I truly love *How Life Works*. Couple the text with the robust online learning system and I think it’s the best introductory biology text/learning system I’ve used.”

– Kari Loomis, University of Massachusetts, Amherst

SAMPLE INSIDE

CHAPTER 7: CELLULAR RESPIRATION

CHAPTER 33: ANIMAL FORM, FUNCTION, AND EVOLUTIONARY HISTORY

James Morris
Daniel Hartl
Andrew Knoll
Robert Lue
Melissa Michael

ANDREW BERRY, ANDREW BIEWENER,
BRIAN FARRELL, N. MICHELE HOLBROOK
ABOUT THE AUTHORS

JAMES R. MORRIS is Professor of Biology and Chair of the Program in Health: Science, Society, and Policy at Brandeis University. He teaches a wide variety of courses for majors and non-majors, including introductory biology, evolution, genetics and genomics, epigenetics, comparative vertebrate anatomy, and a first-year seminar on Darwin’s On the Origin of Species. He is the recipient of numerous teaching awards from Brandeis and Harvard. His research focuses on the rapidly growing field of epigenetics, making use of the fruit fly Drosophila melanogaster as a model organism. He currently pursues this research with undergraduates in order to give them the opportunity to do genuine, laboratory-based research early in their scientific careers. Dr. Morris received a PhD in genetics from Harvard University and an MD from Harvard Medical School. He was a Junior Fellow in the Society of Fellows at Harvard University, and a National Academies Education Fellow and Mentor in the Life Sciences. He also writes short essays on science, medicine, and teaching at his Science Whys blog (http://blogs.brandeis.edu/sciencewhys).

DANIEL L. HARTL is Higgins Professor of Biology in the Department of Organismic and Evolutionary Biology at Harvard University and Professor of Immunology and Infectious Diseases at the Harvard T. H. Chan School of Public Health. He has taught highly popular courses in genetics and evolution at both the introductory and advanced levels. His lab studies molecular evolutionary genetics and population genetics and genomics. Dr. Hartl is the recipient of the Samuel Weiner Outstanding Scholar Award as well as the Gold Medal of the Stazione Zoologica Anton Dohrn, Naples. He is a member of the National Academy of Sciences and the American Academy of Arts and Sciences. He has served as President of the Gordon Society of America and President of the Society for Molecular Biology and Evolution. Dr. Hartl’s PhD is from the University of Wisconsin, and he did postdoctoral studies at the University of California, Berkeley. Before joining the Harvard faculty, he served on the faculties of the University of Minnesota, Purdue University, and Washington University Medical School. In addition to publishing more than 400 scientific articles, Dr. Hartl has authored or coauthored 30 books.

ANDREW H. KNOLL is Fisher Professor of Natural History in the Department of Organismic and Evolutionary Biology at Harvard University. He is also Professor of Earth and Planetary Sciences. Dr. Knoll teaches introductory courses in both departments. His research focuses on the early evolution of life, Precambrian environmental history, and the interconnections between the two. He has also worked extensively on the early evolution of animals, mass extinction, and plant evolution. He currently serves on the science team for NASA’s mission to Mars. Dr. Knoll received the Phi Beta Kappa Book Award in Science for Life on a Young Planet. In 2018, he was awarded the International Prize for Biology. He is a member of the National Academy of Sciences and a foreign member of the Royal Society of London. He received his PhD from Harvard University and then taught at Oberlin College before returning to Harvard.

ROBERT A. LUE is Professor of Molecular and Cellular Biology at Harvard University and the Richard L. Menschel Faculty Director of the Derek Bok Center for Teaching and Learning. Dr. Lue has a longstanding commitment to interdisciplinary teaching and research and chaired the faculty committee that developed the first integrated science foundation in the country to serve science majors as well as pre-medical students. The founding director of Life Sciences Education at Harvard, Dr. Lue led a complete redesign of the introductory curriculum, redefining how the university can more effectively foster new generations of scientists as well as science-literate citizens. Dr. Lue has also developed award-winning multimedia, including the animation “The Inner Life of the Cell.” He has coauthored undergraduate biology textbooks and chaired education conferences on college biology for the National Academies and the National Science Foundation and on diversity in science for the Howard Hughes Medical Institute and the National Institutes of Health. In 2012, Dr. Lue’s extensive work on using technology to enhance learning took a new direction when he became faculty director of university-wide online education initiative HarvardX; he now helps to shape Harvard’s engagement in online learning to reinforce its commitment to teaching excellence. Dr. Lue earned his PhD from Harvard University.

MELISSA MICHAEL is Director for Core Curriculum and Assistant Director for Undergraduate Instruction for the School of Molecular and Cellular Biology at the University of Illinois at Urbana-Champaign. A cell biologist, Dr. Michael primarily focuses on the continuing development of the School’s undergraduate curricula. She is engaged in several projects aimed at improving instruction and assessment at the course and program levels. Her research focuses primarily on how creative assessment strategies affect student learning outcomes and how outcomes in large-enrollment courses can be improved through the use of formative assessment in active classrooms.

ANDREW BERRY is Lecturer in the Department of Organismic and Evolutionary Biology and an undergraduate advisor in the Life Sciences at Harvard University. With research interests in evolutionary biology and history of science, he teaches courses that either focus on one of the areas or combine the two. He has written two books: Infinite Tropics, a collection of the writings of Alfred Russel Wallace, and, with James D. Watson, DNA: The Secret of Life, which is part history, part exploration of the controversies surrounding DNA-based technologies.
ANDREW A. BIEWENER is Charles P. Lyman Professor of Biology in the Department of Organismic and Evolutionary Biology at Harvard University and Director of the Concord Field Station. He teaches both introductory and advanced courses in anatomy, physiology, and biomechanics. His research focuses on the comparative biomechanics and neuromuscular control of mammalian and avian locomotion, with relevance to biorobotics. He is currently Deputy Editor-in-Chief for the Journal of Experimental Biology. He also served as President of the American Society of Biomechanics.

BRIAN D. FARRELL is Director of the David Rockefeller Center for Latin American Studies and Professor of Organismic and Evolutionary Biology and Curator in Entomology at the Museum of Comparative Zoology at Harvard University. He is an authority on coevolution between insects and plants and a specialist on the biology of beetles. He is the author of many scientific papers and book chapters on the evolution of ecological interactions between plants, beetles, and other insects in the tropics and temperate zone. Dr. Farrell also spearheads initiatives to repatriate digital information from scientific specimens of insects in museums to their tropical countries of origin. In 2011–2012, he was a Fulbright Scholar to the Universidad Autónoma de Santo Domingo in the Dominican Republic. Dr. Farrell received a BA in Zoology and Botany from the University of Vermont and MS and PhD from the University of Maryland.

N. MICHELE HOLBROOK is Charles Bullard Professor of Forestry in the Department of Organismic and Evolutionary Biology at Harvard University. She teaches an introductory course on plant biology as well as advanced courses in plant physiology. Her research focuses on the physics and physiology of vascular transport in plants with the goal of understanding how constraints on the movement of water and solutes between soil and leaves influence ecological and evolutionary processes. Dr. Holbrook received her PhD from Stanford University.

ASSESSMENT AUTHORS

JEAN HEITZ is a Distinguished Faculty Associate at the University of Wisconsin in Madison, WI. She has worked with the two-semester introductory sequence for biological sciences majors for over 40 years. Her primary roles include developing both interactive discussion/recitation activities designed to uncover and modify misconceptions in biology and open-ended investigative labs designed to give students a more authentic experience with science. The lab experience includes engaging all second-semester students in independent research, either mentored research or a library-based meta-analysis of an open question in the literature. She is also the advisor to the Peer Learning Association and is actively involved in TA training. She has taught a graduate course in Teaching College Biology, has presented active-learning workshops at a number of national and international meetings, and has published a variety of lab modules, workbooks, and articles related to secondary education.

MARK HENS is Associate Professor of Biology at the University of North Carolina Greensboro, where he has taught introductory biology since 1996. He is a National Academies Education Mentor in the Life Sciences and is the director of his department’s Introductory Biology Program. In this role, he guided the development of a comprehensive set of assessable student learning outcomes for the two-semester introductory biology course required of all science majors at UNCG. In various leadership roles in general education, both on his campus and statewide, he was instrumental in crafting a common set of assessable student learning outcomes for all natural science courses for which students receive general education credit on the 16 campuses of the University of North Carolina system.

ELENA R. LOZOVSKY is Principal Staff Scientist in the Department of Organismic and Evolutionary Biology at Harvard University. She received her PhD in genetics from Moscow State University in Russia and before joining Harvard carried out research at the Institute of Molecular Biology in Moscow, Cornell University, and Washington University School of Medicine in St. Louis. Her research has focused on transposable elements and genome evolution in eukaryotes and on the evolution of drug resistance in malaria parasites. She has also had extensive experience in teaching genetics and evolution.

JOHN MERRILL is Director of the Biological Sciences Program in the College of Natural Science at Michigan State University. This program administers the core biology course sequence required for all science majors. He is a National Academies Education Mentor in the Life Sciences. In recent years, he has focused his research on teaching and learning with emphasis on classroom interventions and enhanced assessment. A particularly active area is the NSF-funded development of computer tools for automatic scoring of students’ open-ended responses to conceptual assessment questions, with the goal of making it feasible to use open-response questions in large-enrollment classes.

RANDALL PHILLIS is Associate Professor of Biology at the University of Massachusetts Amherst. He has taught in the majors introductory biology course at this institution for 19 years and is a National Academies Education Mentor in the Life Sciences. With help from the Pew Center for Academic Transformation (1999), he has been instrumental in transforming the introductory biology course to an active learning format that makes use of classroom communication systems. He also participates in an NSF-funded project to design model-based reasoning assessment tools for use in class and on exams. These tools are being designed to develop and evaluate student scientific reasoning skills, with a focus on topics in introductory biology.

DEBRA PIRES is an Academic Administrator at the University of California, Los Angeles. She teaches the introductory courses in the Life Sciences Core Curriculum. She is also the Instructional Consultant for the Center for Education Innovation & Learning in the Sciences (CEILS). Many of her efforts are focused on curricular redesign of introductory biology courses. Through her work with CEILS, she coordinates faculty development workshops across several departments to facilitate pedagogical changes associated with curricular developments. Her current research focuses on the impact of active learning pedagogies on student performance in lower-division courses, and on concept retention in upper-division courses.
BIOLOGY: HOW LIFE WORKS

has been a revolutionary force for both instructors and students in the majors biology course. It was the first truly comprehensive set of integrated tools for introductory biology, seamlessly incorporating powerful text, media, and assessment to create the best pedagogical experience for students.

THE VISUAL PROGRAM  The already impressive visual program has been greatly improved and expanded. The powerful Visual Synthesis tools, have been reimagined, allowing for more flexibility for both students and instructors. A new Tour Mode allows for learning objective-driven tours of the material. We’ve also added deep-linking from the eText to encourage the student to jump immediately from the reading experience into a more interactive visual representation of the content. Instructors can also create customized tours to use for engaging in-class presentation and active learning opportunities. And finally, new animations have been added to the library, including a new 3D animation to support the animal form and function chapters.

A FOCUS ON SCIENTIFIC SKILLS  The third edition has an increased focus on helping students develop the skills they will need to be successful scientists. We’ve designed skills learning experiences not separate from the core content, but aligned to it. New Skills Primers are self-paced tutorials that guide students to learn, practice, and use skills like data visualization, experimental design, working with numbers, and more. New How Do We Know Activities are digital extensions of the application-based learning tool found in the text, and focus on further developing students’ scientific inquiry skills.

THE HUB  The best teaching resources in the world aren’t of use if instructors can’t find them. The HUB provides a one-stop destination for valuable teaching and learning resources, including all of our well-vetted in-class activities.

IMPROVED ORGANIZATION OF TOPICS  We implemented several organizational changes based on extensive user feedback with the goal of creating an improved narrative for students and a more flexible teaching framework for instructors.

A new chapter on Animal Form, Function, and Evolutionary History leads off the animal anatomy and physiology chapters to provide a whole-body view of structure and function and to provide better context for the more specific systems in following chapters.

The ecology coverage has been enriched and reorganized for a more seamless flow. A new chapter on Ecosystem Ecology combines ecosystem concepts formerly housed in separate chapters to present a more cohesive view of the flow of matter and energy in ecosystems.

All of these changes and improvements represent the next step in the evolution of Biology: How Life Works. We think we have created the best learning resource for introductory biology students, and we think instructors will find joy in the improvements they can make in their classes with these materials.
DEAR STUDENTS AND INSTRUCTORS,

A new edition of *How Life Works* provides an opportunity for us to continue to innovate. It gives us a chance not just to update and organize, but also to rethink and reimagine the resources we develop to support teaching and learning in introductory biology. Many of our revisions are based on what we’ve heard from you—the growing community of students and instructors who use *How Life Works*.

From the start, we have written *How Life Works* to be a streamlined text that focuses on concepts and skills relevant to introductory biology. We take an integrated approach that aims to connect concepts and processes, so students can see their interrelationships. Instead of presenting vast amounts of content, we organize our presentation around a few key core concepts. And we recognize that the text, media, and assessment have to work together to provide a rich and meaningful learning experience for students. Our digital platform is designed to provide maximum flexibility and ease of use. With each edition, we keep these ideas front and center.

The third edition continues and expands on this approach. We are particularly excited about new resources that help to develop skills that students will encounter in introductory biology and beyond, including how to ask questions, develop hypotheses, interpret data, read graphs, use quantitative reasoning, and apply statistical and evolutionary thinking. In short, our new resources emphasize the skills that enable students to think like scientists.

Every chapter includes at least one *How Do We Know Figure*, which takes the time to describe how the scientific community came to know a piece of information, process, or concept presented in the text. These were so well received in the first and second editions that we decided to connect them to *How Do We Know Activities* that ask students to answer questions and explore the figure actively and in depth.

In addition, we have revised and expanded the *Primers* that we developed in earlier editions so that they focus on skills and include media and assessment. In this way, they are interactive and serve as short tutorials on fundamental skills.

We also took a fresh look at the chapters on animal anatomy and physiology. A new case focuses on the exciting field of biology-inspired design. This interdisciplinary field taps into biology, engineering, and material science to build tools and devices inspired by all types of organisms, including animals. In addition, a new chapter on animal form, function, and evolution provides a way to orient students to main concepts before delving into detail in the subsequent chapters. Finally, we have new media and assessment that work closely with this section.

In response to thoughtful feedback from instructors, we reorganized our coverage of ecological systems. We now bring together in a single chapter an integrated discussion of flow of matter and energy in ecosystems. This new arrangement allows us to move seamlessly from organisms to populations to species interactions to interactions with the physical environment to global ecology, ending with a discussion of the impact of human activities on the biosphere.

The pace of change in biology is matched by our ever-growing understanding of how students learn, drawing on the latest findings in neuroscience, psychology, and education. We think about ways to create a classroom that is active, inclusive, and evidence-based. We ask ourselves questions as we work to make our material more student-focused. Can we replace a short lecture with an activity in which students construct their own knowledge? What are some common misconceptions that students might encounter along the way? Do all students feel supported and encouraged?

Toward this end, in our new edition we have added a *Learning Objective Framework* while continuing to diversify our assessments. We focus on high-order questions and visual interpretation questions that ask students to make sense of a graph or figure. We continue to expand our rich collection of in-class activities to provide support for instructors who are leading student-centered classrooms. *Assessments* are found everywhere in *How Life Works*—associated with the text, figures, animations, simulations, maps, and in-class activities.

Finally, our media program continues to be fresh and creative, while staying aligned with our other resources. In this edition, we have redesigned our *Visual Synthesis Maps* to provide new functionality. Students can still freely explore spaces and processes in these maps, but we now offer “tours” based on learning objectives so that students can follow a path as a way to focus their exploration.

As one of our recent adopters said, hearteningly, “Who is the book for?” if not for students. That simple question guides everything we do. With every edition and update, we aim to improve the learning experience as students engage in discovering how life works.

Sincerely,
The *How Life Works* team
The art in the text of *Biology: How Life Works* and the associated media in LaunchPad were developed in coordination with the text and assessments to present an integrated and engaging visual experience for students.

Two of the biggest challenges introductory biology students face are connecting concepts across chapters, and building a contextual picture, or visual framework, of a complex process. To help students think like biologists, we provide *Visual Synthesis Figures* at key points in the text with associated *Visual Synthesis Maps* in the media package. These figures bring together multiple images students have already seen into a visual summary, helping students see how individual concepts connect to tell a single story.

