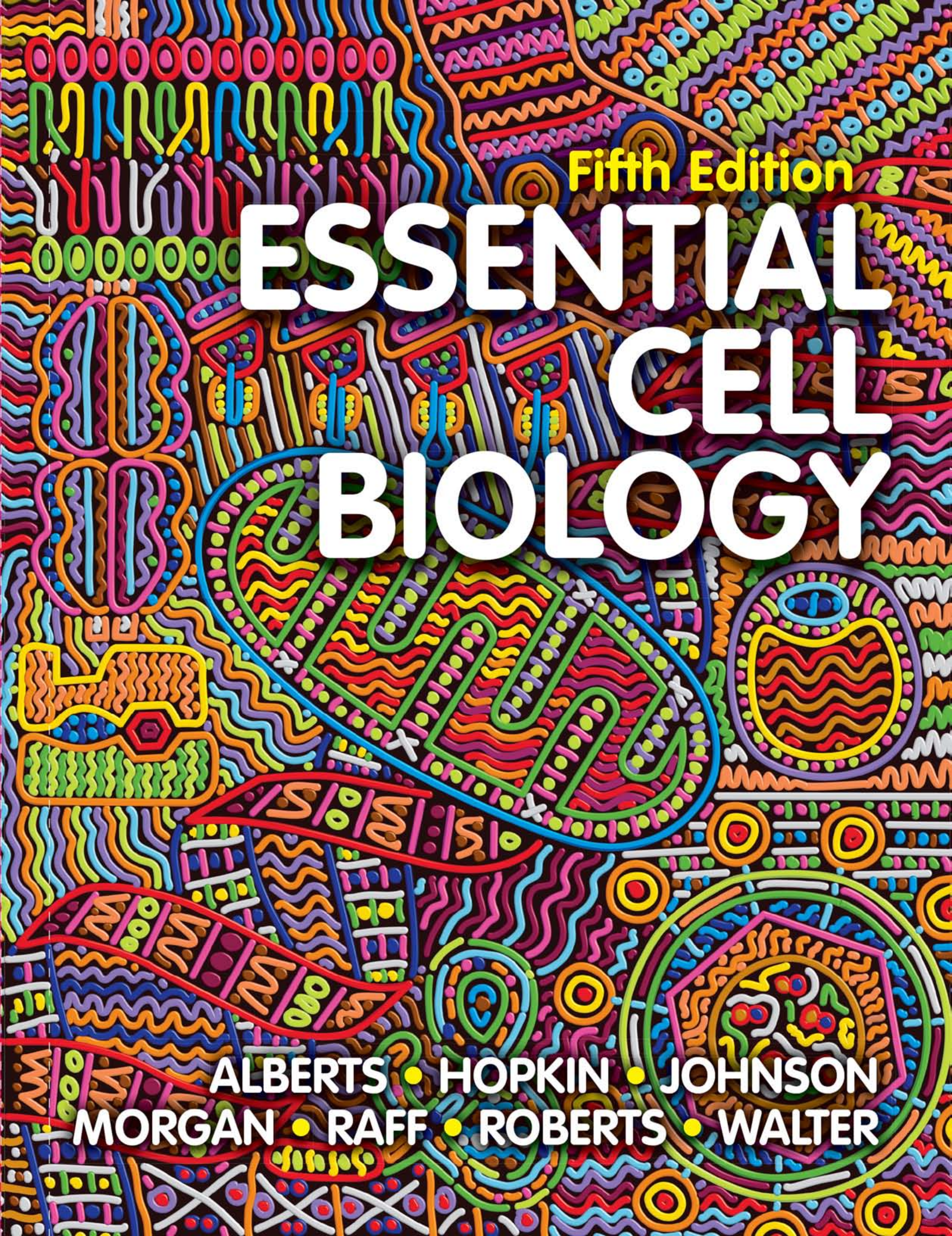
Fifth Edition
ESSENTIAL CELL BIOLOGY
ALBERTS • HOPKIN • JOHNSON
MORGAN • RAFF • ROBERTS • WALTER

ESSENTIAL

CELL BIOLOGY

FIFTH EDITION

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PREFACE

Nobel Prize–winning physicist Richard Feynman once noted that nature has a far, far better imagination than our own. Few things in the universe illustrate this observation better than the cell. A tiny sac of molecules capable of self-replication, this marvelous structure constitutes the fundamental building block of life. We are made of cells. Cells provide all the nutrients we consume. And the continuous activity of cells makes our planet habitable. To understand ourselves—and the world of which we are a part—we need to know something of the life of cells. Armed with such knowledge, we—as citizens and stewards of the global community—will be better equipped to make well-informed decisions about increasingly sophisticated issues, from climate change and food security to biomedical technologies and emerging epidemics.

In *Essential Cell Biology* we introduce readers to the fundamentals of cell biology. The Fifth Edition introduces powerful new techniques that allow us to examine cells and their components with unprecedented precision—such as super-resolution fluorescence microsocopy and cryoelectron microscopy—as well as the latest methods for DNA sequencing and gene editing. We discuss new thinking about how cells organize and encourage the chemical reactions that make life possible, and we review recent insights into human origins and genetics.

With each edition of *Essential Cell Biology*, its authors re-experience the joy of learning something new and surprising about cells. We are also reminded of how much we still don't know. Many of the most fascinating questions in cell biology remain unanswered. How did cells arise on the early Earth, multiplying and diversifying through billions of years of evolution to fill every possible niche—from steaming vents on the ocean floor to frozen mountaintops—and, in doing so, transform our planet's entire environment? How is it possible for billions of cells to seamlessly cooperate and form large, multicellular organisms like ourselves? These are among the many challenges that remain for the next generation of cell biologists, some of whom will begin a wonderful, lifelong journey with this textbook.

Readers interested in learning how scientific inquisitiveness can fuel breakthroughs in our understanding of cell biology will enjoy the stories of discovery presented in each chapter's "How We Know" feature. Packed with experimental data and design, these narratives illustrate how biologists tackle important questions and how experimental results shape future ideas. In this edition, a new "How We Know" recounts the discoveries that first revealed how cells transform the energy locked in food molecules into the forms used to power the metabolic reactions on which life depends.

