also process information that they receive about the environment. Cells sense their environment through proteins in their membranes, and this information is transmitted across the membrane to elaborate signal-transduction chemical pathways that can change the functioning of a cell.

This ability of cells to sense and respond to their environment is critical to the function of tissues and organs in multicellular organisms. A multicellular organism can regulate its internal environment, maintaining constant temperature, pH, and concentrations of vital ions. This homeostasis is possible because of elaborate signaling networks that coordinate the activities of different cells in different tissues.

Living systems exist in a nonequilibrium state

A key feature of living systems is that they are open systems that function far from thermodynamic equilibrium. This has a number of implications for their behavior. A constant supply of energy is necessary to maintain a stable nonequilibrium state. Consider the state of the nucleic acids, and proteins in all of your cells: At equilibrium they are not polymers, they would all be hydrolyzed to monomer nucleotides and amino acids. Second, nonequilibrium systems exhibit self-organizing properties not seen in equilibrium systems.

These self-organizing properties of living systems show up at different levels of the hierarchical organization. At the cellular level, macromolecular complexes such as the spindle necessary for chromosome separation can self-organize. At the population level, a flock of birds, a school of fish, or the bacteria in a biofilm are all also self-organizing. This kind of interacting behavior of individual units leads to emergent properties that are not predictable from the nature of the units themselves.

Emergent properties are properties of collections of molecules, cells, individuals, that are distinct from the categorical properties that can be described by such statistics as mean and standard deviation. The mathematics necessary to describe these kind of interacting systems is nonlinear dynamics. The emerging field of systems biology is beginning to model biological systems in this way. The kinds of feedback and feedforward loops that exist between molecules in cells, or neurons in a nervous system, lead to emergent behaviors like human consciousness.

Learning Outcomes Review 1.4

Biology is a broad and complex field, but we can identify unifying themes in this complexity. Cells are the basic unit of life, and they are information-processing machines. The structures of molecules, macromolecular complexes, cells, and even higher levels of organization are related to their functions. The diversity of life can be classified and organized based on similar features; biologists identify three large domains that encompass six kingdoms. Living organisms are able to use energy to construct complex molecules from simple ones, and are thus not in a state of thermodynamic equilibrium.

- ***How do viruses fit into our definitions of living systems?***

Chapter Review

1.1 The Science of Life

Biology unifies much of natural science.

The study of biological systems is interdisciplinary because solutions require many different approaches to solve a problem.

Life defies simple definition.

Although life is difficult to define, living systems have seven characteristics in common. They are composed of one or more cells; are complex and highly ordered; can respond to stimuli; can grow, reproduce, and transmit genetic information to their offspring; need energy to accomplish work; can maintain relatively constant internal conditions (homeostasis); and are capable of evolutionary adaptation to the environment.

Living systems show hierarchical organization.

The hierarchical organization of living systems progresses from atoms to the biosphere. At each higher level, emergent properties arise that are greater than the sum of the parts.

1.2 The Nature of Science

At its core, science is concerned with understanding the nature of the world by using observation and reasoning.

Much of science is descriptive.

Science is concerned with developing an increasingly accurate description of nature through observation and experimentation.

Science uses both deductive and inductive reasoning.

Deductive reasoning applies general principles to predict specific results. Inductive reasoning uses specific observations to construct general scientific principles.

Hypothesis-driven science makes and tests predictions.

Hypotheses are based on observations, and generate testable predictions. Experiments involve a test where a variable is manipulated, and a control where the variable is not manipulated. If the predictions cannot be verified the hypothesis is rejected.

Reductionism breaks larger systems into their component parts.

Reductionism attempts to understand a complex system by breaking it down into its component parts. It is limited because parts may act differently when isolated from the larger system.

Biologists construct models to explain living systems.

A model provides a way of organizing our thinking about a problem; models may also suggest experimental approaches.

The nature of scientific theories.

Scientists use the word *theory* in two main ways: as a proposed explanation for some natural phenomenon and as a body of concepts that explains facts in an area of study.

Research can be basic or applied.

Basic research extends the boundaries of what we know; applied research seeks to use scientific findings in practical areas such as agriculture, medicine, and industry.

1.3 An Example of Scientific Inquiry: Darwin and Evolution

Darwin's theory of evolution shows how a scientist develops a hypothesis and sets forth evidence, as well as how a scientific theory grows and gains acceptance.

The idea of evolution existed prior to Darwin.

A number of naturalists and philosophers had suggested living things had changed during Earth's history. Darwin's contribution was the concept of natural selection as a mechanism for evolutionary change.

Darwin observed differences in related organisms.

During the voyage of the H.M.S. *Beagle,* Darwin had an opportunity to observe worldwide patterns of diversity.

Darwin proposed natural selection as a mechanism for evolution.

Darwin noted that species produce many more offspring than will survive and reproduce. He observed that traits can be changed by artificial selection. Darwin proposed that individuals possessing traits that increase survival and reproductive success become more numerous in populations over time. Darwin called this descent with modification (natural selection). Alfred Russel Wallace independently came to the same conclusions.

The predictions of natural selection have been tested.

Natural selection has been tested using data from many fields. Among these are the fossil record; the age of the Earth, determined by rates of radioactive decay to be 4.5 billion years; genetic experiments showing that traits can be inherited as discrete units; comparative anatomy and the study of homologous structures; and molecular data that provide evidence for changes in DNA and proteins over time.

Taken together, these findings strongly support evolution by natural selection. No data to conclusively disprove evolution have been found.

1.4 Unifying Themes in Biology

Living systems are organized into cells.

The cell is the basic unit of life and is the foundation for understanding growth and reproduction in all organisms.

The molecular basis of inheritance explains the continuity of life.

Hereditary information, encoded in genes found in the DNA molecule, is passed on from one generation to the next.

The relationship between structure and function underlies living systems.

The function of macromolecules and their complexes is dictated by and dependent on their structure. Similarity of structure and function from one life-form to another may indicate an evolutionary relationship.

The diversity of life arises by evolutionary change.

Living organisms appear to have had a common origin from which a diversity of life arose by evolutionary change. They can be grouped into three domains comprising six kingdoms based on their differences.

Evolutionary conservation explains the unity of living systems.

The underlying similarities in biochemistry and genetics support the contention that all life evolved from a single source.

Cells are information-processing systems.

Cells can sense and respond to environmental changes through proteins located on their cell membranes. Differential expression of stored genetic information is the basis for different cell types.

Living systems exist in a nonequilibrium state.

Organisms are open systems that need a constant supply of energy to maintain their stable nonequilibrium state. Living things are able to self-organize, creating levels of complexity that may exhibit emergent properties.

Review Questions

UNDERSTAND

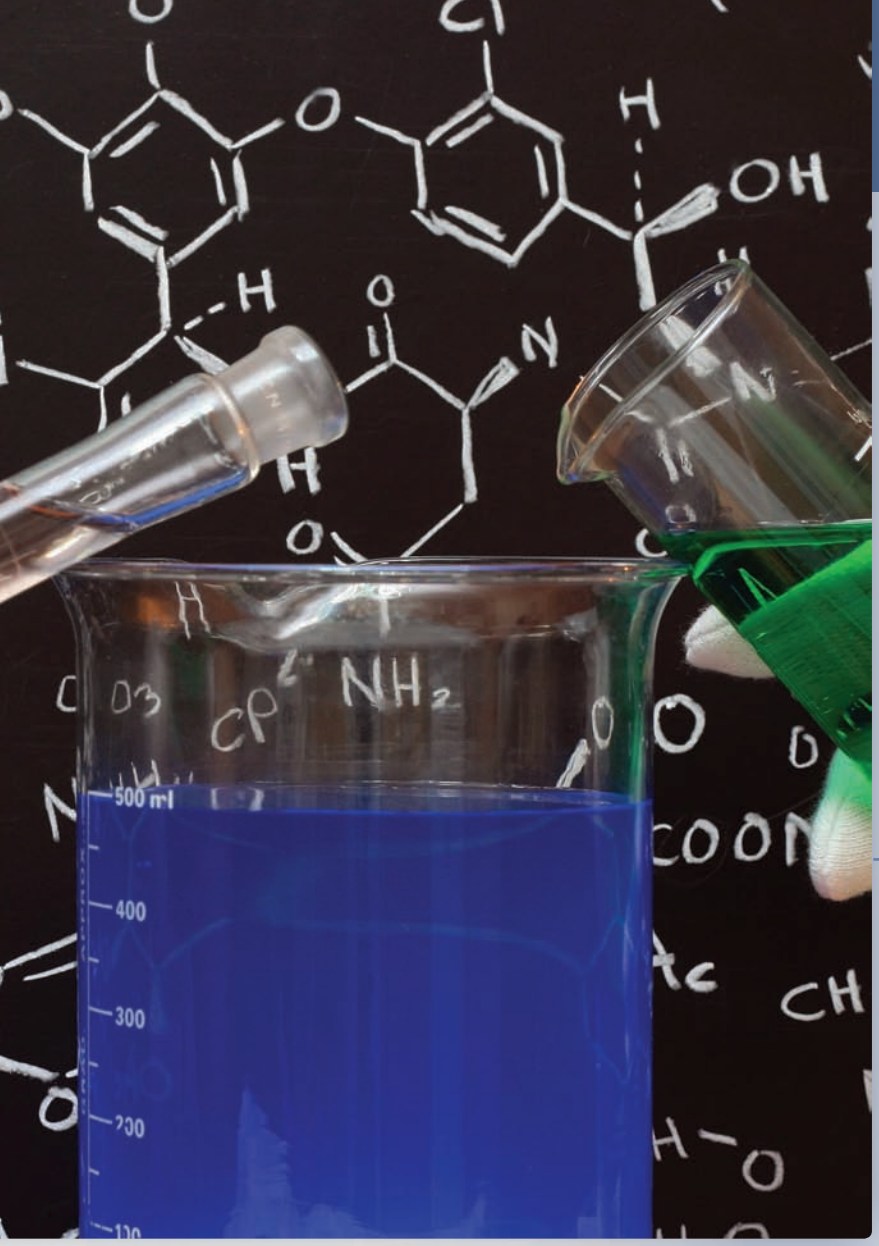
1. Which of the following is NOT a property of life?
   a. Energy utilization
   b. Movement
   c. Order
   d. Homeostasis
2. The process of inductive reasoning involves
   a. the use of general principles to predict a specific result.
   b. the generation of specific predictions based on a belief system.
   c. the use of specific observations to develop general principles.
   d. the use of general principles to support a hypothesis.
3. A hypothesis in biology is best described as
   a. a possible explanation of an observation.
   b. an observation that supports a theory.
   c. a general principle that explains some aspect of life.
   d. an unchanging statement that correctly predicts some aspect of life.
4. A scientific theory is
   a. a guess about how things work in the world.
   b. a statement of how the world works that is supported by experimental data.
   c. a belief held by many scientists.
   d. Both a and c are correct.
5. The cell theory states that
   a. cells are small.
   b. cells are highly organized.
   c. there is only one basic type of cell.
   d. all living things are made up of cells.
6. The molecule DNA is important to biological systems because
   a. it can be replicated.
   b. it encodes the information for making a new individual.
   c. it forms a complex, double-helical structure.
   d. nucleotides form genes.
7. The organization of living systems is
   a. linear with cells at one end and the biosphere at the other.
   b. circular with cells in the center.
   c. hierarchical with cells at the base, and the biosphere at the top.
   d. chaotic and beyond description.
8. The idea of evolution
   a. was original to Darwin.
   b. was original to Wallace.
   c. predated Darwin and Wallace.
   d. Both a and b are correct.

APPLY

1. What is the significance of Pasteur's experiment to test the germ hypothesis?
   a. It proved that heat can sterilize a broth.
   b. It demonstrated that cells can arise spontaneously.
   c. It demonstrated that some cells are germs.
   d. It demonstrated that cells can only arise from other cells.
2. Which of the following is NOT an example of reductionism?
   a. Analysis of an isolated enzyme's function in an experimental assay
   b. Investigation of the effect of a hormone on cell growth in a Petri dish
   c. Observation of the change in gene expression in response to specific stimulus
   d. An evaluation of the overall behavior of a cell
3. How is the process of natural selection different from that of artificial selection?
   a. Natural selection produces more variation.
   b. Natural selection makes an individual better adapted.
   c. Artificial selection is a result of human intervention.
   d. Artificial selection results in better adaptations.
4. If you found a fossil for a modern organism next to the fossil of a dinosaur, this would
   a. argue against evolution by natural selection.
   b. have no bearing on evolution by natural selection.
   c. indicate that dinosaurs may still exist.
   d. Both b and c are correct.
5. The theory of evolution by natural selection is a good example of how science proceeds because
   a. it rationalizes a large body of observations.
   b. it makes predictions that have been tested by a variety of approaches.
   c. it represents Darwin's belief of how life has changed over time.
   d. Both b and c are correct.
6. In which domain of life would you find only single-celled organisms?
   a. Eukarya
   b. Bacteria
   c. Archaea
   d. Both b and c are correct.
7. Evolutionary conservation occurs when a characteristic is
   a. important to the life of the organism.
   b. not influenced by evolution.
   c. no longer functionally important.
   d. found in more primitive organisms.

SYNTHESIZE

1. Exobiology is the study of life on other planets. In recent years, scientists have sent various spacecraft out into the galaxy in search for extraterrestrial life. Assuming that all life shares common properties, what should exobiologists be looking for as they explore other worlds?
2. The classic experiment by Pasteur (figure 1.4) tested the hypothesis that cells arise from other cells. In this experiment cell growth was measured following sterilization of broth in a swan-necked flask or in a flask with a broken neck.
   a. Which variables were kept the same in these two experiments?
   b. How does the shape of the flask affect the experiment?
   c. Predict the outcome of each experiment based on the two hypotheses.
   d. Some bacteria (germs) are capable of producing heat-resistant spores that protect the cell and allow it to continue to grow after the environment cools. How would the outcome of this experiment have been affected if spore-forming bacteria were present in the broth?



CHAPTER 2

The Nature of Molecules and the Properties of Water

Chapter Contents

Introduction

About 12.5 billion years ago (BYA), an enormous explosion probably signaled the beginning of the universe. This explosion started a process of star building and planetary formation that eventually led to the formation of Earth, about 4.5 BYA. Around 3.5 BYA, life began on Earth and started to diversify. To understand the nature of life on Earth, we first need to understand the nature of the matter that forms the building blocks of all life.

The earliest speculations about the world around us included this most basic question, "What is it made of?" The ancient Greeks recognized that larger things may be built of smaller parts. This concept was formed into a solid experimental scientific idea in the early 20th century, when physicists began trying to break atoms apart. From those humble beginnings to the huge particle accelerators used by the modern physicists of today, the picture of the atomic world emerges as fundamentally different from the tangible, macroscopic world around us.

To understand how living systems are assembled, we must first understand a little about atomic structure, about how atoms can be linked together by chemical bonds to make molecules, and about the ways in which these small molecules are joined together to make larger molecules, until finally we arrive at the structures of cells and then of organisms. Our study of life on Earth therefore begins with physics and chemistry. For many of you, this chapter will be a review of material encountered in other courses.

2.1 The Nature of Atoms

Learning Outcomes

1. *Define an element based on its composition.*
2. *Describe the relationship between atomic structure and chemical properties.*
3. *Explain where electrons are found in an atom.*

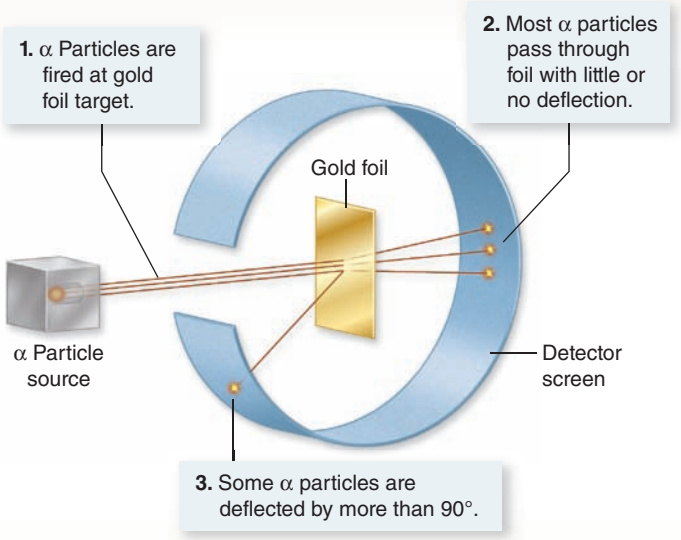
Any substance in the universe that has mass and occupies space is defined as *matter*. All matter is composed of extremely small particles called **atoms.** Because of their size, atoms are difficult to study. Not until early in the 20th century did scientists carry out the first experiments revealing the physical nature of atoms (figure 2.1).

SCIENTIFIC THINKING

Hypothesis: *Atoms are composed of diffuse positive charge with embedded negative charge (electrons).*

Prediction: *If alpha (α) particles, which are helium nuclei, are shot at a thin foil of gold, the α particles will not be deflected much by the diffuse positive charge or by the light electrons.*

Test: *α Particles are shot at a thin sheet of gold foil surrounded by a detector screen, which shows flashes of light when hit by the particles.*



Result: *Most particles are not deflected at all, but a small percentage of particles are deflected at angles of 90° or more.*

Conclusion: *The hypothesis is not supported. The large deflections observed led to a view of the atom as composed of a very small central region containing positive charge (the nucleus) surrounded by electrons.*

Further Experiments: *How does the Bohr atom with its quantized energy for electrons extend this model?*

Figure 2.1 Rutherford scattering experiment. Large-angle scattering of α particles led Rutherford to propose the existence of the nucleus.

Atomic structure includes a central nucleus and orbiting electrons

Objects as small as atoms can be "seen" only indirectly, by using complex technology such as tunneling microscopy (figure 2.2). We now know a great deal about the complexities of atomic structure, but the simple view put forth in 1913 by the Danish physicist Niels Bohr provides a good starting point for understanding atomic theory. Bohr proposed that every atom possesses an orbiting cloud of tiny subatomic particles called *electrons* whizzing around a core, like the planets of a miniature solar system. At the center of each atom is a small, very dense nucleus formed of two other kinds of subatomic particles: *protons* and *neutrons* (figure 2.3).

Atomic number

Different atoms are defined by the number of protons, a quantity called the *atomic number*. Atoms with the same atomic number (that is, the same number of protons) have the same chemical properties and are said to belong to the same element. Formally speaking, an *element* is any substance that cannot be broken down to any other substance by ordinary chemical means.

Within the nucleus, the cluster of protons and neutrons is held together by a force that works only over short, subatomic distances. Each proton carries a positive (+) charge, and each neutron has no charge. Each electron carries a negative (–) charge. Typically, an atom has one electron for each proton and is thus electrically neutral. The chemical behavior of an atom is due to the number and configuration of electrons, as we will see later in this section.

Atomic mass

The terms *mass* and *weight* are often used interchangeably, but they have slightly different meanings. *Mass* refers to the amount of a substance, but *weight* refers to the force gravity exerts on a substance. An object has the same mass whether it is on the Earth or the Moon, but its weight will be greater on the Earth because the Earth's gravitational force is greater than the Moon's. The *atomic mass* of an atom is equal to the sum of the masses of its protons and neutrons. Atoms that occur naturally on Earth contain from 1 to 92 protons and up to 146 neutrons.

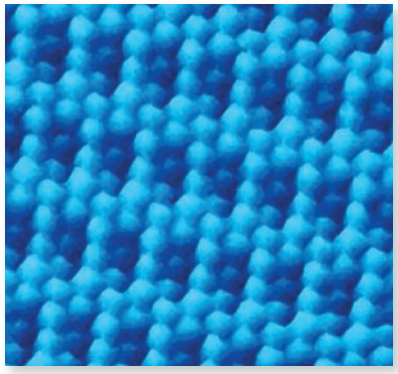


Figure 2.2 Scanning-tunneling microscope image. The scanning-tunneling microscope is a nonoptical way of imaging that allows atoms to be visualized. This image shows a lattice of oxygen atoms *(dark blue)* on a rhodium crystal *(light blue)*.

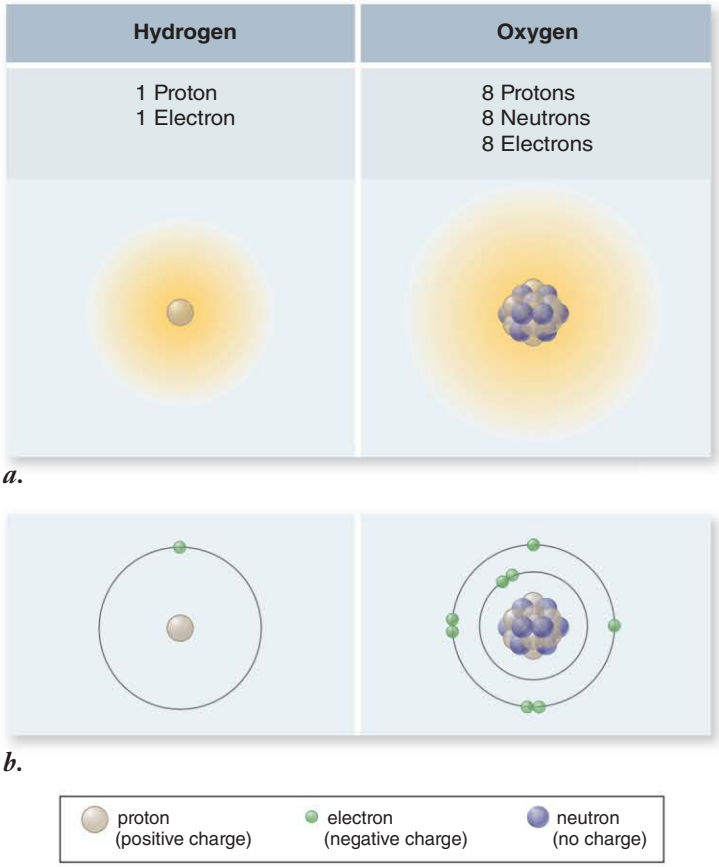


Figure 2.3 Basic structure of atoms. All atoms have a nucleus consisting of protons and neutrons, except hydrogen, the smallest atom, which usually has only one proton and no neutrons in its nucleus. Oxygen typically has eight protons and eight neutrons in its nucleus. In the simple "Bohr model" of atoms pictured here, electrons spin around the nucleus at a relatively far distance. ***a.*** Atoms are depicted as a nucleus with a cloud of electrons (not shown to scale). ***b.*** The electrons are shown in discrete energy levels. These are described in greater detail in the text.

The mass of atoms and subatomic particles is measured in units called *daltons.* To give you an idea of just how small these units are, note that it takes 602 million million billion (6.02×10^{23}) daltons to make 1 gram (g). A proton weighs approximately 1 dalton (actually 1.007 daltons), as does a neutron (1.009 daltons). In contrast, electrons weigh only 1/1840 of a dalton, so they contribute almost nothing to the overall mass of an atom.

Electrons

The positive charges in the nucleus of an atom are neutralized, or counterbalanced, by negatively charged electrons, which are located in regions called **orbitals** that lie at varying distances around the nucleus. Atoms with the same number of protons and electrons are electrically neutral—that is, they have no net charge, and are therefore called *neutral atoms.*

Electrons are maintained in their orbitals by their attraction to the positively charged nucleus. Sometimes other forces overcome this attraction, and an atom loses one or more electrons. In other cases, atoms gain additional electrons. Atoms in which the number of electrons does not equal the number of protons are known as *ions,* and they are charged particles. An atom having more protons than electrons has a net positive charge and is called a **cation.** For example, an atom of sodium (Na) that has lost one electron becomes a sodium ion (Na^+), with a charge of +1. An atom having fewer protons than electrons carries a net negative charge and is called an **anion.** A chlorine atom (Cl) that has gained one electron becomes a chloride ion (Cl^-), with a charge of −1.

Isotopes

Although all atoms of an element have the same number of protons, they may not all have the same number of neutrons. Atoms of a single element that possess different numbers of neutrons are called **isotopes** of that element.

Most elements in nature exist as mixtures of different isotopes. Carbon (C), for example, has three isotopes, all containing six protons (figure 2.4). Over 99% of the carbon found in nature exists as an isotope that also contains six neutrons. Because the total mass of this isotope is 12 daltons (6 from protons plus 6 from neutrons), it is referred to as carbon-12 and is symbolized ^{12}C. Most of the rest of the naturally occurring carbon is carbon-13, an isotope with seven neutrons. The rarest carbon isotope is carbon-14, with eight neutrons. Unlike the other two isotopes, carbon-14 is unstable: This means that its nucleus tends to break up into elements with lower atomic numbers. This nuclear breakup, which emits a significant amount of energy, is called *radioactive decay,* and isotopes that decay in this fashion are **radioactive isotopes.**

Some radioactive isotopes are more unstable than others, and therefore they decay more readily. For any given isotope, however, the rate of decay is constant. The decay time is usually

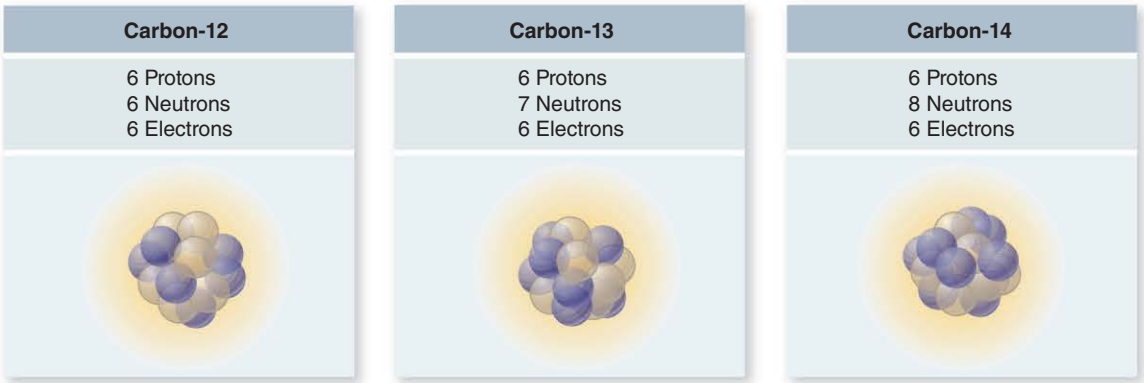


Figure 2.4 The three most abundant isotopes of carbon. Isotopes of a particular element have different numbers of neutrons.

expressed as the *half-life,* the time it takes for one-half of the atoms in a sample to decay. Carbon-14, for example, often used in the carbon dating of fossils and other materials, has a half-life of 5730 years. A sample of carbon containing 1 g of carbon-14 today would contain 0.5 g of carbon-14 after 5730 years, 0.25 g 11,460 years from now, 0.125 g 17,190 years from now, and so on. By determining the ratios of the different isotopes of carbon and other elements in biological samples and in rocks, scientists are able to accurately determine when these materials formed.

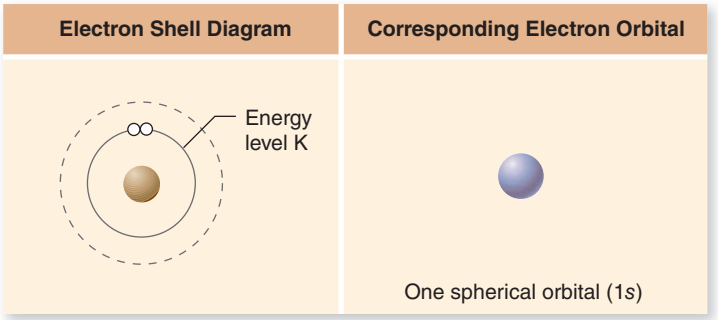
Radioactivity has many useful applications in modern biology. Radioactive isotopes are one way to label, or "tag," a specific molecule and then follow its progress, either in a chemical reaction or in living cells and tissue. The downside, however, is that the energetic subatomic particles emitted by radioactive substances have the potential to severely damage living cells, producing genetic mutations and, at high doses, cell death. Consequently, exposure to radiation is carefully controlled and regulated. Scientists who work with radioactivity follow strict handling protocols and wear radiation-sensitive badges to monitor their exposure over time to help ensure a safe level of exposure.

Electrons determine the chemical behavior of atoms

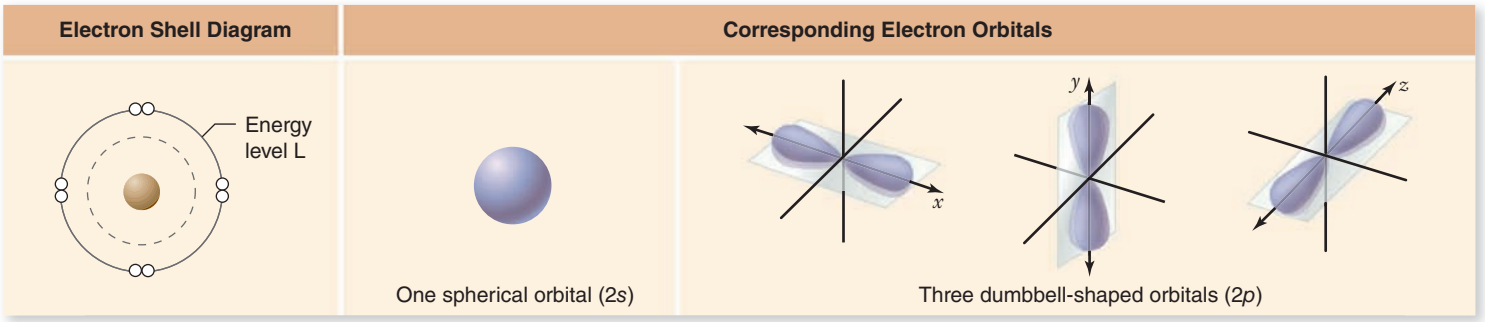
The key to the chemical behavior of an atom lies in the number and arrangement of its electrons in their orbitals. The Bohr model of the atom shows individual electrons as following distinct circular orbits around a central nucleus. The trouble with this simple picture is that it doesn't reflect reality. Modern physics indicates that we cannot pinpoint the position of any individual electron at any given time. In fact, an electron could be anywhere, from close to the nucleus to infinitely far away from it.

A particular electron, however, is more likely to be in some areas than in others. An orbital is defined as the area around a nucleus where an electron is most likely to be found. These orbitals represent probability distributions for electrons—that is, regions more likely to contain an electron. Some electron orbitals near the nucleus are spherical (*s* orbitals), whereas others are dumbbell-shaped (*p* orbitals) (figure 2.5). Still other orbitals, farther away from the nucleus, may have different shapes. Regardless of its shape, no orbital can contain more than two electrons.

Almost all of the volume of an atom is empty space. This is because the electrons are usually far away from the nucleus, relative to its size. If the nucleus of an atom were the size of a golf ball, the orbit of the nearest electron would be a mile away. Consequently, the nuclei of two atoms never come close enough in nature to interact with each other. It is for this reason that an atom's electrons, not its protons or neutrons, determine its chemical behavior, and it also explains why the isotopes of an element, all of which have the same arrangement of electrons, behave the same way chemically.



a.



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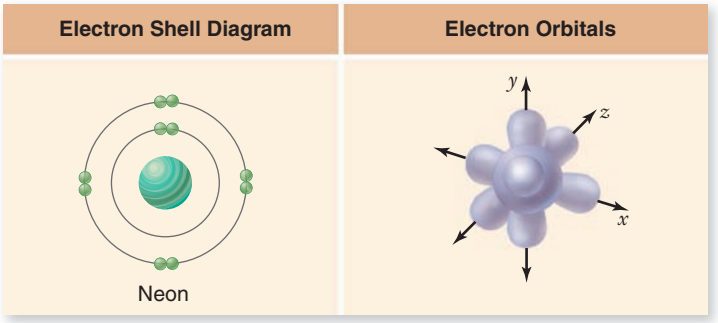


c.