**REIMAGINED VISUAL SYNTHESIS PROGRAM**

The *Visual Synthesis Tool’s* user experience has been reimagined to provide students a more effective visual learning environment, helping them synthesize the connections between biological concepts.
New Tour Mode Functionality: As in previous editions of *How Life Works*, students will still have the opportunity to freely explore these visual concept maps. However, we have now rebuilt the visual synthesis tool to provide students with learning objective–driven tours of the major concepts being visualized in the map. Through these synthesis-focused tours, students follow defined pathways through the core concepts of the maps, as well as measure their understanding of the tours through aligned and assignable assessment opportunities. Instructors will also be able to create their own tours for students to explore in assignments, or for use as in-class teaching resources.

Deep-linking from the eText to the Visual Synthesis Map: Students, with one click of a button, will be taken from their digital reading experience into the exact spot in our Visual Synthesis Maps where a particular figure/visualization from the book appears. These deep links will provide students with additional information about the figure, an enhanced visual opportunity to learn the concept, and the unique experience of seeing how this figure connects into the larger conceptual framework of the map.

REIMAGINED 3D ANIMATIONS

The powerful 3D Animations have been reimagined as more flexible tools for students. While still available as full-length videos, they are also available split into shorter clips of more manageable length with added annotations and an improved alignment of the assessments. New animations have been added to the library, including a new 3D animation to support the revised animal form and function topics.
How Life Works is dedicated to teaching the skills students need to think critically, along with the concepts and content they’ll need for success in later biology courses.

**Skills Primers**

1. Quantitative Reasoning: Working with Numbers
2. Scientific Inquiry: Asking and Answering Questions in Biology
3. Data and Data Visualization: Interpreting and Presenting Results
4. Phylogenetics: Reading and Building Evolutionary Trees
5. Probability and Statistics: Predicting and Analyzing Data
6. Models: Visualizing Biological Structures and Processes

Skills Primers are a new approach to developing the scientific, biological, and cognitive skills students need to be successful in an introductory biology course. The Skills Primers are tutorial-based learning objects that guide students to learn, practice, and use skills like data visualization, experimental design, working with numbers, and many more.

How Do We Know Activities ask students questions connected to How Do We Know Figures in the text. In answering these questions, students explore the figures in depth and develop the skills they need to understand scientific inquiry. These online companion exercises are assignable and gradable.

**How Do We Know?**

**FIG. 33.18**

Do animals tend to get bigger over time?

**BACKGROUND** Cope’s rule, named after the American paleontologist Edward Cope, suggests that there is a trend through time toward increased size among animals. However, it is unclear whether such a general trend actually exists. Large body size can be associated with increased fitness—for example, by making it easier to capture prey or compete with other organisms. Notable examples of very large animals that lived long ago are the dinosaurs. There are also exceptions to this trend in some groups of animals.

**HYPOTHESIS** Animals tend to increase in size over evolutionary time.

**EXPERIMENT** Jonathan Payne and his colleagues at Stanford University decided to test the hypothesis that animals tend to get bigger over time, focusing on marine animals over the last 541 million years. They measured the three major body axes of images of animal specimens to determine the mean volume (as a measure of body size) for more than 17,000 genera of animals, including arthropods, brachiopods, echinoderms, mollusks, and chordates.

**RESULTS** The researchers found that the mean volume for all genera increased over time (the dark black line in the graph). In addition, they found that the range in sizes increased dramatically (the difference between the two light black lines in the graph). Most of this expansion resulted from an increase in the maximum size of animals (the upper light black line in the graph).

**CONCLUSION** The data support the hypothesis that there is an evolutionary trend toward larger body size in many groups of animals.

**FOLLOW-UP WORK** The researchers next asked whether the increase in size is the result of natural selection or genetic drift (Chapter 20). They compiled observed trends in the mean, maximum, and minimum sizes of a number of animal groups and compared them to the predictions of models based on selection and drift. They found that their observations are consistent with models based on selection, and not consistent with models based on drift. These findings suggest that increased body size has selective advantages.

**CONNECTED LEARNING TOOLS**

**The Hub** is the teaching and learning destination of *How Life Works*. The Hub provides an easy way to find teaching and learning resources, including all of our in-class activities.

**Chapter Reading Guides**: Designed to improve and focus the reading experience, the reading guides provide students with easy access to chapter resources, including the Learning Objective Framework and answers to the Self-Assessment Questions.

**In-Class Activities**: Active learning exercises provide students with hands-on exploration and help correct common misconceptions. In-class activities contain all of the resources needed to engage students in an active classroom, including a preparation guide for instructors, in-class presentation slides with assessment questions, and student handouts. This edition of *How Life Works* includes 10 new in-class activities for the second half of the text.

*How Life Works* has always been committed to providing powerful and effective resources for instructors and pedagogical support for students. The third edition expands this support with even better tools for self-study ahead of class and active work in the classroom.
Well-designed assessment is a tremendous tool for instructors preparing students for class, engaging students during class, and gauging student understanding. The *How Life Works* assessment author team applied decades of experience researching and implementing assessment practices to create a variety of questions and activities for pre-class, in-class, homework, and exam settings. All assessment items are carefully aligned with the text and media and have the flexibility to meet the needs of instructors with any experience level, classroom size, or teaching style.

**Objectives:** We’ve authored a two-tier learning objective structure wherein **Level 1 objectives** are broader and more cognitively complex while our **Level 2 objectives** are more granular and typically less complex. Together these objectives describe what the learner should know and be able to do by the end of the learning experience. LaunchPad makes it easy to select assessments associated with these objectives, and to focus on the learning objectives that are most important to your course.

**Improved Assessments:** We have developed more high-order questions, more questions that support the development of quantitative skills, and more questions that require students to engage with figures or consider graphically represented data. Improved data analytics provide insight into student performance.

Toucans are frugivorous (fruit-eating) birds that inhabit tropical forests in Central and South America where they can potentially consume any fruit that is available (generalists). The realized niches of toucans are determined by competition in the consumption of different species of fruits (niche overlap). White-throated toucans are the largest species and very strong competitors who easily scare the mid-sized Cuvier’s and Ivory-billed toucans off the fruiting trees, altering access to the resources among the three species. The graphs shown represent the occupation of niche space at two different sites, where two or three species coexist, in different abundances.

Which of the graphs shown best characterizes the fundamental niche of any of these species of toucans? Assume the X-axis is the niche space available.
Ordinarily, textbooks are developed by first writing chapters, then making decisions about art and images, and finally assembling a test bank and ancillary media. The authors of How Life Works developed the text, visual program, and assessment at the same time. These three threads are tied to the same set of core concepts, share a common language, and use the same visual palette, which ensures a seamless learning experience for students throughout the course.

The text, visuals, and assessments come together most effectively through LaunchPad, Macmillan’s integrated learning management system. In LaunchPad, students and instructors can access all components of How Life Works.

LaunchPad resources for How Life Works are flexible and aligned. Instructors have the ability to select the visuals, assessments, and activities that best suit their classroom and students. All resources are aligned to one another as well as to the text to ensure effectiveness in helping students build skills and develop knowledge necessary for a foundation in biology.

LearningCurve’s game-like quizzing motivates each student to engage with the content, and reporting tools help teachers get a handle on their class needs.
WHAT’S NEW IN THE THIRD EDITION?

MAJOR CHANGES AND UPDATES TO THE BOOK

In developing the third edition of *Biology: How Life Works*, we focused particularly on the form and function chapters and the ecology chapters.

New introductions set the scene for the plant and animal form and function chapters and highlight key themes in structure/function relationships.

- A new chapter, “Animal Form, Function, and Evolutionary History” (Chapter 33), leads off the animal physiology chapters. This chapter provides a whole-body view of structure and function that provides context for the specific systems discussed in the chapters that follow. It focuses on animal body plans and tissue types and introduces homeostasis as the major regulatory theme of the animal physiology chapters.
- The first section of “Plant Form, Function, and Evolutionary History” (Chapter 27) is a completely reconceived introduction to the plant form and function chapters. This section highlights major structure/function differences distinguishing bryophytes and vascular plants. It focuses on how the two groups maintain hydration, specifically on how the reliance on diffusion by bryophytes and bulk flow by vascular plants is reflected in overall structure and cell properties.

Structure/function relationships are placed in a broader evolutionary framework.

- The new “Animal Form, Function, and Evolutionary History” chapter (Chapter 33) concludes with an overview of the history of animal evolution, placing major anatomical and physiological innovations in an evolutionary context.
- “Plant Diversity” (Chapter 31) is now organized around four major structure/function transitions in the evolution of plant life, highlighted in a new Section 31.1.

The relationship between structure and function has been further strengthened in the plant chapters.

We have recrafted several discussions of vascular structure and root structure to further clarify these structures and their effect on the resilience and efficiency of plant systems. In particular, the third edition provides a more thorough and insightful understanding of the mechanism of xylem transport.

The animal physiology chapters begin with a new introductory case that highlights structure/function relationships.

A new and engaging case on Biology-Inspired Design explores how scientists have mimicked nature to solve all kinds of practical problems of real-life interest to students, from Velcro to dialysis machines. Most animal physiology chapters contain a section discussing an example of biology-inspired design.

Ecology coverage has been enriched and reorganized for a more seamless flow.

A new chapter on Ecosystem Ecology, Chapter 46, combines ecosystem concepts such as food webs and trophic pyramids with the material on biogeochemical cycles formerly in separate chapters to present a more cohesive view of the flow of matter and energy in ecosystems. This new arrangement allows us to move seamlessly from organisms to populations to species interactions to interactions with the physical environment to global ecology, ending with a discussion of the impact of human activities on the biosphere.

We continue to expand our treatment of ecological systems, one of our six grand themes. Chapters 44 and 45 (“Population Ecology” and “Species Interactions and Communities”) have been enriched by the addition of new concepts and examples to deepen the discussions of life histories and tradeoffs, island biogeography, the niche, biodiversity, and succession, among other topics.
molecular studies were conducted, however, researchers discovered that they did not support this traditional phylogenetic division of bilaterians into acelomate, coelomate, and pseudocoelomate groups. Similarly, molecular sequence comparisons have not supported the once widespread view that segmented bodies indicate a close relationship between earthworms and lobsters.

**CASE 7 BIOLOGY-INSPIRED DESIGN: USING NATURE TO SOLVE PROBLEMS**

Can we mimic the form and function of animals to build robots?

Scientists who design robots often try to mimic the form and function of animals. Fishes are one of the most popular types of robotic animals. We can learn a great deal about innovations by studying fishes, whose remarkable adaptations have been shaped by natural selection over more than 500 million years.

The first robotic fish was created in the 1980s by a team of scientists and engineers at Massachusetts Institute of Technology. It was called RoboTuna, because it mimicked the form and function of a tuna, allowing it to swim effectively through water. Since then, many more fish-like robots have been made, so that today there are more than 400 different types of robotic fishes. Some, like RoboTuna, have one joint; others have many joints, and still others are made of dynamic materials that can bend nimbly.

Why build a robotic fish? The first and most basic reason is to understand how fish move. Fish are peculiar swimmers. If we can build a robotic fish that swims like a living one, it suggests that we understand how a fish is able to move forward, turn, and navigate its surroundings. Robotic fishes can also be used in studies of fish behavior. A robotic fish that looks and even smells like a real fish, and that has sensors to detect and record its environment, provides a way to quietly “spy” on fish in ways that were not possible by direct observation or by the use of cameras. There are all kinds of practical applications of robotic fishes as well, from mapping coastlines, coral reefs, and the sea floor, to monitoring underwater cables and pipelines, to exploring marine life.

Scientists and engineers have copied the form and function of many animals, including cockroaches, geckos, jellyfish, hummingbirds, and bats, to name just a few. One of the most recent and exciting robots is based on an octopus. Octopuses show incredible dexterity and strength, all without an internal skeleton.

The octobot, called an octobot and designed by researchers at Harvard University, has several remarkable characteristics (Fig. 33.9). It is entirely soft, with no rigid components like metal or even batteries. It is powered by a simple chemical reaction: liquid hydrogen peroxide is converted to a gas in the presence of a catalyst (in this case, platinum), providing pressure that powers movement. Finally, the robot is produced with a 3D printer.

The octobot brings together engineers, material scientists, and chemists to create a robot that is inspired by biology. This truly interdisciplinary effort is the first step toward more flexible and innovative robots for research and diverse applications.

### Self-Assessment Questions

1. Draw a simplified animal tree of life, indicating the relationships among sponges, crinidarians, protostomes, and deuterostomes.
2. Which features distinguish sponges, crinidarians, protostomes, and deuterostomes? Place these features on the phylogeny that you drew for Self-Assessment Question 1.
3. How is cephalization an adaption for forward locomotion?
4. Which animals are more closely related to sponges: crinidarians or bilaterians?
LIST OF NEW TOPICS & OTHER REVISIONS

The following is a detailed list of content changes. These range from small to quite substantial (an entire new chapter in the animal physiology section). Especially important changes are indicated with an asterisk.

- Snottites story replaced with life on Mars story (Case 1)
- A rearranged discussion of DNA structure, DNA function, and process of transcription (Chapter 3)
- Chromatin structure preview removed and discussed in full in Chapter 13 (Chapter 3)
- A new How Do We Know Figure on Anfinsen’s experiment on primary and tertiary structure (Chapter 4)
- An expanded discussion of osmotic pressure (Chapter 5)
- Simplified Figure 7.3, The Four Stages of Cellular Respiration, to show only glucose and glycolysis (Chapter 7)
- A new Figure 7.18 giving an overview of the catalysis of fuel molecules other than glucose (Chapter 7)
- A redesigned bottom panel of the Visual Synthesis Figure 8.20 for clearer and more accurate inputs and outputs (Chapter 8)
- A new section illustrating how individual responses create a whole body response (Chapter 9)
- An expanded discussion of cilia (Chapter 10)
- The section on nondisjunction now moved to Chapter 11 and condensed (Chapter 11)
- Supercorks moved to Section 13.4 from Chapter 3 (Chapter 13)
- A completely revised and expanded explanation of the mechanism of xylem transport (Chapter 27)
- A revised description of the mechanism of filtering by the Casparian strip (Chapter 27)
- A new discussion of the unwanted effects of nitrogen fertilization (Chapter 27)
- A new paragraph on electrical signaling by plants (Chapter 30)
- A new Section 31.1 on the four major transitions in the evolution of plant life (Chapter 31)

Extra explanation of walking through combinatorial control in plants (Chapter 19)

Fruit fly example of Hardy-Weinberg equilibrium replaced by a continuation of Mendel’s pea example (Chapter 20)

Greenish warbler example of populations that differ in reproductive isolation replaced by brier towhee example (Chapter 21)

A new example and figure on the formation of a new species by hybridization: Geospiza fortis finches (Chapter 21)

Figure 23.9 from the second edition removed and replaced by three new figures on different ways of using sequence data for phylogenetic reconstruction (Chapter 23)

A new figure on the carbon cycle (Chapter 24)

Updated bacterial and archaeal phylogenies (Chapter 24)

Updated section on the origin of the eukaryotic cell (Chapter 25)

Discussion of eukaryotic diversity revised in light of recent discoveries from the monumental Tara Ocean Expedition (Chapter 25)

Overall focus changed to feeding a growing population (Case 6)

A new Section 27.1 compares bryophyte and vascular plant structure and function, with a focus on hydration (Chapter 27)

A new, clearer description of xylem conduits (Chapter 27)

In human genetics section, BRCA example replaced by TCF7L2 diabetes example (Chapter 15)
A new table on the “Diversity of Plant Life” (Chapter 31)

Two new figures helping students integrate information from earlier chapters (Chapter 31)

Revised phylogenies and text to reflect the uncertain relationship among the bryophytes (Chapter 31)

A new section on the evolutionary relationship of angiosperms and gymnosperms and their relative diversity (Chapter 31)

A new section on how innovations increased the efficiency of the angiosperm life cycles and xylem transport (Chapter 31)

A revised explanation of diameter increase and vascular bundle distribution in monocot stems (Chapter 31)

More on the release of digestive enzymes from hyphae tips (Chapter 32)

More on spore dispersal mechanisms (Chapter 32)

A new Case on biology-inspired design (Case 7)

A new chapter “Animal Form, Function, and Evolutionary History” providing an introduction to the animal physiology chapters (Chapter 33)

- animal body plans
- tissues and organs
- introduction to homeostasis
- evolutionary history of animals

A new Case section on robots inspired by animals (Chapter 33)

The chapters on Animal Nervous Systems and Animal Sensory Systems now combined into a single chapter, with some material removed or condensed (Chapter 34)

A new Case section on cochlear implants (Chapter 34)

A new Case section on smart materials to heal damaged bones and improve artificial joints (Chapter 35)

A new Case section on artificial heart valves (Chapter 37)

New coverage of insect mandibles (Chapter 38)

A new Case section on dialysis (Chapter 39)

A new Case section on treating sepsis with an artificial spleen (Chapter 41)

Two sections moved to the new chapter on Animal Form, Function, and Evolutionary History (Chapter 42)

A new Table 43.1 summarizing Tinbergen’s four questions (Chapter 43)

A new discussion of altruistic behavior by non-haplodiploid and non-eusocial species (Chapter 43)

Population dynamic equations standardized and further explained (Chapter 44)

A new density-independent factor example: replaced song sparrow example with Scottish Red Deer example (Chapter 44)

Further explanation of life histories and tradeoffs (Chapter 44)

Rearrangements and significant revisions to island biogeography explanation (Chapter 44)

Significant revisions to Case section on island populations and diversity (Chapter 44)

Revision of niche concept figure and textual explanation — replaced generic pond with Connell experiment (Chapter 45)

New example illustrating phylogenetic niche conservation: Anolis and Ameiva lizards (Chapter 45)

New concepts of species richness and evenness in biodiversity section (Chapter 45)

New concepts of primary and secondary succession in succession section (Chapter 45)

A new chapter on Ecosystem Ecology, Chapter 46, combines ecosystem concepts such as food webs and trophic pyramids with the material on biogeochemical cycles formerly in separate chapters to present a more cohesive view of the flow of matter and energy in ecosystems.