As in previous editions, the questions in the margins and at the end of each chapter not only test comprehension but also encourage careful thought and the application of newly acquired information to a broader biological context. Some of these questions have more than one valid answer and others invite speculation. Answers to all of the questions are included at the back of the book, and many provide additional information or an alternative perspective on material presented in the main text.

More than 160 video clips, animations, atomic structures, and high-resolution micrographs complement the book and are available online. The movies are correlated with each chapter and callouts are highlighted in color. This supplemental material, created to clarify complex and critical concepts, highlights the intrinsic beauty of living cells.

For those who wish to probe even more deeply, *Molecular Biology of the Cell*, now in its sixth edition, offers a detailed account of the life of the cell. In addition, *Molecular Biology of the Cell, Sixth Edition: A Problems Approach*, by John Wilson and Tim Hunt, provides a gold mine of thought-provoking questions at all levels of difficulty. We have drawn upon this tour-de-force of experimental reasoning for some of the questions in *Essential Cell Biology*, and we are very grateful to its authors.

Every chapter of *Essential Cell Biology* is the product of a communal effort: both text and figures were revised and refined as drafts circulated from one author to another—many times over and back again! The numerous other individuals who have helped bring this project to fruition are credited in the Acknowledgments that follow. Despite our best efforts, it is inevitable that errors will have crept into the book, and we encourage eagle-eyed readers who find mistakes to let us know, so that we can correct them in the next printing.

Acknowledgments

The authors acknowledge the many contributions of professors and students from around the world in the creation of this Fifth Edition. In particular, we received detailed reviews from the following instructors who had used the fourth edition, and we would like to thank them for their important contributions to our revision:

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Working on this book has been a pleasure, in part due to the many people who contributed to its creation. Nigel Orme again worked closely with author Keith Roberts to generate the entire illustration program with his usual skill and care. He also produced all of the artwork for both cover and chapter openers as a respectful digital tribute to the "squeeze-bottle" paintings of the American artist Alden Mason (1919–2013). As in previous editions, Emma Jeffcock did a brilliant job in laying out the whole book and meticulously incorporated our endless corrections. We owe a special debt to Michael Morales, our editor at Garland Science, who coordinated the whole enterprise. He oversaw the initial reviewing, worked closely with the authors on their chapters, took great care of us at numerous writing meetings, and kept us organized and on schedule. He also orchestrated the wealth of online materials, including all video clips and animations. Our copyeditor, Jo Clayton, ensured that the text was stylistically consistent and error-free. At Garland, we also thank Jasmine Ribeaux, Georgina Lucas, and Adam Sendroff.

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Denise Schanck deserves extra special thanks for providing continuity as she helped shepherd this edition from Garland to Norton. As always, she attended all of our writing retreats and displayed great wisdom in orchestrating everything she touched.

Last but not least, we are grateful, yet again, to our colleagues and our families for their unflagging tolerance and support. We give our thanks to everyone in this long list.

Resources for Instructors and Students

INSTRUCTOR RESOURCES

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Smartwork5

Smartwork5 is an easy-to-use online assessment tool that helps students become better problem solvers through a variety of interactive question types and extensive answer-specific feedback. All Smartwork5 questions are written specifically for the book, are tagged to Bloom's levels and learning objectives, and many include art and animations. Get started quickly with our premade assignments or take advantage of Smartwork5's flexibility by customizing questions and adding your own content. Integration with your campus LMS saves you time by allowing Smartwork5 grades to report right to your LMS gradebook, while individual and class-wide performance reports help you see students' progress.

Interactive Instructor's Guide

An all-in-one resource for instructors who want to integrate active learning into their course. Searchable by chapter, phrase, topic, or learning objective, the Interactive Instructor's Guide compiles the many valuable teaching resources available with *Essential Cell Biology*. This website includes activities, discussion questions, animations and videos, lecture outlines, learning objectives, primary literature suggestions, medical topics guide, and more.

Coursepacks

Easily add high-quality Norton digital media to your online, hybrid, or lecture course. Norton Coursepacks work within your existing learning management system. Content is customizable and includes chapter-based, multiple-choice reading quizzes, text-based learning objectives, access to the full suite of animations, flashcards, and a glossary.

Test Bank

Written by Linda Huang, University of Massachusetts Boston, and Cheryl D. Vaughan, Harvard University Division of Continuing Education, the revised and expanded Test Bank for *Essential Cell Biology* includes 65–80 questions per chapter. Questions are available in multiple-choice, matching, fill-in-the-blank, and short-answer formats, with many using art from the textbook. All questions are tagged to Bloom's taxonomy level, learning objective, book section, and difficulty level, allowing instructors to easily create meaningful exams. The Test Bank is available in ExamView and as downloadable PDFs from wwnorton.com/instructors.

Animations and Videos

Streaming links give access to more than 130 videos and animations, bringing the concepts of cell biology to life. The movies are correlated with each chapter and callouts are highlighted in color.

Figure-integrated Lecture Outlines

All of the figures are integrated in PowerPoint, along with the section and concept headings from the text, to give instructors a head start creating lectures for their course.

Image Files

Every figure and photograph in the book is available for download in PowerPoint and JPG formats from wwnorton.com/instructors.

STUDENT RESOURCES

digital.wwnorton.com/ecb5

Animations and Videos

Streaming links give access to more than 130 videos and animations, bringing the concepts of cell biology to life. Animations can also be accessed via the ebook and in select Smartwork5 questions. The movies are correlated with each chapter and callouts are highlighted in color.

Student Site

Resources for self-study are available on the student site, including multiple-choice quizzes, cell explorer slides, challenge and concept questions, flashcards, and a glossary.