Figure 2.5 Electron orbitals. ***a.*** The lowest energy level, or electron shell—the one nearest the nucleus—is level K. It is occupied by a single *s* orbital, referred to as 1*s*. ***b.*** The next highest energy level, L, is occupied by four orbitals: one *s* orbital (referred to as the 2*s* orbital) and three *p* orbitals (each referred to as a 2*p* orbital). Each orbital holds two paired electrons with opposite spin. Thus, the K level is populated by two electrons, and the L level is populated by a total of eight electrons. ***c.*** The neon atom shown has the L and K energy levels completely filled with electrons and is thus unreactive.

Atoms contain discrete energy levels

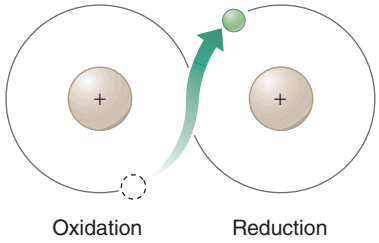
Because electrons are attracted to the positively charged nucleus, it takes work to keep them in their orbitals, just as it takes work to hold a grapefruit in your hand against the pull of gravity. The formal definition of energy is the ability to do work.

The grapefruit held above the ground is said to possess *potential energy* because of its position. If you release it, the grapefruit falls, and its potential energy is reduced. On the other hand, if you carried the grapefruit to the top of a building, you would increase its potential energy. Electrons also have a potential energy that is related to their position. To oppose the attraction of the nucleus and move the electron to a more distant orbital requires an input of energy, which results in an electron with greater potential energy. The chlorophyll that makes plants green captures energy from light during photosynthesis in this way. As you'll see in chapter 8—light energy excites electrons in the chlorophyll molecule. Moving an electron closer to the nucleus has the opposite effect: Energy is released, usually as radiant energy (heat or light), and the electron ends up with less potential energy (figure 2.6).

One of the initially surprising aspects of atomic structure is that electrons within the atom have discrete **energy levels.** These discrete levels correspond to quanta (singular, quantum), which means specific amount of energy. To use the grapefruit analogy again, it is as though a grapefruit could only be raised to particular floors of a building. Every atom exhibits a ladder of potential energy values, a discrete set of orbitals at particular energetic "distances" from the nucleus.

Because the amount of energy an electron possesses is related to its distance from the nucleus, electrons that are the same distance from the nucleus have the same energy, even if they occupy different orbitals. Such electrons are said to occupy the same energy level. The energy levels are denoted with letters K, L, M, and so on (figure 2.6). Be careful not to confuse energy levels, which are drawn as rings to indicate an electron's *energy,* with orbitals, which have a variety of three-dimensional shapes and indicate an electron's most likely *location.* Electron orbitals are arranged so that as they are filled, this fills each energy level in successive order. This filling of orbitals and energy levels is what is responsible for the chemical reactivity of elements.

During some chemical reactions, electrons are transferred from one atom to another. In such reactions, the loss of an electron is called **oxidation,** and the gain of an electron is called *reduction.*



Notice that when an electron is transferred in this way, it keeps its energy of position. In organisms, chemical energy is stored in high-energy electrons that are transferred from one atom to another in reactions involving oxidation and reduction (described in chapter 7). When the processes of oxidation and reduction are coupled, which often happens, one atom or molecule is oxidized, while another is reduced in the same reaction. We call these combinations *redox reactions.*

Learning Outcomes Review 2.1

An atom consists of a nucleus of protons and neutrons surrounded by a cloud of electrons. For each atom, the number of protons is the atomic number; atoms with the same atomic number constitute an element. Atoms of a single element that have different numbers of neutrons are called isotopes. Electrons, which determine the chemical behavior of an element, are located about a nucleus in orbitals representing discrete energy levels. No orbital can contain more than two electrons, but each energy level consists of multiple orbitals, and thus contains many electrons with the same energy.

- ***If the number of protons exceeds the number of neutrons, is the charge on the atom positive or negative?***
- ***If the number of protons exceeds electrons?***

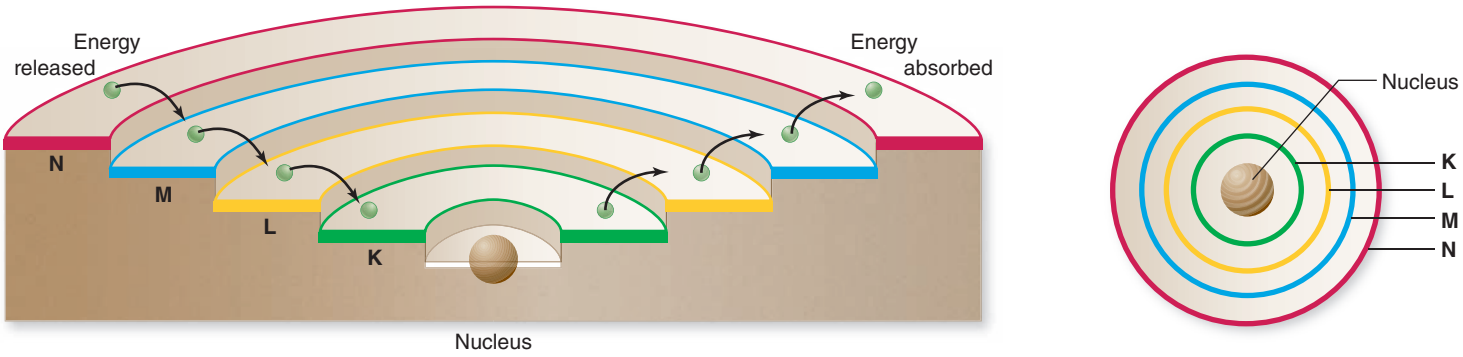


Figure 2.6 Atomic energy levels. Electrons have energy of position. When an atom absorbs energy, an electron moves to a higher energy level, farther from the nucleus. When an electron falls to lower energy levels, closer to the nucleus, energy is released. The first two energy levels are the same as shown in figure 2.5.

2.2 Elements Found in Living Systems

Learning Outcomes

1. *Relate atomic structure to the periodic table of the elements.*
2. *List the important elements found in living systems.*

Ninety elements occur naturally, each with a different number of protons and a different arrangement of electrons. When the 19th-century Russian chemist Dmitri Mendeleev arranged the known elements in a table according to their atomic number, he discovered one of the great generalizations of science: The elements exhibit a pattern of chemical properties that repeats itself in groups of eight. This periodically repeating pattern lent the table its name: the periodic table of elements (figure 2.7).

The periodic table displays elements according to atomic number and properties

The eight-element periodicity that Mendeleev found is based on the interactions of the electrons in the outermost energy level of the different elements. These electrons are called **valence electrons,** and their interactions are the basis for the elements' differing chemical properties. For most of the atoms important to life, the outermost energy level can contain no more than eight electrons; the chemical behavior of an element reflects how many of the eight positions are filled. Elements possessing all eight electrons in their outer energy level (two for helium) are *inert,* or nonreactive. These elements, which include helium (He), neon (Ne), argon (Ar), and so on, are called the *noble gases*. In sharp contrast, elements with seven electrons (one fewer than the maximum number of eight) in their outer energy level, such as fluorine (F), chlorine (Cl), and bromine (Br), are highly reactive. They tend to gain the extra electron needed to fill the energy level. Elements with only one electron in their outer energy level, such as lithium (Li), sodium (Na), and potassium (K), are also very reactive, but they tend to lose the single electron in their outer level.

Mendeleev's periodic table leads to a useful generalization, the **octet rule,** or *rule of eight* (Latin *octo*, "eight"): Atoms tend to establish completely full outer energy levels. For the main group elements of the periodic table, the rule of eight is accomplished by one filled *s* orbital and three filled *p* orbitals (figure 2.8). The exception to this is He, in the first row, which needs only two electrons to fill the 1*s* orbital. Most chemical behavior of biological interest can be predicted quite accurately from this simple rule, combined with the tendency of atoms to balance positive and negative charges. For instance, you read earlier that sodium ion (Na^+) has lost an electron, and chloride ion (Cl^-) has gained an electron. In the section 2.3, we describe how these ions react to form table salt.

Of the 90 naturally occurring elements on Earth, only 12 (C, H, O, N, P, S, Na, K, Ca, Mg, Fe, Cl) are found in living systems in more than trace amounts (0.01% or higher). These elements all have atomic numbers less than 21, and thus, have low atomic masses. Of these 12, the first 4 elements (carbon, hydrogen, oxygen, and nitrogen) constitute 96.3% of the weight of your body. The majority of molecules that make up your body (other than water) are compounds of carbon, which we call *organic* compounds.

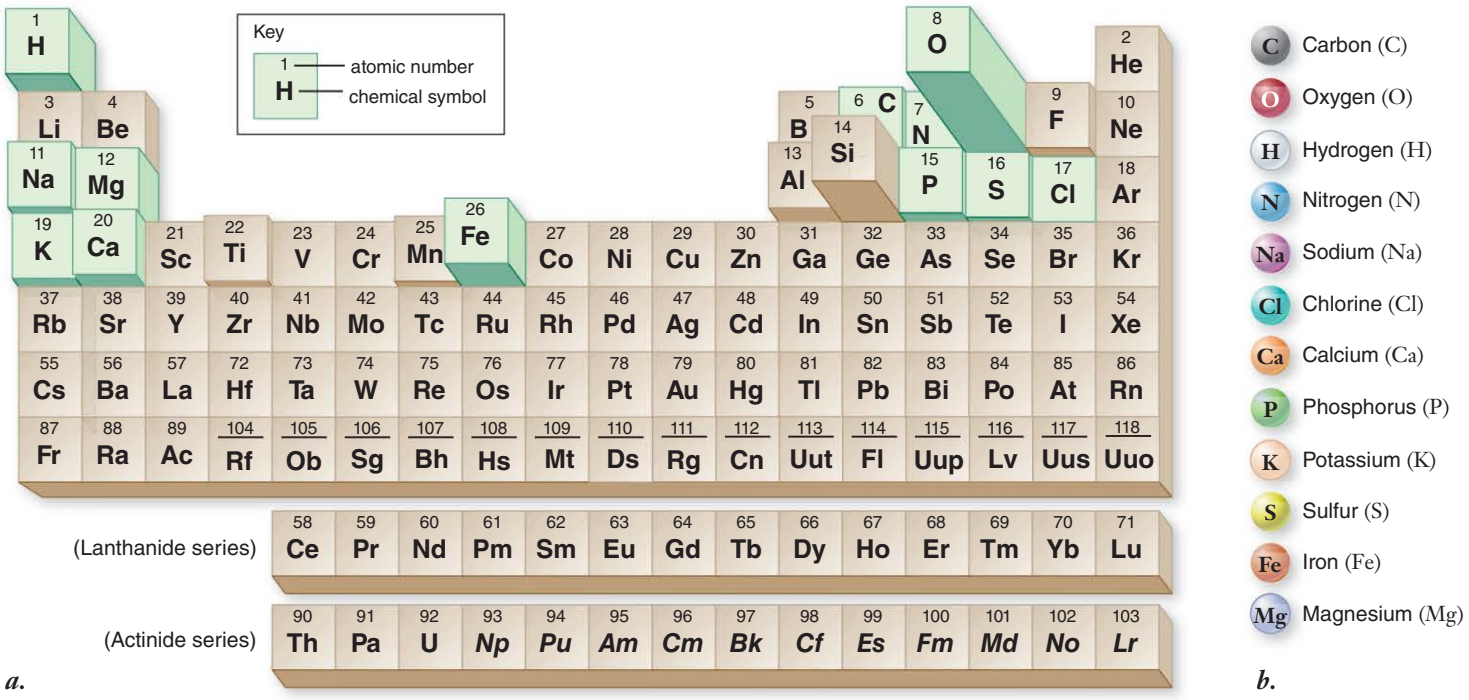


Figure 2.7 Periodic table of the elements. ***a.*** In this representation, the frequency of elements that occur in the Earth's crust is indicated by the height of the block. Elements shaded in green are found in living systems in more than trace amounts. ***b.*** Common elements found in living systems are shown in colors that will be used throughout the text.

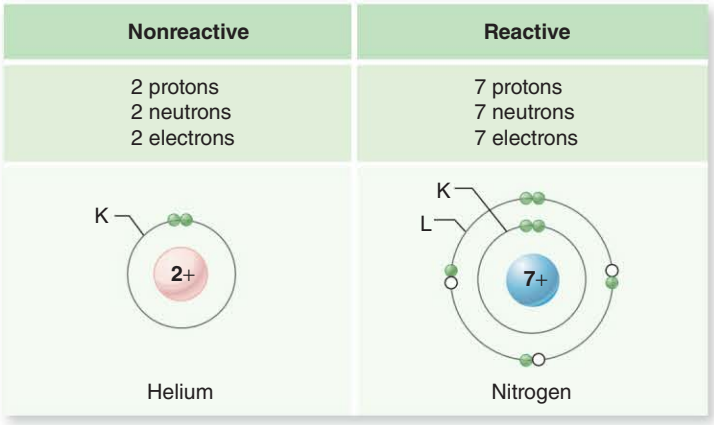


Figure 2.8 Electron energy levels for helium and nitrogen. Green balls represent electrons, blue ball represents the nucleus with number of protons indicated by number of (+) charges. Note that the helium atom has a filled K shell and is thus unreactive, whereas the nitrogen atom has five electrons in the L shell, three of which are unpaired, making it reactive.

These organic compounds contain primarily these four elements (CHON), explaining their prevalence in living systems. Some trace elements, such as zinc (Zn) and iodine (I), play crucial roles in living processes even though they are present in tiny amounts. Iodine deficiency, for example, can lead to enlargement of the thyroid gland, causing a bulge at the neck called a goiter.

Learning Outcomes Review 2.2

The periodic table shows the elements in terms of atomic number and repeating chemical properties. Only 12 elements are found in significant amounts in living organisms: C, H, O, N, P, S, Na, K, Ca, Mg, Fe, and Cl.

- ***Why are the noble gases more stable than other elements in the periodic table?***

2.3 The Nature of Chemical Bonds

Learning Outcomes

1. *Predict which elements are likely to form ions.*
2. *Explain how molecules are formed from atoms joined by covalent bonds.*
3. *Contrast polar and nonpolar covalent bonds.*

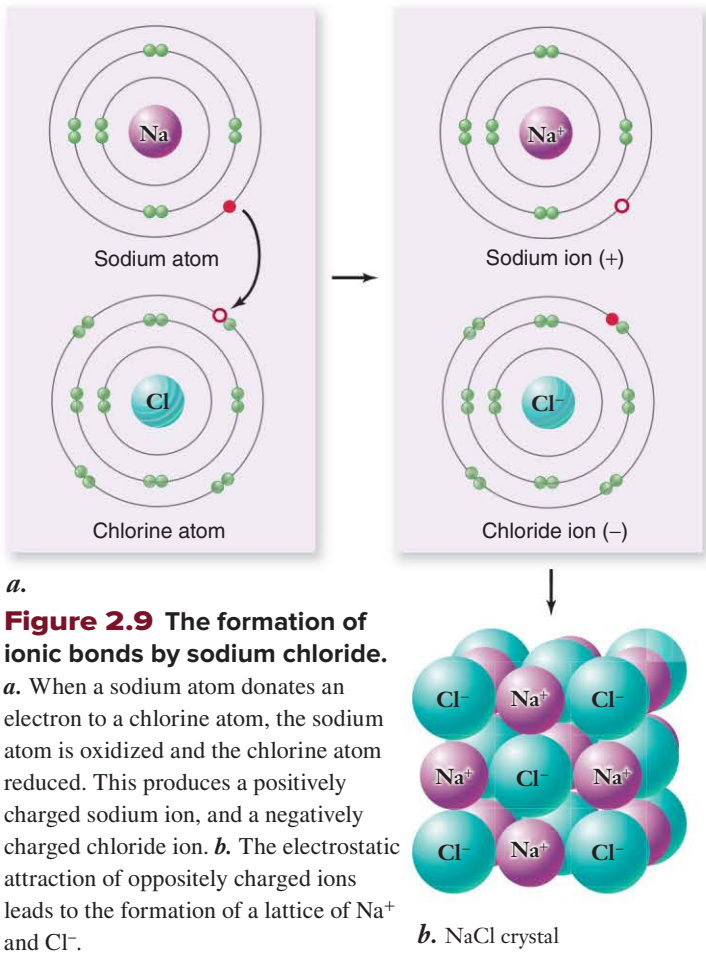
A group of atoms held together by energy in a stable association is called a *molecule.* When a molecule contains atoms of more than one element, it is called a *compound.* The atoms in a molecule are joined by *chemical bonds;* these bonds can result when atoms with opposite charges attract each other (ionic bonds), when two atoms share one or more pairs of electrons (covalent bonds), or when atoms interact in other ways (table 2.1). We will start by examining *ionic bonds,* which form when atoms with opposite electrical charges (ions) attract.

TABLE 2.1 Bonds and Interactions

Name	Basis of Interaction	Strength
Covalent bond	Sharing of electron pairs	Strong
Ionic bond	Attraction of opposite charges	
Hydrogen bond	Sharing of H atom	
Hydrophobic interaction	Forcing of hydrophobic portions of molecules together in presence of polar substances	
van der Waals attraction	Weak attractions between atoms due to oppositely polarized electron clouds	Weak

Ionic bonds form crystals

Common table salt, the molecule sodium chloride (NaCl), is a lattice of ions in which the atoms are held together by ionic bonds (figure 2.9). Sodium has 11 electrons: 2 in the inner energy



a.

Figure 2.9 The formation of ionic bonds by sodium chloride. ***a.*** When a sodium atom donates an electron to a chlorine atom, the sodium atom is oxidized and the chlorine atom reduced. This produces a positively charged sodium ion, and a negatively charged chloride ion. ***b.*** The electrostatic attraction of oppositely charged ions leads to the formation of a lattice of Na^+ and Cl^-.

b. NaCl crystal

level (K), 8 in the next level (L), and 1 in the outer (valence) level (M). The single, unpaired valence electron has a strong tendency to join with another unpaired electron in another atom. A stable configuration can be achieved if the valence electron is lost to another atom that also has an unpaired electron. The loss of this electron results in the formation of a positively charged sodium ion, Na^+.

The chlorine atom has 17 electrons: 2 in the K level, 8 in the L level, and 7 in the M level. As you can see in the figure, one of the orbitals in the outer energy level has an unpaired electron (red circle). The addition of another electron fills that level and causes a negatively charged chloride ion, Cl^-, to form.

When placed together, metallic sodium and gaseous chlorine react swiftly and explosively, as the sodium atoms are oxidized, donating electrons to chlorine atoms, reducing them, and forming Na^+ and Cl^- ions. Because opposite charges attract, the Na^+ and Cl^- remain associated in an *ionic compound,* NaCl, which is electrically neutral. The electrical attractive force holding NaCl together, however, is not directed specifically between individual Na^+ and Cl^- ions, and no individual sodium chloride molecules form. Instead, the force exists between any one ion and *all* neighboring ions of the opposite charge. The ions aggregate in a crystal matrix with a precise geometry. Such aggregations are what we know as salt crystals. If a salt such as NaCl is placed in water, the electrical attraction of the water molecules disrupts the forces holding the ions in their crystal matrix, causing the salt to dissolve into a roughly equal mixture of free Na^+ and Cl^- ions.

Because living systems always include water, ions are more important than ionic crystals. Important ions in biological systems include Ca^{2+}, which is involved in cell signaling, K^+ and Na^+, which are involved in the conduction of nerve impulses.

Covalent bonds build stable molecules

Covalent bonds form when two atoms share one or more pairs of valence electrons. Consider gaseous hydrogen (H_2) as an example. Each hydrogen atom has an unpaired electron and an unfilled outer energy level; for these reasons, the hydrogen atom is unstable. However, when two hydrogen atoms are in close association, each atom's electron is attracted to both nuclei. In effect, the nuclei are able to share their electrons. The result is a diatomic (two-atom) molecule of hydrogen gas.

The molecule formed by the two hydrogen atoms is stable for three reasons:

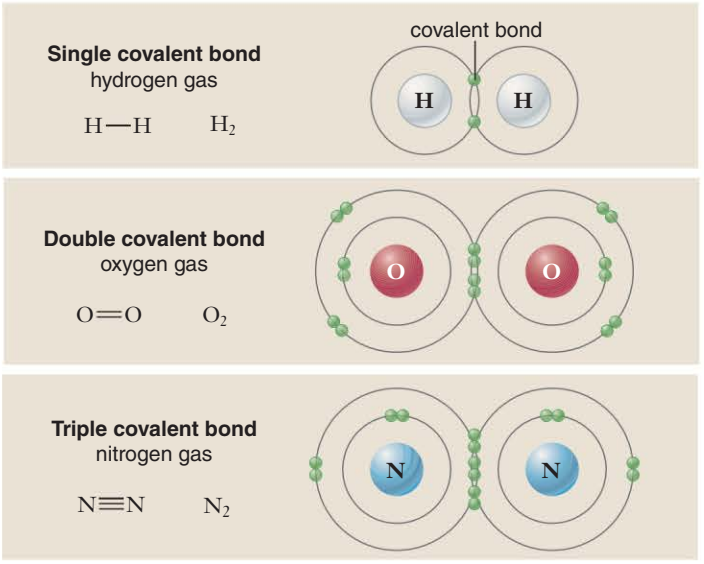
1. **It has no net charge.** The diatomic molecule formed as a result of this sharing of electrons is not charged because it still contains two protons and two electrons.
2. **The octet rule is satisfied.** Each of the two hydrogen atoms can be considered to have two orbiting electrons in its outer energy level. This state satisfies the octet rule, because each shared electron orbits both nuclei and is included in the outer energy level of both atoms.
3. **It has no unpaired electrons.** The bond between the two atoms also pairs the two free electrons.

Unlike ionic bonds, covalent bonds are formed between two individual atoms, giving rise to true, discrete molecules.

The strength of covalent bonds

The strength of a covalent bond depends on the number of shared electrons. Thus *double bonds,* which satisfy the octet rule by allowing two atoms to share two pairs of electrons, are stronger than *single bonds,* in which only one electron pair is shared. In practical terms, more energy is required to break a double bond than a single bond. The strongest covalent bonds are *triple bonds,* such as those that link the two nitrogen atoms of nitrogen gas molecules (N_2).

Covalent bonds are represented in chemical formulas as lines connecting atomic symbols. Each line between two bonded atoms represents the sharing of one pair of electrons. The *structural formulas* of hydrogen gas and oxygen gas are H—H and O═O, respectively, and their *molecular formulas* are H_2 and O_2. The structural formula for N_2 is N≡N.



Molecules with several covalent bonds

A vast number of biological compounds are composed of more than two atoms. An atom that requires two, three, or four additional electrons to fill its outer energy level completely may acquire them by sharing its electrons with two or more other atoms.

For example, the carbon atom (C) contains six electrons, four of which are in its outer energy level and are unpaired. To satisfy the octet rule, a carbon atom must form four covalent bonds. Because four covalent bonds may form in many ways, carbon atoms are found in many different kinds of molecules. CO_2 (carbon dioxide), CH_4 (methane), and C_2H_5OH (ethanol) are just a few examples.

Polar and nonpolar covalent bonds

Atoms differ in their affinity for electrons, a property called **electronegativity.** In general, electronegativity increases left to right across a row of the periodic table and decreases down the column. Thus the elements in the upper-right corner have the highest electronegativity.

For bonds between identical atoms, for example, between two hydrogen or two oxygen atoms, the affinity for electrons is

obviously the same, and the electrons are equally shared. Such bonds are termed **nonpolar.** The resulting compounds (H_2 or O_2) are also referred to as nonpolar.

For atoms that differ greatly in electronegativity, electrons are not shared equally. The shared electrons are more likely to be closer to the atom with greater electronegativity, and less likely to be near the atom of lower electronegativity. In this case, although the molecule is still electrically neutral (same number of protons as electrons), the distribution of charge is not uniform. This unequal distribution results in regions of partial negative charge near the more electronegative atom, and regions of partial positive charge near the less electronegative atom. Such bonds are termed **polar covalent bonds,** and the molecules polar molecules. When drawing polar molecules, these partial charges are usually symbolized by the lowercase Greek letter delta (δ). The partial charge seen in a polar covalent bond is relatively small—far less than the unit charge of an ion. For biological molecules, we can predict polarity of bonds by knowing the relative electronegativity of a small number of important atoms (table 2.2). Notice that although C and H differ slightly in electronegativity, this small difference is negligible, and C—H bonds are considered nonpolar.

Because of its importance in the chemistry of water, we will explore the nature of polar and nonpolar molecules in the section 2.4. Water (H_2O) is a polar molecule with electrons more concentrated around the oxygen atom.

Chemical reactions alter bonds

The formation and breaking of chemical bonds, which is the essence of chemistry, is termed a *chemical reaction.* All chemical reactions involve the shifting of atoms from one molecule or ionic compound to another, without any change in the number or identity of the atoms. For convenience, we refer to the original molecules before the reaction starts as *reactants,* and the molecules resulting from the chemical reaction as *products.* For example:

$$\underset{\textit{reactants}}{6H_2O + 6CO_2} \longrightarrow \underset{\textit{products}}{C_6H_{12}O_6 + 6O_2}$$

You may recognize this reaction as a simplified form of the photosynthesis reaction, in which water and carbon dioxide are combined to produce glucose and oxygen. Most animal life ultimately depends on this reaction, which takes place in plants. (Photosynthetic reactions will be discussed in detail in chapter 8.)

TABLE 2.2 Relative Electronegativities of Some Important Atoms

Atom	Electronegativity
O	3.5
N	3.0
C	2.5
H	2.1

The extent to which chemical reactions occur is influenced by three important factors:

1. **Temperature.** Heating the reactants increases the rate of a reaction because the reactants collide with one another more often. (Care must be taken that the temperature is not so high that it destroys the molecules.)
2. **Concentration of reactants and products.** Reactions proceed more quickly when more reactants are available, allowing more frequent collisions. An accumulation of products typically slows the reaction and, in reversible reactions, may speed the reaction in the reverse direction.
3. **Catalysts.** A catalyst is a substance that increases the rate of a reaction. It doesn't alter the reaction's equilibrium between reactants and products, but it does shorten the time needed to reach equilibrium, often dramatically. In living systems, proteins called enzymes catalyze almost every chemical reaction.

Many reactions in nature are reversible. This means that the products may themselves be reactants, allowing the reaction to proceed in reverse. We can write the preceding reaction in the reverse order:

$$\underset{\textit{reactants}}{C_6H_{12}O_6 + 6O_2} \longrightarrow \underset{\textit{products}}{6H_2O + 6CO_2}$$

This reaction is a simplified version of the oxidation of glucose by cellular respiration, in which glucose is broken down into water and carbon dioxide in the presence of oxygen. Virtually all organisms carry out forms of glucose oxidation; details are covered later, in chapter 7.

Learning Outcomes Review 2.3

An ionic bond is an attraction between ions of opposite charge in an ionic compound. A covalent bond is formed when two atoms share one or more pairs of electrons. Complex biological compounds are formed in large part by atoms that can form one or more covalent bonds: C, H, O, and N. A polar covalent bond is formed by unequal sharing of electrons. Nonpolar bonds exhibit equal sharing of electrons.

- ***How is a polar covalent bond different from an ionic bond?***

2.4 Water: A Vital Compound

Learning Outcomes

1. *Relate how the structure of water leads to hydrogen bonds.*
2. *Describe water's cohesive and adhesive properties.*

Of all the common molecules, only water exists as a liquid at the relatively low temperatures that prevail on the Earth's surface. Three-fourths of the Earth is covered by liquid water (figure 2.10).

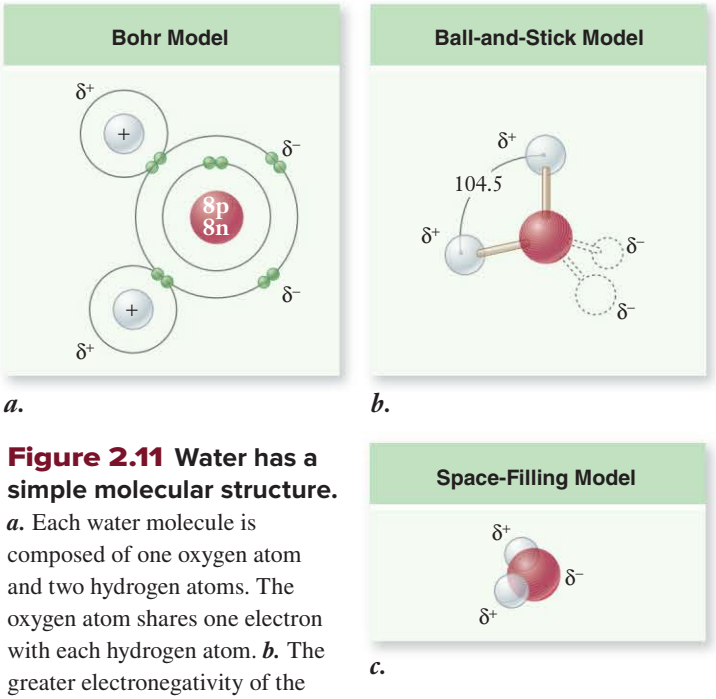
a. Solid ***b.*** Liquid ***c.*** Gas

Figure 2.10 Water takes many forms. ***a.*** When water cools below 0°C, it forms beautiful crystals, familiar to us as snow and ice. ***b.*** Ice turns to liquid when the temperature is above 0°C. ***c.*** Liquid water becomes steam when the temperature rises above 100°C, as seen in this hot spring at Yellowstone National Park.

When life was beginning, water provided a medium in which other molecules could move around and interact, without being held in place by strong covalent or ionic bonds. Life evolved in water for 2 billion years before spreading to land. And even today, life is inextricably tied to water. About two-thirds of any organism's body is composed of water, and all organisms require a water-rich environment, either inside or outside it, for growth and reproduction. It is no accident that tropical rain forests are bursting with life, whereas dry deserts appear almost lifeless except when water becomes temporarily plentiful, such as after a rainstorm.

Water's structure facilitates hydrogen bonding

Water has a simple molecular structure, consisting of an oxygen atom bound to two hydrogen atoms by two single covalent bonds (figure 2.11). The resulting molecule is stable: It satisfies the octet rule, has no unpaired electrons, and carries no net electrical charge. The electronegativity of O is much greater than that of H (see table 2.2), and so the bonds between these atoms are highly polar. *The polarity of water underlies water's chemistry and the chemistry of life.*



a. ***b.*** ***c.***

Figure 2.11 Water has a simple molecular structure. ***a.*** Each water molecule is composed of one oxygen atom and two hydrogen atoms. The oxygen atom shares one electron with each hydrogen atom. ***b.*** The greater electronegativity of the oxygen atom makes the water molecule polar: Water carries two partial negative charges (δ^-) near the oxygen atom and two partial positive charges (δ^+), one on each hydrogen atom. ***c.*** Space-filling model shows what the molecule would look like if it were visible.

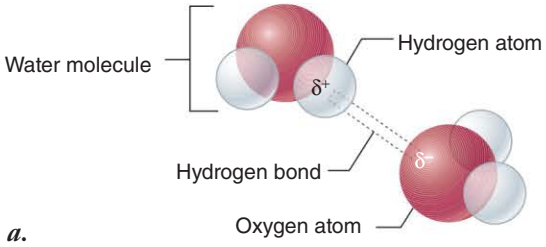
The single most outstanding chemical property of water is its ability to form weak chemical associations, called **hydrogen bonds.** These bonds form between the partially negative O atoms and the partially positive H atoms of two water molecules. Although these bonds have only 5–10% of the strength of covalent bonds, they are important to DNA and protein structure, and thus responsible for much of the chemical organization of living systems.

