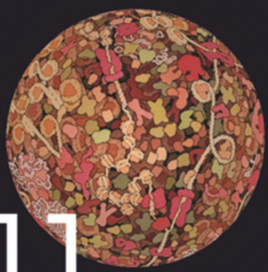

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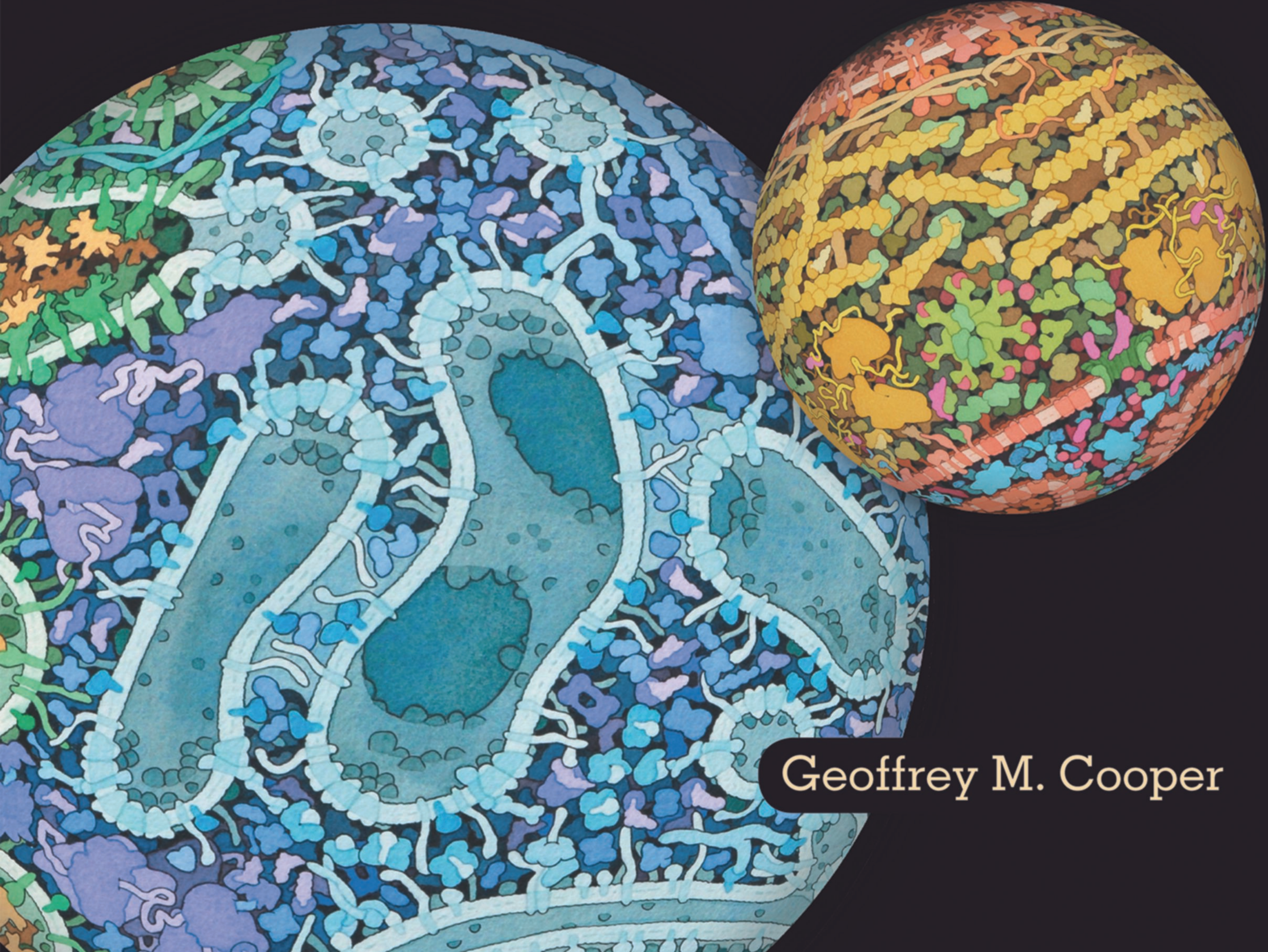

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The Cell

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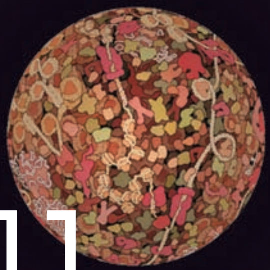