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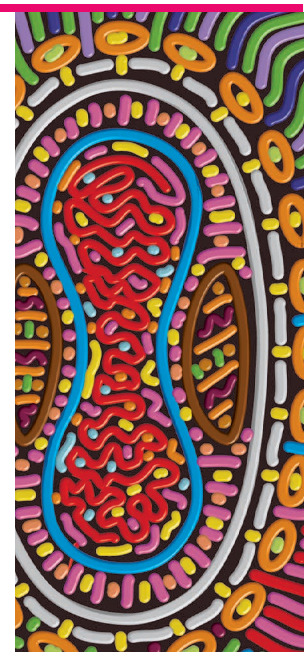

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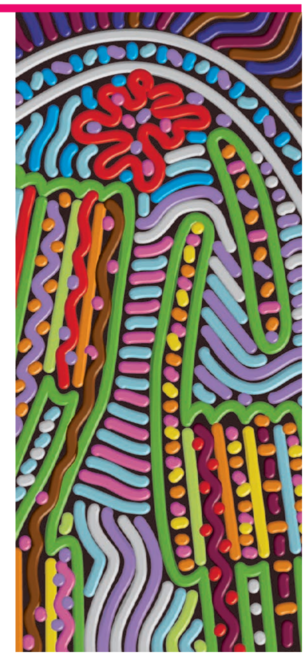

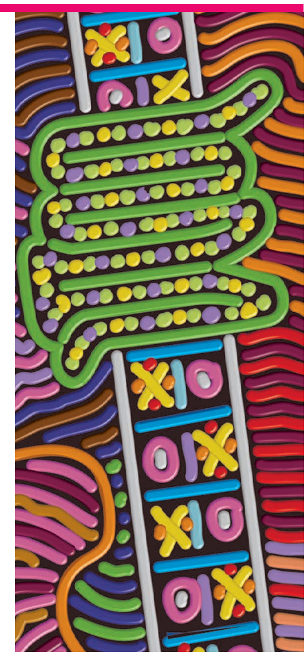

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CHAPTER **ONE** 1

Cells: The Fundamental Units of Life

What does it mean to be living? Petunias, people, and pond scum are all alive; stones, sand, and summer breezes are not. But what are the fundamental properties that characterize living things and distinguish them from nonliving matter?

The answer hinges on a basic fact that is taken for granted now but marked a revolution in thinking when first established more than 175 years ago. All living things (or *organisms*) are built from **cells**: small, membrane-enclosed units filled with a concentrated aqueous solution of chemicals and endowed with the extraordinary ability to create copies of themselves by growing and then dividing in two. The simplest forms of life are solitary cells. Higher organisms, including ourselves, are communities of cells derived by growth and division from a single founder cell. Every animal or plant is a vast colony of individual cells, each of which performs a specialized function that is integrated by intricate systems of cell-to-cell communication.

Cells, therefore, are the fundamental units of life. Thus it is to *cell biology*—the study of cells and their structure, function, and behavior—that we look for an answer to the question of what life is and how it works. With a deeper understanding of cells, we can begin to tackle the grand historical problems of life on Earth: its mysterious origins, its stunning diversity produced by billions of years of evolution, and its invasion of every conceivable habitat on the planet. At the same time, cell biology can provide us with answers to the questions we have about ourselves: Where did we come from? How do we develop from a single fertilized egg cell? How is each of us similar to—yet different from—everyone else on Earth? Why do we get sick, grow old, and die?

In this chapter, we introduce the concept of cells: what they are, where they come from, and how we have learned so much about them. We begin by looking at the great variety of forms that cells can adopt, and we take a preliminary glimpse at the chemical machinery that all cells have in common. We then consider how cells are made visible under the microscope and what we see when we peer inside them. Finally, we discuss how we can exploit the similarities of living things to achieve a coherent understanding of all forms of life on Earth—from the tiniest bacterium to the mightiest oak.

UNITY AND DIVERSITY OF CELLS

Biologists estimate that there may be up to 100 million distinct species of living things on our planet—organisms as different as a dolphin and a rose or a bacterium and a butterfly. Cells, too, differ vastly in form and function. Animal cells differ from those in a plant, and even cells within a single multicellular organism can differ wildly in appearance and activity. Yet despite these differences, all cells share a fundamental chemistry and other common features.

In this section, we take stock of some of the similarities and differences among cells, and we discuss how all present-day cells appear to have evolved from a common ancestor.

Cells Vary Enormously in Appearance and Function

When comparing one cell and another, one of the most obvious places to start is with size. A bacterial cell—say a *Lactobacillus* in a piece of cheese—is a few **micrometers**, or μm, in length. That's about 25 times smaller than the width of a human hair. At the other extreme, a frog egg—which is also a single cell—has a diameter of about 1 millimeter (mm). If we scaled them up to make the *Lactobacillus* the size of a person, the frog egg would be half a mile high.

Cells vary just as widely in their shape (**Figure 1–1**). A typical nerve cell in your brain, for example, is enormously extended: it sends out its electrical signals along a single, fine protrusion (an axon) that is 10,000 times longer than it is thick, and the cell receives signals from other nerve cells through a collection of shorter extensions that sprout from its body like the branches of a tree (see Figure 1–1A). A pond-dwelling *Paramecium*, on the other hand, is shaped like a submarine and is covered with thousands of *cilia*—hairlike projections whose sinuous, coordinated beating sweeps the cell forward, rotating as it goes (Figure 1–1B). A cell in the surface layer of a plant is squat and immobile, surrounded by a rigid box of cellulose with an outer waterproof coating of wax (Figure 1–1C). A macrophage in the body of an animal, by contrast, crawls through tissues, constantly pouring itself into new shapes, as it searches for and engulfs debris, foreign microorganisms, and dead or dying cells (Figure 1–1D). A fission yeast is shaped like a rod (Figure 1–1E), whereas a budding yeast is delightfully spherical (see Figure 1–14). And so on.

Cells are also enormously diverse in their chemical requirements. Some require oxygen to live; for others the gas is deadly. Some cells consume little more than carbon dioxide (CO_2), sunlight, and water as their raw materials; others need a complex mixture of molecules produced by other cells.

These differences in size, shape, and chemical requirements often reflect differences in cell function. Some cells are specialized factories for the production of particular substances, such as hormones, starch, fat, latex, or pigments. Others, like muscle cells, are engines that burn fuel to do mechanical work. Still others are electricity generators, like the modified muscle cells in the electric eel.

Some modifications specialize a cell so much that the cell ceases to proliferate, thus producing no descendants. Such specialization would be senseless for a cell that lived a solitary life. In a multicellular organism, however, there is a division of labor among cells, allowing some cells to become specialized to an extreme degree for particular tasks and leaving them dependent on their fellow cells for many basic requirements. Even the most basic need of all, that of passing on the genetic instructions of the organism to the next generation, is delegated to specialists—the egg and the sperm.