If we consider the shape of a water molecule, we see that its two covalent bonds have a partial charge at each end: δ^- at the oxygen end and δ^+ at the hydrogen end. The most stable arrangement of these charges is a *tetrahedron (a pyramid with a triangle as its base),* in which the two negative and two positive charges are approximately equidistant from one another. The oxygen atom lies at the center of the tetrahedron, the hydrogen atoms occupy two of the apexes (corners), and the partial negative charges occupy the other two apexes (figure 2.11*b*). The bond angle between the two covalent oxygen–hydrogen bonds is 104.5°. This value is slightly less than the bond angle of a regular tetrahedron, which would be 109.5°. In water, the partial negative charges occupy more space than the partial positive regions, so the oxygen–hydrogen bond angle is slightly compressed.

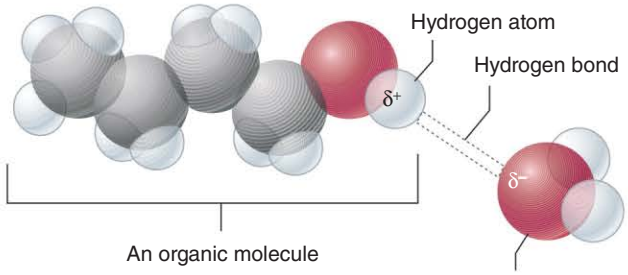
Water molecules are cohesive

The polarity of water allows water molecules to be attracted to one another—that is, water is *cohesive.* The oxygen end of each water molecule, which is δ^-, is attracted to the hydrogen end, which is δ^+, of other molecules. The attraction produces hydrogen bonds among water molecules (figure 2.12). Each hydrogen bond is individually very weak and transient, lasting on average only a hundred-billionth (10^{-11}) of a second. The cumulative effects of large numbers of these bonds, however, can be enormous. Water forms an abundance of hydrogen bonds, which are responsible for many of its important physical properties (table 2.3).

Water's cohesion is responsible for its being a liquid, not a gas, at moderate temperatures. The cohesion of liquid water is also responsible for its **surface tension.** Small insects can walk on water (figure 2.13) because at the air–water interface, all the surface water molecules are hydrogen-bonded to molecules below them.



a.



b.

Figure 2.12 Structure of a hydrogen bond. ***a.*** Hydrogen bond between two water molecules. ***b.*** Hydrogen bond between an organic molecule (*n*-butanol) and water. H in *n*-butanol forms a hydrogen bond with oxygen in water. This kind of hydrogen bond is possible any time H is bound to a more electronegative atom (see table 2.2).

Water molecules are adhesive

The polarity of water causes it to be attracted to other polar molecules as well. This attraction for other polar substances is called *adhesion.* Water adheres to any substance with which it can form hydrogen bonds. This property explains why substances containing polar molecules get "wet" when they are immersed in water, but those that are composed of nonpolar molecules (such as oils) do not.

The attraction of water to substances that have electrical charges on their surface is responsible for capillary action. If a glass tube with a narrow diameter is lowered into a beaker of water, the water will rise in the tube above the level of the water in the beaker, because the adhesion of water to the glass surface, drawing it upward, is stronger than the force of gravity, pulling it downward. The narrower the tube, the greater the electrostatic forces between the water and the glass, and the higher the water rises (figure 2.14).

Figure 2.13 Cohesion. Some insects, such as this water strider, literally walk on water. Because the surface tension of the water is greater than the force of one foot, the strider glides atop the surface of the water rather than sinking. The high surface tension of water is due to hydrogen bonding between water molecules.

Figure 2.14 Adhesion. Capillary action causes the water within a narrow tube to rise above the surrounding water level; the adhesion of the water to the glass surface, which draws water upward, is stronger than the force of gravity, which tends to pull it down. The narrower the tube, the greater the surface area available for adhesion for a given volume of water, and the higher the water rises in the tube.

TABLE 2.3 The Properties of Water

Property	Explanation	Example of Benefit to Life
Cohesion	Hydrogen bonds hold water molecules together.	Leaves pull water upward from the roots; seeds swell and germinate.
High specific heat	Hydrogen bonds absorb heat when they break and release heat when they form, minimizing temperature changes.	Water stabilizes the temperature of organisms and the environment.
High heat of vaporization	Many hydrogen bonds must be broken for water to evaporate.	Evaporation of water cools body surfaces.
Lower density of ice	Water molecules in an ice crystal are spaced relatively far apart because of hydrogen bonding.	Because ice is less dense than water, lakes do not freeze solid, allowing fish and other life in lakes to survive the winter.
Solubility	Polar water molecules are attracted to ions and polar compounds, making these compounds soluble.	Many kinds of molecules can move freely in cells, permitting a diverse array of chemical reactions.

Learning Outcomes Review 2.4

Because of its polar covalent bonds, water can form hydrogen bonds with itself and with other polar molecules. Hydrogen bonding is responsible for water's cohesion, the force that holds water molecules together, and its adhesion, which is its ability to "stick" to other polar molecules. Capillary action results from both of these properties.

- *If water were made of C and H instead of H and O, would it still be cohesive and adhesive?*

2.5 Properties of Water

Learning Outcomes

1. *Illustrate how hydrogen bonding affects the properties of water.*
2. *Explain the relevance of water's unusual properties for living systems.*
3. *Identify the dissociation products of water.*

Water moderates temperature through two properties: its high specific heat and its high heat of vaporization. Water also has the unusual property of being less dense in its solid form, ice, than as a liquid. Water acts as a solvent for polar molecules and exerts an organizing effect on nonpolar molecules. All these properties result from its polar nature.

Water's high specific heat helps maintain temperature

The temperature of any substance is a measure of how rapidly its individual molecules are moving. In the case of water, a large input of thermal energy is required to break the many hydrogen bonds that keep individual water molecules from moving about. Therefore, water is said to have a high **specific heat,** which is defined as the amount of heat 1 g of a substance must absorb or lose to change its temperature by 1 degree Celsius (°C). Specific heat measures the extent to which a substance resists changing its temperature when it absorbs or loses heat. Because polar substances tend to form hydrogen bonds, the more polar it is, the higher is its specific heat. The specific heat of water (1 calorie/g/°C) is twice that of most carbon compounds and nine times that of iron. Only ammonia, which is more polar than water and forms very strong hydrogen bonds, has a higher specific heat than water (1.23 cal/g/°C). Still, only 20% of the hydrogen bonds are broken as water heats from 0° to 100°C.

Because of its high specific heat, water heats up more slowly than almost any other compound and holds its temperature longer. Because organisms have a high water content, water's high specific heat allows them to maintain a relatively constant internal temperature. The heat generated by the chemical reactions inside cells would destroy the cells if not for the absorption of this heat by the water within them.

Water's high heat of vaporization facilitates cooling

The **heat of vaporization** is defined as the amount of energy required to change 1 g of a substance from a liquid to a gas. A considerable amount of heat energy (586 cal) is required to accomplish this change in water. As water changes from a liquid to a gas it requires energy (in the form of heat) to break its many hydrogen bonds. The evaporation of water from a surface cools that surface. Many organisms dispose of excess body heat by evaporative cooling, for example, through sweating in humans and many other vertebrates.

Solid water is less dense than liquid water

At low temperatures, water molecules are locked into a crystal-like lattice of hydrogen bonds, forming solid ice (see figure 2.10*a*). Interestingly, ice is less dense than liquid water because the hydrogen bonds in ice space the water molecules relatively far apart. This unusual feature enables icebergs to float. If water did not have this property, nearly all bodies of water would be ice, with only the shallow surface melting every year. The buoyancy of ice is important ecologically because it means bodies of water freeze from the top down and not the bottom up. Because ice floats on the surface of lakes in the winter and the water beneath the ice remains liquid, fish and other animals keep from freezing.

Polar molecules and ions are soluble in water

Water molecules gather closely around any substance that bears an electrical charge, whether that substance carries a full charge (ion) or a charge separation (polar molecule). For example, sucrose (table sugar) is composed of molecules that contain polar hydroxyl (OH) groups. A sugar crystal dissolves rapidly in water because water molecules can form hydrogen bonds with individual hydroxyl groups of the sucrose molecules. Therefore, sucrose is said to be *soluble* in water. Water is termed the *solvent,* and sugar is called the *solute.* Every time a sucrose molecule dissociates, or breaks away, from a solid sugar crystal, water molecules surround it in a cloud, forming a *hydration shell* that prevents it from associating with other sucrose molecules. Hydration shells also form around ions such as Na^+ and Cl^- (figure 2.15).

Water organizes nonpolar molecules

Water molecules always tend to form the maximum possible number of hydrogen bonds. When nonpolar molecules such as oils, which do not form hydrogen bonds, are placed in water, the water molecules act to exclude them. The nonpolar molecules aggregate, or clump together, thus minimizing their disruption of the hydrogen bonding of water. In effect, they shrink from contact with water, and for this reason they are referred to as **hydrophobic** (Greek *hydros,* "water," and *phobos,* "fearing"). In contrast, polar molecules, which readily form hydrogen bonds with water, are said to be **hydrophilic** ("water-loving").

The tendency of nonpolar molecules to aggregate in water is known as **hydrophobic exclusion.** By forcing the hydrophobic portions of molecules together, water causes these molecules to assume particular shapes. This property can also affect the structure of

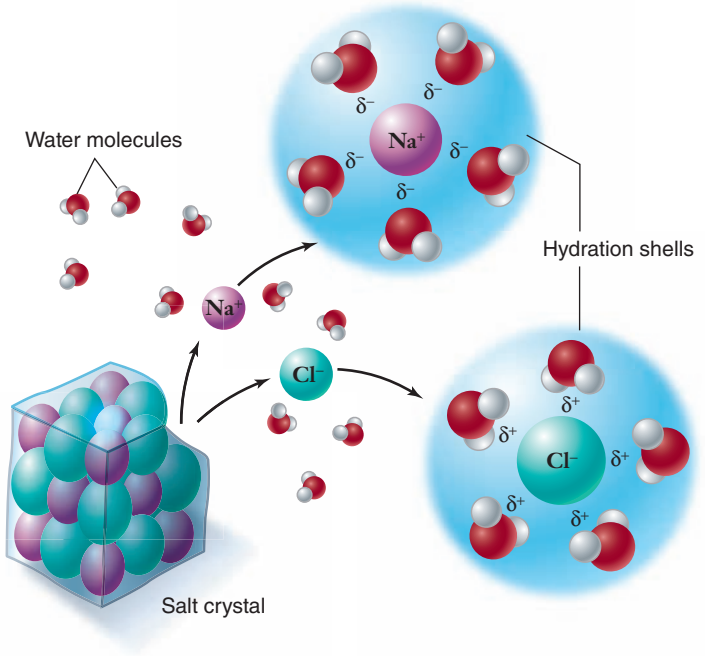


Figure 2.15 Why salt dissolves in water. When a crystal of table salt dissolves in water, individual Na^+ and Cl^- ions break away from the salt lattice and become surrounded by water molecules. Water molecules orient around Na^+ so that their partial negative poles face toward the positive Na^+; water molecules surrounding Cl^- orient in the opposite way, with their partial positive poles facing the negative Cl^-. Surrounded by hydration shells, Na^+ and Cl^- never reenter the salt lattice.

proteins, DNA, and biological membranes. In fact, the interaction of nonpolar molecules and water is critical to living systems.

Water can form ions

The covalent bonds of a water molecule sometimes break spontaneously. In pure water at 25°C, only 1 out of every 550 million water molecules undergoes this process. When it happens, a proton (hydrogen atom nucleus) dissociates from the molecule. Because the dissociated proton lacks the negatively charged electron it was sharing, its positive charge is no longer counterbalanced, and it becomes a hydrogen ion, H^+. The rest of the dissociated water molecule, which has retained the shared electron from the covalent bond, is negatively charged and forms a hydroxide ion, OH^-. This process of spontaneous ion formation is called *ionization:*

$$\underset{\textit{water}}{H_2O} \longrightarrow \underset{\textit{hydroxide ion}}{OH^-} + \underset{\textit{hydrogen ion (proton)}}{H^+}$$

At 25°C, 1 liter (L) of water contains one ten-millionth (or 10^{-7}) mole of H^+ ions. A **mole** (mol) is defined as the weight of a substance in grams that corresponds to the atomic masses of all of the atoms in a molecule of that substance. In the case of H^+, the atomic mass is 1, and a mole of H^+ ions would weigh 1 g. One mole of any substance always contains 6.02×10^{23} molecules of the substance. Therefore, the **molar concentration** of hydrogen ions in pure water, represented as $[H^+]$, is 10^{-7} mol/L. (In reality, the H^+ usually associates with another water molecule to form a hydronium ion, H_3O^+.)

Learning Outcomes Review 2.5

Water has a high specific heat so it does not change temperature rapidly, which helps living systems maintain a near-constant temperature. Water's high heat of vaporization allows cooling by evaporation. Solid water is less dense than liquid water because the hydrogen bonds space the molecules farther apart. Polar molecules are soluble in a water solution, but water tends to exclude nonpolar molecules. Water dissociates to form H^+ and OH^-.

- *How does the fact that ice floats affect life in a lake?*

2.6 Acids and Bases

Learning Outcomes

1. *Define acids, bases, and the pH scale.*
2. *Relate changes in pH to changes in $[H^+]$.*

The concentration of hydrogen ions, and concurrently of hydroxide ions, in a solution is described by the terms *acidity* and *basicity,* respectively. Pure water, having an $[H^+]$ of 10^{-7} mol/L, is considered to be neutral—that is, neither acidic nor basic. Recall that for every H^+ ion formed when water dissociates, an OH^- ion is also formed, meaning that the dissociation of water produces H^+ and OH^- in equal amounts.

The pH scale measures hydrogen ion concentration

The *pH scale* (figure 2.16) is a more convenient way to express the hydrogen ion concentration of a solution. This scale defines *pH,* which stands for "power of hydrogen," as the negative logarithm of the hydrogen ion concentration in the solution:

$$pH = -\log [H^+]$$

Because the logarithm of the hydrogen ion concentration is simply the exponent of the molar concentration of H^+, the pH equals the exponent times −1. For water, therefore, an $[H^+]$ of 10^{-7} mol/L corresponds to a pH value of 7. This is the neutral point—a balance between H^+ and OH^-—on the pH scale. This balance occurs because the dissociation of water produces equal amounts of H^+ and OH^-.

Note that, because the pH scale is *logarithmic,* a difference of 1 on the scale represents a 10-fold change in $[H^+]$. A solution with a pH of 4 therefore has 10 times the $[H^+]$ of a solution with a pH of 5 and 100 times the $[H^+]$ of a solution with a pH of 6.

Acids

Any substance that dissociates in water to increase the $[H^+]$ (and lower the pH) is called an **acid.** The stronger an acid is, the more hydrogen ions it produces and the lower its pH. For example, hydrochloric acid (HCl), which is abundant in your stomach, ionizes completely in water. A dilution of 10^{-1} mol/L of HCl dissociates to form 10^{-1} mol/L of H^+, giving the solution a pH of 1. The pH of champagne, which bubbles because of the carbonic acid dissolved in it, is about 2.

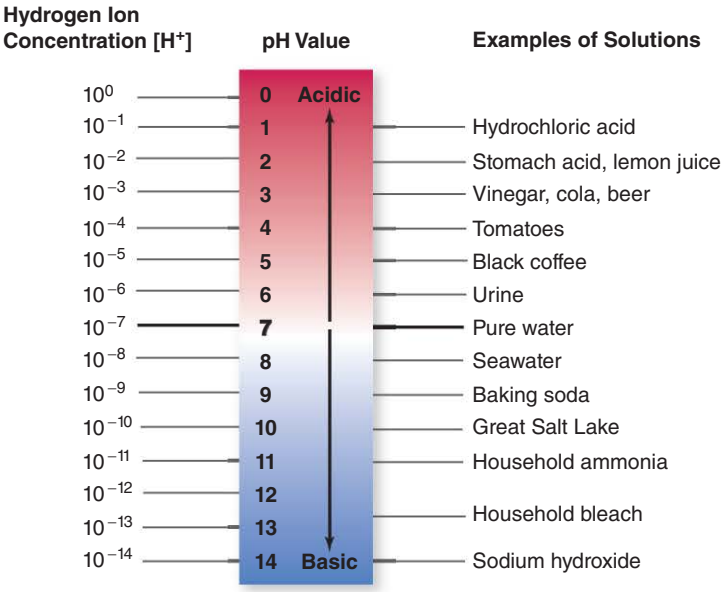


Figure 2.16 The pH scale. The pH value of a solution indicates its concentration of hydrogen ions. Solutions with a pH less than 7 are acidic, whereas those with a pH greater than 7 are basic. The scale is logarithmic, which means that a pH change of 1 represents a 10-fold change in the concentration of hydrogen ions. Thus, lemon juice is 100 times more acidic than tomato juice, and seawater is 10 times more basic than pure water, which has a pH of 7.

Bases

A substance that combines with H^+ when dissolved in water, and thus lowers the $[H^+]$, is called a **base.** Therefore, basic (or alkaline) solutions have pH values above 7. Very strong bases, such as sodium hydroxide (NaOH), have pH values of 12 or more. Many common cleaning substances, such as ammonia and bleach, accomplish their action because of their high pH.

Buffers help stabilize pH

The pH inside almost all living cells, and in the fluid surrounding cells in multicellular organisms, is fairly close to neutral, 7. Most of the enzymes in living systems are extremely sensitive to pH. Often even a small change in pH will alter their shape, thereby disrupting their activities. For this reason, it is important that a cell maintain a constant pH level.

But the chemical reactions of life constantly produce acids and bases within cells. Furthermore, many animals eat substances that are acidic or basic. Cola drinks, for example, are moderately strong (although dilute) acidic solutions. Despite such variations in the concentrations of H^+ and OH^-, the pH of an organism is kept at a relatively constant level by buffers (figure 2.17).

A **buffer** is a substance that resists changes in pH. Buffers act by releasing hydrogen ions when a base is added and absorbing hydrogen ions when acid is added, with the overall effect of keeping $[H^+]$ relatively constant.

Within organisms, most buffers consist of pairs of substances, one an acid and the other a base. The key buffer in human blood is an acid–base pair consisting of carbonic acid (acid) and bicarbonate (base). These two substances interact in a pair of reversible reactions. First, carbon dioxide (CO_2) and H_2O join to form carbonic acid (H_2CO_3), which in a second reaction dissociates to yield bicarbonate ion (HCO_3^-) and H^+.

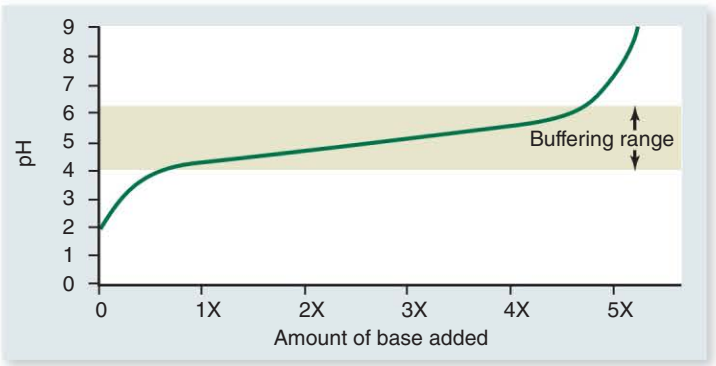
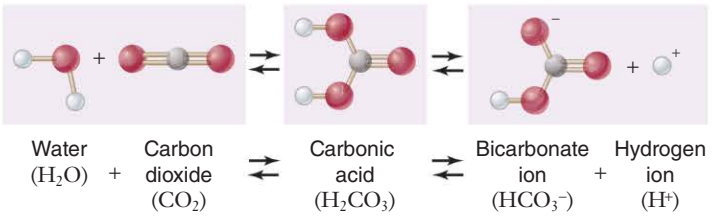


Figure 2.17 Buffers minimize changes in pH. Adding a base to a solution neutralizes some of the acid present, and so raises the pH. Thus, as the curve moves to the right, reflecting more and more base, it also rises to higher pH values. A buffer makes the curve rise or fall very slowly over a portion of the pH scale, called the "buffering range" of that buffer.

Data analysis If we call each step on the *x*-axis one volume of base, how many volumes of base must be added to change the pH from 4 to 6?

If some acid or other substance adds H^+ to the blood, the HCO_3^- acts as a base and removes the excess H^+ by forming H_2CO_3. Similarly, if a basic substance removes H^+ from the blood, H_2CO_3 dissociates, releasing more H^+ into the blood. The forward and reverse reactions that interconvert H_2CO_3 and HCO_3^- thus stabilize the blood's pH:



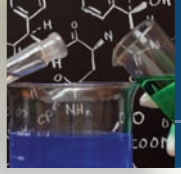
The reaction of carbon dioxide and water to form carbonic acid is a crucial one because it permits carbon, essential to life, to enter water from the air. The Earth's oceans are rich in carbon because of the reaction of carbon dioxide with water.

In a condition called blood acidosis, human blood, which normally has a pH of about 7.4, drops to a pH of about 7.1. This condition is fatal if not treated immediately. The reverse condition, blood alkalosis, involves an increase in blood pH of a similar magnitude and is just as serious.

Learning Outcomes Review 2.6

Acid solutions have a high $[H^+]$, and basic solutions have a low $[H^+]$ (and therefore a high $[OH^-]$). The pH of a solution is the negative logarithm of its $[H^+]$. Low pH values indicate acids, and high pH values indicate bases. Even small changes in pH can be harmful to life. Buffer systems in organisms help to maintain pH within a narrow range.

- ***A change of 2 pH units indicates what change in $[H^+]$?***



Chapter Review

2.1 The Nature of Atoms

All matter is composed of atoms (figure 2.3).

Atomic structure includes a central nucleus and orbiting electrons.

Electrically neutral atoms have the same number of protons as electrons. Atoms that gain or lose electrons are called ions.

Elements are defined by the number of protons in the nucleus, the atomic number. Atomic mass is the sum of the mass of protons and neutrons. Isotopes are forms of a single element with different atomic mass due to different numbers of neutrons. Radioactive isotopes are unstable.

Electrons determine the chemical behavior of atoms.

The potential energy of electrons increases as distance from the nucleus increases. Electron orbitals are probability distributions. *s*-Orbitals are spherical; other orbitals have different shapes, such as the dumbbell-shaped *p*-orbitals.

Atoms contain discrete energy levels.

Energy levels correspond to quanta (singular, quantum) of energy, a "ladder" of energy levels that an electron may have.

The loss of electrons from an atom is called oxidation. The gain of electrons is called reduction. Electrons can be transferred from one atom to another in coupled redox reactions.

2.2 Elements Found in Living Systems

The periodic table displays elements according to atomic number and properties.

Atoms tend to establish completely full outer energy levels (the octet rule). Elements with filled outermost orbitals are inert.

Ninety elements occur naturally in the Earth's crust. Twelve of these elements are found in living organisms in greater than trace amounts: C, H, O, N, P, S, Na, K, Ca, Mg, Fe, and Cl.

Compounds of carbon are called organic compounds. The majority of molecules in living systems are composed of C bound to H, O, and N.

2.3 The Nature of Chemical Bonds

Molecules contain two or more atoms joined by chemical bonds. Compounds contain two or more different elements.

Ionic bonds form crystals.

Ions with opposite electrical charges form ionic bonds, such as NaCl (figure 2.9*b*).

Covalent bonds build stable molecules.

A molecule formed by a covalent bond is stable because it has no net charge, the octet rule is satisfied, and it has no unpaired electrons. Covalent bonds may be single, double, or triple, depending on the number of pairs of electrons shared. Nonpolar covalent bonds involve equal sharing of electrons between atoms. Polar covalent bonds involve unequal sharing of electrons.

Chemical reactions alter bonds.

Temperature, reactant concentration, and the presence of catalysts affect reaction rates. Most biological reactions are reversible, such as the conversion of carbon dioxide and water into carbohydrates.

2.4 Water: A Vital Compound

Water's structure facilitates hydrogen bonding.

Hydrogen bonds are weak interactions between a partially positive H in one molecule and a partially negative O in another molecule (figure 2.11).

Water molecules are cohesive.

Cohesion is the tendency of water molecules to adhere to one another due to hydrogen bonding. The cohesion of water is responsible for its surface tension.

Water molecules are adhesive.

Adhesion occurs when water molecules adhere to other polar molecules. Capillary action results from water's adhesion to the sides of narrow tubes, combined with its cohesion.

2.5 Properties of Water

Water's high specific heat helps maintain temperature.

The specific heat of water is high because it takes a considerable amount of energy to disrupt hydrogen bonds.

Water's high heat of vaporization facilitates cooling.

Breaking hydrogen bonds to turn liquid water into vapor takes a lot of energy. Many organisms lose excess heat through evaporative cooling, such as sweating.

Solid water is less dense than liquid water.

Hydrogen bonds are spaced farther apart in the solid phase of water than in the liquid phase. As a result, ice floats.

Polar molecules and ions are soluble in water.

Water's polarity makes it a good solvent for polar substances and ions. Polar molecules or portions of molecules are attracted to water (hydrophilic). Molecules that are nonpolar are repelled by water (hydrophobic). Water makes nonpolar molecules clump together.

Water organizes nonpolar molecules.

Nonpolar molecules will aggregate to avoid water. This maximizes the hydrogen bonds that water can make. This hydrophobic exclusion can affect the structure of DNA, proteins, and biological membranes.

Water can form ions.

Water dissociates into H^+ and OH^-. The concentration of H^+, shown as $[H^+]$, in pure water is 10^{-7} mol/L.

2.6 Acids and Bases (figure 2.16)

The pH scale measures hydrogen ion concentration.

pH is defined as the negative logarithm of $[H^+]$. Pure water has a pH of 7. A difference of 1 pH unit means a 10-fold change in $[H^+]$.

Acids have a greater $[H^+]$ and therefore a lower pH; bases have a lower $[H^+]$ and therefore a higher pH.

Buffers help stabilize pH.

Carbon dioxide and water react reversibly to form carbonic acid. A buffer resists changes in pH by absorbing or releasing H^+. The key buffer in the human blood is the carbonic acid/bicarbonate pair.

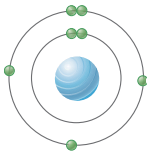
Review Questions

UNDERSTAND

1. The property that distinguishes an atom of one element (carbon, for example) from an atom of another element (oxygen, for example) is
   a. the number of electrons.
   b. the number of protons.
   c. the number of neutrons.
   d. the combined number of protons and neutrons.
2. If an atom has one valence electron—that is, a single electron in its outer energy level—it will most likely form
   a. one polar, covalent bond.
   b. two nonpolar, covalent bonds.
   c. two covalent bonds.
   d. an ionic bond.
3. An atom with a net positive charge must have more
   a. protons than neutrons.
   b. protons than electrons.
   c. electrons than neutrons.
   d. electrons than protons.
4. The isotopes carbon-12 and carbon-14 differ in
   a. the number of neutrons.
   b. the number of protons.
   c. the number of electrons.
   d. Both b and c are correct.
5. Which of the following is NOT a property of the elements most commonly found in living organisms?
   a. The elements have a low atomic mass.
   b. The elements have an atomic number less than 21.
   c. The elements possess eight electrons in their outer energy level.
   d. The elements are lacking one or more electrons from their outer energy level.
6. Ionic bonds arise from
   a. shared valence electrons.
   b. attractions between valence electrons.
   c. charge attractions between valence electrons.
   d. attractions between ions of opposite charge.
7. A solution with a high concentration of hydrogen ions
   a. is called a base.
   b. is called an acid.
   c. has a high pH.
   d. Both b and c are correct.

APPLY

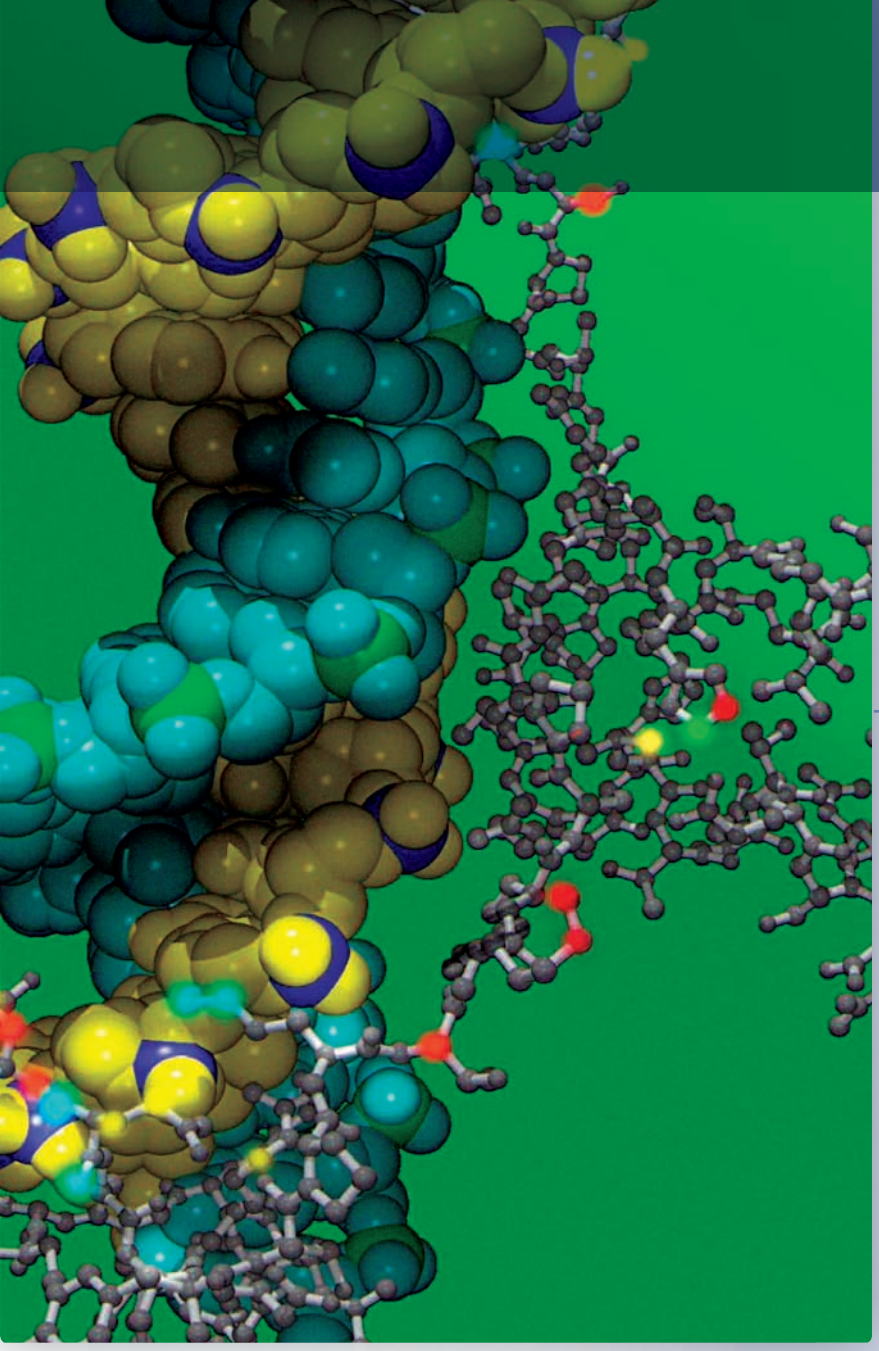
1. Using the periodic table on page 22, which of the following atoms would you predict should form a positively charged ion (cation)?
   a. Fluorine (F)
   b. Neon (Ne)
   c. Potassium (K)
   d. Sulfur (S)
2. Refer to the element pictured. How many covalent bonds could this atom form?
   a. Two
   b. Three
   c. Four
   d. None



3. A molecule with polar covalent bonds would
   a. be soluble in water.
   b. not be soluble in water.
   c. contain atoms with very similar electronegativity.
   d. Both b and c are correct.
4. Hydrogen bonds are formed
   a. between any molecules that contain hydrogen.
   b. only between water molecules.
   c. when hydrogen is part of a polar bond.
   d. when two atoms of hydrogen share an electron.
5. If you shake a bottle of oil and vinegar then let it sit, it will separate into two phases because
   a. the nonpolar oil is soluble in water.
   b. water can form hydrogen bonds with the oil.
   c. polar oil is not soluble in water.
   d. nonpolar oil is not soluble in water.
6. The decay of radioactive isotopes involves changes to the nucleus of atoms. Explain how this differs from the changes in atoms that occur during chemical reactions.