New discussion of lake turnover (Chapter 47)
Chapters are arranged in a familiar way to allow easy use in a range of introductory biology courses. On closer look, there are significant differences that aim to help students understand key concepts in modern biology and think like a scientist.

Key differences are identified by ● and unique chapters by ☀.

### PART 1  FROM CELLS TO ORGANISMS

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**CASE 2** Cancer: Cell Signaling, Form, and Division

| CHAPTER 9 | Cell Signaling                                         |
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### SIX GRAND THEMES: Chapter 1 introduces six themes that act as core concepts for introductory biology. They help students to see biology not as a set of disparate facts, but instead as an integrated whole. They connect and unite the many dimensions of biology, from molecules to the environment. These themes continue to be explored throughout How Life Works. They include scientific inquiry, chemistry and physics, the cell, evolution, ecological systems, and human impacts.

### CASES: Biology is best understood when presented using real and engaging examples as a framework for synthesizing information. Eight carefully positioned Cases help provide this framework. For example, the case about life’s origins is introduced before the first set of chapters to help students understand the fundamental features of a cell, and therefore of life itself. It is then revisited in the subsequent set of chapters. This case has been updated to include recent advances in our search for life on Mars.

### CHEMISTRY: After a brief chapter focusing on chemical principles, chemistry is taught in the context of biological processes in later chapters. This approach helps students to see in action the key principle.

### THE CELL: The cell is the fundamental unit of life. This concept is introduced in Chapter 1. Then, in Chapters 3–8, it is explored by highlighting three fundamental aspects of a cell—information flow (Chapters 3 and 4), homeostasis (Chapter 5), and harnessing energy (Chapters 6–8). Placing these basic points upfront allows students to start with a solid, integrated understanding of the cell.

### CELL DIVISION: Mitosis and meiosis are discussed in one chapter to allow students to see these two forms of cell division side-by-side and understand their similarities, differences, and evolutionary origins.

### GENETICS: The genetics section begins with a timely case on personal genomics that is revisited in the following chapters. The chapters start with genomes and move to inheritance to provide a modern, molecular look at genetic variation and how traits are transmitted. Current techniques such as the gene editing tool CRISPR are discussed.

### VARIATION: Mutation and genetic variation are combined into a single chapter to help students see the interrelationship of mutation, genetic variation, and phenotypic variation.
**CASE 4** Malaria: Coevolution of Humans and a Parasite

CHAPTER 20 Evolution: How Genotypes and Phenotypes Change Over Time
CHAPTER 21 Species and Speciation
CHAPTER 22 Evolutionary Patterns: Phylogeny and Fossils
CHAPTER 23 Human Origins and Evolution

**PART 2 FROM ORGANISMS TO THE ENVIRONMENT**

**CASE 5** The Human Microbiome: Diversity Within

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CHAPTER 33 Animal Form, Function, and Evolutionary History
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**CASE 8** Conserving Biodiversity: Rainforest and Coral Reef Hotspots

CHAPTER 43 Behavior and Behavioral Ecology
CHAPTER 44 Population Ecology
CHAPTER 45 Species Interactions and Communities
CHAPTER 46 Ecosystem Ecology
CHAPTER 47 Biomes and Global Ecology
CHAPTER 48 The Anthropocene: Humans as a Planetary Force

**EVOLUTION:** Evolution provides a thread throughout all of the chapters and resources in *How Life Works*. It is introduced in Chapter 1 as one of six core concepts of biology, allowing us to revisit evolutionary concepts and phylogenetic trees throughout. In this way, evolution provides a way for students to think broadly and in an integrated way about biology. Chapters 20–23 provide a focused discussion of key evolutionary processes, such as natural selection and speciation, and include a chapter devoted to human origins and evolution.

**PROKARYOTIC DIVERSITY:** The diversity of Bacteria and Archaea is discussed in the context of the carbon, nitrogen, and sulfur cycles, providing a conceptual backbone for understanding the tremendous diversity and ecological importance of these organisms.

**UPDATED CASE:** Case 6 has been substantially revised to highlight the challenge of feeding an ever-growing human population.

**PLANT DEFENSE:** The chapter on plant defense provides a strong ecological and case-based perspective on the strategies plants use to survive their exploitation by pathogens and herbivores.

**DIVERSITY:** Diversity follows chapters on anatomy, development, physiology, and life cycles, here and elsewhere, in order to provide a basis for understanding the groupings of organisms and to avoid presenting diversity as a list of names to memorize. When students understand the structure and function of organisms, they can understand the different groups in depth and organize them intuitively. To give instructors flexibility, brief descriptions of unfamiliar organisms and the major groups of organisms are included in the physiology chapters, and the diversity chapters include a brief review of organismal form and function.

**NEW CASE:** Biology-inspired design looks to nature to build a wide variety of tools and devices, from Velcro to prosthetic limbs. This fascinating area combines biology, engineering, and computer science, allowing students to see how different fields come together to solve complex problems. It also serves to emphasize key concepts about the anatomy and physiology of animals.

**NEW CHAPTER 33 — ANIMAL FORM, FUNCTION, AND EVOLUTIONARY HISTORY:** This chapter is new to the third edition and provides an overview of the structure, function, and evolution of animals.

**NERVOUS SYSTEMS:** The biology of nerve cells, sensory systems, and the brain are combined in a single chapter to give students an integrated perspective on these topics and concepts.

**EXPANDED ECOLOGY COVERAGE:** We continue to expand our treatment of ecological systems, one of our six grand themes. In this edition, we progress seamlessly from organisms, to populations and their interactions with other populations, to interactions among species and between species and the physical world, to global patterns of ecology, culminating in an exploration of how human activities are affecting the biosphere in the 21st century.
THE BOOK
Simply, the only textbook for this generation of students. We are no longer bearers of knowledge; the internet and Google have replaced us. So, we must teach students how science works and how we put concepts together into a coherent and meaningful way called biology. This text is designed to teach students within this new paradigm.

– Paul Moore, Bowling Green State University

Students tell me (unsolicited) that they like the textbook and that they can actually “read” it. Some say this is the first text they have actually liked reading.

– Tonya Kane, University of California, Los Angeles

This textbook does a good job of connecting concepts together and provides the student with a logical story throughout a chapter. I appreciate that and so do many of my students.

– Matthew Nusnbaum, Georgia State University

THE CASES
The cases... provide an insightful way to introduce the topics of a particular section. In many instances they show how the text information is applicable and relevant to real life situations.

– Nilo Marin, Broward College
ASSESSMENTS

The LearningCurve assignments have really benefited the students. The feedback I have gotten from students is extremely positive.

– Sally Harmych, University of Toledo

The assessment questions in general are very good and the entire system is pretty flexible and allows instructors to build a learning path and assessments that reflects the way they want their course to be taught.

– Mark Mort, University of Kansas

VISUAL SYNTHESIS MAPS

I love the VSMs! The conceptual depth of each is really quite impressive... I am continually impressed with how deeply students dive into each VSM.

– Jeremy Rose, Oregon State University

I really like the VS maps and the ability to drill down to the level of the atom/molecular group.

– Karen Smith, University of British Columbia
CHAPTER 7

Cellular Respiration
Harvesting Energy from Carbohydrates and Other Fuel Molecules
All living organisms have the ability to harness energy from the environment. We saw in Chapter 6 that energy is needed for all kinds of functions, including cell movement and division, muscle contraction, growth and development, and the synthesis of macromolecules. Organic molecules such as carbohydrates, lipids, and proteins are good sources of chemical energy. Some organisms, such as humans and other heterotrophs, consume organic molecules in their diet. Others, such as plants and other autotrophs, synthesize these molecules from inorganic molecules such as carbon dioxide. Regardless of how they obtain organic molecules, nearly all organisms—animals, plants, fungi, and microbes—break them down in the process of cellular respiration, releasing energy that can be used to do the work of the cell. Cellular respiration is a series of chemical reactions that convert the chemical energy in fuel molecules into the chemical energy of adenosine triphosphate (ATP). ATP can be readily used as a source of energy by all cells.

It is tempting to think that organic molecules are converted into energy in this process, but this is not the case. Recall from Chapter 6 that the first law of thermodynamics states that energy cannot be created or destroyed. Rather than creating energy, cellular respiration converts energy from one form to another. Specifically, it converts the chemical potential energy stored in organic molecules to the chemical potential energy in ATP.

It is also easy to forget that organisms other than animals, such as plants, use cellular respiration. If plants use sunlight as a source of energy, why would they need cellular respiration? As we will see in the next chapter, plants use the energy of sunlight to make carbohydrates. Plants then break down these carbohydrates in the process of cellular respiration to produce ATP.

In this chapter, we discuss the metabolic pathways of cellular respiration that supply the energy needs of a cell: the breakdown, storage, and mobilization of sugars such as glucose, the synthesis of ATP, and the coordination and regulation of these metabolic pathways.

7.1 AN OVERVIEW OF CELLULAR RESPIRATION

In Chapter 6, we saw that catabolism describes the set of chemical reactions that breaks down molecules into smaller units. In the process, these reactions release chemical energy that can be stored in molecules of ATP. Anabolism, by contrast, is the set of chemical reactions that build molecules from smaller units. Anabolic reactions require an input of energy, usually in the form of ATP.

Cellular respiration is one of the major sets of catabolic reactions in a cell. During cellular respiration, fuel molecules such as glucose, fatty acids, and proteins are catabolized into smaller units, releasing the energy stored in their chemical bonds to power the work of the cell.

**Cellular respiration uses chemical energy stored in molecules such as carbohydrates and lipids to produce ATP.**

Cellular respiration is a series of catabolic reactions that converts the energy stored in food molecules, such as glucose, into the energy stored in ATP and that produces carbon dioxide as a waste or by-product. Cellular respiration can occur in the presence of oxygen (termed aerobic respiration) or in its absence (termed anaerobic respiration). Most organisms that you are familiar with are capable of aerobic respiration; some bacteria respire...
an aerobically (Chapter 24). Here we focus on aerobic respiration. Oxygen is consumed in aerobic respiration, and carbon dioxide and water are produced:

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + \text{energy}$$

Glucose Oxygen Carbon dioxide Water

In Chapter 6, we saw that molecules such as carbohydrates and lipids have a large amount of potential energy in their chemical bonds. In contrast, molecules such as carbon dioxide and water have less potential energy in their bonds. Cellular respiration releases a large amount of energy because the sum of the potential energy in all of the chemical bonds of the reactants (glucose and oxygen) is higher than that of the products (carbon dioxide and water). The maximum amount of free energy—energy available to do work—released during cellular respiration is ~686 kcal per mole of glucose. Recall from Chapter 6 that when $\Delta G < 0$, energy is released.

The overall reaction for cellular respiration helps us focus on the starting reactants, final products, and release of energy. However, it misses the many intermediate steps. Tossing a match into the gas tank of a car releases a tremendous amount of energy in the form of an explosion, but this energy is not used to do work. Instead, it is released as light and heat. Similarly, if all the energy stored in glucose were released at once, most of it would be released as heat and the cell would not be able to harness it to do work.

In cellular respiration, energy is released gradually in a series of chemical reactions (Fig. 7.1). As a result, some of this energy can be used to form ATP. On average, 32 molecules of ATP are produced from the aerobic respiration of a single molecule of glucose. The energy needed to form one mole of ATP from ADP and $P_i$ is at least 7.3 kcal. Thus, cellular respiration harnesses at least $32 \times 7.3 = 233.6$ kcal of energy in ATP for every mole of glucose that is broken down in the presence of oxygen.

About 34% of the total energy released by aerobic respiration is harnessed in the form of ATP (233.6/686 = 34%), with the remainder of the energy given off as heat. This degree of efficiency compares favorably with the approximately 25% efficiency of a gasoline engine.

**ATP is generated by substrate-level phosphorylation and oxidative phosphorylation.**

In cellular respiration, ATP is produced in two ways (Fig. 7.1). In the first, an organic molecule transfers a phosphate group directly to ADP, as we saw in Chapter 6. In this case, a single enzyme carries out two coupled reactions: the hydrolysis of an organic molecule to yield a phosphate group and the addition of that phosphate group to ADP. The hydrolysis reaction releases enough free energy to drive the synthesis of ATP. This way of generating ATP is called **substrate-level phosphorylation** because a phosphate group is transferred to ADP from an enzyme substrate, in this case an organic molecule.

**Redox reactions play a central role in cellular respiration.**

Chemical reactions in which electrons are transferred from one atom or molecule to another are called **oxidation–reduction reactions** (“redox reactions” for short). Oxidation is the loss of electrons, and reduction is the gain of electrons. The loss and gain of electrons always occur together in a coupled oxidaction–reduction process.
reaction: electrons are transferred from one molecule to another so that one molecule loses electrons and one molecule gains those electrons. The molecule that loses electrons is oxidized and the molecule that gains electrons is reduced.

We can illustrate oxidation–reduction reactions by looking at the role played by electron carriers in cellular respiration. Two important electron carriers are nicotinamide adenine dinucleotide and flavin adenine dinucleotide. These electron carriers exist in two forms—an oxidized form (NAD$^+$ and FAD) and a reduced form (NADH and FADH$_2$). When fuel molecules such as glucose are catabolized, some of the steps are oxidation reactions. These oxidation reactions are coupled with the reduction of electron carrier molecules. These reduction reactions can be written as:

\[
\begin{align*}
NAD^+ + 2e^- + H^+ &\rightarrow NADH \\
FAD + 2e^- + 2H^+ &\rightarrow FADH_2
\end{align*}
\]

Here, NAD$^+$ and FAD accept electrons and are converted to their reduced forms, NADH and FADH$_2$. Note that in redox reactions involving organic molecules such as NAD$^+$ or FAD, the gain (or loss) of electrons is often accompanied by the gain (or loss) of protons (H$^+$). Therefore, you can easily recognize reduced molecules by an increase in C–H bonds and the corresponding oxidized molecules by a decrease in C–H bonds.

In their reduced forms, NADH and FADH$_2$ can donate electrons. As they are oxidized to NAD$^+$ and FAD, they transfer electrons (and energy) to the electron transport chain:

\[
\begin{align*}
NADH &\rightarrow NAD^+ + 2e^- + H^+ \\
FADH_2 &\rightarrow FAD + 2e^- + 2H^+
\end{align*}
\]

NAD$^+$ and FAD can then accept electrons from the breakdown of fuel molecules. In this way, electron carriers act as shuttles, transferring electrons derived from the oxidation of fuel molecules such as glucose to the electron transport chain.

Cellular respiration can itself be understood as a redox reaction, even though it consists of many steps. In aerobic respiration, glucose is oxidized, releasing carbon dioxide, and at the same time oxygen is reduced, forming water:

\[
C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + \text{energy}
\]

Let’s now consider the reduction reaction (Fig. 7.2b). In oxygen gas, electrons are shared equally between two oxygen atoms. In water, the electrons that are shared between hydrogen and oxygen are more likely to be found near oxygen because oxygen is more electronegative than hydrogen. As a result, oxygen has partially gained electrons and is reduced.

**Cellular respiration occurs in four stages.**

Up to this point, we have focused on the overall reaction of cellular respiration and the chemistry of redox reactions. Let’s now look at the entire process, starting with glucose. Cellular respiration occurs in four stages (Fig. 7.3).
FIG. 7.3 The four stages of cellular respiration. Cellular respiration consists of glycolysis, pyruvate oxidation, the citric acid cycle, and oxidative phosphorylation.

In stage 1, glucose is partially broken down to produce pyruvate, and energy is transferred to ATP and reduced electron carriers, a process known as glycolysis.

In stage 2, pyruvate is oxidized to another molecule called acetyl-coenzyme A (acetyl-CoA), producing reduced electron carriers and releasing carbon dioxide.