Living Cells All Have a Similar Basic Chemistry

Despite the extraordinary diversity of plants and animals, people have recognized from time immemorial that these organisms have something in common, something that entitles them all to be called living things. But while it seemed easy enough to recognize life, it was remarkably difficult to say in what sense all living things were alike. Textbooks had to settle for defining life in abstract general terms related to growth, reproduction, and an ability to actively alter their behavior in response to the environment.

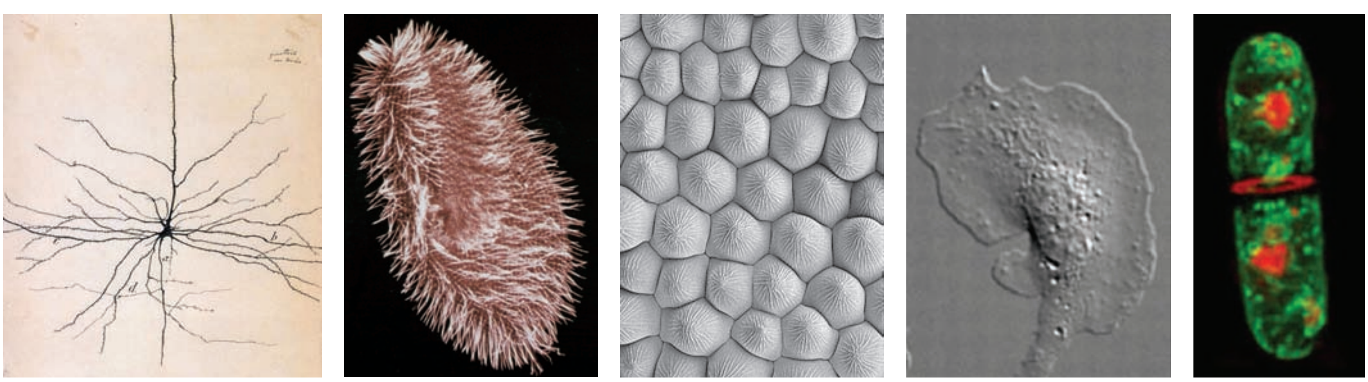
The discoveries of biochemists and molecular biologists have provided an elegant solution to this awkward situation. Although the cells of all living things are enormously varied when viewed from the outside, they are fundamentally similar inside. We now know that cells resemble one another to an astonishing degree in the details of their chemistry. They are composed of the same sorts of molecules, which participate in the same types of chemical reactions (discussed in Chapter 2). In all organisms, genetic information—in the form of *genes*—is carried in DNA molecules. This information is written in the same chemical code, constructed out of the same chemical building blocks, interpreted by essentially the same chemical machinery, and replicated in the same way when a cell or

QUESTION 1–1

"Life" is easy to recognize but difficult to define. According to one popular biology text, living things:

1. Are highly organized compared to natural inanimate objects.
2. Display homeostasis, maintaining a relatively constant internal environment.
3. Reproduce themselves.
4. Grow and develop from simple beginnings.
5. Take energy and matter from the environment and transform it.
6. Respond to stimuli.
7. Show adaptation to their environment.

Score a person, a vacuum cleaner, and a potato with respect to these characteristics.



(A) 100 μm (B) 25 μm (C) 25 μm (D) 5 μm (E) 3 μm

Figure 1–1 Cells come in a variety of shapes and sizes. Note the very different scales of these micrographs. (A) Drawing of a single nerve cell from a mammalian brain. This cell has a single, unbranched extension (axon), projecting toward the top of the image, through which it sends electrical signals to other nerve cells, and it possesses a huge branching tree of projections (dendrites) through which it receives signals from as many as 100,000 other nerve cells. (B) *Paramecium.* This protozoan—a single giant cell—swims by means of the beating cilia that cover its surface. (C) The surface of a snapdragon flower petal displays an orderly array of tightly packed cells. (D) A macrophage spreads itself out as it patrols animal tissues in search of invading microorganisms. (E) A fission yeast is caught in the act of dividing in two. The medial septum (stained *red* with a fluorescent dye) is forming a wall between the two nuclei (also stained *red*) that have been separated into the two daughter cells; in this image, the cells' membranes are stained with a *green* fluorescent dye. (A, Herederos de Santiago Ramón y Cajal, 1899; B, courtesy of Anne Aubusson Fleury, Michel Laurent, and André Adoutte; C, courtesy of Kim Findlay; D, from P.J. Hanley et al., *Proc. Natl Acad. Sci. USA* 107:12145–12150, 2010. With permission from National Academy of Sciences; E, courtesy of Janos Demeter and Shelley Sazer.)

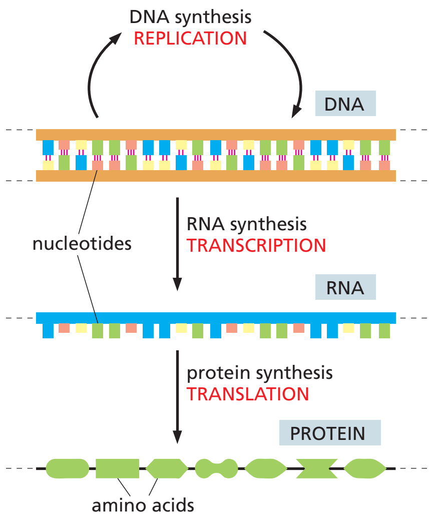


Figure 1–2 In all living cells, genetic information flows from DNA to RNA (transcription) and from RNA to protein (translation)—an arrangement known as the central dogma. The sequence of nucleotides in a particular segment of DNA (a gene) is transcribed into an RNA molecule, which can then be translated into the linear sequence of amino acids of a protein. Only a small part of the gene, RNA, and protein is shown.

organism reproduces. Thus, in every cell, long polymer chains of **DNA** are made from the same set of four monomers, called *nucleotides*, strung together in different sequences like the letters of an alphabet. The information encoded in these DNA molecules is read out, or *transcribed*, into a related set of polynucleotides called **RNA**. Although some of these RNA molecules have their own regulatory, structural, or chemical activities, most are *translated* into a different type of polymer called a **protein**. This flow of information—from DNA to RNA to protein—is so fundamental to life that it is referred to as the *central dogma* (**Figure 1–2**).