SYNTHESIZE

1. Elements that form ions are important for a range of biological processes. You have learned something about the cations sodium (Na^+), calcium ($Ca2^+$), and potassium (K^+) in this chapter. Use your knowledge of the definition of a cation to identify other examples from the periodic table.
2. A popular theme in science fiction literature has been the idea of silicon-based life-forms in contrast to our carbon-based life. Evaluate the possibility of silicon-based life based on the chemical structure and potential for chemical bonding of a silicon atom.
3. Efforts by NASA to search for signs of life on Mars have focused on the search for evidence of liquid water rather than looking directly for biological organisms (living or fossilized). Use your knowledge of the influence of water on life on Earth to construct an argument justifying this approach.



CHAPTER 3

The Chemical Building Blocks of Life

Chapter Contents

Introduction

A cup of water contains more molecules than there are stars in the sky. But many molecules are much larger than water molecules. Many thousands of distinct biological molecules are long chains made of thousands or even billions of atoms. These enormous assemblages, which are almost always synthesized by living things, are *macromolecules*. As you may know, biological macromolecules can be divided into four categories: *carbohydrates, nucleic acids, proteins,* and *lipids,* and they are the basic chemical building blocks from which all organisms are composed.

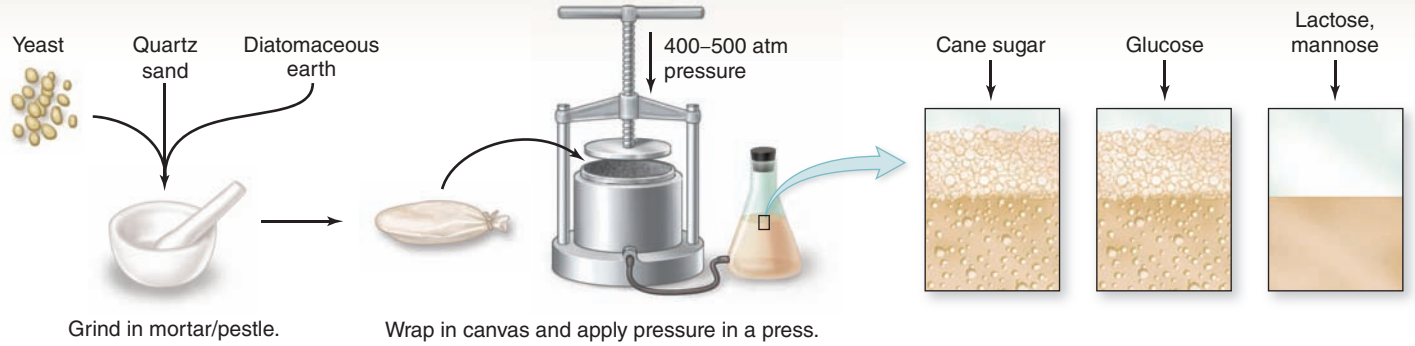
We take the existence of these classes of macromolecules for granted now, but as late as the 19th century many theories of "vital forces" were associated with living systems. One such theory held that cells contained a substance, protoplasm, that was responsible for the chemical reactions in living systems. Any disruption of cells was thought to disturb the protoplasm. Such a view makes studying the chemical reactions of cells in the lab (in vitro) impossible. The demonstration of fermentation in a cell-free system marked the beginning of modern biochemistry (figure 3.1). This approach involves studying biological molecules outside of cells to infer their role inside cells. Because these biological macromolecules all involve carbon-containing compounds, we begin with a brief summary of carbon and its chemistry.

SCIENTIFIC THINKING

Hypothesis: *Chemical reactions, such as the fermentation reaction in yeast, are controlled by enzymes and do not require living cells.*

Prediction: *If yeast cells are broken open, these enzymes should function outside of the cell.*

Test: *Yeast is mixed with quartz sand and diatomaceous earth and then ground in a mortar and pestle. The resulting paste is wrapped in canvas and subjected to 400–500 atm pressure in a press. Fermentable and nonfermentable substrates are added to the resulting fluid, with fermentation being measured by the production of CO_2.*



Result: *When a fermentable substrate (cane sugar, glucose) is used, CO_2 is produced; when a nonfermentable substrate (lactose, mannose) is used, no CO_2 is produced. In addition, visual inspection of the fluid shows no visible yeast cells.*

Conclusion: *The hypothesis is supported. The fermentation reaction can occur in the absence of live yeast.*

Historical Significance: *Although this is not precisely the intent of the original experiment, it represents the first use of a cell-free system. Such systems allow for the study of biochemical reactions in vitro and the purification of proteins involved. We now know that the "fermentation reaction" is actually a complex series of reactions. Would such a series of reactions be your first choice for this kind of demonstration?*

Figure 3.1 The demonstration of cell-free fermentation. The German chemist Eduard Buchner's (1860–1917) demonstration of fermentation by fluid produced from yeast, but not containing any live cells, both argued against the protoplasm theory and provided a method for future biochemists to examine the chemistry of life outside of cells.

3.1 Carbon: The Framework of Biological Molecules

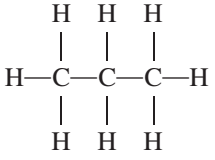
Learning Outcomes

1. *Describe the relationship between functional groups and macromolecules.*
2. *Recognize the different kinds of isomers.*
3. *List the different kinds of biological macromolecules.*

In chapter 2, we reviewed the basics of atomic structure and chemical bonding. Biological systems obey all the laws of chemistry. Thus, chemistry forms the basis of living systems.

The framework of biological molecules consists predominantly of carbon atoms bonded to other carbon atoms or to atoms of oxygen, nitrogen, sulfur, phosphorus, or hydrogen. Because carbon atoms can form up to four covalent bonds, molecules containing carbon can form straight chains, branches, or even rings, balls, tubes, and coils.

Molecules consisting only of carbon and hydrogen are called *hydrocarbons*. Because carbon–hydrogen covalent bonds store considerable energy, hydrocarbons make good fuels. Gasoline, for example, is rich in hydrocarbons, and propane gas, another hydrocarbon, consists of a chain of three carbon atoms, with eight hydrogen atoms bound to it. The chemical formula for propane is C_3H_8. Its structural formula is



Propane structural formula

Theoretically speaking, the length of a chain of carbon atoms is unlimited. As described in the rest of this chapter, the four main types of biological molecules often consist of huge chains of carbon-containing compounds.

Functional groups account for differences in molecular properties

Carbon and hydrogen atoms both have very similar electronegativities. Electrons in C—C and C—H bonds are therefore evenly distributed, with no significant differences in charge over the molecular surface. For this reason, hydrocarbons are nonpolar. Most biological molecules produced by cells, however, also contain other atoms. Because these other atoms frequently have different electronegativities (see table 2.2), molecules containing them exhibit regions of partial positive or negative charge. They are polar.

These molecules can be thought of as a C—H core to which specific molecular groups, called **functional groups,** are attached. One such common functional group is —OH, called a *hydroxyl group.*

Functional groups have definite chemical properties that they retain no matter where they occur. Both the hydroxyl and carbonyl (C═O) groups, for example, are polar because of the electronegativity of the oxygen atoms (see chapter 2). Other common functional groups are the acidic carboxyl (COOH), phosphate (PO_4^-), and the basic amino (NH_2) group. Many of these functional groups can also participate in hydrogen bonding. Hydrogen bond donors and acceptors can be predicted based on their electronegativities shown in table 2.2. Figure 3.2 illustrates these biologically important functional groups and lists the macromolecules in which they are found.

Functional Group	Structural Formula	Example	Found In
Hydroxyl	—OH	Ethanol	carbohydrates, proteins, nucleic acids, lipids
Carbonyl	—C(=O)—	Acetaldehyde	carbohydrates, nucleic acids
Carboxyl	—C(=O)OH	Acetic acid	proteins, lipids
Amino	—N(H)H	Alanine	proteins, nucleic acids
Sulfhydryl	—S—H	Cysteine	proteins
Phosphate	—O—P(=O)(O⁻)—O⁻	Glycerol phosphate	nucleic acids
Methyl	—C(H)(H)H	Alanine	proteins

Figure 3.2 The primary functional chemical groups. These groups tend to act as units during chemical reactions and give specific chemical properties to the molecules that possess them. Amino groups, for example, make a molecule more basic, and carboxyl groups make a molecule more acidic. These functional groups are also not limited to the examples in the "Found In" column but are widely distributed in biological molecules.

Isomers have the same molecular formulas but different structures

Organic molecules having the same molecular or empirical formula can exist in different forms called **isomers.** If there are differences in the actual structure of their carbon skeleton, we call them *structural isomers.* In section 3.2, you will see that glucose and fructose are structural isomers of $C_6H_{12}O_6$. Another form of isomers, called *stereoisomers,* have the same carbon skeleton but differ in how the groups attached to this skeleton are arranged in space.

Enzymes in biological systems usually recognize only a single, specific stereoisomer. A subcategory of stereoisomers, called *enantiomers,* are actually mirror images of each other. A molecule that has mirror-image versions is called a *chiral* molecule. When carbon is bound to four different molecules, this inherent asymmetry exists (figure 3.3).

Chiral compounds are characterized by their effect on polarized light. Polarized light has a single plane, and chiral molecules rotate this plane either to the right (Latin, *dextro*) or left (Latin, *levo*). We therefore call the two chiral forms *D* for *dextrorotatory* and *L* for *levorotatory.* Living systems tend to produce only a single enantiomer of the two possible forms; for example, in most organisms we find primarily D-sugars and L-amino acids.

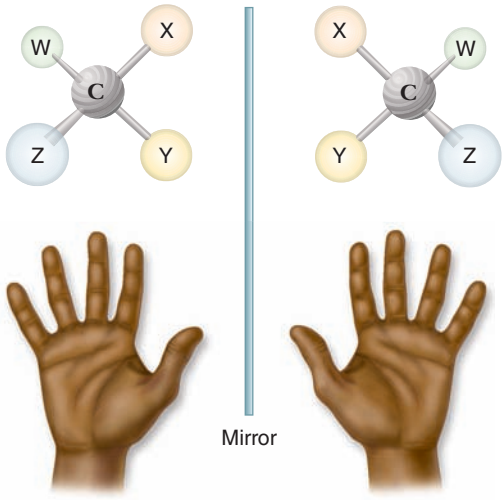


Figure 3.3 Chiral molecules. When carbon is bound to four different groups, the resulting molecule is said to be chiral (from Greek *cheir,* meaning "hand"). A chiral molecule will have stereoisomers that are mirror images. The two molecules shown have the same four groups but cannot be superimposed, much like your two hands cannot be superimposed but must be flipped to match. These types of stereoisomers are called *enantiomers.*

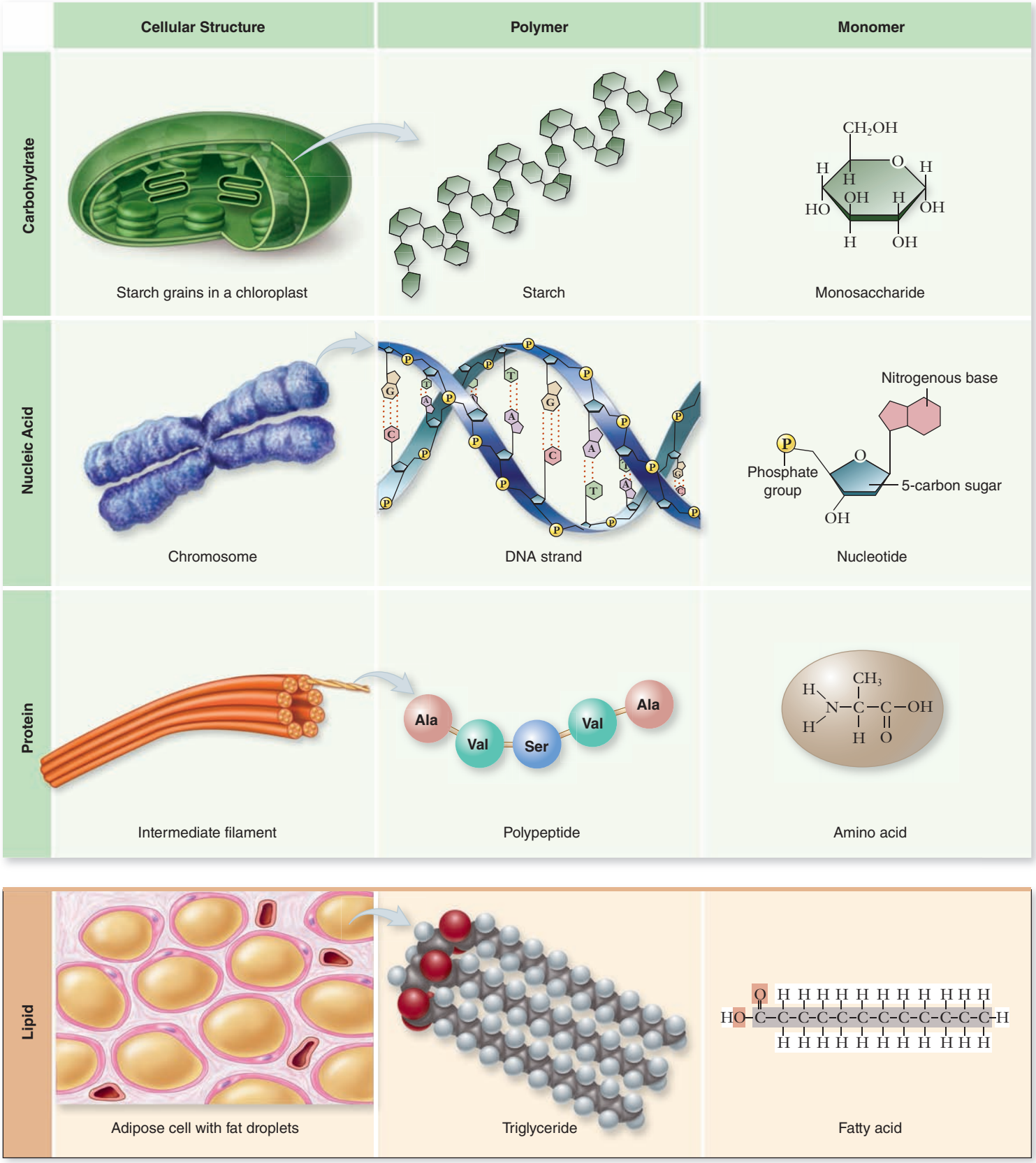


Figure 3.4 Polymer macromolecules. The four major biological macromolecules are shown. Carbohydrates, nucleic acids, and proteins all form polymers and are shown with the monomers used to make them. Lipids do not fit this simple monomer–polymer relationship. The triglyceride shown is constructed from glycerol and fatty acids. All four types of macromolecules are also shown in their cellular context.

TABLE 3.1 Macromolecules

Macromolecule	Subunit	Function	Example
CARBOHYDRATES			
Starch, glycogen	Glucose	Energy storage	Potatoes
Cellulose	Glucose	Structural support in plant cell walls	Paper; strings of celery
Chitin	Modified glucose	Structural support	Crab shells
NUCLEIC ACIDS			
DNA	Nucleotides	Encodes genes	Chromosomes
RNA	Nucleotides	Needed for gene expression	Messenger RNA
PROTEINS			
Functional	Amino acids	Catalysis; transport	Hemoglobin
Structural	Amino acids	Support	Hair; silk
LIPIDS			
Triglycerides (animal fat, oils)	Glycerol and three fatty acids	Energy storage	Butter; corn oil; soap
Phospholipids	Glycerol, two fatty acids, phosphate, and polar R groups	Cell membranes	Phosphatidylcholine
Prostaglandins	Five-carbon rings with two nonpolar tails	Chemical messengers	Prostaglandin E (PGE)
Steroids	Four fused carbon rings	Membranes; hormones	Cholesterol; estrogen
Terpenes	Long carbon chains	Pigments; structural support	Carotene; rubber

Biological macromolecules include carbohydrates, nucleic acids, proteins, and lipids

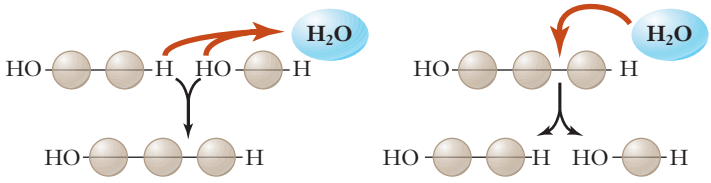
Remember that biological macromolecules are traditionally grouped into carbohydrates, nucleic acids, proteins, and lipids (table 3.1). In many cases, these macromolecules are polymers. A **polymer** is a long molecule built by linking together a large number of small, similar chemical subunits called **monomers.** They are like railroad cars coupled to form a train. The nature of a polymer is determined by the monomers used to build the polymer. Here are some examples. Complex carbohydrates such as starch are polymers composed of simple ring-shaped sugars. Nucleic acids (DNA and RNA) are polymers of nucleotides, and proteins are polymers of amino acids (figure 3.4). These long chains are built via chemical reactions termed *dehydration reactions* and are broken down by *hydrolysis reactions.* Lipids are macromolecules, but they really don't follow the monomer–polymer relationship. However, lipids are formed through dehydration reactions, which link the fatty acids to glycerol.

The dehydration reaction

Despite the differences between monomers of these major polymers, the basic chemistry of their synthesis is similar: To form a covalent bond between two monomers, an —OH group is removed from one monomer, and a hydrogen atom (H) is removed from the other (figure 3.5*a*). This reaction is the same for joining nucleotides when synthesizing DNA or joining glucose units together to make starch. This reaction is also used to link fatty acids to glycerol in lipids. This chemical reaction is called condensation, or a **dehydration reaction,** because the removal of —OH and —H is the same as the removal of a molecule of water (H_2O). For every subunit added to a macromolecule, one water molecule is removed. These and other biochemical reactions require that the reacting substances are held close together and that the correct chemical bonds are stressed and broken. This process of positioning and stressing, termed *catalysis,* is carried out within cells by enzymes.

The hydrolysis reaction

Cells disassemble polymers into their constituent monomers by reversing the dehydration reaction—a molecule of water is added instead of removed (figure 3.5*b*). In this reaction, called hydrolysis, a hydrogen atom is attached to one subunit and a hydroxyl group to the other, breaking the covalent bond joining the subunits. When you eat a potato, which contains starch (see section 3.2), your body breaks the starch down into glucose units by hydrolysis. The potato plant built the starch molecules originally by dehydration reactions.



a. Dehydration reaction ***b.*** Hydrolysis reaction

Figure 3.5 Making and breaking macromolecules.
a. Biological macromolecules are polymers formed by linking monomers together through dehydration reactions. This process releases a water molecule for every bond formed. ***b.*** Breaking the bond between subunits involves hydrolysis, which reverses the loss of a water molecule by dehydration.

Learning Outcomes Review 3.1

Functional groups account for differences in chemical properties in organic molecules. Isomers are compounds with the same empirical formula but different structures. This difference may affect biological function. Macromolecules are polymers consisting of long chains of similar subunits that are joined by dehydration reactions and are broken down by hydrolysis reactions.

- *What is the relationship between dehydration and hydrolysis?*

3.2 Carbohydrates: Energy Storage and Structural Molecules

Learning Outcomes

1. *Describe the structure of simple sugars with three to six carbons.*
2. *Relate the structure of polysaccharides to their functions.*

Monosaccharides are simple sugars

Carbohydrates are a loosely defined group of molecules that all contain carbon, hydrogen, and oxygen in the molar ratio 1:2:1. Their empirical formula (which lists the number of atoms in the molecule with subscripts) is $(CH_2O)_n$, where n is the number of carbon atoms. Because they contain many carbon–hydrogen (C—H) bonds, which release energy when oxidation occurs, carbohydrates are well suited for energy storage. Sugars are among the most important energy-storage molecules, and they exist in several different forms.

The simplest of the carbohydrates are the **monosaccharides** (Greek *mono,* "single," and Latin *saccharum,* "sugar"). Simple sugars contain as few as three carbon atoms, but those that play the central role in energy storage have six (figure 3.6). The empirical formula of 6-carbon sugars is:

$C_6H_{12}O_6$ or $(CH_2O)_6$

Six-carbon sugars can exist in a straight-chain form, but dissolved in water (an aqueous environment) they almost always form rings.

The most important of the 6-carbon monosaccharides for energy storage is glucose, which you first encountered in the examples of chemical reactions in chapter 2. Glucose has seven energy-storing C—H bonds (figure 3.7). Depending on the orientation of the carbonyl group (C═O) when the ring is closed, glucose can exist in two different forms: alpha (α) or beta (β).

Sugar isomers have structural differences

Glucose is not the only sugar with the formula $C_6H_{12}O_6$. Both structural isomers and stereoisomers of this simple 6-carbon skeleton exist in nature. Fructose is a structural isomer that differs in the position of the carbonyl carbon (C═O); galactose is a stereoisomer that differs in the position of —OH and —H groups relative to the ring (figure 3.8). These differences often account for substantial functional differences between the isomers. Your taste buds can discern them: Fructose tastes much sweeter than glucose, despite the fact that both sugars have identical chemical composition. Enzymes that act on different sugars can distinguish both the structural and stereoisomers of this basic 6-carbon skeleton. The different stereoisomers of glucose are also important in the polymers that can be made using glucose as a monomer, as you will see later in this section.

Disaccharides serve as transport molecules in plants and provide nutrition in animals

Most organisms transport sugars within their bodies. In humans, the glucose that circulates in the blood does so as a simple monosaccharide. In plants and many other organisms, however, glucose is converted into a transport form before it is moved from place to place within the organism. In such a form, it is less readily metabolized during transport.

Transport forms of sugars are commonly made by linking two monosaccharides together to form a **disaccharide** (Greek *di,* "two"). Disaccharides serve as effective reservoirs of glucose because the enzymes that normally use glucose in the organism cannot break the bond linking the two monosaccharide subunits. Enzymes that can do so are typically present only in the tissue that uses glucose.

Transport forms differ depending on which monosaccharides are linked to form the disaccharide. Glucose forms transport disaccharides with itself and with many other monosaccharides,

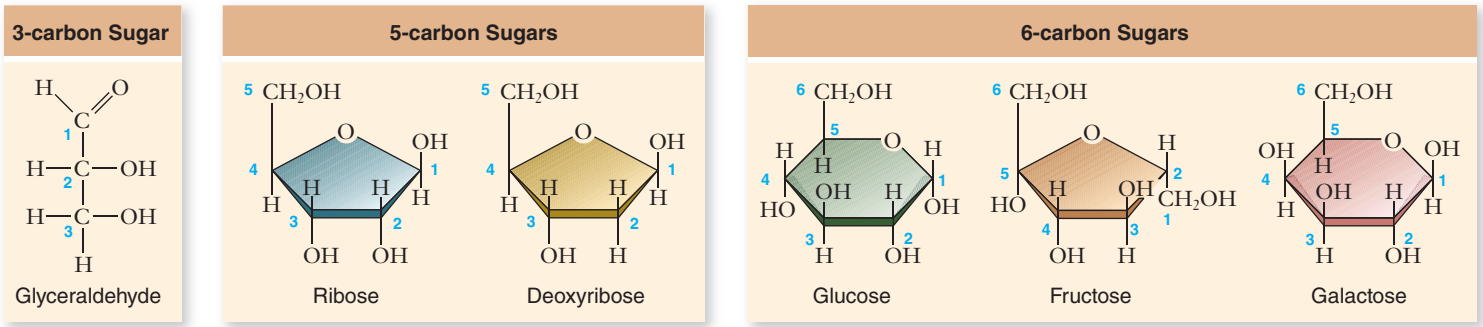


Figure 3.6 Monosaccharides. Monosaccharides, or simple sugars, can contain as few as three carbon atoms and are often used as building blocks to form larger molecules. The 5-carbon sugars ribose and deoxyribose are components of nucleic acids (see figure 3.15). The carbons are conventionally numbered (in *blue*) from the more oxidized end.

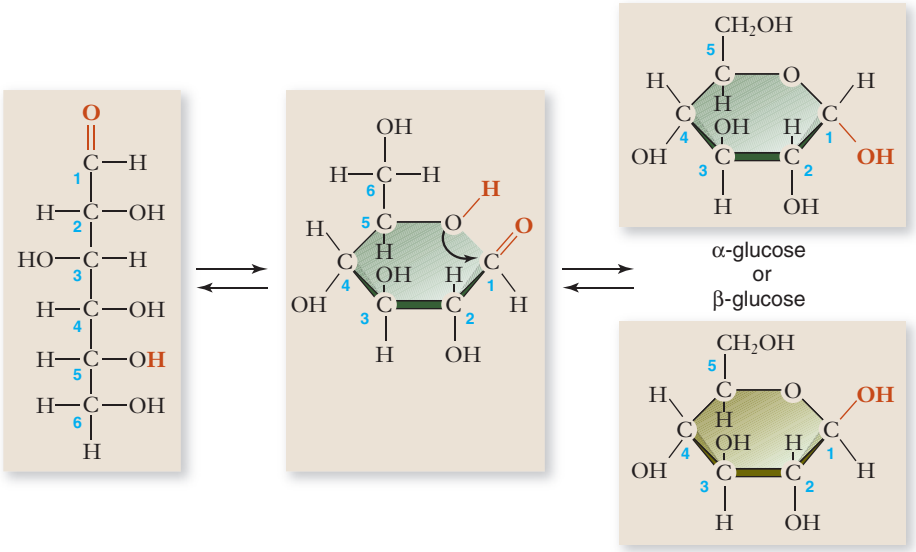


Figure 3.7 Structure of the glucose molecule. Glucose is a linear, 6-carbon molecule that forms a six-membered ring in solution. Ring closure occurs such that two forms can result: α-glucose and β-glucose. These structures differ only in the position of the —OH bound to carbon 1. The structure of the ring can be represented in many ways; shown here are the most common, with the carbons conventionally numbered so that the forms can be compared easily. The heavy lines in the ring structures represent portions of the molecule that are projecting out of the page toward you.

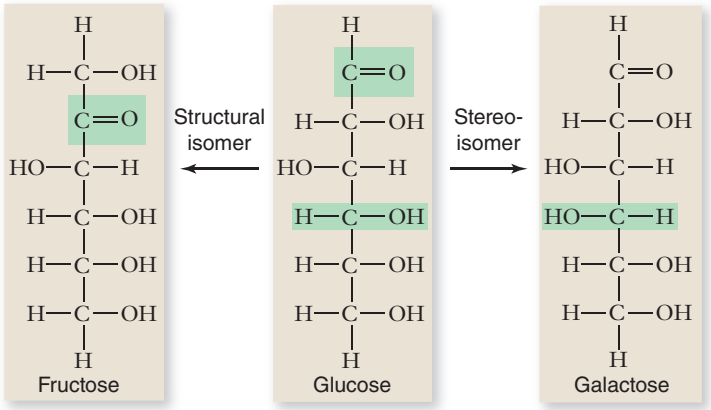


Figure 3.8 Isomers and stereoisomers. Glucose, fructose, and galactose are isomers with the empirical formula $C_6H_{12}O_6$. A structural isomer of glucose, such as fructose, has identical chemical groups bonded to different carbon atoms. Notice that this results in a five-membered ring in solution (see figure 3.6). A stereoisomer of glucose, such as galactose, has identical chemical groups bonded to the same carbon atoms but in different orientations (the —OH at carbon 4).

including fructose and galactose. When glucose forms a disaccharide with the structural isomer fructose, the resulting disaccharide is *sucrose,* or table sugar (figure 3.9*a*). Sucrose is the form most plants use to transport glucose and is the sugar that most humans and other animals eat. Sugarcane and sugar beets are rich in sucrose.

When glucose is linked to the stereoisomer galactose, the resulting disaccharide is *lactose,* or milk sugar. Many mammals supply energy to their young in the form of lactose. Adults often have greatly reduced levels of lactase, the enzyme required to cleave lactose into its two monosaccharide components, and thus they cannot metabolize lactose efficiently. This can result in lactose intolerance in humans. Most of the energy that is channeled into lactose production is therefore reserved for offspring. For this reason, lactose as an energy source is primarily for offspring in mammals.

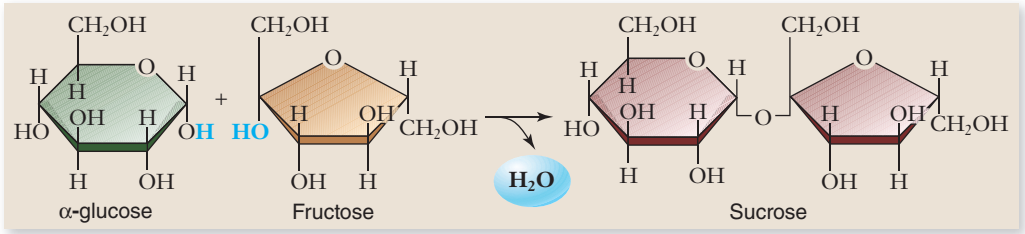
Polysaccharides provide energy storage and structural components

Polysaccharides are longer polymers made up of monosaccharides that have been joined through dehydration reactions. **Starch,** a storage polysaccharide, consists entirely of α-glucose molecules linked in long chains. **Cellulose,** a structural polysaccharide, also consists of glucose molecules linked in chains, but these molecules are β-glucose. Because starch is built from α-glucose we call the linkages α linkages; cellulose has β linkages.

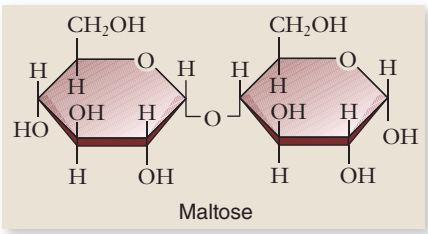
Starches and glycogen

Organisms store the metabolic energy contained in monosaccharides by converting them into disaccharides, such as *maltose* (figure 3.9*b*). These are then linked together into the insoluble polysaccharides called *starches.* These polysaccharides differ mainly in how the polymers branch.

The starch with the simplest structure is *amylose.* It is composed of many hundreds of α-glucose molecules linked together in long, unbranched chains. Each linkage occurs between the carbon 1 (C-1) of one glucose molecule and the C-4 of another, making them α-(1⟶4) linkages (figure 3.10*a*). The long chains of amylose tend to coil up in water, a property that renders amylose insoluble. Potato starch is about 20% amylose (figure 3.10*b*).



a.



b.

Figure 3.9 How disaccharides form. Some disaccharides are used to transport glucose from one part of an organism's body to another; one example is sucrose ***(a)***, which is found in sugarcane. Other disaccharides, such as maltose ***(b)***, are used in grain for storage.