Acetyl-CoA enters stage 3, the citric acid cycle, also called the tricarboxylic (TCA) cycle or the Krebs cycle. In this series of chemical reactions, the acetyl group is completely oxidized to carbon dioxide and energy is transferred to ATP and reduced electron carriers. The amount of energy transferred to ATP and reduced electron carriers in this stage is nearly twice that transferred by stages 1 and 2 combined.

Stage 4 is oxidative phosphorylation. In this series of reactions, reduced electron carriers generated in stages 1–3 donate electrons to the electron transport chain and a large amount of ATP is produced.

Each stage of cellular respiration consists of a series of reactions, some of which are redox reactions. Therefore, glucose is not oxidized all at once to carbon dioxide. Instead, it is oxidized slowly and in a controlled manner, allowing for energy to be harnessed. Some of this energy is used to synthesize ATP directly and some of it is stored temporarily in reduced electron carriers and then used to generate ATP by oxidative phosphorylation.

Fig. 7.4 shows the change of free energy at each step in the catabolism of glucose. As you can see, the individual reactions allow the initial chemical energy present in a molecule of glucose to be “packaged” into molecules of ATP and reduced electron carriers. Note that the change in free energy is much greater for the steps that generate reduced electron carriers than for those that produce ATP directly.

In eukaryotes, glycolysis takes place in the cytoplasm, and pyruvate oxidation, the citric acid cycle, and oxidative phosphorylation all take place in mitochondria. The electron transport chain is made up of proteins and small molecules associated with the inner mitochondrial membrane (Chapter 5). In some bacteria, these reactions take place in the cytoplasm, and the electron transport chain is located in the plasma membrane.

Self-Assessment Questions

1. What are the four major stages of cellular respiration? Briefly describe each one.
2. What is an oxidation–reduction reaction? Why is the breakdown of glucose in the presence of oxygen to produce carbon dioxide and water an example of an oxidation–reduction reaction?
3. For each of the following pairs of molecules, indicate which member of the pair is reduced and which is oxidized, and which has more chemical energy and which has less chemical energy: NAD+/NADH; FAD/FADH2; CO2/C6H12O6.
4. What are two different ways in which ATP is generated in cellular respiration?
CHAPTER 7  CELLULAR RESPIRATION: HARVESTING ENERGY FROM CARBOHYDRATES AND OTHER FUEL MOLECULES

Glycolysis is a series of 10 chemical reactions (Fig. 7.5). These reactions can be divided into three phases.

The first phase prepares glucose for the next two phases by the addition of two phosphate groups to glucose. This phase requires an input of energy. To supply that energy and provide the phosphate groups, two molecules of ATP are hydrolyzed per molecule of glucose. In other words, the first phase of glycolysis is an endergonic process. The phosphorylation of glucose has two important consequences. Whereas glucose enters and exits cells through specific membrane transporters, phosphorylated glucose is trapped inside the cell. In addition, the presence of two negatively charged phosphate groups in proximity destabilizes the molecule so that it can be broken apart in the second phase of glycolysis.

The second phase is the cleavage phase, in which the 6-carbon molecule is split into two 3-carbon molecules. For each molecule of glucose entering glycolysis, two 3-carbon molecules enter the third phase of glycolysis.

The third and final phase of glycolysis is sometimes called the payoff phase because ATP and the electron carrier NADH are produced. Later, NADH will contribute to the synthesis of ATP during oxidative phosphorylation. This phase ends with the production of two molecules of pyruvate.

In summary, glycolysis begins with a single molecule of glucose (six carbons) and produces two molecules of pyruvate (three carbons each). These reactions yield four molecules of ATP and two molecules of NADH. However, two ATP molecules are consumed during the initial phase of glycolysis, resulting in a net gain of two ATP molecules and two molecules of NADH (Fig. 7.5).

7.2 GLYCOLYSIS

Glucose is the most common fuel molecule in animals, plants, and microbes. It is the starting molecule for glycolysis, which results in the partial oxidation of glucose and the synthesis of a relatively small amount of both ATP and reduced electron carriers. Glycolysis literally means “splitting sugar,” an apt name because a 6-carbon sugar (glucose) is split in two in this process, yielding two 3-carbon molecules. Glycolysis is anaerobic because oxygen is not consumed. It evolved very early in the evolution of life, when oxygen was not present in Earth’s atmosphere. It occurs in nearly all living organisms and is therefore probably the most widespread metabolic pathway among organisms.

Glycolysis is the partial breakdown of glucose.

Glycolysis begins with a molecule of glucose and produces two 3-carbon molecules of pyruvate and a net total of two molecules of ATP and two molecules of the electron carrier NADH. ATP is produced directly by substrate-level phosphorylation.
FIG. 7.5 Glycolysis. Glucose is partially oxidized to pyruvate, with the net production of two ATP and two NADH.
7.3 PYRUVATE OXIDATION

Glycolysis occurs in almost all living organisms, but it does not generate very much energy in the form of ATP. The end product, pyruvate, still contains a good deal of chemical potential energy in its bonds. In the presence of oxygen, pyruvate can be further oxidized to release more energy, first to acetyl-CoA and then even further in the series of reactions in the citric acid cycle. Pyruvate oxidation to acetyl-CoA is a key step that links glycolysis to the citric acid cycle.

The oxidation of pyruvate connects glycolysis to the citric acid cycle.

In eukaryotes, pyruvate oxidation is the first step that takes place inside the mitochondria. Mitochondria are rod-shaped organelles surrounded by a double membrane (Fig. 7.6; Chapter 5). The inner membrane has folds that project inward. These membranes define two spaces: the space between the inner and outer membranes is called the intermembrane space, and the space enclosed by the inner membrane is called the mitochondrial matrix.

Pyruvate is transported into the mitochondrial matrix, where it is converted into acetyl-CoA (Fig. 7.7). First, part of the pyruvate molecule is oxidized and splits off to form carbon dioxide, the most oxidized (and therefore the least energetic) form of carbon. The electrons lost in this process are donated to NAD⁺, which is reduced to NADH. The remaining part of the pyruvate molecule, an acetyl group (COCH₃), still contains a large amount of potential energy. It is transferred to coenzyme A (CoA), a molecule that carries the acetyl group to the next set of reactions.

Overall, the synthesis of one molecule of acetyl-CoA from pyruvate results in the formation of one molecule of carbon dioxide and one molecule of NADH. Recall, however, that a single molecule of glucose forms two molecules of pyruvate during glycolysis. Therefore, two molecules of carbon dioxide, two molecules of NADH, and two molecules of acetyl-CoA are produced from a single glucose molecule in this stage of cellular respiration. Acetyl-CoA is the substrate of the first step in the citric acid cycle.

Self-Assessment Question

7. At the end of pyruvate oxidation, but before the subsequent stages of cellular respiration, which molecules contain the energy held in the original glucose molecule?
### 7.4 THE CITRIC ACID CYCLE

During the citric acid cycle, fuel molecules are completely oxidized. Specifically, the acetyl group of acetyl-CoA is completely oxidized to carbon dioxide and the chemical energy is transferred to ATP by substrate-level phosphorylation and to the reduced electron carriers NADH and FADH$_2$. In this way, the citric acid cycle supplies electrons to the electron transport chain, leading to the production of much more energy in the form of ATP than is obtained by glycolysis alone.

**The citric acid cycle produces ATP and reduced electron carriers.**

Like the synthesis of acetyl-CoA, the citric acid cycle takes place in the mitochondrial matrix. It is composed of eight reactions and is called a cycle because the starting molecule, oxaloacetate, is regenerated at the end (Fig. 7.8).

---

**FIG. 7.8 The citric acid cycle.** The acetyl group of acetyl-CoA is completely oxidized, with the net production of one ATP, three NADH, and one FADH$_2$. 

![Citric acid cycle diagram](image-url)
In the first reaction, the 2-carbon acetyl group of acetyl-CoA is transferred to a 4-carbon molecule of oxaloacetate to form the 6-carbon molecule citric acid or tricarboxylic acid (hence the alternative names “citric acid cycle” and “tricarboxylic acid cycle”). The molecule of citric acid is then oxidized in a series of reactions. The last reaction of the cycle regenerates a molecule of oxaloacetate, which can join to a new acetyl group and allow the cycle to continue.

The citric acid cycle results in the complete oxidation of the acetyl group of acetyl-CoA. Because the first reaction creates a molecule with six carbons and the last reaction regenerates a 4-carbon molecule, two carbons are eliminated during the cycle. These carbons are released as carbon dioxide. Along with the release of carbon dioxide from pyruvate during pyruvate oxidation, these reactions are the sources of carbon dioxide released during cellular respiration and therefore the sources of the carbon dioxide that we exhale when we breathe.

Four redox reactions, including the two that release carbon dioxide, produce the reduced electron carriers NADH and FADH₂. In this way, energy released in the oxidation reactions is transferred to a large quantity of reduced electron carriers: three molecules of NADH and one molecule of FADH₂ per turn of the cycle. These electron carriers donate electrons to the electron transport chain.

A single substrate-level phosphorylation reaction generates a molecule of GTP (Fig. 7.8). GTP can transfer its terminal phosphate to a molecule of ADP to form ATP.

Overall, two molecules of acetyl-CoA produced from a single molecule of glucose yield two molecules of ATP, six molecules of NADH, and two molecules of FADH₂ in the citric acid cycle.

**CASE 1 LIFE’S ORIGINS: INFORMATION, HOMEOSTASIS, AND ENERGY**

**What were the earliest energy-harnessing reactions?**

Some bacteria run the citric acid cycle in reverse, incorporating carbon dioxide into organic molecules instead of liberating it. Running the citric acid cycle in reverse requires energy, which is supplied by sunlight (Chapter 8) or chemical reactions (Chapter 24).

Why would an organism run the citric acid cycle backward? The answer is that running the cycle in reverse allows an organism to build, rather than break down, organic molecules. Whether the cycle is run in the reverse or forward direction, the intermediates generated step by step as the cycle turns provide the building blocks for synthesizing the cell’s key organic molecules (Fig. 7.9). Pyruvate, for example, is the starting point for the synthesis of sugars and the amino acid alanine; acetate is the starting point for the synthesis of the cell’s lipids; oxaloacetate is modified to form different amino acids and pyrimidine bases; and α-(alpha-)ketoglutarate is modified to form other amino acids.

Therefore, for organisms that run the cycle in the forward direction, the citric acid cycle is used to generate both energy-storing molecules (ATP and reduced electron carriers) and intermediates in the synthesis of other molecules. For organisms that run the cycle in reverse, it is used to generate intermediates in the synthesis of other molecules and also to incorporate carbon into organic molecules.

The citric acid cycle is thus central to both the synthesis of organic molecules and to meeting the energy requirements of cells, suggesting that it evolved early in some of the first cells to feature metabolism. The early appearance of the citric acid cycle, in turn, implies that the great variety of biosynthetic and energy-yielding pathways found in modern cells evolved through the extension and modification of this deeply rooted cycle. As typical of evolution, new cellular capabilities arose by the modification of simpler, more general sets of reactions.

**Self-Assessment Question**

8. At the end of the citric acid cycle, but before the subsequent stages of cellular respiration, which molecules contain the energy held in the original glucose molecule?
7.5 THE ELECTRON TRANSPORT CHAIN AND OXIDATIVE PHOSPHORYLATION

The complete oxidation of glucose during the first three stages of cellular respiration results in the production of two kinds of reduced electron carriers: NADH and FADH₂. We are now going to see how the energy stored in these electron carriers is used to synthesize ATP.

The energy in these electron carriers is released in a series of redox reactions that occur as electrons pass through a chain of protein complexes in the inner mitochondrial membrane to the final electron acceptor, oxygen, which is reduced to water. The energy released by these redox reactions is not converted directly into the chemical energy of ATP, however. Instead, the passage of electrons is coupled to the transfer of protons (H⁺) across the inner mitochondrial membrane, creating a concentration and charge gradient (Chapter 5). This electrochemical gradient provides a source of potential energy that is then used to drive the synthesis of ATP.

We next explore the properties of the electron transport chain, the role of the proton gradient, and the synthesis of ATP.

The electron transport chain transfers electrons and pumps protons.

The electron transport chain is made up of four large protein complexes (known as complexes I to IV) that are embedded in the inner mitochondrial membrane (Fig. 7.10). The inner mitochondrial membrane contains one of the highest concentrations of proteins found in eukaryotic membranes.

Electrons donated by NADH and FADH₂ are transported along this series of protein complexes. Electrons enter the electron transport chain at either complex I or II. Electrons donated by NADH enter through complex I, and electrons donated by FADH₂ enter through complex II. (Complex II is the same enzyme that catalyzes step 6 in the citric acid cycle.) These electrons are transported through either complex I or II to complex III and then through complex IV.

Within each protein complex of the electron transport chain, electrons are passed from electron donors to electron acceptors. Each donor and acceptor is a redox couple, consisting of an oxidized and a reduced form of a molecule. The electron transport chain contains many of these redox couples. When oxygen accepts electrons at the end of the electron transport chain, it is reduced to form water:

\[ \text{O}_2 + 4e^- + 4H^+ \rightarrow 2\text{H}_2\text{O} \]

This reaction is catalyzed by complex IV.

Electrons also must be transported between the four complexes (Fig. 7.10). Coenzyme Q (CoQ), also called ubiquinone, accepts electrons from both complexes I and II. In this reaction, two electrons and two protons are transferred to CoQ from the mitochondrial matrix, forming CoQH₂. Once formed, CoQH₂ diffuses in the inner membrane to complex III.

In complex III, electrons are transferred from CoQH₂ to cytochrome c and protons are released into the intermembrane space. When it accepts an electron, cytochrome c is reduced, diffuses in the intermembrane space, and passes the electron to complex IV.

The electron transfer steps within complexes are each associated with the release of energy. Some of this energy is used to reduce the next electron acceptor in the chain, but in complexes I, III, and IV, some of it is used to pump protons (H⁺) across the inner mitochondrial membrane, from the mitochondrial matrix to the intermembrane space (Fig. 7.10). Thus, the transfer of electrons through complexes I, III, and IV is coupled with the pumping of protons. The result is an accumulation of protons in the intermembrane space.

The proton gradient is a source of potential energy.

Like all membranes, the inner mitochondrial membrane is selectively permeable; protons cannot passively diffuse across this membrane, and the movement of other molecules is controlled by transporters and channels (Chapter 5). We have just seen that the movement of electrons through membrane-embedded protein complexes is coupled to the pumping of protons from the mitochondrial matrix into the intermembrane space. The result is a proton gradient, a difference in proton concentration across the inner membrane.

The proton gradient has two components: a chemical gradient that results from the difference in concentration and an electrical gradient that results from the difference in charge between the two sides of the membrane. To reflect the dual contribution of the two gradients, the proton gradient is also called an electrochemical gradient.

The proton gradient is a source of potential energy, as discussed in Chapters 5 and 6. It stores energy in much the same way that a battery or a dam does. Protons in this gradient have a high concentration in the intermembrane space and a low concentration in the mitochondrial matrix. As a result, there is a tendency for protons to diffuse back to the mitochondrial matrix, driven by a difference in concentration and charge on the two sides of the membrane. This movement, however, is blocked by the membrane. The gradient stores potential energy because, if a pathway is opened through the membrane, the resulting movement of the protons through the membrane can be used to perform work.

In sum, the oxidation of the electron carriers NADH and FADH₂ leads to the generation of a proton electrochemical gradient. This gradient is a source of potential energy used to synthesize ATP.

ATP synthase converts the energy of the proton gradient into the energy of ATP.

In 1961, Peter Mitchell proposed a hypothesis to explain how the energy stored in the proton electrochemical gradient is used
FIG. 7.10 The electron transport chain. (a) The electron transport chain consists of four complexes (I to IV) in the inner mitochondrial membrane. (b) Electrons flow from electron carriers to oxygen, the final electron acceptor. (c) The proton gradient formed from the electron transport chain has potential energy that is used to synthesize ATP.

a. The electron transport chain in cellular respiration

b. Electron transport

Coenzymes Q is reduced to CoQH₂ and transfers electrons from complexes I and II to complex III.

Cytochrome c moves to complex IV where oxygen is reduced to form water.

ATP synthase uses the electrochemical proton gradient to drive the synthesis of ATP.

The transport of electrons in complexes I, III, and IV is coupled with the transport of protons across the inner membrane, from the mitochondrial matrix to the intermembrane space.
to synthesize ATP. In 1978, he was awarded the Nobel Prize in Chemistry for work that fundamentally changed the way we understand how a cell harnesses energy.