The appearance and behavior of a cell are dictated largely by its protein molecules, which serve as structural supports, chemical catalysts, molecular motors, and much more. Proteins are built from *amino acids*, and all organisms use the same set of 20 amino acids to make their proteins. But the amino acids are linked in different sequences, giving each type of protein molecule a different three-dimensional shape, or *conformation*, just as different sequences of letters spell different words. In this way, the same basic biochemical machinery has served to generate the whole gamut of life on Earth (**Figure 1–3**).

Living Cells Are Self-Replicating Collections of Catalysts

One of the most commonly cited properties of living things is their ability to reproduce. For cells, the process involves duplicating their genetic material and other components and then dividing in two—producing a pair of daughter cells that are themselves capable of undergoing the same cycle of replication.

It is the special relationship between DNA, RNA, and proteins—as outlined in the central dogma (see Figure 1–2)—that makes this self-replication possible. DNA encodes information that ultimately directs the assembly of proteins: the sequence of nucleotides in a molecule of DNA dictates the sequence of amino acids in a protein. Proteins, in turn, catalyze the replication of DNA and the transcription of RNA, and they participate in the translation of RNA into proteins. This feedback loop between proteins and polynucleotides underlies the self-reproducing behavior of living things (**Figure 1–4**). We discuss this complex interdependence between DNA, RNA, and proteins in detail in Chapters 5 through 8.

In addition to their roles in polynucleotide and protein synthesis, proteins also catalyze the many other chemical reactions that keep the self-replicating system shown in Figure 1–4 running. A living cell can break down

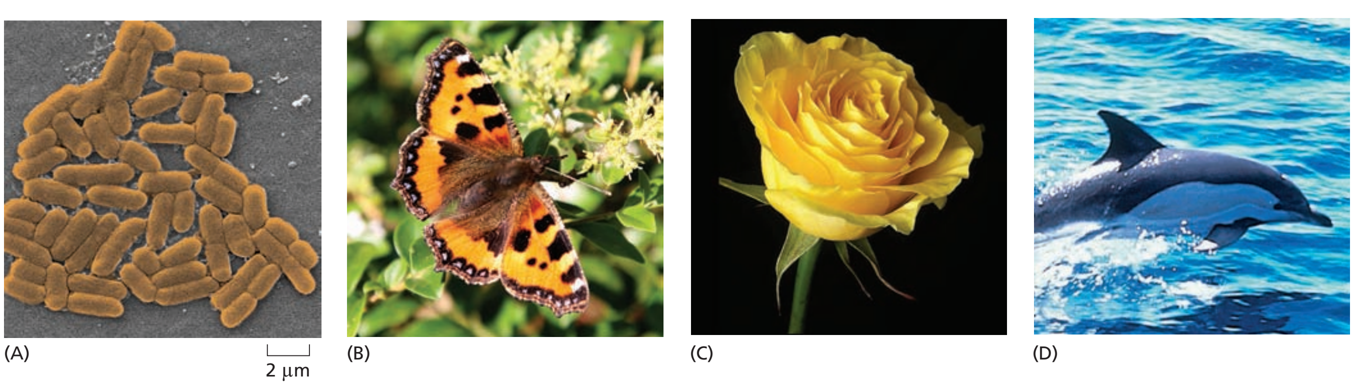


Figure 1–3 All living organisms are constructed from cells. (A) A colony of bacteria, (B) a butterfly, (C) a rose, and (D) a dolphin are all made of cells that have a fundamentally similar chemistry and operate according to the same basic principles. (A, courtesy of Janice Carr; D, courtesy of Jonathan Gordon, IFAW.)

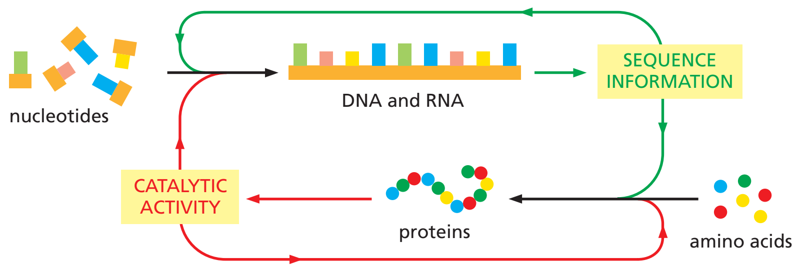


Figure 1–4 Life is an autocatalytic process. DNA and RNA provide the sequence information (*green* arrows) that is used to produce proteins and to copy themselves. Proteins, in turn, provide the catalytic activity (*red* arrows) needed to synthesize DNA, RNA, and themselves. Together, these feedback loops create the self-replicating system that endows living cells with their ability to reproduce.

nutrients and use the products to both make the building blocks needed to produce polynucleotides, proteins, and other cell constituents and to generate the energy needed to power these biosynthetic processes. We discuss these vital metabolic reactions in detail in Chapters 3 and 13.

Only living cells can perform these astonishing feats of self-replication. Viruses also contain information in the form of DNA or RNA, but they do not have the ability to reproduce by their own efforts. Instead, they parasitize the reproductive machinery of the cells that they invade to make copies of themselves. Thus, viruses are not truly considered living. They are merely chemical zombies: inert and inactive outside their host cells but able to exert a malign control once they gain entry. We review the life cycle of viruses in Chapter 9.

All Living Cells Have Apparently Evolved from the Same Ancestral Cell

When a cell replicates its DNA in preparation for cell division, the copying is not always perfect. On occasion, the instructions are corrupted by *mutations* that change the sequence of nucleotides in the DNA. For this reason, daughter cells are not necessarily exact replicas of their parent.

Mutations can create offspring that are changed for the worse (in that they are less able to survive and reproduce), changed for the better (in that they are better able to survive and reproduce), or changed in a neutral way (in that they are genetically different but equally viable). The struggle for survival eliminates the first, favors the second, and tolerates the third. The genes of the next generation will be the genes of the survivors.

For many organisms, the pattern of heredity may be complicated by sexual reproduction, in which two cells of the same species fuse, pooling their DNA. The genetic cards are then shuffled, re-dealt, and distributed in new combinations to the next generation, to be tested again for their ability to promote survival and reproduction.