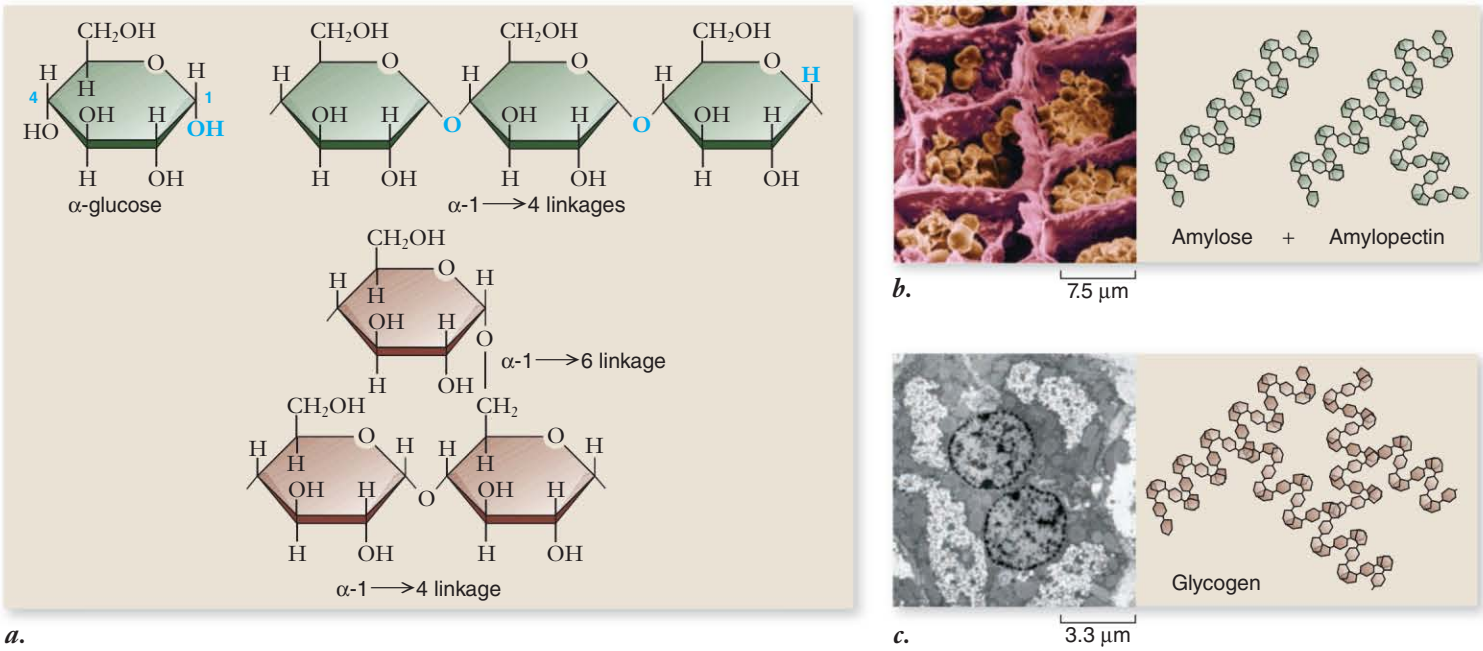


Figure 3.10 Polymers of glucose: Starch and glycogen. ***a.*** Starch chains consist of polymers of α-glucose subunits joined by α-(1⟶4) glycosidic linkages. These chains can be branched by forming similar α-(1⟶6) glycosidic bonds. These storage polymers then differ primarily in their degree of branching. ***b.*** Starch is found in plants and is composed of amylose and amylopectin, which are unbranched and branched, respectively. The branched form is insoluble and forms starch granules in plant cells. ***c.*** Glycogen is found in animal cells and is highly branched and also insoluble, forming glycogen granules.

Most plant starch, including the remaining 80% of potato starch, is a somewhat more complicated variant of amylose called *amylopectin.* Pectins are branched polysaccharides with the branches occurring due to bonds between the C-1 of one molecule and the C-6 of another [α-(1⟶6) linkages]. These short amylose branches consist of 20 to 30 glucose subunits (figure 3.10*b*).

The comparable molecule to starch in animals is **glycogen.** Like amylopectin, glycogen is an insoluble polysaccharide containing branched amylose chains. Glycogen has a much longer average chain length and more branches than plant starch (figure 3.10*c*).

Cellulose

Although some chains of sugars store energy, others serve as structural material for cells. For two glucose molecules to link together, the glucose subunits must be of the same form. *Cellulose* is a polymer of β-glucose (figure 3.11). The bonds between adjacent

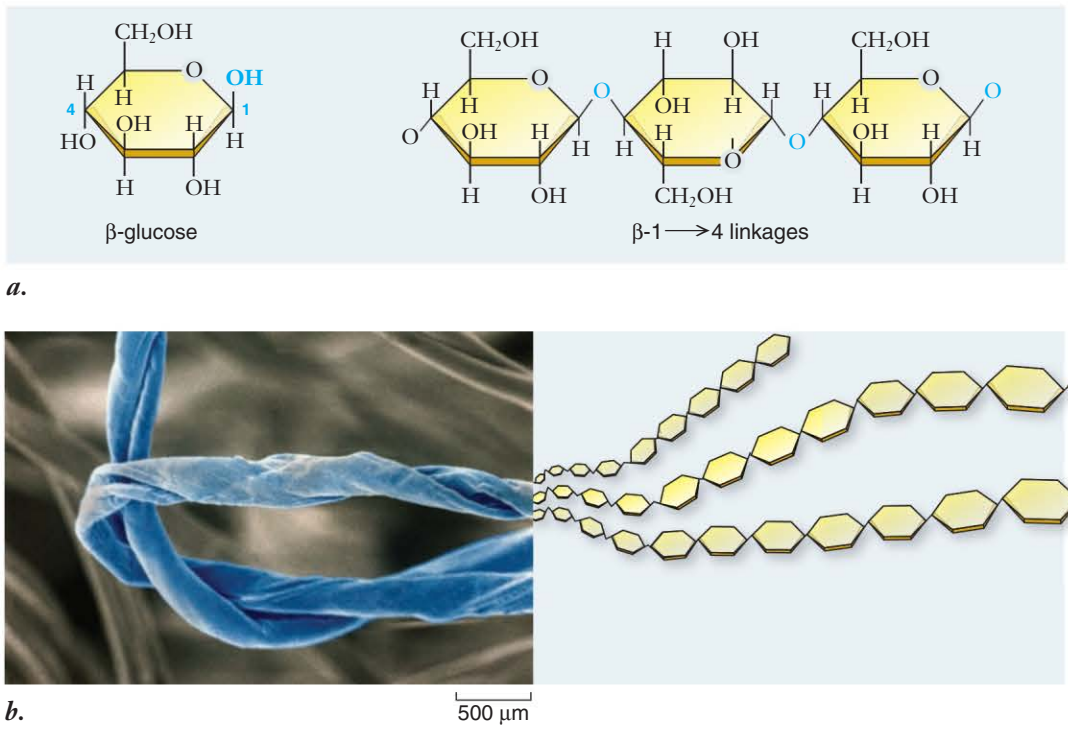


Figure 3.11 Polymers of glucose: Cellulose. Starch chains consist of α-glucose subunits, and cellulose chains consist of β-glucose subunits. ***a.*** Thus the bonds between adjacent glucose molecules in cellulose are β-(1⟶4) glycosidic linkages. ***b.*** Cellulose is unbranched and forms long fibers. Cellulose fibers can be very strong and are quite resistant to metabolic breakdown, which is one reason wood is such a good building material.

glucose molecules still exist between the C-1 of the first glucose and the C-4 of the next glucose, but these are β-(1⟶4) linkages.

The properties of a chain of glucose molecules consisting of all β-glucose are very different from those of starch. These long, unbranched β-linked chains make tough fibers. Cellulose is the chief component of plant cell walls (see figure 3.11*b*). It is chemically similar to amylose, with one important difference: The starch-hydrolyzing enzymes that occur in most organisms cannot break the bond between two β-glucose units because they only recognize α linkages.

Because cellulose cannot be broken down readily by most animals, it works well as a biological structural material. But some animals, such as cows, are able to utilize cellulose aided by symbiotic bacteria and protists in their digestive tracts. These organisms provide the necessary enzymes for cleaving the β-(1⟶4) linkages, thus providing access to a rich source of energy.

Chitin

Chitin, the structural material found in arthropods and many fungi, is a polymer of *N*-acetylglucosamine, a substituted version of glucose. When cross-linked by proteins, it forms a tough, resistant surface material that serves as the hard exoskeleton of insects and crustaceans (figure 3.12; see chapter 34). Few organisms are able to digest chitin, but most possess a chitinase enzyme, probably to protect against fungi.

Learning Outcomes Review 3.2

Monosaccharides have three to six or more carbon atoms typically arranged in a ring form. Disaccharides consist of two linked monosaccharides; polysaccharides are long chains of monosaccharides. Structural differences between sugar isomers can lead to functional differences. Starches are branched polymers of α-glucose used for energy storage. Cellulose in plants consists of unbranched chains of β-glucose that are not easily digested.

- *How do the structures of starch, glycogen, and cellulose affect their function?*

Figure 3.12 Chitin. Chitin is the principal structural element in the external skeletons of many invertebrates, such as this lobster.

3.3 Nucleic Acids: Information Molecules

Learning Outcomes

1. *Describe the structure of nucleotides.*
2. *Contrast the structures of DNA and RNA.*
3. *Discuss the functions of DNA and RNA.*
4. *Recognize other nucleotides involved in energy metabolism.*

The biochemical activity of a cell depends on production of a large number of proteins, each with a specific sequence. The information necessary to produce the correct proteins is passed through generations of organisms, even though the proteins themselves are not inherited.

Nucleic acids carry information inside cells, just as disks contain the information in a computer or road maps display information needed by travelers. Two main varieties of nucleic acids are **deoxyribonucleic acid** (**DNA;** figure 3.13) and **ribonucleic acid (RNA).**

Genetic information is stored in DNA, and short-lived copies of this are made in the form of RNA, which is then used to direct the synthesis of proteins during the process of gene expression (as discussed in detail in chapter 15). Unique among macromolecules, nucleic acids are able to serve as templates for producing precise copies of themselves. This characteristic allows genetic information to be preserved during cell division and during the reproduction of organisms.

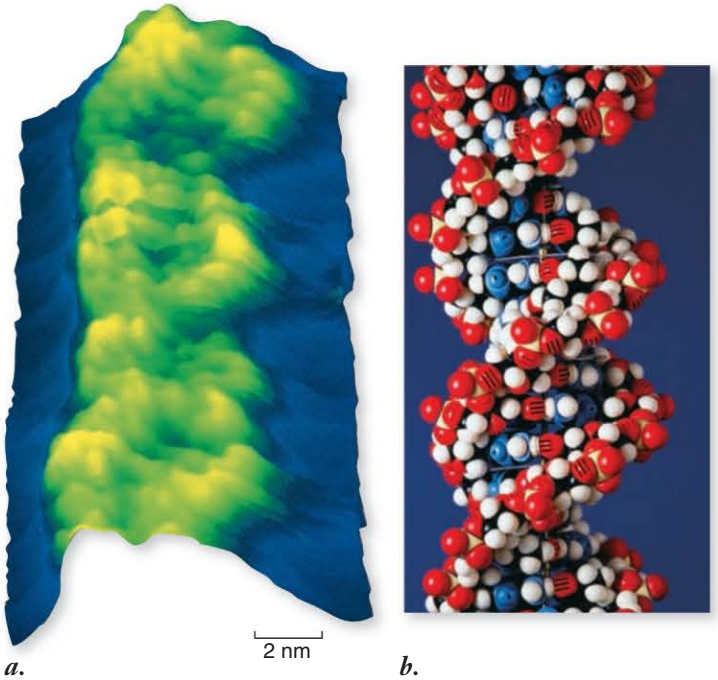


Figure 3.13 Images of DNA. ***a.*** A scanning-tunneling micrograph of DNA (false color; 2,000,000×) showing approximately three turns of the DNA double helix. ***b.*** A space-filling model for comparison to the image of actual DNA in ***(a)***.

The role of RNA in cells is much more complicated: RNA carries information, is part of the organelle responsible for protein synthesis, and recent work indicates it is also involved in the control of gene expression. As a carrier of information, the form of RNA called **messenger RNA (mRNA)** consists of transcribed single-stranded copies of portions of the DNA. These transcripts serve as blueprints specifying the amino acid sequences of proteins. This process will be described in detail in chapter 15.

Nucleic acids are nucleotide polymers

Nucleic acids are long polymers of repeating subunits called **nucleotides.** Each nucleotide consists of three components: a pentose, or 5-carbon sugar (ribose in RNA and deoxyribose in DNA); a phosphate ($—PO_4^-$) group; and an organic nitrogenous (nitrogen-containing) base (figure 3.14). Nucleotides can form polymers by joining the phosphate of one nucleotide to a hydroxyl group on the sugar of another nucleotide by a dehydration reaction. This forms a *phosphodiester bond* linking the two sugars through a phosphate. A **nucleic acid,** then, is simply a chain of 5-carbon sugars linked together by phosphodiester bonds with a nitrogenous base protruding from each sugar (see figure 3.15*a*). These chains of nucleotides, *polynucleotides,* have polarity, or different ends: a phosphate on one end and an —OH from a sugar on the other end. We conventionally refer to these ends as 5′ ("five-prime," $—PO_4^-$) and 3′ ("three-prime," —OH) taken from the carbon numbering of the sugar (figure 3.15*a*).

Nucleotides have five types of nitrogenous bases (figure 3.15*b*). Two of these are large, double-ring molecules called *purines* that are each found in both DNA and RNA; the two purines are adenine (A) and guanine (G). The other three bases are single-ring molecules

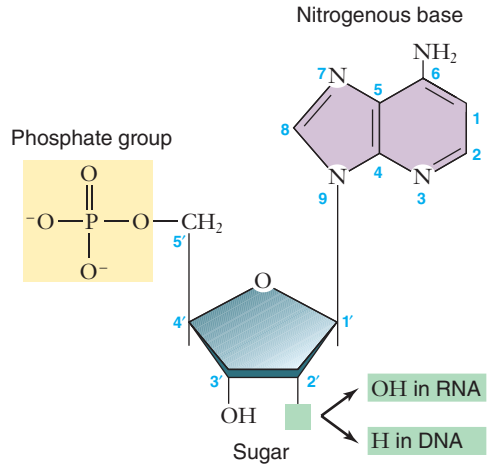
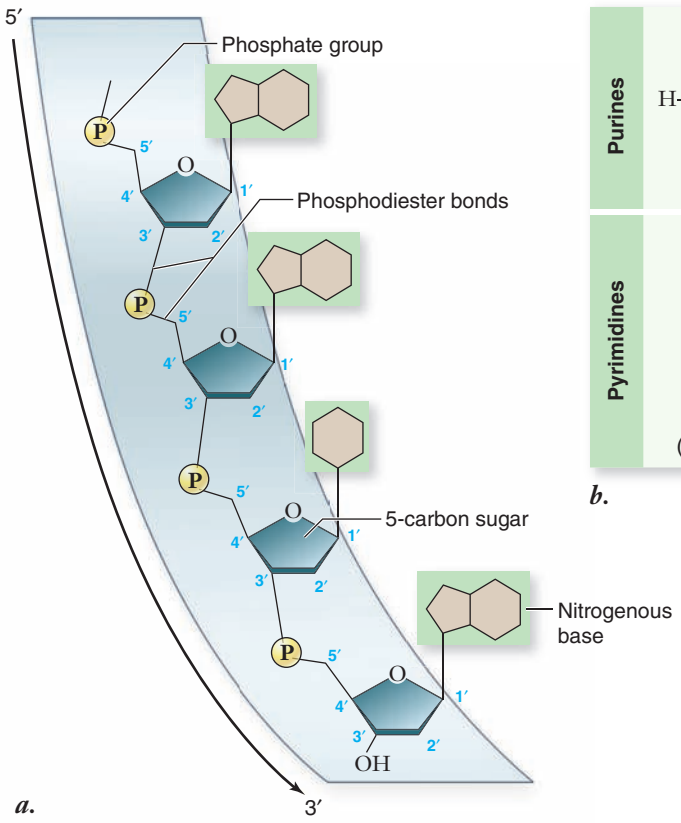


Figure 3.14 Structure of a nucleotide. The nucleotide subunits of DNA and RNA are made up of three elements: a 5-carbon sugar (ribose or deoxyribose), an organic nitrogenous base (adenine is shown here), and a phosphate group. Notice that all the numbers on the sugar are given as "primes" (1′, 2′, etc.) to distinguish them from the numbering on the rings of the bases.

called *pyrimidines* that include cytosine (C, in both DNA and RNA), thymine (T, in DNA only), and uracil (U, in RNA only).

DNA stores genetic information

Organisms use sequences of nucleotides in DNA to encode the information specifying the amino acid sequences of their proteins. This method of encoding information is very similar to the way in which sequences of letters encode information in a sentence.



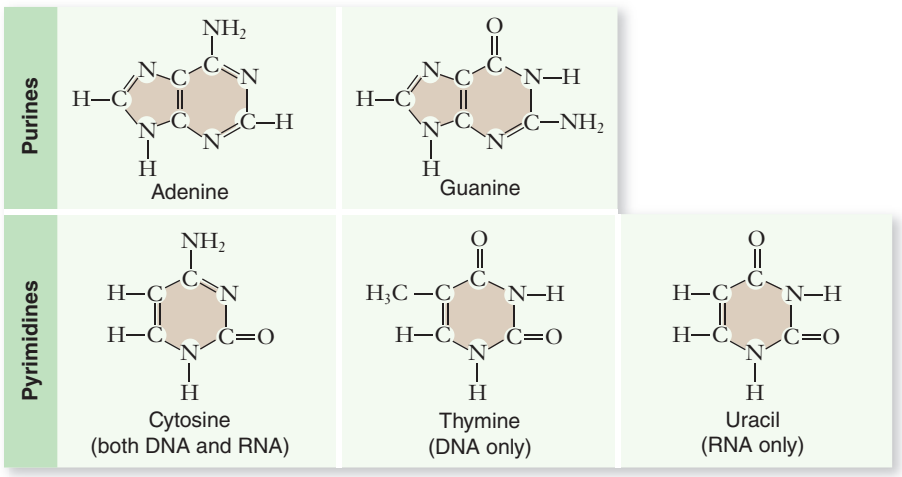


Figure 3.15 The structure of a nucleic acid and the organic nitrogenous bases. ***a.*** In a nucleic acid, nucleotides are linked to one another via phosphodiester bonds formed between the phosphate of one nucleotide and the sugar of the next nucleotide. We call this the sugar-phosphate backbone, with the organic bases protrude from this chain. The backbone also has different ends: a 5′ phosphate end and a 3′ hydroxyl end (the blue numbers come from the numbers in the sugars). ***b.*** The organic nitrogenous bases can be either purines or pyrimidines. The base thymine is found in DNA. The base uracil is found in RNA.

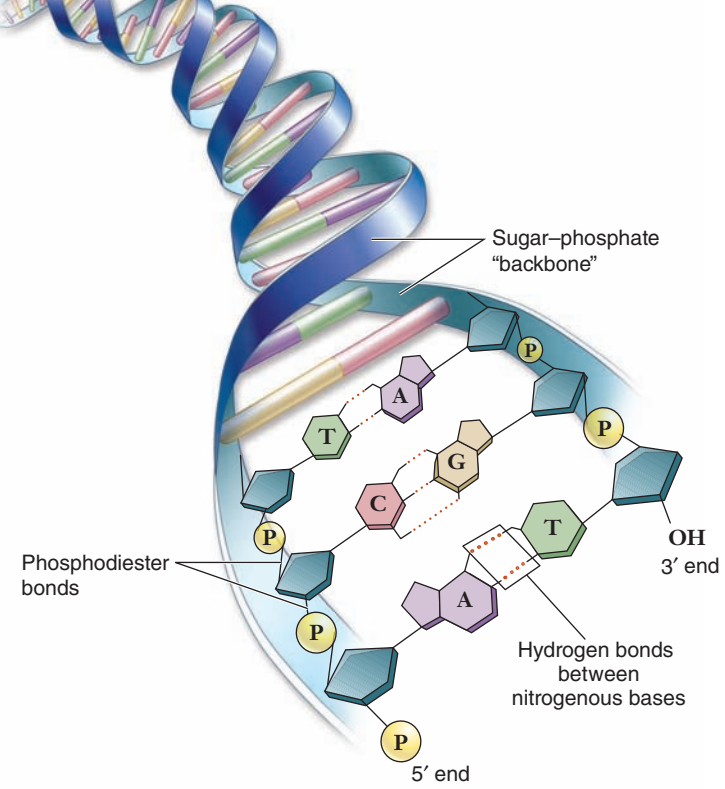


Figure 3.16 The structure of DNA. DNA consists of two polynucleotide chains running in opposite directions wrapped about a single helical axis. Hydrogen bond formation (dashed lines) between the nitrogenous bases, called base-pairing, causes the two chains of DNA to bind to each other and form a double helix.

A sentence written in English consists of a combination of the 26 different letters of the alphabet in a certain order; the code of a DNA molecule consists of different combinations of the four types of nucleotides in specific sequences, such as CGCTTACG.

DNA molecules in organisms exist as two chains wrapped about each other in a long linear molecule in eukaryotes, and a circular molecule in most prokaryotes. The two strands of a DNA polymer wind around each other like the outside and inside rails of a spiral staircase. Such a spiral shape is called a helix, and a helix composed of two chains is called a **double helix.** Each step of DNA's helical staircase is composed of a base-pair. The pair consists of a base in one chain attracted by hydrogen bonds to a base opposite it on the other chain (figure 3.16).

The base-pairing rules arise from the most stable hydrogen bonding configurations between the bases: Adenine pairs with thymine (in DNA) or with uracil (in RNA), and cytosine pairs with guanine. The bases that participate in base-pairing are said to be **complementary** to each other. Additional details of the structure of DNA and how it interacts with RNA in the production of proteins are presented in chapters 14 and 15.

In eukaryotic organisms, the DNA is further complexed with protein to form structures we call chromosomes. This actually forms a higher order structure that affects the function of DNA as it is involved in the control of gene expression (see chapter 16).

RNA has many roles in a cell

RNA is similar to DNA, but with two major chemical differences. First, RNA molecules contain ribose sugars, in which the C-2 is bonded to a hydroxyl group. (In DNA, a hydrogen atom replaces this hydroxyl group.) Second, RNA molecules use uracil in place of thymine. Uracil has a similar structure to thymine, except that one of its carbons lacks a methyl (—CH_3) group.

RNA is produced by transcription (copying) from DNA, and is usually single-stranded (figure 3.17). The role of RNA in cells is quite varied: it carries information in the form of **mRNA,** it is part of the ribosome, in the form of **ribosomal RNA (rRNA),** and it carries amino acids in the form of **transfer RNA (tRNA).** There has been a revolution of late in how we view RNA since it has been found to function as an enzyme, and other forms of RNA are involved in regulating gene expression (explored in more detail in chapter 16).

Other nucleotides are vital components of energy reactions

In addition to serving as subunits of DNA and RNA, nucleotide bases play other critical roles in the life of a cell. For example, adenine is a key component of the molecule **adenosine triphosphate**

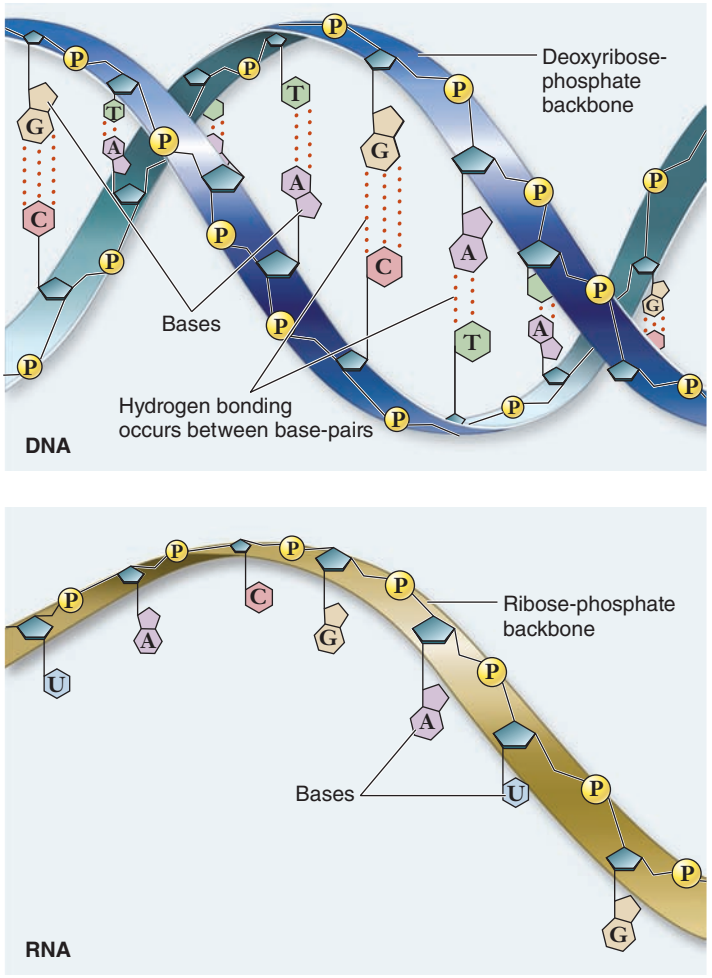


Figure 3.17 DNA versus RNA. DNA forms a double helix, uses deoxyribose as the sugar in its sugar–phosphate backbone, and uses thymine among its nitrogenous bases. RNA is usually single-stranded, uses ribose as the sugar in its sugar–phosphate backbone, and uses uracil in place of thymine.

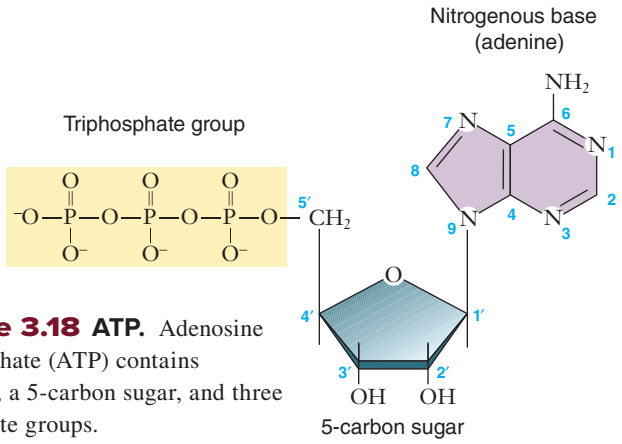


Figure 3.18 ATP. Adenosine triphosphate (ATP) contains adenine, a 5-carbon sugar, and three phosphate groups.

(**ATP;** figure 3.18)—the energy currency of the cell. Cells use ATP as energy in a variety of transactions, the way we use money in society. ATP is used to drive energetically unfavorable chemical reactions, to power transport across membranes, and to power the movement of cells.

Two other important nucleotide-containing molecules are **nicotinamide adenine dinucleotide (NAD^+)** and **flavin adenine dinucleotide (FAD).** These molecules function as electron carriers in a variety of cellular processes. You will see the action of these molecules in detail when we discuss photosynthesis and respiration (see chapters 7 and 8).

Learning Outcomes Review 3.3

A nucleic acid is a polymer composed of alternating phosphate and 5-carbon sugar groups with a nitrogenous base protruding from each sugar. In DNA, this sugar is deoxyribose. In RNA, the sugar is ribose. RNA also contains the base uracil instead of thymine. DNA is a double-stranded helix that stores hereditary information as a specific sequence of nucleotide bases. RNA has multiple roles in a cell, including carrying information from DNA and forming part of the ribosome.

- ***If an RNA molecule is copied from a DNA strand, what is the relationship between the sequence of bases in RNA and each DNA strand?***

3.4 Proteins: Molecules with Diverse Structures and Functions

Learning Outcomes

1. *Describe the possible levels of protein structure.*
2. *Explain how motifs and domains contribute to protein structure.*
3. *Understand the relationship between amino acid sequence and their three-dimensional structure.*

Proteins are the most diverse group of biological macromolecules, both chemically and functionally. Because proteins have so many different functions in cells we could not begin to list them all. We can, however, group these functions into the following seven categories. This list is a summary only, however; the function of proteins is relevant to most topics in biology:

1. **Enzyme catalysis.** Enzymes are biological catalysts that facilitate specific chemical reactions. Because of this property, the appearance of enzymes was one of the most important events in the evolution of life. Enzymes are three-dimensional globular proteins that fit snugly around the molecules they act on. This fit facilitates chemical reactions by stressing particular chemical bonds.
2. **Defense.** Other globular proteins use their shapes to "recognize" foreign microbes and cancer cells. These cell-surface receptors form the core of the body's endocrine and immune systems.
3. **Transport.** A variety of globular proteins transport small molecules and ions. The transport protein hemoglobin, for example, transports oxygen in the blood. Membrane transport proteins help move ions and molecules across the membrane.
4. **Support.** Protein fibers play structural roles. These fibers include keratin in hair, fibrin in blood clots, and collagen. The last one, collagen, forms the matrix of skin, ligaments, tendons, and bones and is the most abundant protein in a vertebrate body.
5. **Motion.** Muscles contract through the sliding motion of two kinds of protein filaments: actin and myosin. Contractile proteins also play key roles in the cell's cytoskeleton and in moving materials within cells.
6. **Regulation.** Small proteins called hormones serve as intercellular messengers in animals. Proteins also play many regulatory roles within the cell—turning on and shutting off genes during development, for example. In addition, proteins receive information, acting as cell-surface receptors.
7. **Storage.** Calcium and iron are stored in the body by binding as ions to storage proteins.

Table 3.2 summarizes these functions and includes examples of the proteins that carry them out in the human body.

Proteins are polymers of amino acids

Proteins are linear polymers made with 20 different amino acids. **Amino acids,** as their name suggests, contain an amino group (—NH_2) and an acidic carboxyl group (—COOH). The specific order of amino acids determines the protein's structure and function. Many scientists believe amino acids were among the first molecules formed on the early Earth. It seems highly likely that the oceans that existed early in the history of the Earth contained a wide variety of amino acids.

Amino acid structure

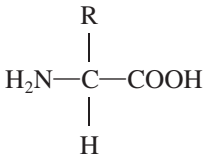
The generalized structure of an amino acid is shown as amino and carboxyl groups bonded to a central carbon atom, with an additional hydrogen and a functional side group indicated

TABLE 3.2 The Many Functions of Protein

Function	Class of Protein	Examples	Examples of Use
Enzyme catalysis	Enzymes	Glycosidases	Cleave polysaccharides
		Proteases	Break down proteins
		Polymerases	Synthesize nucleic acids
		Kinases	Phosphorylate sugars and proteins
Defense	Immunoglobulins	Antibodies	Mark foreign proteins for elimination
	Toxins	Snake venom	Blocks nerve function
	Cell-surface antigens	MHC* proteins	"Self"-recognition
Transport	Circulating transporters	Hemoglobin	Carries O_2 and CO_2 in blood
		Myoglobin	Carries O_2 and CO_2 in muscle
		Cytochromes	Electron transport
	Membrane transporters	Sodium–potassium pump	Excitable membranes
		Proton pump	Chemiosmosis
		Glucose transporter	Transports glucose into cells
Support	Fibers	Collagen	Forms cartilage
		Keratin	Forms hair, nails
		Fibrin	Forms blood clots
Motion	Muscle	Actin	Contraction of muscle fibers
		Myosin	Contraction of muscle fibers
Regulation	Osmotic proteins	Serum albumin	Maintains osmotic concentration of blood
	Gene regulators	*lac* Repressor	Regulates transcription
	Hormones	Insulin	Controls blood glucose levels
		Vasopressin	Increases water retention by kidneys
		Oxytocin	Regulates uterine contractions and milk production
Storage	Ion-binding	Ferritin	Stores iron, especially in spleen
		Casein	Stores ions in milk
		Calmodulin	Binds calcium ions

*MHC, major histocompatibility complex.

by R. These components completely fill the bonds of the central carbon:



The unique character of each amino acid is determined by the nature of the R group. Notice that unless the R group is an H atom, as in glycine, amino acids are chiral and can exist as two enantiomeric forms: D or L. In living systems, only the L-amino acids are found in proteins, and D-amino acids are rare.