According to Mitchell’s hypothesis, the gradient of protons provides a source of potential energy that is converted into chemical energy stored in ATP. First, for the potential energy of the proton gradient to be released, there must be an opening in the membrane for the protons to flow through. Mitchell suggested that protons in the intermembrane space diffuse down their electrical and concentration gradients through a transmembrane protein channel into the mitochondrial matrix. Second, the movement of protons through the channel must be coupled with the synthesis of ATP. This coupling is made possible by ATP synthase, an enzyme composed of two distinct subunits called $F_0$ and $F_1$ (Fig. 7.11). $F_0$ forms the channel in the inner mitochondrial membrane through which protons flow; $F_1$ is the catalytic unit that synthesizes ATP. Proton flow through the channel makes it possible for the enzyme to synthesize ATP.

Proton flow through the $F_0$ channel causes it to rotate, converting the energy of the proton gradient into mechanical rotational energy, a form of kinetic energy. The rotation of the $F_0$ subunit leads to rotation of the $F_1$ subunit in the mitochondrial matrix (Fig. 7.11). The rotation of the $F_1$ subunit in turn causes conformational changes that allow it to catalyze the synthesis of ATP from ADP and $P_i$. In this way, mechanical rotational energy is converted into the chemical energy of ATP.

Direct experimental evidence for Mitchell’s idea, called the chemiosmotic hypothesis, did not come for over a decade. One of the key experiments that provided support for his ideas is illustrated in Fig. 7.12.

Approximately 2.5 molecules of ATP are produced for each NADH that donates electrons to the chain and 1.5 molecules of ATP for each FADH$_2$. Overall, the complete oxidation of glucose yields about 32 molecules of ATP from all four stages of cellular respiration (Table 7.1). Some of the energy held in the bonds of glucose is now available in a molecule that can be readily used by cells.

It is worth taking a moment to follow the flow of energy in cellular respiration, illustrated in its full form in Fig. 7.13. We began with glucose and noted that it holds chemical potential energy in its covalent bonds. This energy is released in a series of reactions and captured in chemical form. Some of these

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**TABLE 7.1** Approximate Total ATP Yield in Cellular Respiration

<table>
<thead>
<tr>
<th>PATHWAY</th>
<th>SUBSTRATE-LEVEL PHOSPHORYLATION</th>
<th>OXIDATIVE PHOSPHORYLATION</th>
<th>TOTAL ATP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycolysis (glucose → 2 pyruvate)</td>
<td>2 ATP</td>
<td>2 NADH = 5 ATP</td>
<td>7</td>
</tr>
<tr>
<td>Pyruvate oxidation (2 pyruvate → 2 acetyl-CoA)</td>
<td>0 ATP</td>
<td>2 NADH = 5 ATP</td>
<td>5</td>
</tr>
<tr>
<td>Citric acid cycle (2 turns, 1 for each acetyl-CoA)</td>
<td>2 ATP</td>
<td>6 NADH = 15 ATP</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>4 ATP</td>
<td>28 ATP</td>
<td>32</td>
</tr>
</tbody>
</table>

---

**FIG. 7.11** ATP synthase. ATP synthase drives the synthesis of ATP by means of an electrochemical proton gradient.
Reactions generate ATP directly by substrate-level phosphorylation. Others are redox reactions that transfer energy to the electron carriers NADH and FADH$_2$. These electron carriers donate electrons to the electron transport chain.

The electron transport chain uses the energy stored in the electron carriers to pump protons across the inner membrane of the mitochondria. In other words, the energy of the reduced electron carriers is transformed into energy stored in a proton electrochemical gradient. ATP synthase then converts the energy of the proton gradient to rotational energy, which drives the synthesis of ATP. The cell now has a form of energy that it can use in many ways to perform work.

**FIG. 7.12**
Can a proton gradient drive the synthesis of ATP?

**BACKGROUND** Peter Mitchell’s hypothesis that a proton gradient can drive the synthesis of ATP was met with skepticism because he proposed the idea before experimental evidence existed to support it. In the 1970s, biochemist Efraim Racker and his collaborator Walther Stoeckenius tested the hypothesis.

**EXPERIMENT** Racker and Stoeckenius built an artificial system consisting of a collection of vesicle-shaped membranes, each with ATP synthase and a bacterial proton pump that was activated by light.

They measured the concentration of protons (pH) in the external medium and the amount of ATP produced in the presence and absence of light.

**RESULTS** In the presence of light, the pH of the external medium increased. An increase in pH indicates a decrease in concentration of protons as a result of movement of protons from the outside to the inside of the vesicles. This result demonstrates that the proton pump was activated and the vesicles were taking up protons. In the dark, the pH returned to the starting level.

Furthermore, ATP was generated in the light, but not in the dark.

**INTERPRETATION** In the presence of light, the proton pump was activated and protons were pumped to one side of the membrane, leading to the formation of a proton gradient. The proton gradient, in turn, powered synthesis of ATP by ATP synthase.

**CONCLUSION** A membrane, proton gradient, and ATP synthase are sufficient to synthesize ATP. This result provided experimental evidence for Mitchell’s hypothesis.


**Self-Assessment Questions**

9. Animals breathe in air that contains more oxygen than the air they breathe out. Where is oxygen consumed?
10. How does the movement of electrons along the electron transport chain lead to the generation of a proton gradient?
11. How is a proton gradient used to generate ATP?
12. Uncoupling agents are proteins spanning the inner mitochondrial membrane that allow protons to pass through the membrane and bypass the channel of ATP synthase. Describe the consequences for the proton gradient and ATP production.
### 7.6 ANAEROBIC METABOLISM

Up to this point, we have followed a single metabolic path: the breakdown of glucose in the presence of oxygen to produce carbon dioxide and water. However, metabolic pathways more often resemble intersecting roads rather than a single, linear path. As an example, we saw earlier that intermediates of the citric acid cycle often feed into other metabolic pathways.

One of the major forks in the metabolic road occurs at pyruvate, the end product of glycolysis. When oxygen is present, it is converted to acetyl-CoA, which then enters the citric acid cycle. When oxygen is not present, pyruvate is metabolized along a number of different pathways. These pathways occur in many living organisms today and played an important role in the early evolution of life on Earth.

**Fermentation extracts energy from glucose in the absence of oxygen.**

Pyruvate has many possible fates in the cell. In the absence of oxygen, it can be broken down by fermentation, a process for extracting energy from fuel molecules that does not rely on oxygen or an electron transport chain, but instead uses an organic molecule as an electron acceptor. Fermentation is accomplished through a wide variety of metabolic pathways. These pathways are important for anaerobic organisms that live without oxygen, as well as yeast and some other organisms that favor fermentation over oxidative phosphorylation, even in the presence of oxygen. Aerobic organisms sometimes use fermentation when oxygen cannot be delivered fast enough to meet the cell’s metabolic needs, as in exercising muscle.

Recall that during glycolysis, glucose is oxidized to form pyruvate and NAD\(^+\) is reduced to form NADH. For glycolysis to continue, NADH must be oxidized to NAD\(^+\); otherwise, glycolysis would grind to a halt. In the presence of oxygen, NAD\(^+\) is regenerated when NADH donates its electrons to the electron transport chain. In the absence of oxygen during fermentation, NADH is oxidized to NAD\(^+\) when pyruvate or a derivative of pyruvate is reduced.

Two of the major fermentation pathways are **lactic acid fermentation** and **ethanol fermentation** (Fig. 7.14). Lactic acid fermentation occurs in animals and bacteria. During lactic acid fermentation, electrons from NADH are transferred to pyruvate to produce lactic acid and NAD\(^+\) (Fig. 7.14a). The overall chemical reaction is written as follows:

\[
\text{Glucose} + 2 \text{ADP} + 2 \text{P} \rightarrow 2 \text{lactic acid} + 2 \text{ATP} + 2\text{H}_2\text{O}
\]

Ethanol fermentation occurs in plants and fungi. During ethanol fermentation, pyruvate releases carbon dioxide to form acetaldehyde, and electrons from NADH are transferred to acetaldehyde to produce ethanol and NAD\(^+\) (Fig. 7.14b). The overall chemical reaction is written as follows:

\[
\text{Glucose} + 2 \text{ADP} + 2 \text{P} \rightarrow 2 \text{ethanol} + 2\text{CO}_2 + 2 \text{ATP} + 2\text{H}_2\text{O}
\]
In both fermentation pathways, NADH is oxidized to NAD\(^+\). However, NADH and NAD\(^+\) do not appear in the overall chemical equations because there is no net production or loss of either molecule. NAD\(^+\) molecules that are reduced during glycolysis are oxidized when lactic acid or ethanol is formed.

The breakdown of a molecule of glucose by fermentation yields only two molecules of ATP. The energetic gain is relatively small compared with the yield of aerobic respiration because the end products, lactic acid and ethanol, are not fully oxidized and still contain a large amount of chemical energy in their bonds. Organisms that produce ATP by fermentation therefore must consume a large quantity of fuel molecules to power the cell.

**Case 1 Life’s Origins: Information, Homeostasis, and Energy**

**How did early cells meet their energy requirements?**

The four stages of cellular respiration lead to the full oxidation of glucose and the release of a large amount of energy stored in its chemical bonds. In the first stage, glycolysis, glucose is only partially oxidized, so just some of the energy held in its chemical bonds is released. Nearly all organisms are capable of partially breaking down glucose, suggesting that glycolysis evolved very early in the history of life.

The atmosphere contained no oxygen when life first evolved about 4 billion years ago. The earliest organisms probably used one of the fermentation pathways to generate ATP. Fermentation occurs in the cytoplasm, does not require atmospheric oxygen, and does not require proteins embedded in specialized membranes.

As we have seen, cellular respiration makes use of an electron transport chain, composed of proteins embedded in a membrane and capable of transferring electrons from one protein to the next and pumping protons. The resulting proton gradient powers the synthesis of ATP. Like fermentation, cellular respiration can occur in the absence of oxygen, but in that case molecules other than oxygen, such as sulfate and nitrate, are the final electron acceptor (Chapter 26). This form of respiration is known as anaerobic respiration and occurs in some present-day bacteria. The electron transport chain in these bacteria is located in the plasma membrane, not in an internal membrane.

How might such a system have evolved? An intriguing possibility is that early prokaryotes evolved pumps to drive protons out of the cell in response to an increasingly acidic environment (Fig. 7.15). Some pumps might have used the energy of ATP to pump protons, while others used the energy from electron transport to pump protons (Fig. 7.15a). At some point, proton pumps powered by electron transport might have generated a large enough electrochemical gradient that the protons could pass back through the ATP-driven pumps, running them in reverse to synthesize ATP (Fig. 7.15b).
Organisms capable of producing oxygen, the cyanobacteria, did not evolve until about 2.5 billion years ago, or maybe earlier. The evolution of this new form of life introduced oxygen into Earth’s atmosphere. This dramatic change led to the evolution of new life forms with new possibilities for extracting energy from fuel molecules such as glucose. Aerobic respiration, in which oxygen serves as the final electron acceptor in the electron transport chain, generates much more energy than does anaerobic respiration or fermentation.

The evolution of cellular respiration illustrates that evolution often works in a stepwise fashion, building on what is already present. In this case, aerobic respiration picked up where anaerobic respiration left off, making it possible to harness more energy from organic molecules to power the work of the cell.

**Self-Assessment Questions**

13. Bread making involves ethanol fermentation and typically uses yeast, sugar, flour, and water. Why are yeast and sugar used?

14. What are two different metabolic pathways that pyruvate can enter?

**7.7 METABOLIC INTEGRATION**

In this chapter, we have focused on the breakdown of glucose. What happens if there is more glucose than the cell needs? As well as glucose, organisms consume diverse carbohydrates, lipids, and proteins. How are these broken down? And how are the various metabolic pathways that break down fuel molecules coordinated so that the intracellular level of ATP is maintained in a narrow range? In this final section, we consider how the cell responds to these challenges.

**Excess glucose is stored as glycogen in animals and starch in plants.**

Glucose is a readily available form of energy in organisms, but it is not always broken down immediately. Excess glucose can be stored in cells and then mobilized when necessary. Glucose can be stored in two major forms: as glycogen in animals and as starch in plants (Fig. 7.16). Both these molecules are large branched polymers of glucose.

Carbohydrates in the diet are broken down into glucose and other simple sugars and circulate in the blood. The level of glucose in the blood is tightly regulated (Chapter 37). When the blood glucose level is high, as it is after a meal, glucose molecules that are not consumed by glycolysis are linked together to form glycogen in liver and muscle. Glycogen stored in muscle is used to provide ATP for muscle contraction. By contrast, the liver does not store glycogen primarily for its own use, but is a glycogen storehouse for the whole body. Glucose molecules located at the end of glycogen chains can be cleaved one by one and released in the form of glucose 1-phosphate. Glucose 1-phosphate is converted into glucose 6-phosphate, an intermediate in glycolysis (see Fig. 7.5). One glucose molecule cleaved off a glycogen chain produces three and not two molecules of ATP by glycolysis because the ATP-consuming step 1 of glycolysis is bypassed.

**Sugars other than glucose contribute to glycolysis.**

The carbohydrates in your diet are digested to produce a variety of sugars. Some of these are disaccharides (maltose, lactose, and sucrose) with two sugar units; others are monosaccharides (fructose, mannose, and galactose) with one sugar unit (Fig. 7.17). The disaccharides are hydrolyzed into monosaccharides, which are transported into cells.
Glucose molecules released during digestion directly enter glycolysis. What happens to other sugars? They, too, enter glycolysis, although not as glucose. Instead, they are converted into intermediates of glycolysis that come later in the pathway (Fig. 7.18). For example, fructose is produced by the hydrolysis of sucrose (table sugar) and receives a phosphate group to form either fructose 6-phosphate or fructose 1-phosphate. In the liver, fructose 1-phosphate is cleaved and converted into glyceraldehyde 3-phosphate, which enters glycolysis at reaction 6 (see Fig. 7.5).

**Fatty acids and proteins are useful sources of energy.**

We know from common experience that lipids are also a good source of energy. Butter, oils, ice cream, and the like all contain lipids and are high in calories, which are units of energy. We can also infer that lipids are a good source of energy from their chemical structure. Recall from Chapter 2 that a type of fat called triacylglycerol is composed of three fatty acid molecules bound to a...
glycerol backbone (see Fig. 2.25). These fatty acid molecules are rich in carbon–carbon and carbon–hydrogen bonds, which, as we saw earlier, carry chemical potential energy.

Following a meal, the small intestine very quickly absorbs triacylglycerols, which are then transported by the bloodstream and either consumed or stored in fat (adipose) tissue. Triacylglycerols are broken down inside cells to glycerol and fatty acids (Fig. 7.18). Then, the fatty acids themselves are shortened by a series of reactions that sequentially remove two carbon units from their ends. This process is called \( \beta \)-\textit{(beta-)oxidation}. It does not generate ATP, but produces NADH and FADH\(_2\), molecules that provide electrons for the synthesis of ATP by oxidative phosphorylation. In addition, the end product of the reaction is acetyl-CoA, which feeds the citric acid cycle and leads to the production of additional reduced electron carriers.

The oxidation of fatty acids produces a large amount of ATP. For example, the complete oxidation of a molecule of palmitic acid, a fatty acid containing 16 carbons, yields about 106 molecules of ATP. By contrast, glycolysis yields just 2 molecules of ATP, and the complete oxidation of a glucose molecule produces about 32 molecules of ATP (Table 7.1). Fatty acids therefore are a useful and efficient source of energy. But they cannot be used by all tissues of the body. Notably, the brain and red blood cells depend primarily on glucose for energy.

Proteins, like fatty acids, are a source of chemical energy that can be broken down, if necessary, to power the cell. Proteins are typically first broken down to amino acids, which enter at various points in glycolysis, pyruvate oxidation, and the citric acid cycle (Fig. 7.18).

The intracellular level of ATP is a key regulator of cellular respiration.

ATP is the key end product of cellular respiration. ATP is constantly being turned over in a cell, broken down to ADP and P\(_i\) to supply the cell’s energy needs, and re-synthesized by fermentation and cellular respiration. The level of ATP inside a cell can therefore be an indicator of how much energy a cell has available. When ATP levels are high, the cell has a high amount of free energy and is poised to carry out cellular processes. In this case, pathways that generate ATP are slowed, or down-regulated. By contrast, when ATP levels are low, pathways that generate ATP
regulation of enzymes that control key steps of the pathway. One of these key reactions is reaction 3 of glycolysis. In this reaction, fructose 6-phosphate is converted to fructose 1,6-bisphosphate, and a molecule of ATP is consumed. This is a key step in glycolysis because it is highly endergonic and irreversible. As a result, it is considered a “committed” step and is subject to tight control. This reaction is catalyzed by the enzyme phosphofructokinase-1 (PFK-1). You can think of this enzyme as a metabolic valve that regulates the rate of glycolysis.