These simple principles of genetic change and selection, applied repeatedly over billions of cell generations, are the basis of **evolution**—the process by which living species become gradually modified and adapted to their environment in more and more sophisticated ways. Evolution offers a startling but compelling explanation of why present-day cells are so similar in their fundamentals: they have all inherited their genetic instructions from the same common ancestral cell. It is estimated that this cell existed between 3.5 and 3.8 billion years ago, and we must suppose that it contained a prototype of the universal machinery of all life on Earth today. Through a very long process of mutation and natural selection, the descendants of this ancestral cell have gradually diverged to fill every habitat on Earth with organisms that exploit the potential of the machinery in a seemingly endless variety of ways.

QUESTION 1–2

Mutations are mistakes in the DNA that change the genetic plan from that of the previous generation. Imagine a shoe factory. Would you expect mistakes (i.e., unintentional changes) in copying the shoe design to lead to improvements in the shoes produced? Explain your answer.

Genes Provide Instructions for the Form, Function, and Behavior of Cells and Organisms

A cell's **genome**—that is, the entire sequence of nucleotides in an organism's DNA—provides a genetic program that instructs a cell how to behave. For the cells of plant and animal embryos, the genome directs the growth and development of an adult organism with hundreds of different cell types. Within an individual plant or animal, these cells can be extraordinarily varied, as we discuss in detail in Chapter 20. Fat cells, skin cells, bone cells, and nerve cells seem as dissimilar as any cells could be. Yet all these *differentiated cell types* are generated during embryonic development from a single fertilized egg cell, and they contain identical copies of the DNA of the species. Their varied characters stem from the way that individual cells use their genetic instructions. Different cells *express* different genes: that is, they use their genes to produce some RNAs and proteins and not others, depending on their internal state and on cues that they and their ancestor cells have received from their surroundings—mainly signals from other cells in the organism.

The DNA, therefore, is not just a shopping list specifying the molecules that every cell must make, and a cell is not just an assembly of all the items on the list. Each cell is capable of carrying out a variety of biological tasks, depending on its environment and its history, and it selectively uses the information encoded in its DNA to guide its activities. Later in this book, we will see in detail how DNA defines both the parts list of the cell and the rules that decide when and where these parts are to be made.

CELLS UNDER THE MICROSCOPE

Today, we have access to many powerful technologies for deciphering the principles that govern the structure and activity of the cell. But cell biology started without these modern tools. The earliest cell biologists began by simply looking at tissues and cells, and later breaking them open or slicing them up, attempting to view their contents. What they saw was to them profoundly baffling—a collection of tiny objects whose relationship to the properties of living matter seemed an impenetrable mystery. Nevertheless, this type of visual investigation was the first step toward understanding tissues and cells, and it remains essential today in the study of cell biology.

Cells were not made visible until the seventeenth century, when the **microscope** was invented. For hundreds of years afterward, all that was known about cells was discovered using this instrument. *Light microscopes* use visible light to illuminate specimens, and they allowed biologists to see for the first time the intricate structure that underpins all living things.

Although these instruments now incorporate many sophisticated improvements, the properties of light—specifically its wavelength—limit the fineness of detail these microscopes reveal. *Electron microscopes*, invented in the 1930s, go beyond this limit by using beams of electrons instead of beams of light as the source of illumination; because electrons have a much shorter wavelength, these instruments greatly extend our ability to see the fine details of cells and even render some of the larger molecules visible individually.

In this section, we describe various forms of light and electron microscopy. These vital tools in the modern cell biology laboratory continue to improve, revealing new and sometimes surprising details about how cells are built and how they operate.

The Invention of the Light Microscope Led to the Discovery of Cells

By the seventeenth century, glass lenses were powerful enough to permit the detection of structures invisible to the naked eye. Using an instrument equipped with such a lens, Robert Hooke examined a piece of cork and in 1665 reported to the Royal Society of London that the cork was composed of a mass of minute chambers. He called these chambers "cells," based on their resemblance to the simple rooms occupied by monks in a monastery. The name stuck, even though the structures Hooke described were actually the cell walls that remained after the plant cells living inside them had died. Later, Hooke and his Dutch contemporary Antoni van Leeuwenhoek were able to observe living cells, seeing for the first time a world teeming with motile microscopic organisms.

For almost 200 years, such instruments—the first light microscopes—remained exotic devices, available only to a few wealthy individuals. It was not until the nineteenth century that microscopes began to be widely used to look at cells. The emergence of cell biology as a distinct science was a gradual process to which many individuals contributed, but its official birth is generally said to have been signaled by two publications: one by the botanist Matthias Schleiden in 1838 and the other by the zoologist Theodor Schwann in 1839. In these papers, Schleiden and Schwann documented the results of a systematic investigation of plant and animal tissues with the light microscope, showing that cells were the universal building blocks of all living tissues. Their work, and that of other nineteenth-century microscopists, slowly led to the realization that all living cells are formed by the growth and division of existing cells—a principle sometimes referred to as the *cell theory* (**Figure 1–5**). The implication that living organisms do not arise spontaneously but can be generated only from existing organisms was hotly contested, but it was finally confirmed