The R group also determines the chemistry of amino acids. Serine, in which the R group is —CH_2OH, is a polar molecule. Alanine, which has —CH_3 as its R group, is nonpolar. The 20 common amino acids are grouped into five chemical classes, based on their R group:

1. Nonpolar amino acids, such as leucine, often have R groups that contain —CH_2 or —CH_3.
2. Polar uncharged amino acids, such as threonine, have R groups that contain oxygen (or —OH).
3. Charged amino acids, such as glutamic acid, have R groups that contain acids or bases that can ionize.
4. Aromatic amino acids, such as phenylalanine, have R groups that contain an organic (carbon) ring with alternating single and double bonds. These are also nonpolar.
5. Amino acids that have special functions have unique properties. Some examples are methionine, which is often the first amino acid in a chain of amino acids; proline, which causes kinks in chains; and cysteine, which links chains together.

Each amino acid affects the shape of a protein differently, depending on the chemical nature of its side group. For example, portions of a protein chain with numerous nonpolar amino acids tend to fold into the interior of the protein by hydrophobic exclusion.

Peptide bonds

In addition to its R group, each amino acid, when ionized, has a positive amino (NH_3^+) group at one end and a negative carboxyl (COO^-) group at the other. The amino and carboxyl groups on a pair of amino acids can undergo a dehydration reaction to form a covalent bond. The covalent bond that links two amino acids is called a **peptide bond** (figure 3.19). The two amino acids linked by such a bond are not free to rotate around the N—C linkage because the peptide bond has a partial double-bond character. This is different from the N—C and C—C bonds to the central carbon of the amino acid. This lack of rotation about the peptide bond is one factor that determines the structural character of the coils and other regular shapes formed by chains of amino acids.

A protein is composed of one or more long unbranched chains. Each chain is called a **polypeptide** and is composed of amino acids linked by peptide bonds. The terms *protein* and *polypeptide* tend to be used loosely and may be confusing. For proteins that include only a single polypeptide chain, the two terms are synonymous.

The pioneering work of Frederick Sanger in the early 1950s provided the evidence that each kind of protein has a specific amino acid sequence. Using chemical methods to remove successive amino acids and then identify them, Sanger succeeded in determining the amino acid sequence of insulin. In so doing he demonstrated clearly that this protein had a defined sequence, which was the same for all insulin molecules in the solution. Although many different amino acids occur in nature, only 20 commonly occur in proteins. Of these 20, 8 are called essential amino acids because humans cannot synthesize them and thus must get them from their diets. Figure 3.20 illustrates these 20 amino acids and their side groups.

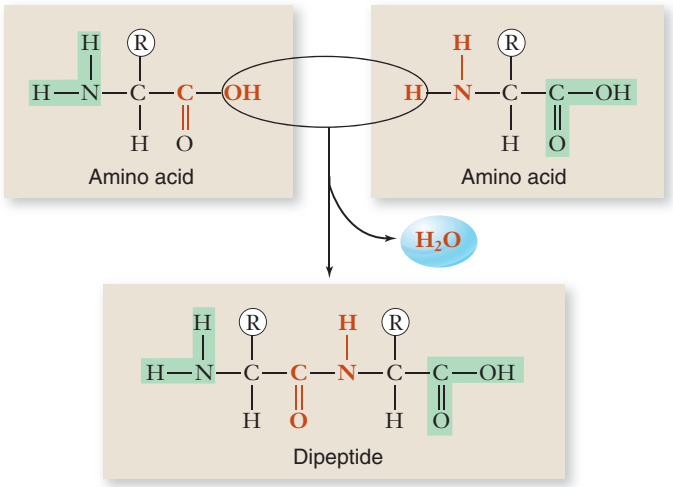


Figure 3.19 The peptide bond. A peptide bond forms when the amino end of one amino acid joins to the carboxyl end of another. Reacting amino and carboxyl groups are shown in red and nonreacting groups are highlighted in green. Notice that the resulting dipeptide still has an amino end and a carboxyl end. Because of the partial double-bond nature of peptide bonds, the resulting peptide chain cannot rotate freely around these bonds.

Proteins have levels of structure

The shape of a protein determines its function. One way to study the shape of something as small as a protein is to look at it with very short wavelength energy—in other words, with X-rays. X-rays can be passed through a crystal of protein to produce a diffraction pattern. This pattern can then be analyzed by a painstaking procedure that allows the investigator to build up a three-dimensional picture of the position of each atom. The first protein to be analyzed in this way was myoglobin, and the related protein hemoglobin was analyzed soon thereafter.

As more and more proteins were studied, a general principle became evident: In every protein studied, essentially all the internal amino acids are nonpolar ones—amino acids such as leucine, valine, and phenylalanine. Water's tendency to hydrophobically exclude nonpolar molecules literally shoves the nonpolar portions of the amino acid chain into the protein's interior (figure 3.21). This tendency forces the nonpolar amino acids into close contact with one another, leaving little empty space inside. Polar and charged amino acids are restricted to the surface of the protein, except for the few that play key functional roles.

The structure of proteins is usually discussed in terms of a hierarchy of four levels: *primary, secondary, tertiary,* and *quaternary* (figure 3.22). We will examine this view and then integrate it with a more modern approach arising from our increasing knowledge of protein structure.

Primary structure: Amino acid sequence

The **primary structure** of a protein is its amino acid sequence. Because the R groups that distinguish the amino acids play no role in the peptide backbone of proteins, a protein can consist of any sequence of amino acids. Thus, because any of 20 different amino acids might appear at any position, a protein containing 100 amino acids could form any of 20^{100} different amino acid sequences (that's the same as 10^{130}, or 1 followed by 130 zeros—more than the number of atoms known in the universe). This important property of proteins permits great diversity.

Consider the protein hemoglobin, the protein your blood uses to transport oxygen. Hemoglobin is composed of two α-globin peptide chains and two β-globin peptide chains. The α-globin chains differ from the β-globin ones in the sequence of amino acids. Furthermore, any alteration in the normal sequence of either of the types of globin proteins, even by a single amino acid, can have drastic effects on how the protein functions.

Secondary structure: Hydrogen bonding patterns

The amino acid side groups are not the only portions of proteins that form hydrogen bonds. The peptide groups of the main chain can also do so. These hydrogen bonds can be with water or with other peptide groups. If the peptide groups formed too many hydrogen bonds with water, the proteins would tend to behave like a random coil and wouldn't produce the kinds of globular

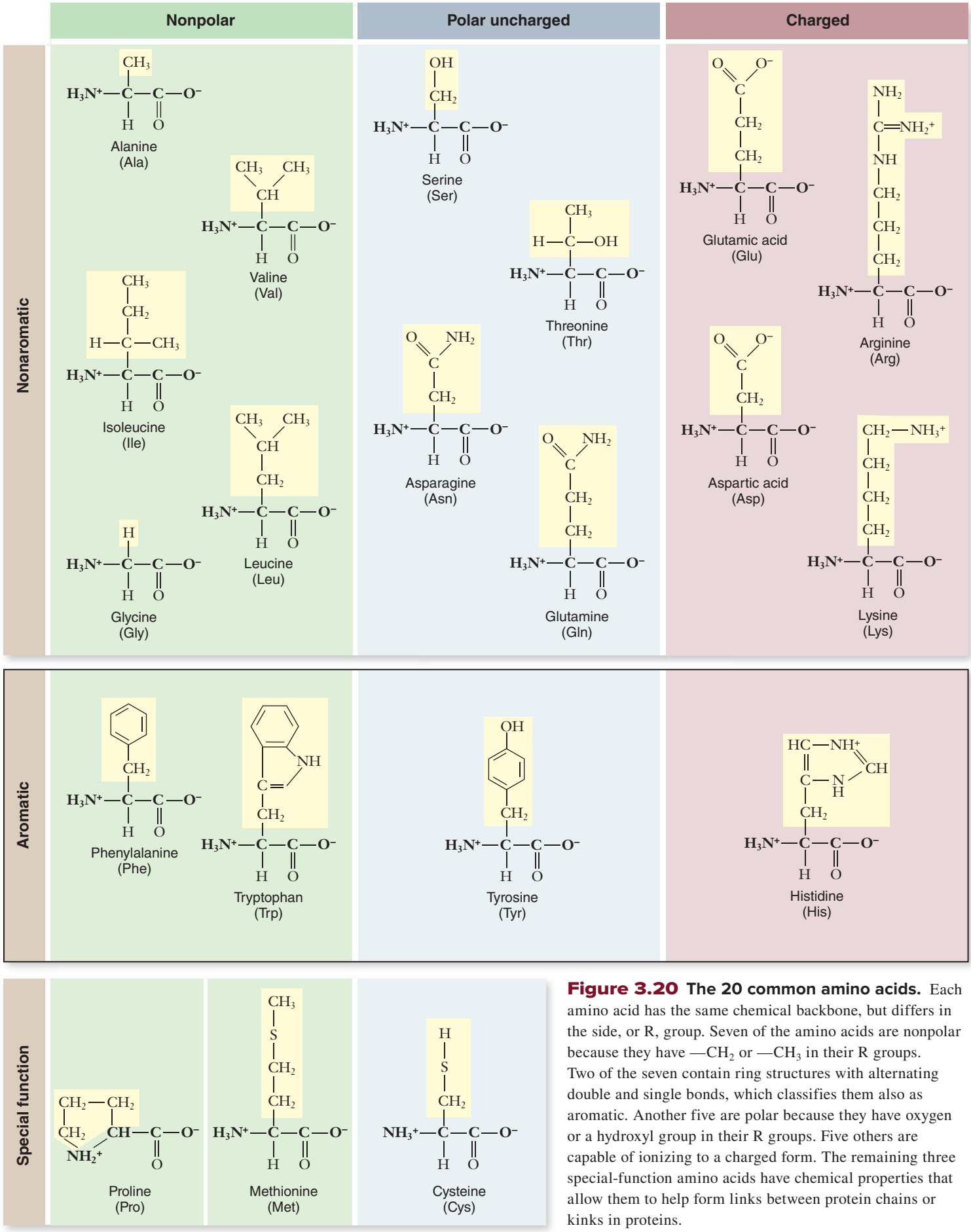
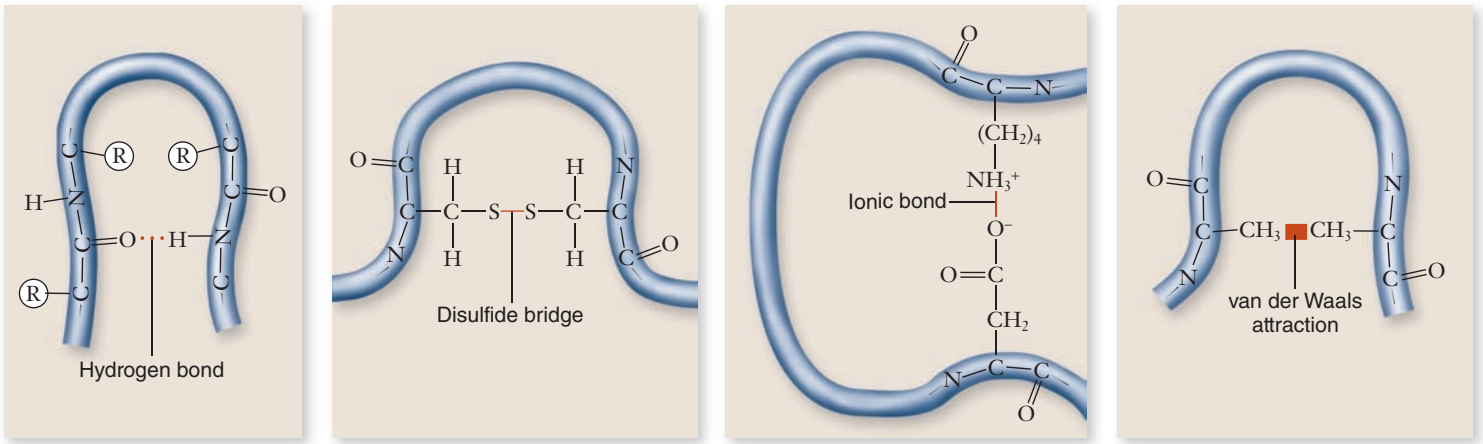


Figure 3.20 The 20 common amino acids. Each amino acid has the same chemical backbone, but differs in the side, or R, group. Seven of the amino acids are nonpolar because they have $—CH_2$ or $—CH_3$ in their R groups. Two of the seven contain ring structures with alternating double and single bonds, which classifies them also as aromatic. Another five are polar because they have oxygen or a hydroxyl group in their R groups. Five others are capable of ionizing to a charged form. The remaining three special-function amino acids have chemical properties that allow them to help form links between protein chains or kinks in proteins.



a. *b.* *c.* *d.* *e.*

Figure 3.21 Interactions that contribute to a protein's shape. Aside from the bonds that link together the amino acids in a protein, several other weaker forces and interactions stabilize protein structure. ***a.*** Hydrogen bonds can form between the different amino acids. ***b.*** Covalent disulfide bridges can form between two cysteine side chains. ***c.*** Ionic bonds can form between groups with opposite charge. ***d.*** van der Waals attractions, which are weak attractions between atoms due to oppositely polarized electron clouds, can occur. ***e.*** Polar portions of the protein tend to gather on the outside of the protein and interact with water, whereas the hydrophobic portions of the protein, including nonpolar amino acid chains, are shoved toward the interior of the protein.

structures that are common in proteins. Linus Pauling suggested that the peptide groups could interact with one another if the peptide was coiled into a spiral that he called the **α helix.** We now call this sort of regular interaction of groups in the peptide backbone **secondary structure.** Another form of secondary structure can occur between regions of peptide aligned next to each other to form a planar structure called a **β sheet.** These can be either parallel or antiparallel depending on whether the adjacent sections of peptide are oriented in the same direction, or opposite direction.

These two kinds of secondary structure create regions of the protein that are cylindrical (α helices) and planar (β sheets). A protein's final structure can include regions of each type of secondary structure. For example, DNA-binding proteins usually have regions of α helix that can lay across DNA and interact directly with the bases of DNA. Porin proteins that form holes in membranes are composed of β sheets arranged to form a pore in the membrane. Finally in hemoglobin, the α- and β-globin peptide chains that make up the final molecule each have characteristic regions of secondary structure.

Tertiary structure: Folds and links

The final folded shape of a globular protein is called its **tertiary structure.** This tertiary structure contains regions that have secondary structure and determines how these are further arranged in space to produce the overall structure. A protein is initially driven into its tertiary structure by hydrophobic exclusion from water. Ionic bonds between oppositely charged R groups bring regions into close proximity, and disulfide bonds (covalent links between two cysteine R groups) lock particular regions together. The final folding of a protein is determined by its primary structure—the chemical nature of its side groups (see figures 3.21 and 3.22). Many small proteins can be fully unfolded ("denatured") and will spontaneously refold into their characteristic shape. Other larger proteins tend to associate together and form insoluble clumps when denatured, such as the film that can form when you heat milk for hot chocolate.

The tertiary structure is stabilized by a number of forces including hydrogen bonding between R groups of different amino acids, electrostatic attraction between R groups with opposite charge (also called salt bridges), hydrophobic exclusion of nonpolar R groups, and covalent bonds in the form of disulfides. The stability of a protein, once it has folded into its tertiary shape, is strongly influenced by how well its interior fits together. When two nonpolar chains in the interior are very close together, they experience a form of molecular attraction called van der Waals forces. Individually quite weak, these forces can add up to a strong attraction when many of them come into play, like the combined strength of hundreds of hooks and loops on a strip of Velcro. These forces are effective only over short distances, however. No "holes" or cavities exist in the interior of proteins. The variety of different nonpolar amino acids, with a different-sized R group with its own distinctive shape, allows nonpolar chains to fit very precisely within the protein interior.

It is therefore not surprising that changing a single amino acid can drastically alter the structure, and thus the function of a

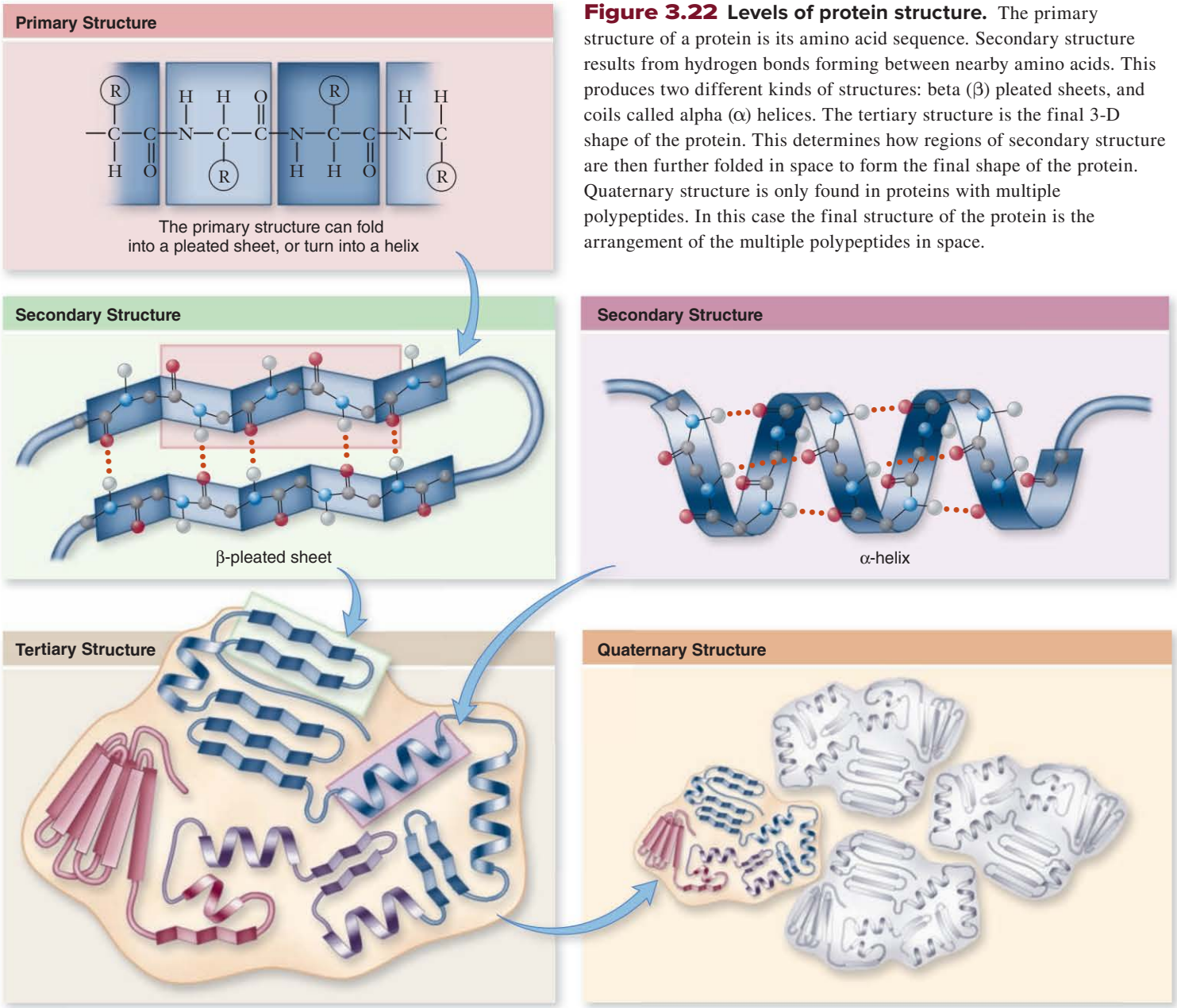


Figure 3.22 Levels of protein structure. The primary structure of a protein is its amino acid sequence. Secondary structure results from hydrogen bonds forming between nearby amino acids. This produces two different kinds of structures: beta (β) pleated sheets, and coils called alpha (α) helices. The tertiary structure is the final 3-D shape of the protein. This determines how regions of secondary structure are then further folded in space to form the final shape of the protein. Quaternary structure is only found in proteins with multiple polypeptides. In this case the final structure of the protein is the arrangement of the multiple polypeptides in space.

protein. The sickle cell version of hemoglobin (HbS), for example, is a change of a single glutamic acid for a valine in the β-globin chain. This change substitutes a charged amino acid for a nonpolar one on the surface of the protein, leading the protein to become sticky and form clumps. Another variant of hemoglobin called HbE, actually the most common in human populations, causes a change from glutamic acid to lysine at a different site in the β-globin chain. In this case the structural change is not as dramatic, but it still impairs function, resulting in blood disorders called anemia and thalassemia. More than 700 structural variants of hemoglobin are known, with up to 7% of the world's population being carriers of forms that are medically important.

Quaternary structure: Subunit arrangements

When two or more polypeptide chains associate to form a functional protein, the individual chains are referred to as subunits of the protein. The arrangement of these subunits is termed its **quaternary structure.** In proteins composed of subunits, the interfaces where the subunits touch one another are often nonpolar, and they play a key role in transmitting information between the subunits about individual subunit activities.

Remember that the protein hemoglobin is composed of two α-chain subunits and two β-chain subunits. Each α- and β-globin chain has a primary structure consisting of a specific sequence of amino acids. This then assumes a characteristic secondary structure consisting of α helices and β sheets that are then arranged into a specific tertiary structure for each α- and β-globin subunit. Lastly, these subunits are then arranged into their final quaternary structure. This is the final structure of the protein. For proteins that consist of only a single peptide chain, the enzyme lysozyme for example, the tertiary structure is the final structure of the protein.

Motifs and domains are structural elements of proteins

To directly determine the sequence of amino acids in a protein is a laborious task. Although the process has been automated, it remains slow and difficult.

The ability to sequence DNA changed this situation rather suddenly. Originally done manually, the Human Genome Project drove the development of automated sequencing. This increased throughput significantly, but the advent of next-generation sequencing technologies resulted in quantum increases in sequence data. Today, over 40,000 bacterial genomes have been sequenced, and almost 8000 eukaryotic genomes, including more than 80 mammalian genomes. Because the DNA sequence is directly related to amino acid sequence in proteins, biologists now have an enormous database of protein sequences to compare and analyze. This new information has also stimulated thought about the logic of the genetic code and whether underlying patterns exist in protein structure. Our view of protein structure has evolved with these data. Researchers still view the four-part hierarchical structure as important, but two additional terms have entered the biologist's vocabulary: motif and domain.

Motifs

As biologists discovered the three-dimensional structure of proteins (an even more laborious task than determining the sequence), they noticed similarities between otherwise dissimilar proteins. These similar structures are called **motifs,** or sometimes "supersecondary structure." The term *motif* is borrowed from the arts and refers to a recurring thematic element in music or design.

One very common protein motif is the β-α-β motif, which creates a fold or crease; the so-called "Rossmann fold" at the core of nucleotide-binding sites in a wide variety of proteins. A second motif that occurs in many proteins is the β barrel, which is a β sheet folded around to form a tube. A third type of motif, the helix-turn-helix, consists of two α helices separated by a bend. This motif is important because many proteins use it to bind to the DNA double helix (figure 3.23; see also chapter 16).

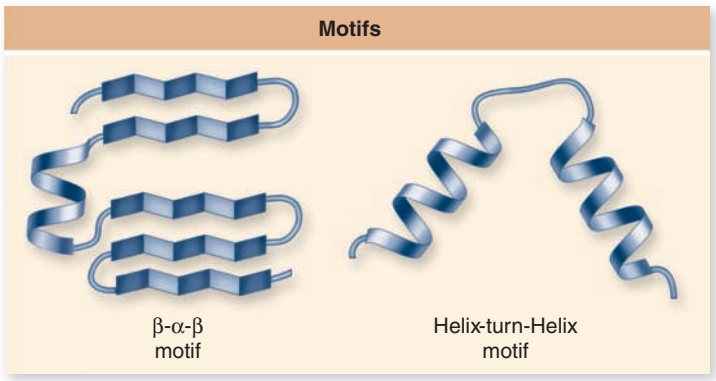
Motifs indicate a logic to structure that investigators still do not understand. Do they simply represent a reuse by evolution of something that already works, or are they an optimal solution to a problem, such as how to bind a nucleotide? One way to think about it is that if amino acids are letters in the language of proteins, then motifs represent repeated words or phrases. Motifs have been useful in determining the function of unknown proteins. Databases of protein motifs are used to search new unknown proteins. Finding motifs with known functions may allow an investigator to infer the function of a new protein.

Domains

Domains of proteins are functional units within a larger structure. They can be thought of as substructure within the tertiary structure of a protein (figure 3.23). To continue the metaphor: Amino acids are letters in the protein language, motifs are words or phrases, and domains are paragraphs.

Most proteins are made up of multiple domains that perform different parts of the protein's function. In many cases, these domains can be physically separated. For example, transcription factors (discussed in chapter 16) are proteins that bind to DNA and initiate its transcription. If the DNA-binding region is exchanged with a different transcription factor, then the specificity of the factor for DNA can be changed without changing its ability to stimulate transcription. Such "domain-swapping" experiments have been performed with many transcription factors, and they indicate, among other things, that the DNA-binding and activation domains are functionally separate.

These functional domains of proteins may also help the protein to fold into its proper shape. As a polypeptide chain folds, the



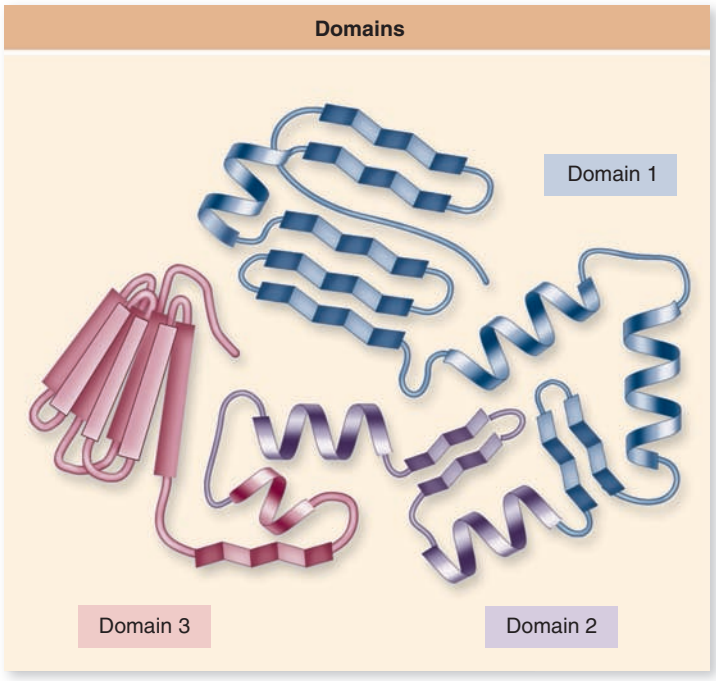


Figure 3.23 Motifs and domains. The elements of secondary structure can combine, fold, or crease to form motifs. These motifs are found in different proteins and can be used to predict function. Proteins also are made of larger domains, which are functionally distinct parts of a protein. The arrangement of these domains in space is the tertiary structure of a protein.

domains take their proper shape, each more or less independently of the others. This action can be demonstrated experimentally by artificially producing the fragment of a polypeptide that forms the domain in the intact protein, and showing that the fragment folds to form the same structure as it exhibits in the intact protein. A single polypeptide chain connects the domains of a protein, like a rope tied into several adjacent knots.

Domains can also correspond to the structure of the genes that encode them. Later, in chapter 15, you will see that genes in eukaryotes are often in pieces within the genome, and these pieces, called *exons,* sometimes encode the functional domains of a protein. This finding led to the idea of evolution acting by shuffling protein-encoding domains.

The process of folding relies on chaperone proteins

Originally, biochemists thought that newly made proteins fold spontaneously, randomly trying out different configurations as hydrophobic interactions with water shoved nonpolar amino acids into the protein's interior until the final structure was arrived at. We now know this view is too simple. Protein chains can fold in so many different ways that trial and error would simply take too long. In addition, as the open chain folds its way toward its final form, nonpolar "sticky" interior portions are exposed during intermediate stages. If these intermediate forms are placed in a test tube in an environment identical to that inside a cell, they stick to other, unwanted protein partners, forming a gluey mess.

How do cells avoid having their proteins clump into a mass? A vital clue came in studies of unusual mutations that prevent viruses from replicating in bacterial cells. It turns out that the virus proteins produced inside the cells could not fold properly. Further study revealed that normal cells contain **chaperone proteins,** which help other proteins to fold correctly.

Molecular biologists have now identified many proteins that act as molecular chaperones. This large class of proteins can be divided into subclasses, and representatives have been found in essentially every organism that has been examined. At least some of these proteins have been shown to be necessary for viability, illustrating their fundamental importance. Many are so-called heat shock proteins, produced in large amounts in response to elevated temperature. High temperatures cause proteins to unfold, and heat shock chaperone proteins help the cell's proteins to refold properly.

One class of these proteins, called chaperonins, has been extensively studied. In the bacterium *Escherichia coli (E. coli),* one example is the essential protein GroE chaperonin. In mutants in which the GroE chaperonin is inactivated, fully 30% of the bacterial proteins fail to fold properly. Chaperonins associate to form a large macromolecular complex that resembles a cylindrical container. Proteins can move into the container, and the container itself can change its shape considerably (figure 3.24). Experiments have shown that an improperly folded protein can enter the chaperonin and be refolded. Although we don't know exactly how this happens, it seems to involve changes in the hydrophobicity of the interior of the chamber.

The flexibility of the structure of chaperonins is amazing. We tend to think of proteins as being fixed structures, but this is clearly not the case for chaperonins and this flexibility is necessary for their function. It also illustrates that even domains that may be very widely separated in a very large protein are still functionally connected. The folding process within a chaperonin harnesses the hydrolysis of ATP to power these changes in structure necessary for function. This entire process can occur in a cyclic manner until the appropriate structure is achieved. Cells use these chaperonins both to accomplish the original folding of some proteins and to restore the structure of incorrectly folded ones.

Improper folding of proteins can result in disease

Chaperone protein deficiencies may be implicated in certain diseases in which key proteins are improperly folded. Cystic fibrosis is a hereditary disorder in which a mutation disables a vital protein

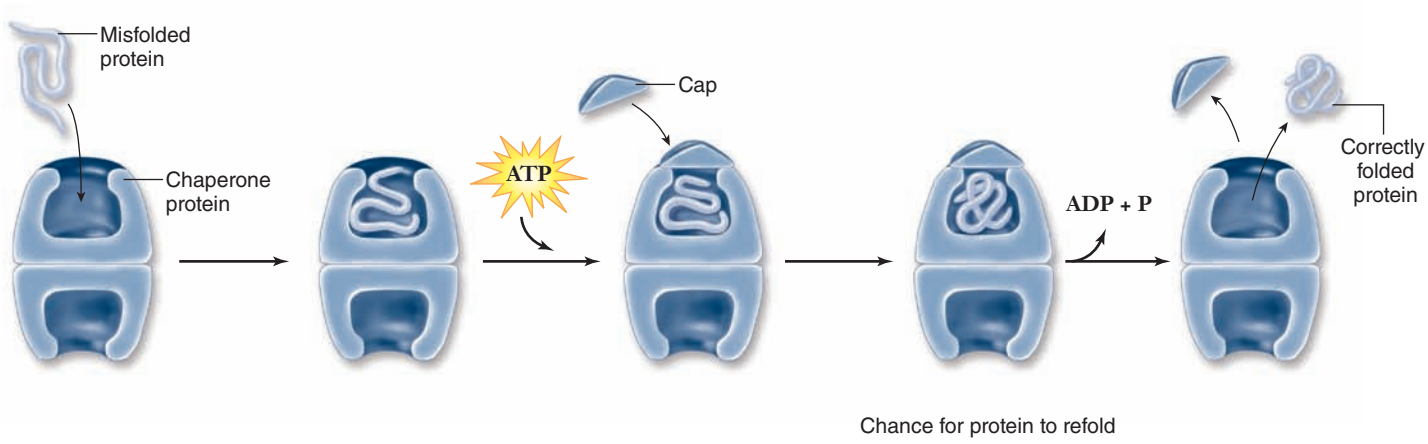


Figure 3.24 How one type of chaperone protein works. This barrel-shaped chaperonin is from the GroE family of chaperone proteins. It is composed of two identical rings each with seven identical subunits, each of which has three distinct domains. An incorrectly folded protein enters one chamber of the barrel, and a cap seals the chamber. Energy from the hydrolysis of ATP fuels structural alterations to the chamber, changing it from hydrophobic to hydrophilic. This change allows the protein to refold. After a short time, the protein is ejected, either folded or unfolded, and the cycle can repeat itself.

that moves ions across cell membranes. As a result, people with cystic fibrosis have thicker than normal mucus. This results in breathing problems, lung disease, and digestive difficulties, among other things. One interesting feature of the molecular analysis of this disease has been the number of different mutations found in human populations. One diverse class of mutations all result in problems with protein folding. The number of different mutations that can result in improperly folded proteins may be related to the fact that the native protein often fails to fold properly.