PFK-1 is an allosteric enzyme with many activators and inhibitors (Fig. 7.20). Recall from Chapter 6 that an allosteric enzyme changes its shape and activity in response to the binding of molecules at a site other than the active site. ADP and AMP are allosteric activators of PFK-1. When ADP and AMP are abundant, one or the other binds to the enzyme and causes the enzyme’s shape to change. The shape change activates the enzyme, increasing the rate of glycolysis and the synthesis of ATP. When ATP is in abundance, it binds to the same site on the enzyme as ADP and AMP, but in this case binding inhibits the enzyme’s catalytic activity. As a result, glycolysis and the rate of ATP production slow down.

PFK-1 is also regulated by one of its downstream products, citrate, an intermediate in the citric acid cycle (see Fig. 7.8). Citrate acts as an allosteric inhibitor of the enzyme, slowing its activity. High levels of citrate indicate that it is not being consumed by the citric acid cycle and glucose breakdown can be slowed. The role of citrate in controlling glycolysis is an example of how the activity of glycolysis and the citric acid cycle is coordinated.

Exercise requires several types of fuel molecules and the coordination of metabolic pathways.

In the last two chapters, we considered what energy is and how it is harnessed by cells. Let’s apply the concepts we discussed to a familiar example: exercise. Exercise such as running, walking, and swimming is a form of kinetic energy, powered by ATP in muscle cells. Where does this ATP come from?

Muscle cells, like all cells, do not contain a lot of ATP, and stored ATP is depleted by exercise in a matter of seconds. As a result, muscle cells rely on fuel molecules to generate ATP. For a short sprint or a burst of activity, muscle can convert stored glycogen to glucose, and then break down glucose anaerobically to pyruvate and lactic acid by lactic acid fermentation. This pathway is rapid, but it does not generate a lot of ATP.

For longer, more sustained exercise, other metabolic pathways come into play. Muscle cells contain many mitochondria, which produce ATP by aerobic respiration. The energy yield of aerobic respiration is much greater than that of fermentation, but the process is slower. This slower production of ATP by aerobic respiration in part explains why runners cannot maintain the pace of a sprint for longer runs.

For even longer exercise, liver glycogen supplements muscle glycogen: the liver releases glucose into the blood that is taken up by muscle cells and oxidized to produce ATP. In addition,
Fatty acids are released from adipose tissue and taken up by muscle cells, where they are broken down by β-oxidation. β-oxidation yields even more ATP than does the complete oxidation of glucose, but the process is again slower. Storage forms of energy molecules, such as fatty acids and glycogen, contain large reservoirs of energy, but are slow to mobilize. Thus, exercise takes coordination between different cells, tissues, and metabolic pathways to ensure adequate ATP to meet the needs of working muscle.

Self-Assessment Question

15. How does muscle tissue generate ATP during short-term and long-term exercise?

Core Concepts Summary

7.1 An Overview of Cellular Respiration: Cellular respiration is a series of catabolic reactions that convert the energy in fuel molecules into energy in ATP.

- During cellular respiration, sugar molecules such as glucose are broken down in the presence of oxygen to produce carbon dioxide and water. page 135
- Cellular respiration releases energy because the potential energy of the reactants is greater than that of the products. page 136
- ATP is generated in two ways during cellular respiration: substrate-level phosphorylation and oxidative phosphorylation. page 136
- Cellular respiration is an oxidation–reduction reaction. page 136
- In oxidation–reduction reactions, electrons are transferred from one molecule to another. Oxidation is the loss of electrons, and reduction is the gain of electrons. page 136
- Electron carriers transfer electrons to an electron transport chain, which harnesses the energy of these electrons to generate ATP. page 137

7.2 Glycolysis: Glycolysis is the partial oxidation of glucose and results in the production of pyruvate, as well as ATP and reduced electron carriers.

- Glycolysis takes place in the cytoplasm. page 138
- Glycolysis is a series of 10 reactions in which glucose is oxidized to pyruvate. page 139
- Glycolysis consists of preparatory, cleavage, and payoff phases. page 139
- For each molecule of glucose broken down during glycolysis, a net gain of two molecules of ATP and two molecules of NADH is produced. page 139
- The synthesis of ATP in glycolysis results from the direct transfer of a phosphate group from a substrate to ADP, a process called substrate-level phosphorylation. page 139

7.3 Pyruvate Oxidation: Pyruvate is oxidized to acetyl-CoA, connecting glycolysis to the citric acid cycle.
The conversion of pyruvate to acetyl-CoA results in the production of one molecule of NADH and one molecule of carbon dioxide. page 141

Pyruvate oxidation occurs in the mitochondrial matrix. page 141

7.4 THE CITRIC ACID CYCLE: The citric acid cycle results in the complete oxidation of fuel molecules and the generation of ATP and reduced electron carriers.

The citric acid cycle takes place in the mitochondrial matrix. page 142

The acetyl group of acetyl-CoA is completely oxidized in the citric acid cycle. page 142

The citric acid cycle is a cycle because the acetyl group of acetyl-CoA combines with oxaloacetate, and then a series of reactions regenerates oxaloacetate. page 143

A complete turn of the citric acid cycle results in the production of one molecule of GTP (which is converted to ATP), three molecules of NADH, and one molecule of FADH2. page 143

Citric acid cycle intermediates are starting points for the synthesis of many different organic molecules. page 143

7.5 THE ELECTRON TRANSPORT CHAIN AND OXIDATIVE PHOSPHORYLATION: The electron transport chain transfers electrons from electron carriers to oxygen, using the energy to pump protons and synthesize ATP by oxidative phosphorylation.

NADH and FADH2 donate electrons to the electron transport chain. page 144

In the electron transport chain, electrons move from one redox couple to the next. page 144

The electron transport chain is made up of four complexes. Complexes I and II accept electrons from NADH and FADH2, respectively. The electrons are transferred from these two complexes to coenzyme Q. page 144

Reduced coenzyme Q transfers electrons to complex III and cytochrome c transfers electrons to complex IV. Complex IV reduces oxygen to water. page 144

The transfer of electrons through the electron transport chain is coupled with the movement of protons across the inner mitochondrial membrane into the intermembrane space. page 144

The buildup of protons in the intermembrane space results in a proton electrochemical gradient, which stores potential energy. page 144

The movement of protons back into the mitochondrial matrix through the F0 subunit of ATP synthase is coupled with the formation of ATP, a reaction catalyzed by the F1 subunit of ATP synthase. page 146

Complete oxidation of one glucose molecule by the four stages of aerobic cellular respiration nets approximately 32 molecules of ATP. page 146

7.6 ANAEROBIC METABOLISM: Glucose can be broken down in the absence of oxygen by fermentation, producing a modest amount of ATP.

Pyruvate, the end product of glycolysis, is processed differently in the presence and the absence of oxygen. page 148

In the absence of oxygen, pyruvate enters one of several fermentation pathways. page 148

In lactic acid fermentation, pyruvate is reduced to lactic acid. page 148

In ethanol fermentation, pyruvate is converted to acetaldehyde, which is reduced to ethanol. page 148

During fermentation, NADH is oxidized to NAD+, allowing glycolysis to proceed. page 148

Glycolysis and fermentation are ancient biochemical pathways and were likely used in the common ancestor of all organisms living today. page 149

7.7 METABOLIC INTEGRATION: Metabolic pathways are integrated, allowing control of the energy level of cells.

Excess glucose molecules are linked together and stored in polymers called glycogen (in animals) and starch (in plants). page 150

Other monosaccharides derived from the digestion of dietary carbohydrates are converted into intermediates of glycolysis. page 151

Fatty acids contained in triacylglycerols are an important form of energy storage in cells. The breakdown of fatty acids is called β-oxidation. page 151

Phosphofructokinase-1 controls a key step in glycolysis. It has many allosteric activators, including ADP and AMP, and allosteric inhibitors, including ATP and citrate. page 153

The ATP in muscle cells used to power exercise is generated by lactic acid fermentation, aerobic respiration, and β-oxidation. page 153

Log in to LaunchPad to check your answers to the Self-Assessment Questions and to access additional learning tools.
33.1 ANIMAL BODY PLANS: Animals have a limited number of distinct body plans.

33.2 TISSUES AND ORGANS: Most animals have four different types of tissue, which combine to form organs.

33.3 HOMEOSTASIS: Homeostasis actively maintains a stable internal environment.

33.4 EVOLUTIONARY HISTORY: Animals evolved more than 600 million years ago in the oceans, and by 500 million years ago the major body plans were in place.

Animals move, feed, and behave in many different ways. Indeed, animals have evolved a remarkable variety of structures to carry out these and other functions. As an example, consider the ways in which animals move (Chapter 35). Sponges have no muscle cells at all; rooted to the ground, they don't move from place to place. Jellyfish have muscle fibers that contract to squeeze a fluid-filled cavity, powering movement by jet propulsion. Mammals have limbs for locomotion, which are powered by the coordinated actions of muscles attached to an internal skeleton. Insects move in much the same way, but their skeleton is external. Other organ systems show comparable variation among animals. The wide range of anatomical and physiological variations has permitted animals to diversify to a remarkable degree.

Biologists have described approximately 1.8 million species of eukaryotic organisms from the world's forests, deserts, grasslands, and oceans. Of these, some 1.3 million species are animals. There is reason to believe that animal diversification began in the oceans, but today most animal species are found on land. Indeed, the majority of all animal species are insects. In this chapter, we look at animals as a group, focusing on their basic form, function, and evolutionary history.

33.1 ANIMAL BODY PLANS

As discussed in Chapter 22, it is relatively easy to understand how the body plans of humans, chimpanzees, and gorillas show them to be more closely related to one another than any of them is to other animal species. Furthermore, it isn’t hard to see that humans, chimpanzees, and gorillas are more closely related to monkeys than they are to lemurs, and that humans, chimpanzees, gorillas, and monkeys are more closely related to lemurs than they are to horses. Anatomy and morphology reveal key evolutionary relationships among vertebrate animals, but how do we come to understand the place of vertebrates in a broader tree that includes all animals? More generally, how can we construct an animal phylogeny that includes organisms with body plans as different as those of sponges, jellyfish, earthworms, mussels, sea stars, and humans?

What is an animal?

Let’s begin by asking what an animal is. Which features differentiate animals from all other organisms? And, more specifically, which features differentiate animals from their nearest relatives?

As introduced in Chapter 25, the organisms most closely related to animals are choanoflagellates, a group of single-celled eukaryotes. This relationship was first proposed in the nineteenth century by scientists who noticed similarities in cell shape between choanoflagellates and the feeding cells of sponges; it was confirmed in the twenty-first century through comparisons of molecular sequences. Choanoflagellates are unicellular, whereas animals are multicellular. But multicellularity is not a unique feature of animals: plants and fungi are also multicellular. Thus, we need to find another feature to distinguish animals from other organisms.

Animals are heterotrophs, gaining energy and carbon from preformed organic molecules (Chapter 6). This character differentiates animals from plants, but not from fungi, which are also heterotrophs. Animal cells lack cell walls, allowing them to move during development and in the adult animal (Chapter 26). This character differentiates animals from both...
plants and fungi. Animals have a pattern of early embryological development that begins with a hollow ball of cells called a blastula and includes the movement of embryonic cells, usually to form a gastrula (Chapters 19, 26, and 40), a process unique to animals.

Animals, therefore, can be described as multicellular heterotrophic eukaryotes with a distinctive mode of early development. Other features also distinguish animals from other organisms, but as we learn more about choanoflagellates, some of these lines have blurred. For example, collagen, long considered to be unique to animals, is now known to occur in choanoflagellates.

**Animals can be classified based on type of symmetry.** Early in the history of biology, taxonomists such as Carl Linnaeus recognized that for all their diversity, animals have a limited number of distinctive body plans. Animals with the same type of body plan can be placed into a group called a phylum. The problem for biologists has long been how to understand the evolutionary relationships among animal phyla. Indeed, this is still an active field of research.

In Chapter 21, we saw that the fundamental mechanism by which biological diversity increases is speciation, the divergence of two populations from a common ancestor. Played out repeatedly through time, speciation gives rise to a treelike pattern of evolutionary relatedness: more closely related groups diverge from branch points closer to the tips of the tree, whereas more distantly related groups diverge from branch points nearer its base. Distinctive features of organisms, called characters, evolve throughout evolutionary history. We can estimate when a character arose from its shared presence in the descendants of the population in which the character first evolved. Often the characters analyzed are anatomical traits.

**Fig. 33.1** shows a phylogenetic tree of animals. Most animals can be divided into three groups based on the symmetry of their bodies. **Porifera** (sponges) are irregular in form, with no clearly developed plane of symmetry. **Cnidaria** (the group that includes jellyfish, corals, and sea anemones) display radial symmetry. Their bodies have an axis that runs from mouth to base, with many planes of symmetry cutting through this axis (**Fig. 33.2a**). Because of this structure, jellyfish can move up and down in the water column by flexing the muscles around their bell-like bodies, and many sea anemones and corals can wave their ring of food-gathering tentacles in all directions at once.

**Bilateria** (most other animals, including humans, insects, and snails) show bilateral symmetry. Their bodies have a distinct front and back, top and bottom, and right and left, with a single plane of symmetry running between right and left at the midline (**Fig. 33.2b**). Animals with bilateral symmetry are able to move in a horizontal direction to capture prey, find shelter, and escape from enemies. These animals develop specialized sensory organs at the front end for guidance (Chapter 34), and specialized appendages along both sides for locomotion, grasping, and defense.

The phylogenetic tree in **Fig. 33.1** also indicates that animals are closely related to choanoflagellates, but differ from them in having persistent multicellularity and in forming a blastula during early development. **Poriferans** have only a few different cell types, and these cells are organized into only simple tissues, not the well-defined tissues and complex organs found in other animals (Section 33.2). Cnidarians have well-defined tissues, but lack complex organs. Bilaterians have both well-defined tissues and complex organs. These organs are specialized for movement, digestion, gas exchange, and other functions.

Note that the phylogenetic tree shown in **Fig. 33.1** does not tell us that sponges are older than other animals. Instead, it says that sponges and other animals diverged from a common ancestor, but it doesn’t tell us what that common ancestor looked like. Similarly, cnidarians and animals with bilateral symmetry diverged from their last common ancestor at a single point in time and so are equally old, but structurally distinct.

**Many animals have a brain and specialized sensory organs at the front of the body.** A notable feature of many bilaterian animals is that nervous system tissue, including specialized sense organs such as eyes, becomes concentrated at one end of the body. For example,
Cephalization is a key feature of the body plan of most animals, including vertebrates. Cephalization is considered an adaptation for locomotion because it allows animals to take in sensory information.

The eyespots of flatworms are located at one end of its body, as are the brain and sense organs of earthworms, insects, and vertebrates (Fig. 33.3). The concentration of nervous system components at one end of the body, defined as the “front,” is referred to as cephalization. Cephalization is a key feature of the body plan of most animals, including vertebrates.

FIG. 33.2 Symmetry in animal form. (a) Radial versus (b) bilateral symmetry distinguishes cnidarians and bilaterian animals.

FIG. 33.3 Cephalization. (a) Flatworms, (b) earthworms, (c) insects, and (d) vertebrates all have a distinct head region with specialized sense organs.

Photo sources: (left to right) Science History Images/Alamy Stock Photo; bazilfoto/iStock/Getty Images; marcouliana/Getty Images; taviphoto/Getty Images.
from the environment ahead of them as they move forward. In addition, the proximity of the sensory organs to the brain makes it possible to process this information quickly, thereby enabling a suitable behavioral response. As the quality and amount of sensory information taken in by animals increased, their brain size and complexity also increased. Cephalization is also considered to be an adaptation for predation, since animals with cephalization can better detect and capture prey, and for predator avoidance, providing a means of escaping capture.

Although cephalization is a feature of many animals, it has been particularly well studied in vertebrates. In vertebrates, the brain, many sense organs, and the mouth are all located in the head. Vertebrates have also evolved several novel features located in the head, including a jaw, teeth, and tongue. These structures are all thought to be adaptations for predation, or more generally the acquisition and processing of food.

As a result of evolutionary selection for enhanced sensory perception and the ability to respond to important cues in the environment, the brain, sensory organs, and nervous system of many animals are complex in their organization. Notably, they are linked to more sophisticated abilities that allow for a broad range of behaviors. Such abilities are critical to the success of both predators and prey, and they underlie the complex interactions that occur among members of a species when they mate, reproduce, disperse, and care for their young.

**Some animals also show segmentation.**

In addition to cephalization, another broad pattern that is evident among the body plans of bilaterian animals is segmentation. **Segmentation** is the organization of the body into units, or segments, that are repeated from front to back (along the anterior–posterior axis), but modified depending on where they are located in the body.

Insects, for example, have a head, thorax, and abdomen (Fig. 33.4). Each of these regions can be further subdivided into segments. For example, each of three pairs of legs grows from one of the three segments that make up the thorax. In Chapter 19, we considered some of the genetic mechanisms that generate this segmented pattern in the fruit fly *Drosophila*. Humans and other vertebrates also develop in a segmented fashion, as is evident in the repeated pattern of vertebrae and nerves that make up the backbone and spinal cord.