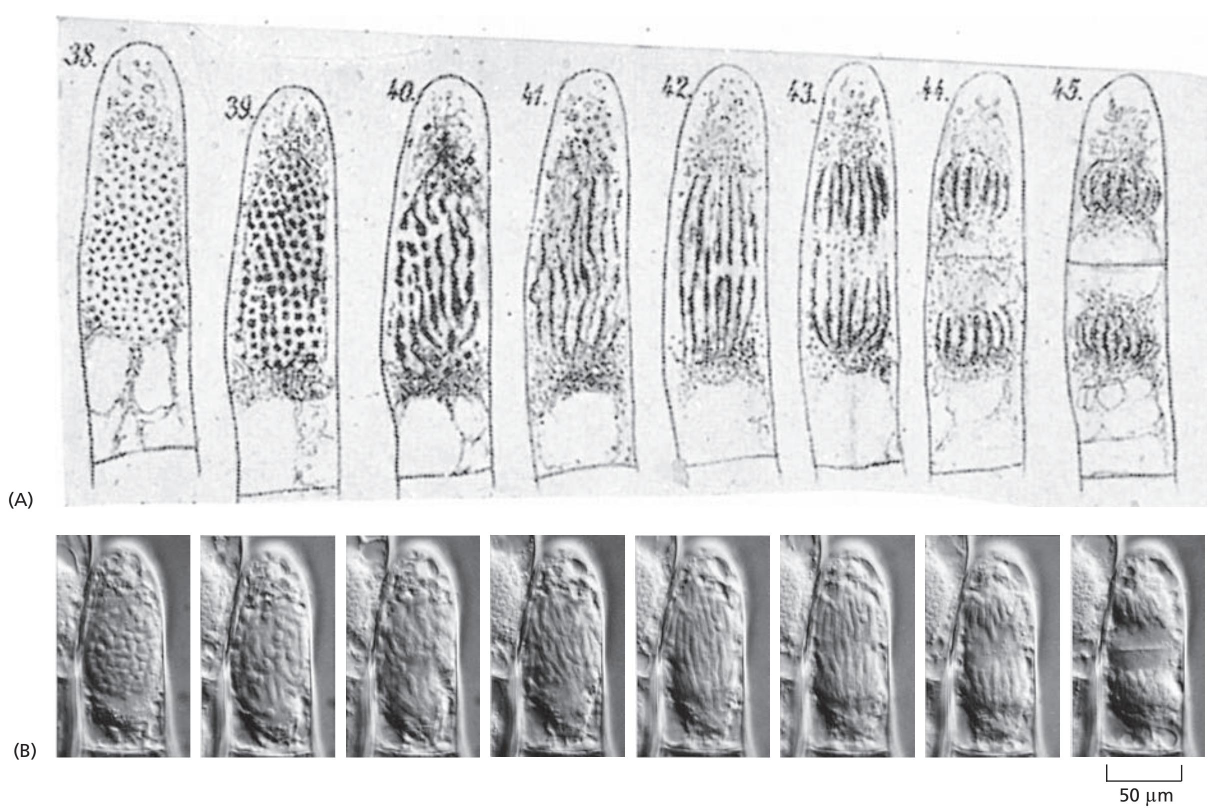


Figure 1–5 New cells form by growth and division of existing cells. (A) In 1880, Eduard Strasburger drew a living plant cell (a hair cell from a *Tradescantia* flower), which he observed dividing in two over a period of 2.5 hours. Inside the cell, DNA (*black*) can be seen condensing into chromosomes, which are then segregated into the two daughter cells. (B) A comparable living plant cell photographed through a modern light microscope. (B, from P.K. Hepler, *J. Cell Biol.* 100:1363–1368, 1985. With permission from Rockefeller University Press.)

in the 1860s by an elegant set of experiments performed by Louis Pasteur (see Question 1–3).

QUESTION 1–3

You have embarked on an ambitious research project: to create life in a test tube. You boil up a rich mixture of yeast extract and amino acids in a flask, along with a sprinkling of the inorganic salts known to be essential for life. You seal the flask and allow it to cool. After several months, the liquid is as clear as ever, and there are no signs of life. A friend suggests that excluding the air was a mistake, since most life as we know it requires oxygen. You repeat the experiment, but this time you leave the flask open to the atmosphere. To your great delight, the liquid becomes cloudy after a few days, and, under the microscope, you see beautiful small cells that are clearly growing and dividing. Does this experiment prove that you managed to generate a novel life-form? How might you redesign your experiment to allow air into the flask, yet eliminate the possibility that contamination by airborne microorganisms is the explanation for the results? (For a ready-made answer, look up the classic experiments of Louis Pasteur.)

The principle that cells are generated only from preexisting cells and inherit their characteristics from them underlies all of biology and gives the subject a unique flavor: in biology, questions about the present are inescapably linked to conditions in the past. To understand why present-day cells and organisms behave as they do, we need to understand their history, all the way back to the misty origins of the first cells on Earth. Charles Darwin provided the key insight that makes this history comprehensible. His theory of evolution, published in 1859, explains how random variation and natural selection gave rise to diversity among organisms that share a common ancestry. When combined with the cell theory, the theory of evolution leads us to view all life, from its beginnings to the present day, as one vast family tree of individual cells. Although this book is primarily about how cells work today, we will encounter the theme of evolution again and again.

Light Microscopes Reveal Some of a Cell's Components

If a very thin slice is cut from a suitable plant or animal tissue and viewed using a light microscope, it is immediately apparent that the tissue is divided into thousands of small cells. In some cases, the cells are closely packed; in others, they are separated from one another by an *extracellular matrix*—a dense material often made of protein fibers embedded in a gel of long sugar chains. Each cell is typically about 5–20 μm in diameter. If care has been taken to keep the specimen alive, particles will be seen moving around inside its individual cells. On occasion, a cell may even be seen slowly changing shape and dividing into two (see Figure 1–5 and **Movie 1.1**).

Distinguishing the internal structure of a cell is difficult, not only because the parts are small, but also because they are transparent and mostly colorless. One way around the problem is to stain cells with dyes that color particular components differently (**Figure 1–6**). Alternatively, one can exploit the fact that cell components differ slightly from one another in refractive index, just as glass differs in refractive index from water, causing light rays to be deflected as they pass from the one medium into

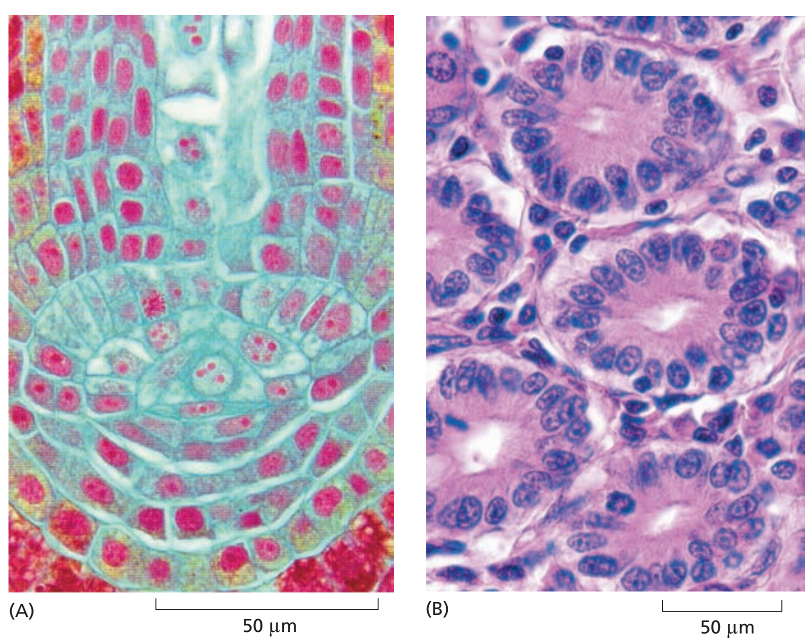


Figure 1–6 Cells form tissues in plants and animals. (A) Cells in the root tip of a fern. The DNA-containing nuclei are stained *red*, and each cell is surrounded by a thin cell wall (*light blue*). The *red* nuclei of densely packed cells are seen at the bottom corners of the preparation. (B) Cells in the crypts of the small intestine. Each crypt appears in this cross section as a ring of closely packed cells (with nuclei stained *blue*). The ring is surrounded by extracellular matrix, which contains the scattered cells that produced most of the matrix components. (A, courtesy of James Mauseth; B, Jose Luis Calvo/Shutterstock.)