Denaturation inactivates proteins

If a protein's environment is altered, the protein may change its shape or even unfold completely. This process is called **denaturation** (figure 3.25). Proteins can be denatured when the pH, temperature, or ionic concentration of the surrounding solution changes.

Denatured proteins are usually biologically inactive. This action is particularly significant in the case of enzymes. Because practically every chemical reaction in a living organism is catalyzed by a specific enzyme, it is vital that a cell's enzymes work properly.

The traditional methods of food preservation, salt curing and pickling, involve denaturation of proteins. Prior to the general availability of refrigerators and freezers, the only practical way to keep microorganisms from growing in food was to keep the food in

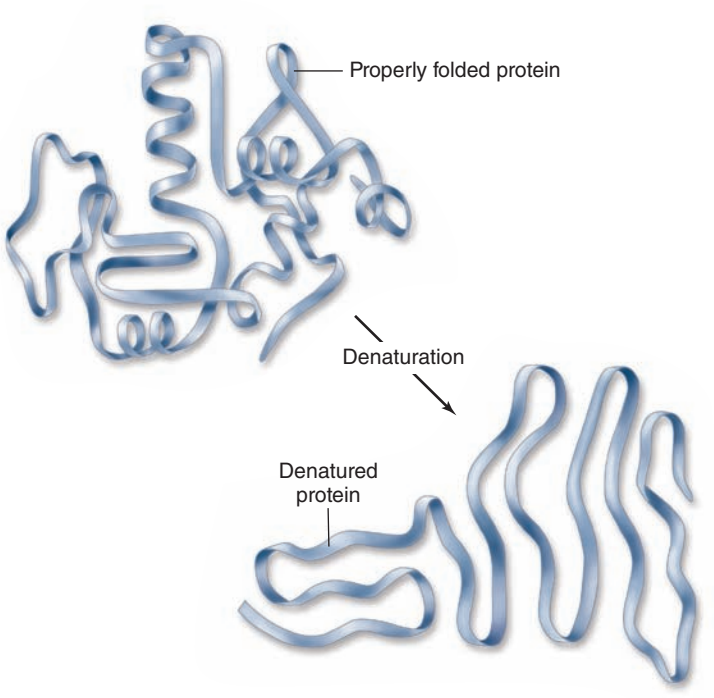


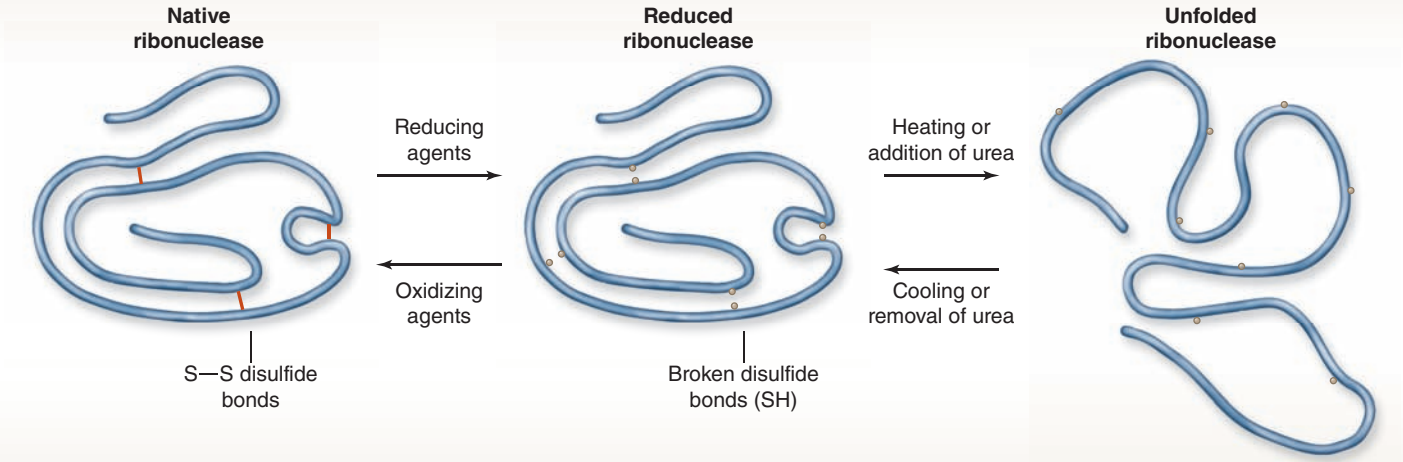
Figure 3.25 Protein denaturation. Environmental changes, such as variation in temperature or pH, can cause a protein to unfold and lose its shape. This loss of structure is called denaturation. Denatured proteins are biologically inactive.

SCIENTIFIC THINKING

Hypothesis: *The 3-D structure of a protein is the thermodynamically stable structure. It depends only on the primary structure of the protein and the solution conditions.*

Prediction: *If a protein is denatured and allowed to renature under native conditions, it will refold into the native structure.*

Test: *Ribonuclease is treated with a reducing agent to break disulfide bonds and is then treated with urea to completely unfold the protein. The disulfide bonds are re-formed under nondenaturing conditions to see if the protein refolds properly.*



Result: *Denatured ribonuclease refolds properly under nondenaturing conditions.*

Conclusion: *The hypothesis is supported. The information in the primary structure (amino acid sequence) is sufficient for refolding to occur. This implies that protein folding results in the thermodynamically stable structure.*

Further Experiments: *If the disulfide bonds were allowed to re-form under denaturing conditions, would we get the same result? How can we rule out that the protein had not been completely denatured and therefore retained some structure?*

Figure 3.26 Primary structure determines tertiary structure.

a solution containing a high concentration of salt or vinegar, which denatured the enzymes of most microorganisms and prevented them from growing on the food.

Most enzymes function within a very narrow range of environmental conditions. Blood-borne enzymes that course through a human body at a pH of about 7.4 would rapidly become denatured in the highly acidic environment of the stomach. Conversely, the protein-degrading enzymes that function at a pH of 2 or less in the stomach would be denatured in the relatively basic pH of the blood. Similarly, organisms that live near oceanic hydrothermal vents have enzymes that work well at these extremes of temperature (over 100°C). They cannot survive in cooler waters, because their enzymes do not function properly at lower temperatures. Any given organism usually has a tolerance range of pH, temperature, and salt concentration. Within that range, its enzymes maintain the proper shape to carry out their biological functions.

When a protein's normal environment is reestablished after denaturation, a small protein may spontaneously refold into its natural shape, driven by the interactions between its nonpolar amino acids and water (figure 3.26). This process is termed *renaturation,* and it was first established for the enzyme ribonuclease (RNase). The renaturation of RNase led to the doctrine that primary structure determines tertiary structure. Larger proteins can rarely refold spontaneously, however, because of the complex nature of their final shape, so this simple idea needs to be qualified.

The fact that some proteins can spontaneously renature implies that tertiary structure is strongly influenced by primary structure. In an extreme example, the *E. coli* ribosome can be taken apart and put back together experimentally. Although this process requires temperature and ion concentration shifts, it indicates an amazing degree of self-assembly. That complex structures can arise by self-assembly is a key idea in the study of modern biology.

It is important to distinguish denaturation from **dissociation.** For proteins with quaternary structure, the subunits may be dissociated (separated) without losing their individual tertiary structure. For example, the four subunits of hemoglobin may dissociate into four individual molecules (two α-globins and two β-globins) without denaturation of the folded globin proteins. They readily reassume their four-subunit quaternary structure.

Learning Outcomes Review 3.4

Proteins are molecules with diverse functions. They are constructed from 20 different kinds of amino acids. Protein structure can be viewed at four levels: (1) the amino acid sequence, or primary structure; (2) coils and sheets, called secondary structure; (3) the three-dimensional shape, called tertiary structure; and (4) individual polypeptide subunits associated in a quaternary structure. Different proteins often have similar substructures called motifs and can be broken down into functional domains. Proteins have a narrow range of conditions in which they fold properly; outside that range, proteins tend to unfold (denaturation). Under some conditions, denatured proteins can refold and become functional again (renaturation).

- ***How does our knowledge of protein structure help us to predict the function of unknown proteins?***

3.5 Lipids: Hydrophobic Molecules

Learning Outcomes

1. *Describe the structure of triglycerides.*
2. *Explain how fats function as energy-storage molecules.*
3. *Apply knowledge of the structure of phospholipids to the formation of membranes.*

Lipids are a somewhat loosely defined group of molecules with one main chemical characteristic: They are insoluble in water. Storage fats such as animal fat are one kind of lipid. Oils such as those from olives, corn, and coconut are also lipids, as are waxes such as beeswax and earwax. Even some vitamins are lipids!

Lipids have a very high proportion of nonpolar carbon–hydrogen (C—H) bonds, and so long-chain lipids cannot fold up like a protein to confine their nonpolar portions away from the surrounding aqueous environment. Instead, when they are placed in water, many lipid molecules spontaneously cluster together and expose what polar (hydrophilic) groups they have to the surrounding water, while confining the nonpolar (hydrophobic) parts of the molecules together within the cluster. You may have noticed this effect when you add oil to a pan containing water, and the oil beads up into cohesive drops on the water's surface. This spontaneous assembly of lipids is of paramount importance to cells, as it underlies the structure of cellular membranes.

Fats consist of complex polymers of fatty acids attached to glycerol

Many lipids are built from a simple skeleton made up of two main kinds of molecules: fatty acids and glycerol. Fatty acids are long-chain hydrocarbons with a carboxylic acid (COOH) at one end. Glycerol is a 3-carbon polyalcohol (three —OH groups). Many lipid molecules consist of a glycerol molecule with three fatty acids attached, one to each carbon of the glycerol backbone. Because it contains three fatty acids, a fat molecule is commonly called a **triglyceride** (the more accurate chemical name is *triacylglycerol*). This basic structure is depicted in figure 3.27. The three fatty acids of a triglyceride need not be identical, and often they are very different from one another. The hydrocarbon chains of fatty acids vary in length. The most common are even-numbered chains of 14 to 20 carbons. The many C—H bonds of fats serve as a form of long-term energy storage.

If all of the internal carbon atoms in a fatty acid chain are bonded to two hydrogen atoms, we call this **saturated,** which refers to its having the maximum hydrogen atoms possible (figure 3.27). A fatty acid with double bonds between one or more pairs of successive carbon atoms will have fewer hydrogen atoms, and thus is said to be **unsaturated.** Fatty acids with one double bond are called monounsaturated, and those with more than one double bond are termed **polyunsaturated.** Most naturally occurring unsaturated fatty acids have double bonds with a *cis* configuration, where the carbon chain is on the same side before and after the double bond

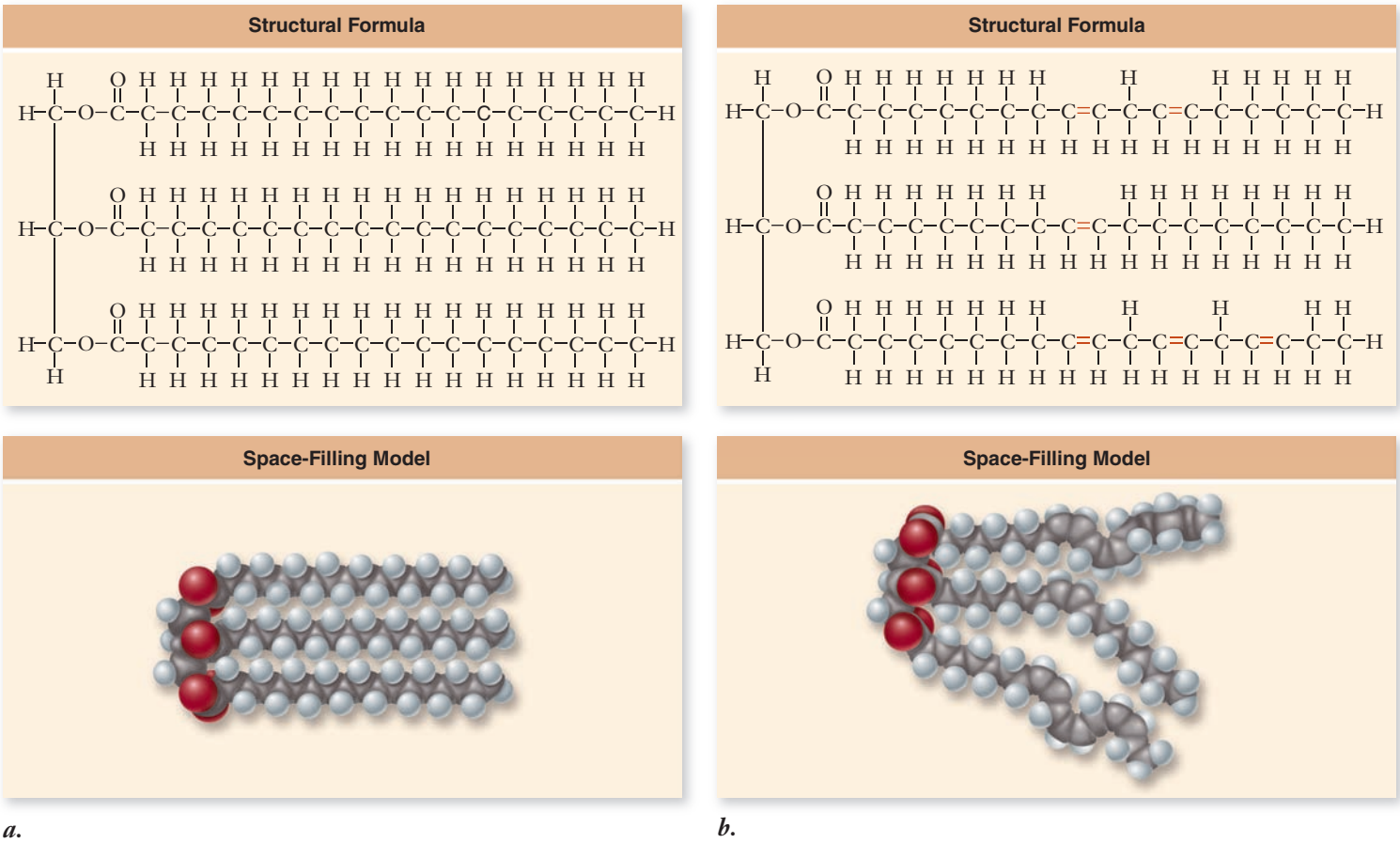


Figure 3.27 Saturated and unsaturated fats. ***a.*** A saturated fat is composed of triglycerides that contain three saturated fatty acids (the kind that have no double bonds). A saturated fat therefore has the maximum number of hydrogen atoms bonded to its carbon chain. Most animal fats are saturated. ***b.*** Unsaturated fat is composed of triglycerides that contain three unsaturated fatty acids (the kind that have one or more double bonds). These have fewer than the maximum number of hydrogen atoms bonded to the carbon chain. This example includes both a monounsaturated and two polyunsaturated fatty acids. Plant fats are typically unsaturated. The many kinks of the double bonds prevent the triglyceride from closely aligning, which makes them liquid oils at room temperature.

(double bonds in fatty acids in figure 3.27*b* are all *cis*). When fats are partially hydrogenated industrially, this can produce double bonds with a *trans* configuration where the carbon chain is on opposite sides before and after the double bond. These are the so-called trans fats. These have been linked to elevated levels of low-density lipoprotein (LDL) "bad cholesterol" and lowered levels of high-density lipoprotein (HDL) "good cholesterol." This condition is thought to be associated with an increased risk for coronary heart disease.

The correlation of dietary trans fats and coronary artery disease led the FDA in the United States to remove trans fats from the list of generally regarded as safe (GRAS) compounds. This is not the same as a ban, as they can be used as a dietary supplement, but along with product labeling, it has been effective in helping to remove trans fats from most common sources.

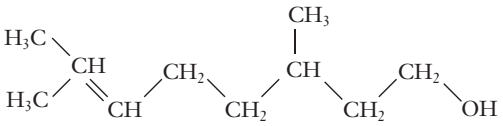
Having double bonds changes the behavior of the molecule because free rotation cannot occur about a C═C double bond as it can with a C—C single bond. This characteristic mainly affects melting point—that is, whether the fatty acid is a solid fat or a liquid oil at room temperature. Fats containing polyunsaturated fatty acids have low melting points because their fatty acid chains bend at the double bonds, preventing the fat molecules from aligning closely with one another. Most saturated fats, such as animal fat or those in butter, are solid at room temperature.

Placed in water, triglycerides spontaneously associate together, forming fat globules that can be very large relative to the size of the individual molecules. Because fats are insoluble in water, they can be deposited at specific locations within an organism, such as in vesicles of adipose tissue.

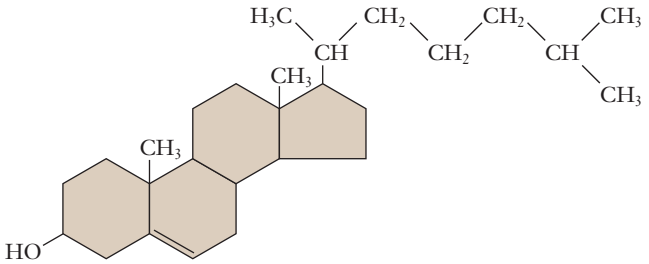
Organisms contain many other kinds of lipids besides fats (figure 3.28). *Terpenes* are long-chain lipids that are components of many biologically important pigments, such as chlorophyll and the visual pigment retinal. Rubber is also a terpene. *Steroids,* another class of lipid, are composed of four carbon rings. Most animal cell membranes contain the steroid cholesterol. Other steroids, such as testosterone and estrogen, function as hormones in multicellular animals. *Prostaglandins* are a group of about 20 lipids that are modified fatty acids, with two nonpolar "tails" attached to a 5-carbon ring. Prostaglandins act as local chemical messengers in many vertebrate tissues. Chapter 45 explores the effects of some of these complex fatty acids.

Fats are excellent energy-storage molecules

Most fats contain over 40 carbon atoms. The ratio of energy-storing C—H bonds in fats is more than twice that of carbohydrates (see section 3.2), making fats much more efficient molecules for



a. Terpene (citronellol)



b. Steroid (cholesterol)

Figure 3.28 Other kinds of lipids. ***a.*** Terpenes are found in biological pigments, such as chlorophyll and retinal, and ***(b)*** steroids play important roles in membranes and as the basis for a class of hormones involved in chemical signaling.

storing chemical energy. On average, fats yield about 9 kilocalories (kcal) of chemical energy per gram, as compared with about 4 kcal/g for carbohydrates.

Most fats produced by animals are saturated (except some fish oils), whereas most plant fats are unsaturated (see figure 3.27). The exceptions are the tropical plant oils (palm oil and coconut oil), which are saturated even though they are liquid at room temperature.

When an organism consumes excess carbohydrate, it is converted into starch, glycogen, or fats reserved for future use. The reason that many humans in developed countries gain weight as they grow older is that the amount of energy they need decreases with age, but their intake of food does not. Thus, an increasing proportion of the carbohydrates they ingest is converted into fat.

A diet heavy in fats is one of several factors thought to contribute to heart disease, particularly atherosclerosis. In atherosclerosis, sometimes referred to as "hardening of the arteries," fatty substances called plaque adhere to the lining of blood vessels, blocking the flow of blood. Fragments of a plaque can break off from a deposit and clog arteries to the brain, causing a stroke.

Phospholipids form membranes

Complex lipid molecules called **phospholipids** are among the most important molecules of the cell because they form the core of all biological membranes. An individual phospholipid can be thought of as a substituted triglyceride—that is, a triglyceride with a phosphate replacing one of the fatty acids. The basic structure of a phospholipid includes three kinds of subunits:

1. *Glycerol,* a 3-carbon alcohol, in which each carbon bears a hydroxyl group. Glycerol forms the backbone of the phospholipid molecule.
2. *Fatty acids,* long chains of —CH_2 groups (hydrocarbon chains) ending in a carboxyl (—COOH) group. Two fatty acids are attached to the glycerol backbone in a phospholipid molecule.
3. *A phosphate group* (—PO_4^{2-}) attached to one end of the glycerol. The charged phosphate group usually has a charged organic molecule linked to it, such as choline, ethanolamine, or the amino acid serine.

The phospholipid molecule can be thought of as having a polar "head" at one end (the phosphate group) and two long, very nonpolar "tails" at the other (figure 3.29). This structure is essential for how these molecules function, although it first appears

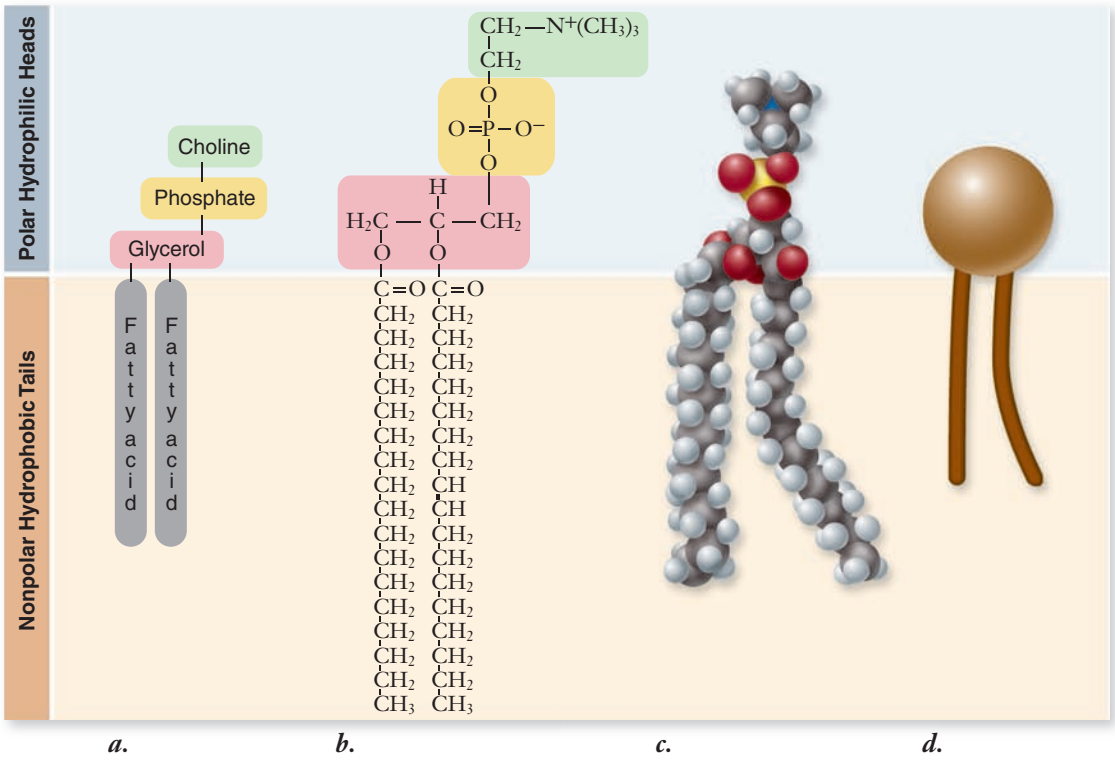


Figure 3.29 Phospholipids. The phospholipid phosphatidylcholine is shown as ***(a)*** a schematic, ***(b)*** a formula, ***(c)*** a space-filling model, and ***(d)*** an icon used in depictions of biological membranes.

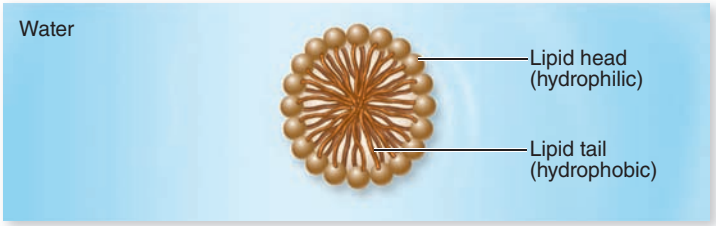
paradoxical. Why would a molecule need to be soluble in water, but also not soluble in water? The formation of a membrane shows the unique properties of such a structure.

In water, the nonpolar tails of nearby lipid molecules aggregate away from the water, forming spherical *micelles,* with the tails facing inward (figure 3.30*a*). This is actually how detergent molecules work to make grease soluble in water. The grease is soluble within the nonpolar interior of the micelle and the polar surface of the micelle is soluble in water. With phospholipids, a more complex structure forms in which two layers of molecules line up, with the hydrophobic tails of each layer pointing toward one another, or inward, leaving the hydrophilic heads oriented outward, forming a bilayer (figure 3.30*b*). Lipid bilayers are the basic framework of biological membranes, discussed in detail in chapter 5.

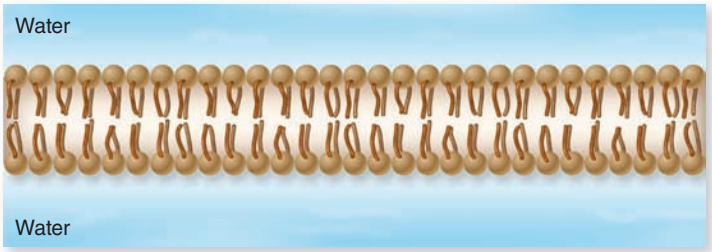
Learning Outcomes Review 3.5

Triglycerides are made of fatty acids linked to glycerol. Fats can contain twice as many C—H bonds as carbohydrates and thus they store energy efficiently. Because the C—H bonds in lipids are nonpolar, they are not water-soluble and aggregate together in water. Phospholipids replace one fatty acid with a hydrophilic phosphate group. This allows them to spontaneously form bilayers, which are the basis of biological membranes.

- ***Why do phospholipids form membranes while triglycerides form insoluble droplets?***

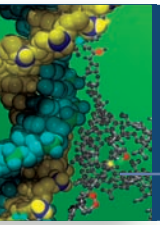


a.



b.

Figure 3.30 Lipids spontaneously form micelles or lipid bilayers in water. In an aqueous environment, lipid molecules orient so that their polar (hydrophilic) heads are in the polar medium, water, and their nonpolar (hydrophobic) tails are held away from the water. ***a.*** Droplets called micelles can form, or ***(b)*** phospholipid molecules can arrange themselves into two layers; in both structures, the hydrophilic heads extend outward and the hydrophobic tails inward. This second example is called a phospholipid bilayer.



Chapter Review

3.1 Carbon: The Framework of Biological Molecules

Carbon, the backbone of all biological molecules, can form four covalent bonds and make long chains. Hydrocarbons consist of carbon and hydrogen, and their bonds store considerable energy.

Functional groups account for differences in molecular properties.

Functional groups are small molecular entities that confer specific chemical characteristics when attached to a hydrocarbon.

Carbon and hydrogen have similar electronegativity so C—H bonds are not polar. Oxygen and nitrogen have greater electronegativity, leading to polar bonds.

Isomers have the same molecular formulas but different structures.

Structural isomers are molecules with the same formula but different structures; stereoisomers differ in how groups are attached. Enantiomers are mirror-image stereoisomers.

Biological macromolecules include carbohydrates, nucleic acids, proteins, and lipids.

Most important biological macromolecules are polymers—long chains of monomer units. Biological polymers are formed by elimination of water (H and OH) from two monomers (dehydration reaction). They are broken down by adding water (hydrolysis).

3.2 Carbohydrates: Energy Storage and Structural Molecules

The empirical formula of a carbohydrate is $(CH_2O)_n$. Carbohydrates are used for energy storage and as structural molecules.

Monosaccharides are simple sugars.

Simple sugars contain three to six or more carbon atoms. Examples are glyceraldehyde (3 carbons), deoxyribose (5 carbons), and glucose (6 carbons).

Sugar isomers have structural differences.

The general formula for 6-carbon sugars is $C_6H_{12}O_6$, and many isomeric forms are possible. Living systems often have enzymes for converting isomers from one to the other.

Disaccharides serve as transport molecules in plants and provide nutrition in animals.

Plants convert glucose into the disaccharide sucrose for transport within their bodies. Female mammals produce the disaccharide lactose to nourish their young.

Polysaccharides provide energy storage and structural components.

Glucose is used to make three important polymers: glycogen (in animals), and starch and cellulose (in plants). Chitin is a related structural material found in arthropods and many fungi.

3.3 Nucleic Acids: Information Molecules

Deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) are polymers composed of nucleotide monomers. Cells use nucleic acids for information storage and transfer.

Nucleic acids are nucleotide polymers.

Nucleic acids contain four different nucleotide bases. In DNA these are adenine, guanine, cytosine, and thymine. In RNA, thymine is replaced by uracil.

DNA stores genetic information.

DNA exists as a double helix held together by specific base pairs: adenine with thymine and guanine with cytosine. The nucleic acid sequence constitutes the genetic code.

RNA has many roles in a cell.

RNA is made by copying DNA. RNA carries information from DNA and forms part of the ribosome. RNA can also be an enzyme and affect gene expression.

Other nucleotides are vital components of energy reactions.

Adenosine triphosphate (ATP) provides energy in cells; NAD^+ and FAD transport electrons in cellular processes.

3.4 Proteins: Molecules with Diverse Structures and Functions

Most enzymes are proteins. Proteins also provide defense, transport, motion, and regulation, among many other roles.

Proteins are polymers of amino acids.

Amino acids are joined by peptide bonds to make polypeptides. The 20 common amino acids are characterized by R groups that determine their properties.

Proteins have levels of structure.

Protein structure is defined by the following hierarchy: primary (amino acid sequence), secondary (hydrogen bonding patterns), tertiary (three-dimensional folding), and quaternary (associations between two or more polypeptides).

Motifs and domains are structural elements of proteins.

Motifs are similar structural elements found in dissimilar proteins. They can create folds, creases, or barrel shapes. Domains are functional subunits or sites within a tertiary structure.

The process of folding relies on chaperone proteins.

Chaperone proteins assist in the folding of proteins. Heat shock proteins are an example of chaperone proteins.

Improper folding of proteins can result in disease.

Some forms of cystic fibrosis and Alzheimer disease are associated with misfolded proteins.

Denaturation inactivates proteins.

Denaturation refers to an unfolding of tertiary structure, which usually destroys function. Some denatured proteins may recover function when conditions are returned to normal. This implies that primary structure strongly influences tertiary structure.

Dissociation refers to separation of quaternary subunits with no changes to their tertiary structure.

3.5 Lipids: Hydrophobic Molecules

Lipids are insoluble in water because they have a high proportion of nonpolar C—H bonds.

Fats consist of complex polymers of fatty acids attached to glycerol.

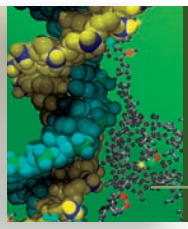
Many lipids exist as triglycerides, three fatty acids connected to a glycerol molecule. Saturated fatty acids contain the maximum number of hydrogen atoms. Unsaturated fatty acids contain one or more double bonds between carbon atoms.

Fats are excellent energy-storage molecules.