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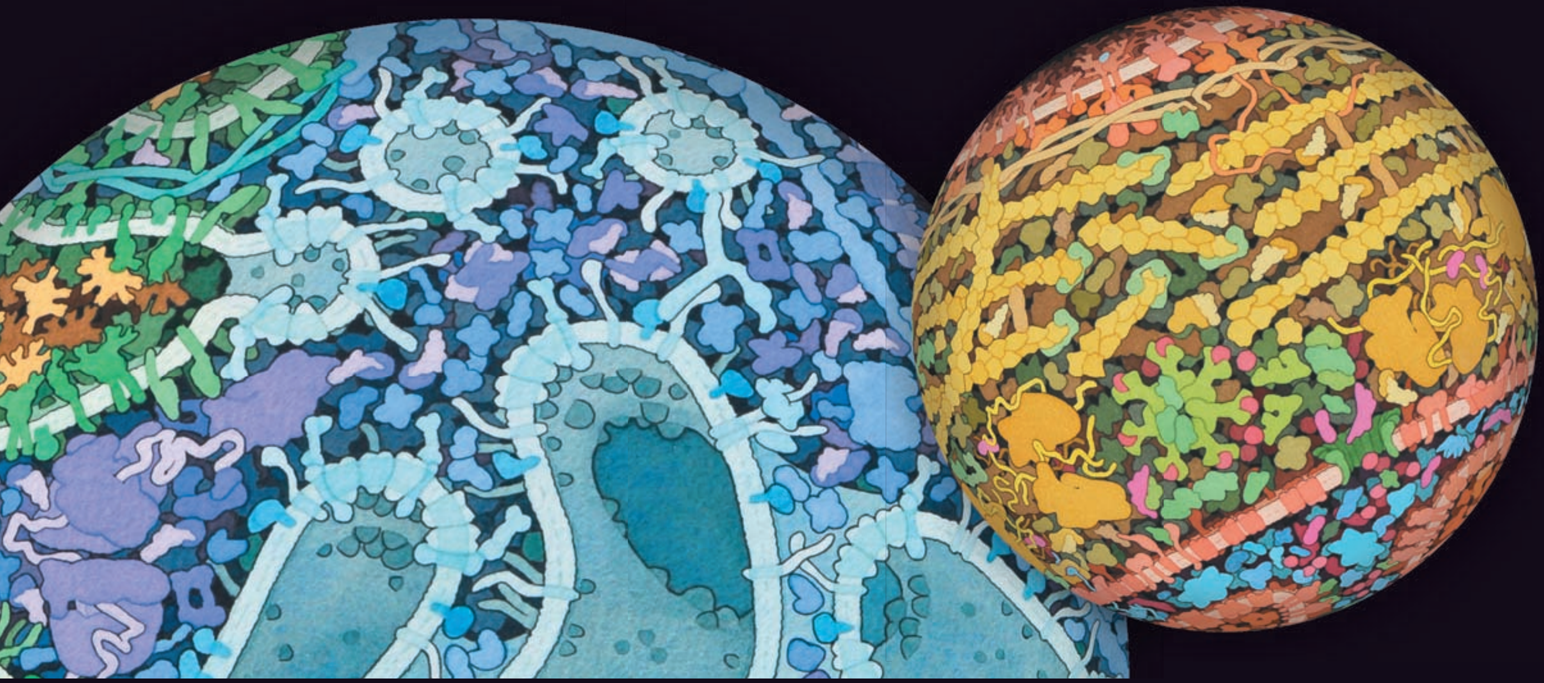

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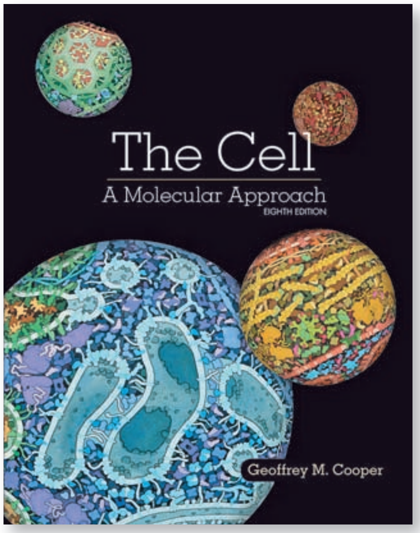

The Cover

The cover is a composite of David S. Goodsell paintings from previous editions of *The Cell*. They illustrate formation of a clathrin-coated pit, the interior of a nucleus, apoptosis, and formation of an autophagosome (clockwise from the upper left).