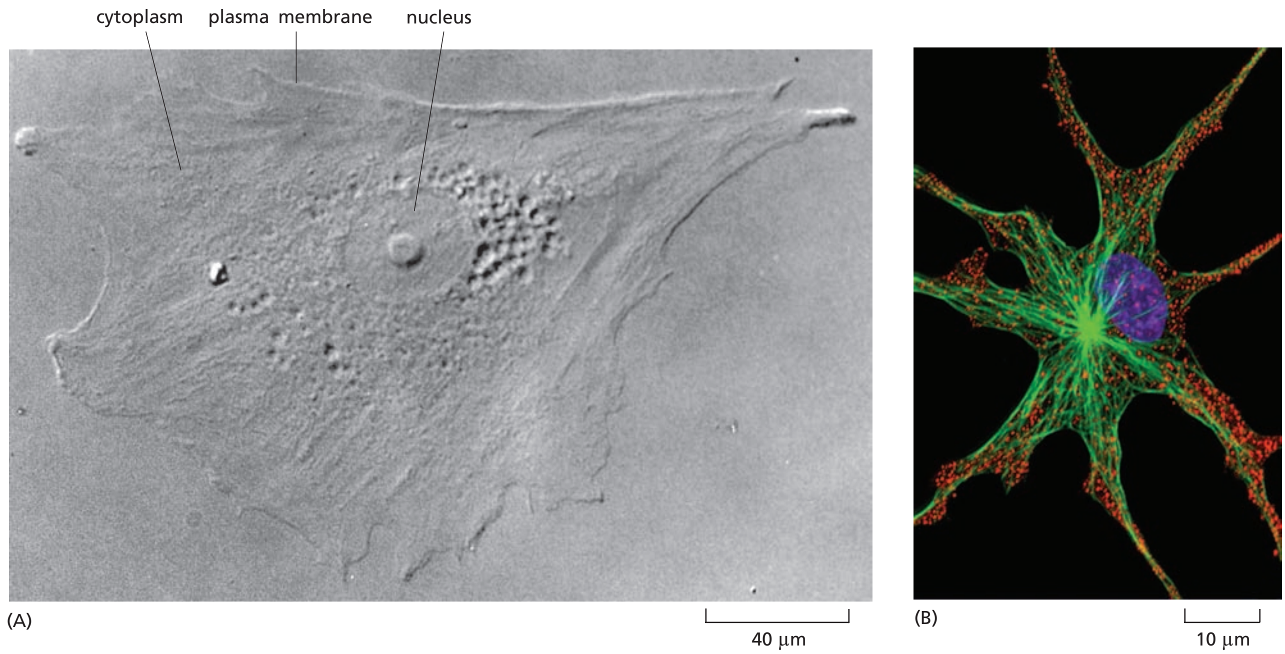


Figure 1–7 Some of the internal structures of a cell can be seen with a light microscope. (A) A cell taken from human skin and grown in culture was photographed through a light microscope using interference-contrast optics (described in Panel 1–1, pp. 12–13). The nucleus is especially prominent, as is the small, round nucleolus within it (discussed in Chapter 5 and see Panel 1–2, p. 25). (B) A pigment cell from a frog, stained with fluorescent dyes and viewed with a confocal fluorescence microscope (discussed in Panel 1–1). The nucleus is shown in *purple*, the pigment granules in *red*, and the microtubules—a class of protein filaments in the cytoplasm—in *green*. (A, courtesy of Casey Cunningham; B, courtesy of Stephen Rogers and the Imaging Technology Group of the Beckman Institute, University of Illinois, Urbana.)

the other. The small differences in refractive index can be made visible by specialized optical techniques, and the resulting images can be enhanced further by electronic processing (**Figure 1–7A**).

As shown in Figures 1–6B and 1–7A, typical animal cells visualized in these ways have a distinct anatomy. They have a sharply defined boundary, indicating the presence of an enclosing membrane, the **plasma membrane**. A large, round structure, the *nucleus*, is prominent near the middle of the cell. Around the nucleus and filling the cell's interior is the **cytoplasm**, a transparent substance crammed with what seems at first to be a jumble of miscellaneous objects. With a good light microscope, one can begin to distinguish and classify some of the specific components in the cytoplasm, but structures smaller than about 0.2 μm—about half the wavelength of visible light—cannot normally be resolved; points closer than this are not distinguishable and appear as a single blur.

In recent years, however, new types of light microscope called **fluorescence microscopes** have been developed that use sophisticated methods of illumination and electronic image processing to see fluorescently labeled cell components in much finer detail (**Figure 1–7B**). The most recent super-resolution fluorescence microscopes, for example, can push the limits of resolution down even further, to about 20 nanometers (nm). That is the size of a single **ribosome**, a large macromolecular complex in which RNAs are translated into proteins. These super-resolution techniques are described further in Panel 1–1 (pp. 12–13).

The Fine Structure of a Cell Is Revealed by Electron Microscopy

For the highest magnification and best resolution, one must turn to an **electron microscope**, which can reveal details down to a few nanometers. Preparing cell samples for the electron microscope is a painstaking process. Even for light microscopy, a tissue often has to be *fixed* (that is, preserved by pickling in a reactive chemical solution), supported by *embedding* in a solid wax or resin, cut, or *sectioned,* into thin slices, and *stained* before it is viewed. (The tissues in Figure 1–6 were prepared in