The energy stored in the C—H bonds of fats is more than twice that of carbohydrates: 9 kcal/g compared with 4 kcal/g. For this reason, excess carbohydrate is converted to fat for storage.

Phospholipids form membranes.

Phospholipids contain two fatty acids and one phosphate attached to glycerol. In phospholipid-bilayer membranes, the phosphate heads are hydrophilic and cluster on the two faces of the membrane, and the hydrophobic tails are in the center.



Review Questions

UNDERSTAND

1. How is a polymer formed from multiple monomers?
   a. From the growth of the chain of carbon atoms
   b. By the removal of an —OH group and a hydrogen atom
   c. By the addition of an —OH group and a hydrogen atom
   d. Through hydrogen bonding
2. Why are carbohydrates important molecules for energy storage?
   a. The C—H bonds found in carbohydrates store energy.
   b. The double bonds between carbon and oxygen are very strong.
   c. The electronegativity of the oxygen atoms means that a carbohydrate is made up of many polar bonds.
   d. They can form ring structures in the aqueous environment of a cell.
3. Plant cells store energy in the form of _____, and animal cells store energy in the form of _____.
   a. fructose; glucose
   b. disaccharides; monosaccharides
   c. cellulose; chitin
   d. starch; glycogen
4. Which carbohydrate would you find as part of a molecule of RNA?
   a. Galactose
   b. Deoxyribose
   c. Ribose
   d. Glucose
5. A molecule of DNA or RNA is a polymer of
   a. monosaccharides.
   b. nucleotides.
   c. amino acids.
   d. fatty acids.

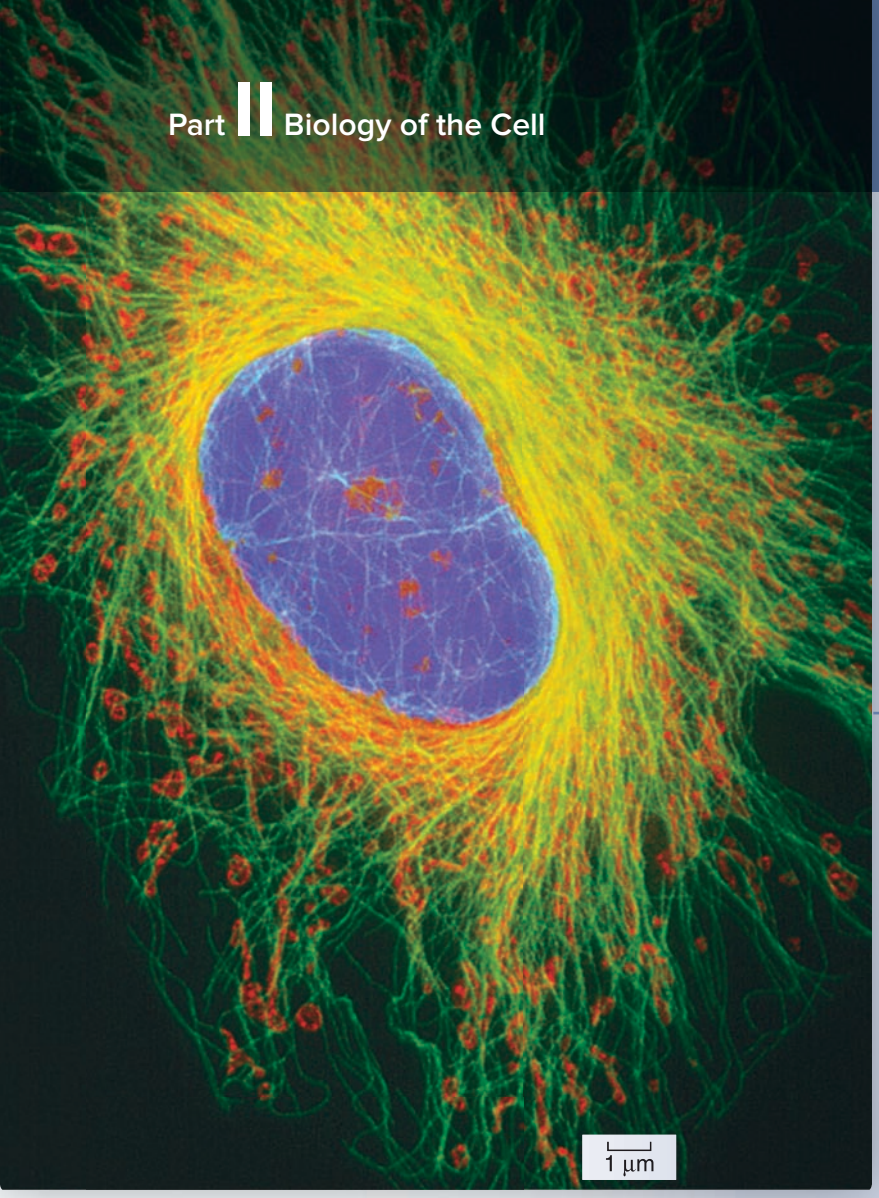
6. What makes cellulose different from starch?
   a. Starch is produced by plant cells, and cellulose is produced by animal cells.
   b. Cellulose forms long filaments, and starch is highly branched.
   c. Starch is insoluble, and cellulose is soluble.
   d. All of the choices are correct.
7. What monomers make up a protein?
   a. Monosaccharides
   b. Nucleotides
   c. Amino acids
   d. Fatty acids
8. A triglyceride is a form of _____ composed of _____.
   a. lipid; fatty acids and glucose
   b. lipid; fatty acids and glycerol
   c. carbohydrate; fatty acids
   d. lipid; cholesterol

APPLY

1. You can use starch or glycogen as an energy source, but not cellulose because
   a. starch and cellulose have similar structures.
   b. cellulose and glycogen have similar structures.
   c. starch and glycogen have similar structures.
   d. your body makes starch but not cellulose.
2. Which of the following is NOT a difference between DNA and RNA?
   a. Deoxyribose sugar versus ribose sugar
   b. Thymine versus uracil
   c. Double-stranded versus single-stranded
   d. Phosphodiester versus hydrogen bonds
3. Which part of an amino acid has the greatest influence on the overall structure of a protein?
   a. The (—NH_2) amino group
   b. The R group
   c. The (—COOH) carboxyl group
   d. Both a and c are correct.
4. A mutation that alters a single amino acid within a protein can alter
   a. the primary level of protein structure.
   b. the secondary level of protein structure.
   c. the tertiary level of protein structure.
   d. All of the choices are correct.
5. Two different proteins have the same domain in their structure. From this we can infer that they have
   a. the same primary structure.
   b. similar function.
   c. very different functions.
   d. the same primary structure but different function.
6. What aspect of triglyceride structure accounts for their insolubility in water?
   a. The COOH group of fatty acids
   b. The nonpolar C—H bonds in fatty acids
   c. The OH groups in glycerol
   d. The C═C bonds found in unsaturated fatty acids
7. The spontaneous formation of a lipid bilayer in an aqueous environment occurs because
   a. the polar head groups of the phospholipids can interact with water.
   b. the long fatty acid tails of the phospholipids can interact with water.
   c. the fatty acid tails of the phospholipids are hydrophobic.
   d. Both a and c are correct.

SYNTHESIZE

1. How do the four biological macromolecules differ from one another? How does the structure of each relate to its function?
2. Hydrogen bonds and hydrophobic interactions each play an important role in stabilizing and organizing biological macromolecules. Consider the four macromolecules discussed in this chapter. Describe how these affect the form and function of each type of macromolecule. Would a disruption in the hydrogen bonds affect form and function? Hydrophobic interactions?
3. Plants make both starch and cellulose. Would you predict that the enzymes involved in starch synthesis could also be used by the plant for cellulose synthesis? Construct an argument to explain this based on the structure and function of the enzymes and the polymers synthesized.



CHAPTER 4

Cell Structure

Chapter Contents

Introduction

All organisms are composed of cells. The gossamer wing of a butterfly is a thin sheet of cells and so is the glistening outer layer of your eyes. The burger or tomato you eat is composed of cells, and its contents soon become part of your cells. Some organisms consist of a single cell too small to see with the unaided eye. Others, such as humans, are composed of many specialized cells, such as the fibroblast cell shown in the striking fluorescence micrograph on this page. Cells are so much a part of life that we cannot imagine an organism that is not cellular in nature. In this chapter, we take a close look at the internal structure of cells. In chapters 5 to 10, we will focus on cells in action—how they communicate with their environment, grow, and reproduce.

4.1 Cell Theory

Learning Outcomes

1. *Discuss the cell theory.*
2. *Describe the factors that limit cell size.*
3. *Categorize structural and functional similarities in cells.*

Cells are characteristically microscopic in size. Although there are exceptions, a typical eukaryotic cell is 10 to 100 micrometers (µm) (10 to 100 millionths of a meter) in diameter, although most prokaryotic cells are only 1 to 10 µm in diameter.

Because cells are so small, they were not discovered until the invention of the microscope in the 17th century. English natural philosopher Robert Hooke was the first to observe cells in 1665, naming the shapes he saw in cork *cellulae* (Latin, "small rooms"). This is known to us as *cells.* Another early microscopist, Dutch Anton van Leeuwenhoek, first observed living cells, which he termed "animalcules," or little animals. After these early efforts, a

century and a half passed before biologists fully recognized the importance of cells. In 1838, German botanist Matthias Schleiden stated that all plants "are aggregates of fully individualized, independent, separate beings, namely the cells themselves." In 1839, German physiologist Theodor Schwann reported that all animal tissues also consist of individual cells. Thus, the cell theory was born.

Cell theory is the unifying foundation of cell biology

The cell theory was proposed to explain the observation that all organisms are composed of cells. It sounds simple, but it is a far-reaching statement about the organization of life.

In its modern form, the *cell theory* includes the following three principles:

1. All organisms are composed of one or more cells, and the life processes of metabolism and heredity occur within these cells.
2. Cells are the smallest living things, the basic units of organization of all organisms.
3. Cells arise only by division of a previously existing cell.

Although life likely evolved spontaneously in the environment of early Earth, biologists have concluded that no additional cells are originating spontaneously at present. Rather, life on Earth represents a continuous line of descent from those early cells.

Cell size is limited

Most cells are relatively small for reasons related to the diffusion of substances into and out of them. The rate of diffusion is affected by a number of variables, including (1) surface area available for diffusion, (2) temperature, (3) concentration gradient of diffusing substance, and (4) the distance over which diffusion must occur. As the size of a cell increases, the length of time for diffusion from the outside membrane to the interior of the cell increases as well. Larger cells need to synthesize more macromolecules, have correspondingly higher energy requirements, and produce a greater quantity of waste. Molecules used for energy and biosynthesis must be transported through the membrane. Any metabolic waste produced must be removed, also passing through the membrane. The rate at which this transport occurs depends on both the distance to the membrane and the area of membrane available. For this reason, an organism made up of many relatively small cells has an advantage over one composed of fewer, larger cells.

The advantage of small cell size is readily apparent in terms of the **surface area-to-volume ratio.** As a cell's size increases, its volume increases much more rapidly than its surface area. For a spherical cell, the surface area is proportional to the square of the radius, whereas the volume is proportional to the cube of the radius. Thus, if the radii of two cells differ by a factor of 10, the larger cell will have 10^2, or 100 times, the surface area, but 10^3, or 1000 times, the volume of the smaller cell (figure 4.1).

The cell surface provides the only opportunity for interaction with the environment, because all substances enter and exit a cell via this surface. The membrane surrounding the cell plays a key role in controlling cell function. Because small cells have more surface area per unit of volume than large ones, control over cell contents is more effective when cells are relatively small.

Although most cells are small, some quite large cells do exist. These cells have apparently overcome the surface area-to-volume problem by one or more adaptive mechanisms. For example, some cells, such as skeletal muscle cells, have more than one nucleus, allowing genetic information to be spread around a large cell. Some other large cells, such as neurons, are long and skinny, so that any given point within the cell is close to the plasma membrane. This permits diffusion between the inside and outside of the cell to still be rapid.

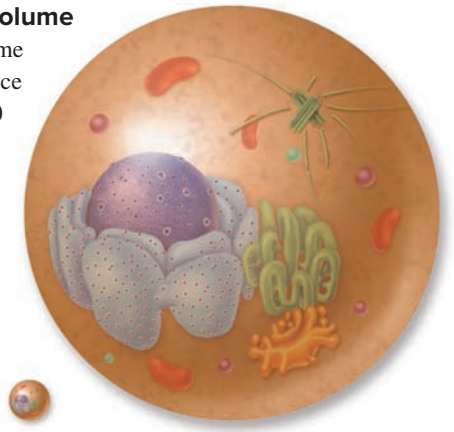


Figure 4.1 Surface area-to-volume ratio. As a cell gets larger, its volume increases at a faster rate than its surface area. If the cell radius increases by 10 times, the surface area increases by 100 times, but the volume increases by 1000 times. A cell's surface area must be large enough to meet the metabolic needs of its volume.

Cell radius (r)	1 unit	10 unit
Surface area ($4\pi r^2$)	12.57 unit^2	1257 unit^2
Volume ($\frac{4}{3}\pi r^3$)	4.189 unit^3	4189 unit^3
Surface Area / Volume	3	0.3

Microscopes allow visualization of cells and components

Other than egg cells, not many cells are visible to the naked eye (figure 4.2). Most are less than 50 μm in diameter, far smaller than the period at the end of this sentence. So, to visualize cells we need the aid of technology. The development of microscopes and their refinement over the centuries has allowed us to continually explore cells in greater detail.

The resolution problem

How do we study cells if they are too small to see? The key is to understand why we can't see them. The reason we can't see such small objects is the limited resolution of the human eye. *Resolution* is the minimum distance two points can be apart and still be distinguished as two separate points. When two objects are closer together than about 100 μm, the light reflected from each strikes the same photoreceptor cell at the rear of the eye. Only when the objects are farther than 100 μm apart can the light from each strike different cells, allowing your eye to resolve them as two distinct objects rather than one.

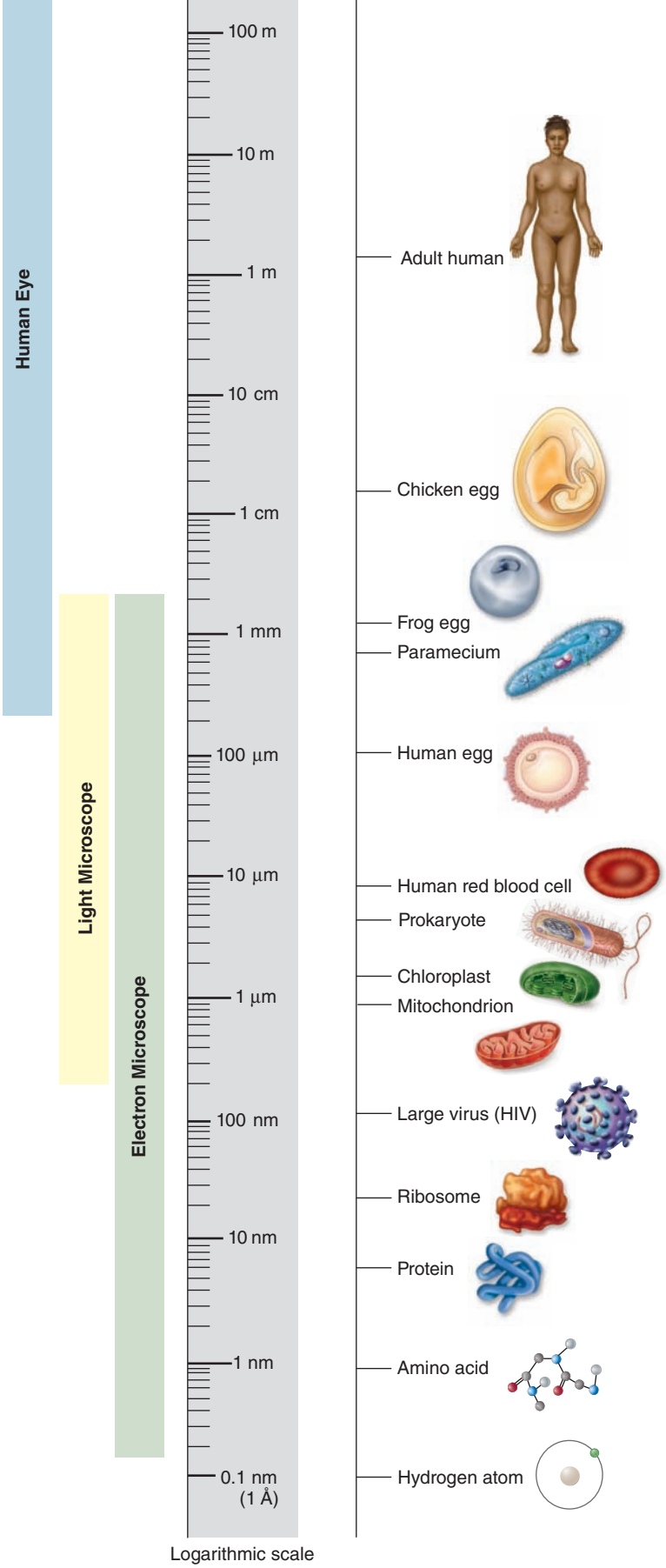


Figure 4.2 The size of cells and their contents. Except for vertebrate eggs, which can typically be seen with the unaided eye, most cells are microscopic in size. Prokaryotic cells are generally 1 to 10 µm across.
$1\ m = 10^2\ cm = 10^3\ mm = 10^6\ \mu m = 10^9\ nm$

Types of microscopes

One way to overcome the limitations of our eyes is to increase magnification so that small objects appear larger. The first microscopists used glass lenses to magnify small cells and cause them to appear larger than the 100-µm limit imposed by the human eye. The glass lens increases focusing power. Because the glass lens makes the object appear closer, the image on the back of the eye is bigger than it would be without the lens.

Modern *light microscopes,* which operate with visible light, use two magnifying lenses (and a variety of correcting lenses) to achieve very high magnification and clarity (table 4.1). The first lens focuses the image of the object on the second lens, which magnifies it again and focuses it on the back of the eye. Microscopes that magnify in stages using several lenses are called *compound microscopes.* They can resolve structures that are separated by at least 200 nanometers (nm).

Light microscopes, even compound ones, are not powerful enough to resolve many of the structures within cells. For example, a cell membrane is only 5 nm thick. Why not just add another magnifying stage to the microscope to increase its resolving power? This doesn't work because when two objects are closer than a few hundred nanometers, the light beams reflecting from the two images start to overlap each other. The only way two light beams can get closer together and still be resolved is if their wavelengths are shorter. One way to avoid overlap is by using a beam of electrons rather than a beam of light. Electrons have a much shorter wavelength, and an *electron microscope,* employing electron beams, has 1000 times the resolving power of a light microscope. *Transmission electron microscopes,* so called because the electrons used to visualize the specimens are transmitted through the material, are capable of resolving objects only 0.2 nm apart—which is only twice the diameter of a hydrogen atom!

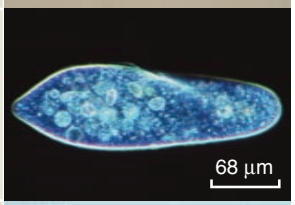
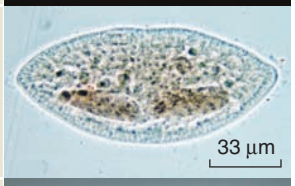
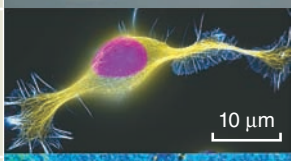
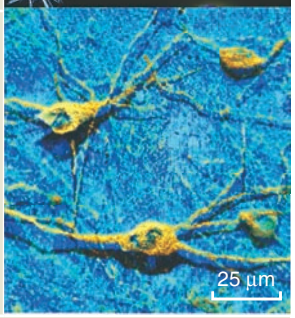
A second kind of electron microscope, the *scanning electron microscope,* beams electrons onto the surface of the specimen. The electrons reflected back from the surface, together with other electrons that the specimen itself emits as a result of the bombardment, are amplified and transmitted to a screen, where the image can be viewed and photographed. Scanning electron microscopy yields striking three-dimensional images. This technique has improved our understanding of many biological and physical phenomena (table 4.1).

Using stains to view cell structure

Although resolution remains a physical limit, we can improve the images we see by altering the sample. Certain chemical stains increase the contrast between different cellular components. Structures within the cell absorb or exclude the stain differentially, producing contrast that aids resolution.

Stains that bind to specific types of molecules have made these techniques even more powerful. This method uses antibodies that bind, for example, to a particular protein. This process, called *immunohistochemistry,* uses antibodies generated in animals such as rabbits or mice. When these animals are injected with specific proteins, they produce antibodies that bind to the injected protein. The antibodies are then purified and chemically bonded to enzymes, to stains, or to fluorescent molecules. When cells are incubated in a solution containing the antibodies, the antibodies bind to cellular structures that contain the target molecule and can

TABLE 4.1 Microscopes

LIGHT MICROSCOPES	
Bright-field microscope: Light is transmitted through a specimen, giving little contrast. Staining specimens improves contrast but requires that cells be fixed (not alive), which can distort or alter components.	
Dark-field microscope: Light is directed at an angle toward the specimen. A condenser lens transmits only light reflected off the specimen. The field is dark, and the specimen is light against this dark background.	
Phase-contrast microscope: Components of the microscope bring light waves out of phase, which produces differences in contrast and brightness when the light waves recombine.	
Differential-interference–contrast microscope: Polarized light is split into two beams that have slightly different paths through the sample. Combining these two beams produces greater contrast, especially at the edges of structures.	
Fluorescence microscope: Fluorescent stains absorb light at one wavelength, then emit it at another. Filters transmit only the emitted light.	
Confocal microscope: Light from a laser is focused to a point and scanned across the fluorescently stained specimen in two directions. This produces clear images of one plane of the specimen. Other planes of the specimen are excluded to prevent the blurring of the image. Multiple planes can be used to reconstruct a 3-D image.	
ELECTRON MICROSCOPES	
Transmission electron microscope: A beam of electrons is passed through the specimen. Electrons that pass through are used to expose film. Areas of the specimen that scatter electrons appear dark. False coloring enhances the image.	
Scanning electron microscope: An electron beam is scanned across the surface of the specimen, and electrons are knocked off the surface. Thus, the topography of the specimen determines the contrast and the content of the image. False coloring enhances the image.	

be seen with light microscopy. This approach has been used extensively in the analysis of cell structure and function.

All cells share many structural features

The general plan of cellular organization varies between different organisms, but despite these modifications, all cells resemble one another in certain fundamental ways. Before we begin a detailed examination of cell structure, let's first summarize four major features all cells have in common: (1) a nucleoid or nucleus where genetic material is located, (2) cytoplasm, (3) *ribosomes* to synthesize proteins, and (4) a plasma membrane.

Centrally located genetic material

Every cell contains DNA, the hereditary molecule. In **prokaryotes,** the simplest organisms, most of the genetic material lies in a single circular molecule of DNA. It typically resides near the center of the cell in an area called the **nucleoid.** This area is not segregated, however, from the rest of the cell's interior by membranes.

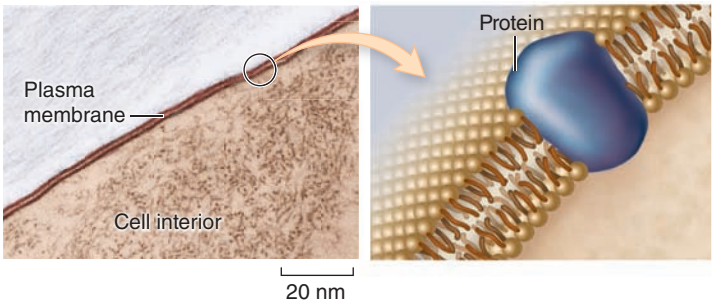
By contrast, the DNA of eukaryotes, which are more complex organisms, is contained in the nucleus, which is surrounded by a double-membrane structure called the **nuclear envelope.** In both types of organisms, the DNA contains the genes that code for the proteins synthesized by the cell. (Details of nucleus structure are described in section 4.3.)

The cytoplasm

A semifluid matrix called the **cytoplasm** fills the interior of the cell. The cytoplasm contains all of the sugars, amino acids, and proteins the cell uses to carry out its everyday activities. Although it is an aqueous medium, cytoplasm is more like Jell-O than water due to the high concentration of proteins and other macromolecules. We call any discrete macromolecular structure in the cytoplasm specialized for a particular function an **organelle.** The part of the cytoplasm that contains organic molecules and ions in solution is called the **cytosol** to distinguish it from the larger organelles suspended in this fluid.

The plasma membrane

The **plasma membrane** encloses a cell and separates its contents from its surroundings. The plasma membrane is a phospholipid bilayer about 5 to 10 nm (5 to 10 billionths of a meter) thick, with proteins embedded in it. Viewed in cross section with the electron microscope, such membranes appear as two dark lines separated by a lighter area. This distinctive appearance arises from the tail-to-tail packing of the phospholipid molecules that make up the membrane (see chapter 5).



The proteins of the plasma membrane are generally responsible for a cell's ability to interact with the environment. *Transport proteins* help molecules and ions move across the plasma membrane, either from the environment to the interior of the cell or vice versa. *Receptor proteins* induce changes within the cell when they come in contact with specific molecules in the environment, such as hormones, or with molecules on the surface of neighboring cells. These molecules can function as *markers* that identify the cell as a particular type. This interaction between cell surface molecules is especially important in multicellular organisms, whose cells must be able to recognize one another as they form tissues.

We'll examine the structure and function of cell membranes more thoroughly in chapter 5.

Learning Outcomes Review 4.1

All organisms are single cells or aggregates of cells, and all cells arise from preexisting cells. Cell size is limited primarily by the efficiency of diffusion across the plasma membrane. As a cell becomes larger, its volume increases more quickly than its surface area. Past a certain point, diffusion cannot support the cell's needs. All cells are bounded by a plasma membrane and filled with cytoplasm. The genetic material is found in the central portion of the cell; and in eukaryotic cells, it is contained in a membrane-bounded nucleus.

- ***Would finding life on Mars change our view of cell theory?***

4.2 Prokaryotic Cells

Learning Outcomes

1. *Describe the organization of prokaryotic cells.*
2. *Distinguish between bacterial and archaeal cell types.*

When cells were visualized with microscopes, two basic cellular architectures were recognized: eukaryotic and prokaryotic. These terms refer to the presence or absence, respectively, of a membrane-bounded nucleus that contains genetic material. We have already mentioned that in addition to lacking a nucleus, prokaryotic cells do not have an internal membrane system or numerous membrane-bounded organelles.

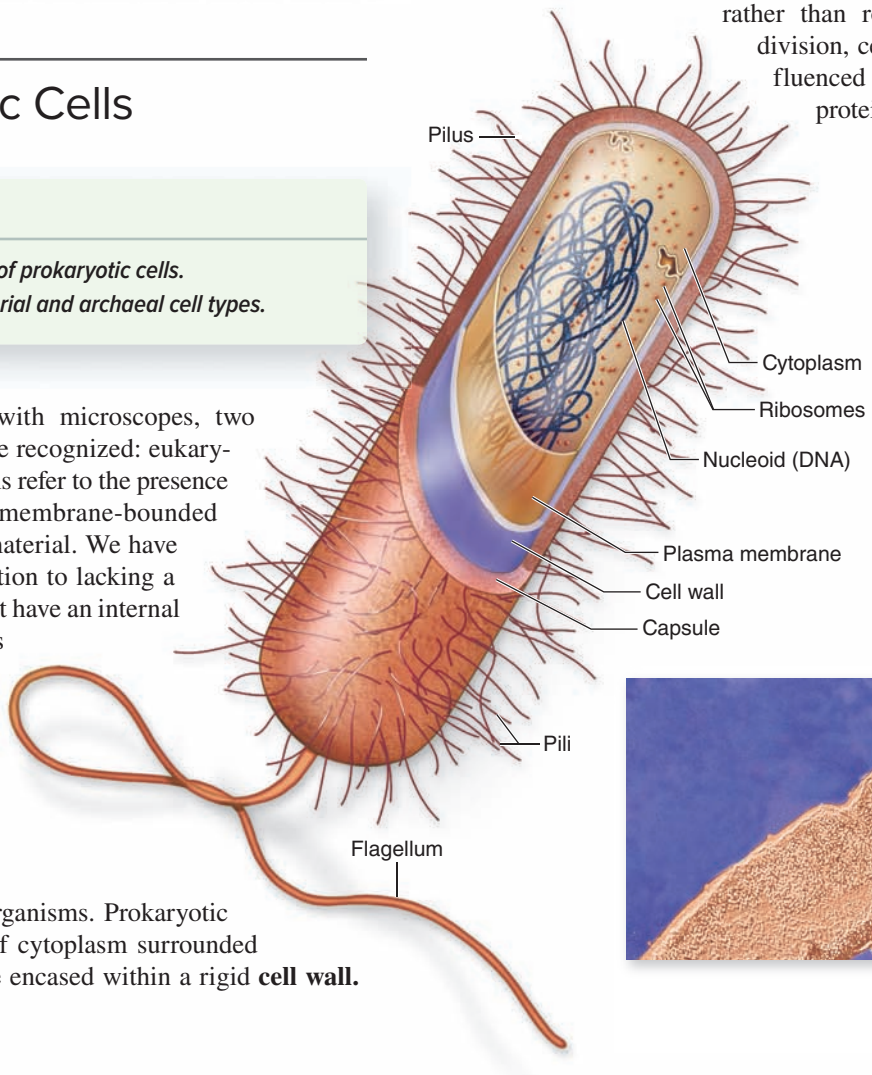
Prokaryotic cells have relatively simple organization

Prokaryotes are the simplest organisms. Prokaryotic cells are small. They consist of cytoplasm surrounded by a plasma membrane and are encased within a rigid **cell wall.** They have no distinct interior compartments (figure 4.3). A prokaryotic cell is like a one-room cabin in which eating, sleeping, and watching TV all occur.

Prokaryotes are very important in the ecology of living organisms. Some harvest light by photosynthesis, others break down dead organisms and recycle their components. Still others cause disease or have uses in many important industrial processes. Prokaryotes have two main domains: archaea and bacteria. Chapter 28 covers prokaryotic diversity in more detail.

? Inquiry question What modifications would you include if you wanted to make a cell as large as possible?

Although prokaryotic cells do contain organelles like **ribosomes,** which carry out protein synthesis, most lack the membrane-bounded organelles characteristic of eukaryotic cells. It was long thought that prokaryotes also lack the elaborate cytoskeleton found in eukaryotes, but we have now found they have molecules related to both actin and tubulin, which form two of the cytoskeletal elements described in section 4.6. The strength and shape of the cell is determined by the cell wall and not these cytoskeletal elements (figure 4.3). However, cell wall structure is influenced by the cytoskeleton. For instance, the presence of actin like MreB fibers running the length of the cell lead to perpendicular cell-wall fibers that produce a rod-shaped cell. This can be seen when MreB protein is removed, cells become spherical rather than rod-shaped. During cell division, cell-wall deposition is influenced by the tubulin-like FtsZ protein (see chapter 10).



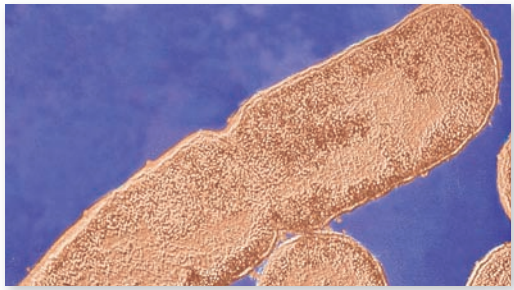


Figure 4.3
Structure of a prokaryotic cell.
Generalized cell organization of a prokaryote. The nucleoid is visible as a dense central region segregated from the cytoplasm. Some prokaryotes have hairlike growths (called pili [singular, *pilus*]) on the outside of the cell.