The Artist

David S. Goodsell is an Associate Professor of Molecular Biology at the Scripps Research Institute. His illustrated books, *The Machinery of Life* and *Our Molecular Nature*, explore biological molecules and their diverse roles within living cells, and his new book, *Bionanotechnology: Lessons from Nature*, presents the growing connections between biology and nanotechnology. More information may be found at: http://mgl.scripps.edu/people/goodsell

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About the Author

Geoffrey M. Cooper is a Professor of Biology at Boston University. Receiving a Ph.D. in Biochemistry from the University of Miami in 1973, he pursued postdoctoral work with Howard Temin at the University of Wisconsin, where he developed gene transfer assays to characterize the proviral DNAs of Rous sarcoma virus and related retroviruses. He then joined the faculty of Dana-Farber Cancer Institute and Harvard Medical School in 1975, where he pioneered the discovery of oncogenes in human cancers. He moved to Boston University as Chair of Biology in 1998 and subsequently served as Associate Dean of the Faculty for Natural Sciences, as well as teaching undergraduate cell biology and continuing his research on the roles of oncogenes in the signaling pathways that regulate cell proliferation and programmed cell death. He has authored over 100 research papers, two textbooks on cancer, and an award-winning novel, *The Prize*, dealing with fraud in medical research.

Preface

Learning cell biology can be a daunting task because the field is so vast and rapidly moving, characterized by a continual explosion of new information. The challenge is how to master the fundamental concepts without becoming bogged down in details. Students need to understand the principles of cell biology and be able to appreciate new advances, rather than just memorizing "the facts" as we see them today. At the same time, the material must be presented in sufficient depth to thoughtfully engage students and provide a sound basis for further studies. The Eighth Edition of *The Cell* emphasizes the fundamental concepts of cell biology and includes new features designed to meet the needs of today's students and their teachers.

This edition of *The Cell* continues the goal of helping students understand the principles and concepts of cell biology while gaining an appreciation of the excitement and importance of ongoing research in this rapidly moving field. Our understanding of cell and molecular biology has progressed in many ways over the last three years, and these important advances have been incorporated into the current edition. Some of the most striking advances have continued to come from progress in genomics and understanding the complex mechanisms of gene regulation in higher eukaryotes. A new chapter in the current edition-—Transcriptional Regulation and Epigenetics—highlights these rapidly advancing areas. Other notable advances covered in the current edition include progress in proteomics, synthetic biology, mitochondrial replacement therapy, splicing therapy for Duchenne's muscular dystrophy, and immunotherapy of cancer.

Beyond incorporating new material, the Eighth Edition of *The Cell* has been extensively revised to improve its utility as a teachable text for today's students. It has become abundantly clear that teaching in the sciences is most effective when it is done with a focus on active student engagement. To facilitate this and to avoid overwhelming students with too much information, I have minimized unnecessary detail to focus on concepts and shorten the text. In addition, recognizing that students with many different backgrounds take cell biology, additional introductory material on the nature of chemical bonds and thermodynamics has been added. Even with these additions, *The Cell* has been substantially shortened, ensuring that it remains an accessible and readable text for undergraduates who are taking their first course in cell and molecular biology.

The reorganization of this edition includes the division of each chapter into self-contained sections, enabling instructors to readily change the order in which material is covered. To optimize student engagement, each section begins with Learning Objectives, includes marginal notes that highlight key concepts, and concludes with a summary and expanded series of questions.

The questions in this edition span several levels of Bloom's taxonomy, ranging from knowledge and comprehension to analysis and synthesis.

Distinguishing features of *The Cell* include the Molecular Medicine and Key Experiment essays, which highlight clinical applications and describe seminal research papers, respectively. Additional questions have been added to these essays, designed to focus attention on key aspects of the material and give students a sense of how progress in our field is made. A new feature of this edition is the addition of Data Analysis Problems to the end of each chapter. These problems, which present data and figures from original research papers, engage students in the analysis of experimental methods and results. They were included in the Instructor's Resource Library of the Seventh Edition and a number of instructors found them to be a valuable resource, so a selection has been incorporated directly into the text of the current edition (with answers in the back of the book). Like the Key Experiment and Molecular Medicine essays, they provide excellent material for discussions and opportunities for student participation in active learning. An Active Learning Guide is included in the Instructor's Resource Library of this edition of *The Cell* to facilitate this important approach to student engagement.

My hope is that these changes to *The Cell* will stimulate students and help to convey the excitement and challenges of contemporary cell and molecular biology. The opportunities in our field are greater than ever, and today's students will be responsible for the advances of tomorrow.

Acknowledgments

I am particularly grateful to Marianna Pap and Jozsef Szeberenyi for providing the Data Analysis Problems.