Three animal phyla are known for showing a segmented body plan: arthropods (including insects, spiders, and crustaceans), annelids (segmented worms), and chordates (including vertebrates). Segmentation allows for the differentiation of segments into distinct body parts and may have evolved as an adaptation for higher motility.

**Animals can be classified based on the number of their germ layers.**

New insights about animals became possible with the advent of microscopes that enabled the direct study of early animal embryos. One important observation was that some animals that look very different as adults share patterns of early embryological development. For example, adult sea stars and catfish look very different from each other, but their embryos show a number of key similarities, including the way that the early cell divisions occur and the number of embryonic tissue layers they develop.

In cnidarians (radially symmetrical animals), the embryo has two germ layers, the endoderm and the ectoderm, from which the adult tissues develop. Because of this characteristic, these animals are called diploblastic (Fig. 33.5). In bilaterians (bilaterally symmetrical animals), the embryo has three germ layers, with the mesoderm between the endoderm and ectoderm. These animals are called triploblastic (Fig. 33.5). The evolution of the mesoderm in triploblasts allowed for the development of new types of tissues and organs, such as muscles and circulatory systems. These new types of tissues and organs, in turn, facilitated the evolution of new modes of locomotion, feeding, and behavior.

Comparative embryology also enabled biologists to divide bilaterian animals into the two groups shown in Fig. 33.6: the **protostomes** (from the Greek for “first mouth”) and the **deuterostomes** (from the Greek for “second mouth”). In protostomes, the earliest-forming opening to the internal cavity of the developing embryo, called the blastopore, becomes the mouth. Protostomes include such groups as nematodes (roundworms), arthropods (including insects, spiders, and crustaceans), mollusks ( gastropods like snails and slugs; bivalves like clams and mussels; and cephalopods like squids and octopus), annelids (segmented worms), and flatworms (Fig. 33.7).
In deuterostomes, the blastopore becomes the anus, and the mouth forms second. Deuterostomes include chordates, such as vertebrates, and echinoderms, such as sea stars, sea urchins, and sand dollars (Fig. 33.7).

While the names of the protostomes and deuterostomes focus our attention on which structure the blastopore becomes, these groups exhibit a host of other differences. For example, they differ in the nature of the early divisions of the embryo, the origin of the mesoderm, and the position of the nerve cord running the length of the body. Only in the age of molecular sequence comparisons have the relationships among phyla within each of these two groups become clear.

**FIG. 33.5 Variation in embryonic development.** Early development of germ tissues in the embryo separates the diploblastic cnidarians from the triploblastic bilaterians.

**FIG. 33.6 A phylogenetic tree of bilaterian animals.** Embryological features and molecular sequences of genes show that bilaterian animals can be organized into two major groups, deuterostomes and protostomes. 

Photo sources: (top) Glenn Nagel/iStockphoto; (bottom) Lal/Getty Images.
Molecular sequence comparisons have confirmed some relationships and raised new questions.

Early biologists laid the groundwork for understanding animal phylogeny by relying on their observations of comparative anatomy and embryonic development. Yet as was true for phylogenetic relationships in Bacteria, Archaea, and Eukarya as a whole, a modern understanding of evolutionary relationships among animals had to wait for the revolution in molecular sequencing. Over the past two decades, comparisons among DNA, RNA, and amino acid sequences have greatly improved our understanding of animal phylogeny. Molecular comparisons support many of the conclusions reached by the early biologists, including the early divergence of sponges and the separation of radially and bilaterally symmetrical animals. Moreover, molecular sequence comparisons confirm that choanoflagellates are the closest protistan relatives of animals.

Other hypotheses have been rejected. For example, some biologists pointed to the presence or absence of a cavity, or coelom, surrounding the gut, as a character that could be used to organize bilaterians into three groups: those without a body cavity (acoelomates) and those with a body cavity (coelomates and pseudocoelomates, which differ in the embryonic origin of the cells lining the cavity). These body plans are shown in Fig. 33.8. The coelom cushions
the internal organs against hard blows to the body and enables the body to turn without twisting these organs. Once molecular studies were conducted, however, researchers discovered that they did not support this traditional phylogenetic division of bilaterians into acoelomate, coelomate, and pseudocoelomate groups. Similarly, molecular sequence comparisons have not supported the once widespread view that segmented bodies indicate a close relationship between earthworms and lobsters.

**CASE 7 BIOLOGY-INSPIRED DESIGN: USING NATURE TO SOLVE PROBLEMS**

*Can we mimic the form and function of animals to build robots?*

Scientists who design robots often try to mimic the form and function of animals. Fishes are one of the most popular types of robotic animals. We can learn a great deal about innovations by studying fishes, whose remarkable adaptations have been shaped by natural selection over more than 500 million years.

The first robotic fish was created in the 1980s by a team of scientists and engineers at Massachusetts Institute of Technology. It was called RoboTuna because it mimicked the form and function of a tuna, allowing it to swim effectively through water. Since then, many more fish-like robots have been made, so that today there are more than 400 different types of robotic fishes. Some, like RoboTuna, have one joint; others have many joints; and still others are made of dynamic materials that can bend fluidly.

Why build a robotic fish? The first and most basic reason is to understand how fish move. Fish are spectacular swimmers. If we can build a robotic fish that swims like a living one, it suggests that we understand how a fish is able to move forward, turn, and navigate its surroundings. Robotic fishes can also be used in studies of fish behavior. A robotic fish that looks and even smells like a real fish, and that has sensors to detect and record its surroundings, provides a way to quietly “spy” on fish in a way that is not possible by direct observation or by the use of cameras. There are all kinds of practical applications of robotic fish as well, from mapping coastlines, coral reefs, and the sea floor, to monitoring underwater cables and pipelines, to exploring marine life.

Scientists and engineers have copied the form and function of many animals, including cockroaches, geckos, jellyfish, hummingbirds, and bats, to name just a few. One of the most recent and exciting robots is based on an octopus. Octopuses show incredible dexterity and strength, all without an internal skeleton.

The robot octopus, called an octobot and designed by researchers at Harvard University, has several remarkable characteristics ([Fig. 33.9](#)). It is entirely soft, with no rigid components like metal or even batteries. It is powered by a simple chemical reaction: liquid hydrogen peroxide is converted to a gas in the presence of a catalyst (in this case, platinum), providing pressure that powers movement. Finally, the robot is produced with a 3D printer.

The octobot brings together engineers, material scientists, and chemists to create a robot that is inspired by biology. This truly interdisciplinary effort is the first step toward more flexible and innovative robots for research and diverse applications.

### Self-Assessment Questions

1. Draw a simplified animal tree of life, indicating the relationships among sponges, cnidarians, protostomes, and deuterostomes.
2. Which features distinguish sponges, cnidarians, protostomes, and deuterostomes? Place these features on the phylogeny that you drew for Self-Assessment Question 1.
3. How is cephalization an adaption for forward locomotion?
4. Which animals are more closely related to sponges: cnidarians or bilaterians?

### 33.2 TISSUES AND ORGANS

As we have seen, animals show a diversity of form. Nevertheless, the cells of most animals are organized into just four types of tissues: epithelial, connective, muscle, and nervous. Tissues are collections of cells that carry out a specific
Epithelial tissue is classified based on certain characteristics. The first characteristic is layering: a single layer of cells is considered simple, and more than one layer is labeled as stratified. The second characteristic is the shape of the cells: flat cells are squamous, round or square cells are cuboidal, and tall cells are columnar. For example, a single layer of flat cells is called simple squamous epithelium; this type of epithelial tissue lines the inside of blood vessels and the interior surface of the lung. Some epithelial tissues have special features, such as a layer of the protein keratin in the case of the skin, or cilia in the case of the upper airways.

Epithelial tissue not only forms a boundary, but also may absorb substances from and secrete substances into the space it surrounds. In the gut, for example, the epithelial lining absorbs nutrients. Notably, epithelial tissue has no blood vessels, so it gets its blood supply from the underlying tissue, which is connective tissue.

Connective tissue underlies epithelial tissues and is found elsewhere as well. In contrast to epithelial tissue, which is composed of closely packed cells, connective tissue has an extensive extracellular matrix and few cells. The extracellular matrix is an insoluble meshwork composed of proteins and polysaccharides. Its components are synthesized, secreted, and modified by the cells that reside within the connective tissue. Many different forms of extracellular matrix exist, which differ in the amount, type, and organization of the proteins and polysaccharides that compose them. The extracellular matrix not only contributes structural support, but also provides informational cues that determine the activity of the cells that are in contact with it (Chapter 10).

Connective tissue is characterized by the properties of the specific extracellular matrix. For example, two layers of connective tissue lie beneath the epidermis of the skin: first a specialized type of connective tissue called the basal lamina, and then the dermis, a type of connective tissue made up of cells that secrete the components of the extracellular matrix (Fig. 33.10). The dermis is strong and flexible because its extracellular matrix is composed of tough protein fibers. This layer contains blood vessels that nourish both the dermis and the overlying epidermis. The dermis also provides a cushion for the body.

The dermis of the skin is one of several types of connective tissue found in the body. Other connective tissues, such as bones, cartilage, tendons, and ligaments, help support the body and provide a system of levers for movement (Chapter 35). Finally, specialized connective tissues also include adipose tissue (fat) and blood.

Muscle tissue is made up of cells (called fibers) that are able to shorten or contract (Chapter 35). These specialized cells contain actin thin filaments and myosin thick filaments. Myosin is a motor protein that uses the energy of ATP to change conformation. This conformational change moves the thin filament relative to the thick filament. As a result, individual muscle
Fig. 33.11  Skeletal muscle. Viewed under the microscope, skeletal muscle cells have a striated, or striped, appearance. Photo source: Photo Researchers/Getty Images.

Vertebrate animals have three types of muscle tissues. Skeletal muscle attaches to bone and makes voluntary movements possible (Fig. 33.11). Cardiac muscle is found in the heart and contracts to make the heart beat. Smooth muscle can be found in such places as the gut, where it causes waves of contraction that push food along the digestive tract, and blood vessels, which constrict and relax to control blood flow.

Nervous tissue is the fourth type of animal tissue (Chapter 34). It can be found, for example, in the nerve nets of cnidarians and in the brain, spinal cord, and peripheral nerves of vertebrates. Nervous tissue takes in sensory information from the environment, processes information, and sends signals to target organs to elicit a response. For example, signals sent to muscles direct movement, and signals sent to organs help the body maintain a relatively constant internal state, called homeostasis (Section 33.3).

Nervous tissue is made up primarily of neurons (nerve cells) that send electrical impulses from one end of the cell to the other (Fig. 33.12). They communicate with each other at specialized junctions called synapses, where chemical signals are released by one nerve cell and received by another. The ability of nerve cells to communicate quickly and specifically and to form networks underlies rapid decision making and complex behaviors.

Tissues are organized into organs that carry out specific functions.

In bilaterians, multiple tissues can combine to make an organ. For example, the intestine is an organ that includes all four types of tissues: epithelial, connective, muscle, and nervous. In turn, organs may combine to form an organ system. For example, the intestine is one organ of the digestive system, which also includes the stomach, liver, pancreas, and other organs (Chapter 38).

Sponges have only simple epithelia that line the surface of the body. In contrast, jellyfish, corals, and sea anemones (cnidarians) have some tissues, but not true organs (see Fig. 33.1). These organisms have a set of nerves called a nerve net, but their nerves are not organized into a brain or central nervous system. Moreover, cnidarians have muscle cells, but not well-developed
how animals are able to maintain homeostasis.

Critical feature of cells and of life itself. In this section, we examine what goes out (Chapter 5). For example, the plasma membrane passage of others, allowing the cell to regulate what goes in and pumps lets some molecules through freely but restricts the life. The lipid bilayer with its embedded protein channels and actively maintains intracellular conditions compatible with concentration.

Within a narrow range of conditions, such as pH range or salt and protein folding, for example, are carried out efficiently only critical for many functions that support life. Chemical reactions inside of cells remains relatively constant. This consistency is environment outside of cells may change, but the environment internal conditions is called homeostasis. Homeostasis is a critical feature of cells and of life itself. In this section, we examine how animals are able to maintain homeostasis.

**Homeostasis is the active maintenance of stable conditions inside of cells and organisms.**

In Chapter 5, we looked at how cells maintain homeostasis. The environment outside of cells may change, but the environment inside of cells remains relatively constant. This consistency is critical for many functions that support life. Chemical reactions and protein folding, for example, are carried out efficiently only within a narrow range of conditions, such as pH range or salt concentration.

For cells, the selectively permeable plasma membrane actively maintains intracellular conditions compatible with life. The lipid bilayer with its embedded protein channels and pumps lets some molecules through freely but restricts the passage of others, allowing the cell to regulate what goes in and what goes out (Chapter 5). For example, the plasma membrane keeps ion concentrations within narrow ranges. The firing of action potentials by neurons is an example of a cell function that requires particular ion concentrations on either side of the membrane. Recent evidence suggests that nerve cell firing rates are maintained at a steady level in the brain of rats, regardless of sensory stimulus or deprivation, or whether the animals are awake or asleep. Temperature and pH are other parameters that do not vary much, because enzymes often work effectively only in narrow temperature and pH ranges. For example, cells found in the highly acidic waters associated with mine drainage nevertheless maintain an internal pH that is roughly neutral. To do so, they actively pump protons across the cell membrane.

Homeostasis is also maintained for the body as a whole. Many physiological parameters are maintained in a narrow range of conditions throughout the body, including temperature, heart rate, blood pressure, blood sugar, blood pH, and other ion concentrations. Similarly, the water content of the body as a whole is kept stable through the careful regulation of ions and other solutes, as discussed in Chapter 39.

The concept of homeostasis was first described as regulation of the body’s "interior milieu" in the late 1800s by the French physiologist Claude Bernard, who is often credited with bringing scientific methods to the field of medicine. The term “homeostasis” was coined by the American physiologist Walter Cannon, whose book *The Wisdom of the Body* (first published in 1932) popularized the concept.

Maintaining steady and stable conditions takes work in the face of changing environmental conditions. That is, a cell or organism actively performs various processes that maintain homeostasis. For example, long periods of drought challenge an animal’s ability to remain hydrated and maintain a stable water and ion balance. Animals facing drought must respond rapidly by changing the permeability of their skin and respiratory organs so that they can retain as much water as possible.

**Homeostasis is often achieved by negative feedback.**

How does the body maintain homeostasis? Homeostatic regulation often depends on negative feedback (Fig. 33.13). In negative feedback, a stimulus acts on a sensor that communicates with an effector, which produces a response that opposes the initial stimulus. For example, negative feedback is used to maintain a constant temperature in a house. Cool temperature (the stimulus) is detected by a thermostat (the sensor). The thermostat sends a signal to the furnace or other heating system (the effector), prompting it to generate heat (the response). The response (heat) opposes the initial stimulus (cool temperature) until the temperature setting of the thermostat is reached. No additional heat is produced until the temperature drops below the temperature setting. In this way, a stable temperature is maintained (Fig. 33.13a).

In a similar way, humans and other mammals maintain a steady body temperature even as the temperature outside fluctuates. Nerve cells in the hypothalamus (located in the base of the brain) act as the body’s thermostat or sensor (Fig. 33.13b). When a decrease in the temperature in the environment causes a drop in body temperature (the stimulus), the hypothalamus (the sensor) activates the nervous system to induce shivering and the production of metabolic heat (the effectors), as discussed in Chapter 36. At the same time, the hypothalamus...
are essentially unknown because they lack mineralized body parts (Chapter 22). In contrast, the fossilized shells and bones of bivalve mollusks (such as clams and mussels), brachiopods (marine shelled animals), echinoderms (such as sea stars and sea urchins), and mammals preserve an excellent record of evolutionary history within these groups. Fossils also provide a record of now extinct species that often resemble, yet are distinct from, modern groups. They can show combinations of traits not seen in living animals—think, for example, of dinosaurs. In addition, they underscore the evolutionary importance of extinctions: a small number of events removed a majority of existing species, paving the way for renewed diversification among survivors. If we step back and look at the big picture, what do fossils tell us about the evolutionary history of the animal kingdom?

Fig. 33.13 Temperature regulation by negative feedback in (a) a house and (b) a mammal. In negative feedback, a response (such as heat) opposes the stimulus (cold), leading to a stable state (a steady temperature).

activates nerves that cause peripheral blood vessels to constrict (additional effectors). The reduction in blood flow near the body’s surface reduces heat loss to the surrounding air. Conversely, an increase in temperature signals sweat glands to secrete moisture and peripheral blood vessels to dilate to aid heat loss from the skin.

Homeostatic regulation, therefore, relies on negative feedback to maintain a set point, or steady-state value. In the example, the set point is an animal’s preferred body temperature. The ability to maintain a constant body temperature is known as thermoregulation, and preferred body temperature is just one of many physiological set points that the body actively maintains, as we discuss in subsequent chapters.

Self-Assessment Question

6. What is homeostasis? Provide one example of a condition that is maintained by homeostasis.

33.4 EVOLUTIONARY HISTORY

Because many animals form hard, mineralized skeletons, sedimentary rocks deposited throughout their evolutionary history over the past 541 million years contain a rich fossil record of shells and bones. Animals also leave sedimentary calling cards in the form of their tracks, trails, and burrows, which are also widespread in sedimentary rocks. Nevertheless, not all animal phyla are well represented in the fossil record. For example, fossil earthworms are rare and fossil flatworms are essentially unknown because they lack mineralized body parts (Chapter 22). In contrast, the fossilized shells and bones of bivalve mollusks (such as clams and mussels), brachiopods (marine shelled animals), echinoderms (such as sea stars and sea urchins), and mammals preserve an excellent record of evolutionary history within these groups.

Fossils also provide a record of now extinct species that often resemble, yet are distinct from, modern groups. They can show combinations of traits not seen in living animals—think, for example, of dinosaurs. In addition, they underscore the evolutionary importance of extinctions: a small number of events removed a majority of existing species, paving the way for renewed diversification among survivors. If we step back and look at the big picture, what do fossils tell us about the evolutionary history of the animal kingdom?

Fossils and phylogeny show that animal forms were initially simple but rapidly evolved complexity.

In Chapter 22, we discussed how to interpret and build phylogenetic trees based on morphological, developmental, and molecular traits of organisms. Phylogeny suggests that animals are relative latecomers in evolutionary history, and the fossil record supports this hypothesis. Life originated more than 3.5 billion years ago, but microorganisms were the only members of ecosystems for most of our planet’s history. As noted in Chapter 26, macroscopic fossils of organisms thought to be animals first appear in rocks deposited only 575 million years ago. Called Ediacaran fossils after the Ediacara Hills of South Australia where they were discovered, these fossils have
SECTION 33.4 EVOLUTIONARY HISTORY

FIG. 33.14 Dickinsonia, an Ediacaran fossil. Dickinsonia and similar fossils are structurally simple, showing that the earliest animals had not yet evolved the complex morphologies and organ systems seen today in bilaterians. Source: O. Louis Mazzatenta/Getty Images.


simple shapes that are not easily classified among living animal groups (Fig. 33.14).

Based on phylogenetic trees, we should look for sponges, cnidarians (jellyfish, corals, and sea anemones), and other diploblastic animals among the oldest animal fossils. Sponges, at least, are rare among Ediacaran fossils, probably because early sponges did not make mineralized parts. Instead, the majority of the organisms preserved as Ediacaran fossils show simple, fluid-filled tubes, without identifiable mouths or other organs. Many may have formed colonies, gaining complexity through colonial growth and differentiation, as some living cnidarians do. These early animals had epithelia and are thought to have obtained food by taking in dissolved organic matter or phagocytosing small particles. They would have exchanged gases by diffusion. Most Ediacaran fossils probably branched from an early node or nodes on the animal tree.

Why did the first observable animal radiation occur so late in the history of life? Scientists continue to debate this question, but part of the answer appears to lie in Earth’s environmental history. Geochemical data suggest that only during the Ediacaran Period did the atmosphere and oceans come to contain sufficient amounts of oxygen to support the metabolism of large, active animals.

The animal body plans we see today emerged during the Cambrian Period.

Ediacaran fossils differ markedly from the shapes of living animals. In contrast, in the next interval of geologic history, the Cambrian Period (541–485 million years ago), we begin to see the fossilized remains of animals with familiar body plans (Fig. 33.15). Cambrian fossils commonly include skeletons made of the minerals silica, calcium carbonate, and calcium phosphate, and they record the presence of arthropods (the group that today includes insects, spiders, crabs, and their close relatives), echinoderms, mollusks, brachiopods, and other bilaterian animals in the oceans. The rocks also preserve complex tracks and burrows made by early organisms. And in a few places, notably at Chengjiang in China and the Burgess Shale in Canada, unusual environmental conditions have preserved a treasure trove of animals that did not form mineralized skeletons (Chapter 22).

These exceptional windows into early animal evolution show that, during the first 40 million years of the Cambrian Period, the body plans characteristic of most bilaterian phyla took shape. This period of rapid diversification in the fossil record is sometimes called the Cambrian explosion. Sponges and cnidarians radiated as well, producing through time the diverse habitats of reefs and imparting an ecological structure to life in the sea broadly similar to what we see today.
Scientists sometimes argue about whether the name “Cambrian explosion” is apt. The fossil record makes it clear that bilaterian body plans did not suddenly appear fully formed, so the event was not truly “explosive.” Rather, fossils demonstrate a large accumulation of new characters in a relatively short period of time during which the key attributes of modern animal phyla emerged. For example, living arthropods have segmented bodies with a protective cuticle, jointed legs, other appendages specialized for feeding or sensing the environment, and compound eyes with many lenses. Cambrian fossils include the remains of organisms with some, but not all, of the major features present today in arthropods. In short, the first 40 million years of the Cambrian Period ushered in a world utterly distinct from anything known in the preceding 3 billion years.

**Five mass extinctions have changed the trajectory of animal evolution during the past 500 million years.**

The wealth of paleontological data we have show a dynamic history of animal radiations and extinctions through time (Chapter 22). Fig. 33.16 is a graph of fossil occurrences through time, compiled from the paleontological literature by American paleontologist Jack Sepkoski. A notable feature of this graph is that great reductions in the number of animal genera appear to have occurred five times (indicated by the arrows), suggesting events that we call mass extinctions. A mass extinction is a large, widespread, and relatively rapid loss of life on Earth.

In Fig. 33.16, we also see that despite the burst of body plan evolution recorded by Cambrian fossils, there were still relatively few genera at the end of the Cambrian Period. The following Ordovician Period (485–444 million years ago) was a time of renewed animal diversification. In particular, heavily skeletonized animals evolved in the world’s oceans. The number of genera recorded by fossils increased fivefold during this period, suggesting that species diversity might have increased by an order of magnitude (most genera contain multiple species). The Ordovician radiation established a marine ecosystem that persisted for more than 200 million years.

One interesting note: if you had walked along an Ordovician beach, the shells washing about your feet would have been far different from the ones you see today. The dominant shells were those of brachiopods, not clams (Fig. 33.17). The broken corals in the Ordovician surf were the skeletons of now-extinct cnidarians exoskeletons, molted during growth, were those of now-extinct trilobites, not lobsters or crabs. Why was the Ordovician world so distinct from our own?

Another look at Fig. 33.16 provides the answer. At the end of the Permian Period, 252 million years ago, a mass extinction eliminated most genera in the oceans. Early coral-like cnidarians
become extinct, as did the trilobites. Brachiopods survived as a group, but most species disappeared. As noted in Chapter 22, the likely trigger for this devastation was a massive eruption of volcanos that unleashed global warming, ocean acidification, and oxygen loss from subsurface oceans.

As ecosystems recovered from this mass extinction, they came to be dominated by new groups descended from survivors of the extinction. Notably, bivalves and gastropods (two groups of mollusks) diversified. New groups of arthropods also radiated, including the ancestors of the crabs and shrimps we see today. In addition, the surviving cnidarians evolved a new ability to make skeletons of calcium carbonate, resulting in the corals that build modern reefs. In short, mass extinction reset the course of evolution, as it did four other times during the past 500 million years (see Fig. 33.16).

Animals began to colonize the land 420 million years ago.

The movement from water to land presented numerous challenges for animals, just as it did for plants (Chapter 27). In particular, animals had to develop ways to move about without the buoyancy provided by water (Chapter 35), extract oxygen from air rather than water (Chapter 37), and reproduce on land (Chapter 40).

Animals began to colonize land only after plants had already established themselves there. Land plants evolved during the Ordovician Period, about 460 million years ago. The first animals to colonize the land were arthropods, which moved onto land during the Silurian Period, about 420 million years ago. These arthropods included insects and chelicerates (the group that today includes spiders, mites, and scorpions).

The radiation of the major groups of insects began about 360 million years ago with a marked diversification of dragonflies and the ancestors of cockroaches and grasshoppers. Some of the dragonfly-like insects that darted among the plants of this period had bodies the size of a lobster and 75-cm wing spans! You might well wonder what prevents insects from attaining this size today. Scientists debate this question, but part of the answer probably implicates flying vertebrates—first now-extinct groups such as pterosaurs, and later, birds and bats—which competed with and preyed upon large insects.

Flies, beetles, bees, wasps, butterflies, and moths radiated later. Their rise in diversity parallels that of the flowering plants and reflects the coevolution of these pollinators and flowering plants.

Fossils of tetrapods (four-legged land vertebrates, such as amphibians) first appear in sedimentary rocks deposited near the end of the Devonian Period, about the same time as the early insect radiations of 360 million years ago. As discussed in Chapter 22 (see Fig. 22.22), the fossil record documents in some detail the shifts in skull, trunk, and limb morphology that allowed vertebrate animals to colonize land. These include the evolution of muscled, articulated legs from fins, together with a set of strong, articulated digits where the limbs meet the ground; lungs and a rib cage to support the muscles that control breathing; and an erect, elevated head with eyes oriented for forward vision.

Amniotes (the large group that includes reptiles, birds, and mammals) evolved later, about 310 million years ago. A key innovation that separates amniotes from amphibians is the evolution of a water-tight, or amniotic, egg (Chapter 40). This feature allowed land vertebrates to reproduce on land without returning to the water. The appearance in the fossil record of amphibians and then amniotes follows the predictions of phylogenies based on comparative biology.

During this time, new species of land animals continued to diversify, including small bipedal species that gave rise to some of the most remarkable creatures ever to walk on land: the dinosaurs. From their beginnings approximately 240 million years ago, dinosaurs radiated to produce many hundreds of species, dominating terrestrial ecosystems until the end of the Cretaceous Period, 66 million years ago. At that time, another mass extinction, caused by a catastrophic asteroid impact, eliminated nearly all dinosaur species (Chapter 1). We say "nearly all" because the fossil record documents the evolutionary divergence of birds from a specific subgroup of dinosaurs approximately 150 million years ago (Chapter 22).

Mammals have been the dominant vertebrates on land since the extinction of dinosaurs. This group actually originated much earlier, at least 210 million years ago. During the age of dinosaurs, most mammals were small nocturnal or tree-dwelling animals that stayed out of the way of large dinosaurs, although fossils from China show clearly that the largest mammals of this interval ate small dinosaurs and their eggs. Mammals are dominant components of terrestrial ecosystems today in part because they survived the end-Cretaceous mass extinction.

Some animals show a trend toward increase body size over time.

In our brief overview of animal evolution, we have seen giant dragonflies and large dinosaurs. A newly described dinosaur, *Patagotitan mayorum*, is thought to be the largest animal ever to have walked on land. The blue whale (*Balaenoptera musculus*) is the largest animal to have ever existed on Earth. These are just a few examples, but it turns out that many groups of animals show increases in body sizes over time (Fig. 33.18). These groups include the brachiopods, chordates (including vertebrates), and echinoderms (such as sea stars, sea urchins, and sand dollars).

Large body size presents distinct challenges. Within those large bodies, animals need to transport oxygen, nutrients, and signaling molecules over long distances. Diffusion, the random motion of molecules, is effective only over short distances. In Chapter 27, we discussed how bulk flow can transport...
The issue with a large ant is that it increases in size but keeps its overall shape. This kind of change is called isometry ("same measure"). By contrast, increases in size are possible if they are accompanied by changes in shape. This kind of change is called allometry ("different measure"). For example, in the 1600s, Galileo Galilei noticed that the bones of larger animals are not simply scaled-up versions of the bones of smaller animals. Instead, in many cases, the bones of larger animals are disproportionately wider than those of smaller animals so as to support the increased weight.

As an animal (or any three-dimensional object) gets bigger, both surface area and volume increase, but surface area increases more slowly than does volume (Chapter 26). Therefore, shape changes often accompany size differences to balance the two. For example, nutrients are absorbed through the lining of the gut, which is one large surface area, but they support the entire body, which represents a volume. Larger organisms, therefore, have adaptations of the lining of the gut to increase the surface area over the long distances present in larger organisms. In some animals, for example, blood is circulated throughout the body by the pumping action of the heart, and oxygen is transported into the lungs by contraction of the muscular diaphragm (Chapter 37).

More generally, the form of animals is in part determined by their size. Therefore, as animals got bigger, their form changed as well. To understand why this is so, consider what happens if the size of an ant increases 10-fold without a change in its form. The strength of the legs would increase as the square of the scale factor, or \(10^2\) (100 times), because strength is proportional to the cross-sectional area of the legs. However, the weight of the ant would increase as the cube of the scale factor, or \(10^3\) (1000 times), because weight is proportional to volume. Therefore, as an ant gets bigger, its weight would quickly outstrip the strength of its legs, and it would not be able to support itself. So, an ant looks like an ant in part because of its size.
area, enabling them to “keep up” with the increased volume. These adaptations include folds of the lining of gut (called villi) and projections of the surface of the intestinal cells (called microvilli) that greatly increase the surface area available to absorb nutrients (Chapter 38).

The British biologist J. B. S. Haldane wrote, “For every type of animal there is a most convenient size, and a large change in size inevitably carries with it a change of form.” In the subsequent chapters, we will see many examples of adaptations that can be explained at least in part by considering the size of the animal.

### 33.1 ANIMAL BODY PLANS: Animals have a limited number of distinct body plans.

Animals are multicellular heterotrophic eukaryotes that form a blastula and, commonly, a gastrula during development. page 740

Early biologists grouped animals on the basis of shared features of adult bodies, such as symmetry. page 740

Poriferans (sponges) have no well-defined plane of symmetry; cnidarians (jellyfish, corals, and sea anemones) are radially symmetric; and bilaterians (insects and vertebrates, for example) are bilaterally symmetric. page 740

Cephalization is the concentration of the nervous system and special sensory organs at the front of the body. page 741

Segmentation is the organization of the body into repeated units along the anterior–posterior (head–tail) axis. page 742

Cnidarians have two germ layers (ectoderm and endoderm), whereas bilaterians have three germ layers (ectoderm, mesoderm, and endoderm). page 742

### 33.2 TISSUES AND ORGANS: Most animals have four different types of tissues, which combine to form organs.

Most animals organize their cells into tissues. page 746

The four types of tissues found in animals are epithelial, connective, muscle, and nervous. page 746

Epithelial tissue lines spaces, such as cavities or the outside of the body. page 746

Connective tissue is characterized by an extensive extracellular matrix and few cells. It provides nutrients and a cushion for the overlying epithelial tissue, among other functions. page 746

Muscle tissue is able to shorten, or contract. page 746

Nervous tissue is specialized for transmitting electrical impulses, thereby allowing animals to take in information from the environment, process it, and elicit a response. page 747

Most animals with tissues, with the exception of cnidarians, have organs, which are collections of tissues that perform a specific function. page 747

Organs often work with other organs form an organ system. page 747

### 33.3 HOMEOSTASIS: Homeostasis actively maintains a stable internal environment.

Homeostasis is an active process that is often maintained for individual cells as well as for an organism as a whole. page 748

Many parameters, such as blood pH, ion concentrations, and body temperature, are actively maintained in a narrow range by homeostasis. page 748

Homeostasis is often achieved by negative feedback, in which the response inhibits the stimulus to maintain a set point. page 748

Self-Assessment Questions

7. What is the evolutionary significance of the Cambrian explosion?

8. What are two examples of how mass extinctions changed the ecological structure of life on Earth?

9. Which has more surface area relative to volume: a grape or a grapefruit?
33.4 EVOLUTIONARY HISTORY: Animals evolved more than 600 million years ago in the oceans, and by 500 million years ago the major body plans were in place.

Ediacaran fossils from 575 million years ago provide evidence of early animals. page 749

Most of the animal body plans we see today first evolved during the Cambrian explosion, a time of rapid diversification that began 541 million years ago. page 750

Animal diversity has been shaped by five mass extinctions, which were followed by adaptive radiations, over the past 500 million years. page 751

Arthropods were the first animals to colonize the land, sometime around 420 million years ago. page 752

Four-legged vertebrates (tetrapods) first appear in the fossil record approximately 360 million years ago. page 752

Mammals originated at least 210 million years ago, but became dominant only after the extinction of the non-avian dinosaurs 66 million years ago. page 752

Some animal groups show a tendency toward larger sizes over time, resulting in changes in form. page 753

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– Paul Moore, Bowling Green State University

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– Matthew Nusnbaum, Georgia State University

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