The book has also benefited from the comments and suggestions of reviewers, colleagues, and instructors who used the previous edition. I am pleased to thank the following reviewers for their thoughtful comments and advice:

Nancy Bae	*Midwestern University*
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Jason Bush	*California State University, Fresno*
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Tricia A. Van Laar	*California State University Fresno*
Leticia Vega	*Barry University*
Liu Zhiming	*Eastern New Mexico University*

It is also a pleasure to thank Andy Sinauer for his continuing support of this project over the last twenty-plus years. Andy and his colleagues Dean Scudder and Chris Small were once again full of enthusiasm and ideas that made them a pleasure to work with. Ann Chiara did a beautiful job on the page layout of Donna DiCarlo's design. Tracy Marton was a fantastically helpful and supportive production editor, assisted in her efforts by Kathaleen Emerson. I am grateful for their patient and careful work, as well as that of their colleagues at Sinauer Associates.

Geoffrey M. Cooper
July, 2018

Organization and Features of *The Cell*, Eighth Edition

The Cell has been designed to be an approachable and teachable text that can be covered in a single semester while allowing students to master the material in the entire book. It is assumed that most students will have had introductory biology and general chemistry courses, but will not have had previous courses in organic chemistry, biochemistry, or molecular biology. Several aspects of the organization and features of the book will help students to approach and understand its subject matter.

Organization

The Cell is divided into four parts, each of which is self-contained, so that the order and emphasis of topics can be easily varied according to the needs of individual courses.

Part I provides background chapters on the evolution of cells, methods for studying cells, the chemistry of cells (including reviews of chemical bonds and thermodynamics), the fundamentals of molecular biology, and the fields of genomics and systems biology. For those students who have a strong background from either a comprehensive introductory biology course or a previous course in cell biology, various parts of these chapters can be skipped or used for review.

Part II focuses on the molecular biology of cells and contains chapters dealing with genome organization and sequences; DNA replication and repair; transcription and RNA processing; and the synthesis, processing, and regulation of proteins.

Part III contains chapters on cell structure and function, including chapters on the nucleus, cytoplasmic organelles, the cytoskeleton, the plasma membrane, and the extracellular matrix. This part of the book starts with coverage of the nucleus, which puts the molecular biology of Part II within the context of the eukaryotic cell, and then works outward through cytoplasmic organelles and the cytoskeleton to the plasma membrane and the exterior of the cell. These chapters are relatively self-contained, however, and could be used in a different order should that be more appropriate for a particular course.

Finally, Part IV focuses on the exciting and fast-moving area of cell regulation, including coverage of topics such as cell signaling, the cell cycle, programmed cell death, and stem cells. This part of the book concludes with a chapter on cancer, which synthesizes the consequences of defects in basic cell regulatory mechanisms.

Features

Several pedagogical features have been incorporated into *The Cell* in order to help students master and integrate its contents. These features are reviewed below as a guide to students studying from this book.

CHAPTER ORGANIZATION Each chapter is divided into three to five major sections, which are further divided into a similar number of subsections. An outline listing the major sections at the beginning of each chapter provides a brief overview of its contents. The major sections are numbered and self-contained to facilitate assignability.

LEARNING OBJECTIVES Each of the major sections begins with Learning Objectives, which help to organize and focus students' attention on the material.

SUMMARY AND QUESTIONS The major sections conclude with a review, including a section summary and questions (with answers in the back of the book). The questions span several levels of Bloom's taxonomy, ranging from knowledge and comprehension to analysis and synthesis.

MARGINAL NOTES Major points are summarized as marginal notes throughout the text, providing a running outline of the material.

KEY TERMS AND GLOSSARY Key terms are identified as boldfaced words when they are introduced in each chapter and defined in the glossary at the end of the book.

ILLUSTRATIONS AND MICROGRAPHS An illustration program of full-color art and micrographs has been carefully developed to complement and visually reinforce the text.

KEY EXPERIMENT AND MOLECULAR MEDICINE ESSAYS Each chapter contains either two Key Experiment essays or one Key Experiment and one Molecular Medicine essay. These features are designed to provide the student with a sense of both the experimental basis of cell and molecular biology and its applications to modern medicine. Additional questions have been added to these essays, designed to focus attention on key aspects of the material. These essays are also a useful basis for student discussions, which can be accompanied with a review of the original paper upon which the Key Experiments are based.

DATA ANALYSIS PROBLEMS Each chapter concludes with Data Analysis Problems that present data from original research papers, together with questions that engage students in the analysis of experimental methods and results (with answers in the back of the book). Like the Key Experiment and Molecular Medicine essays, the Data Analysis Problems provide excellent material for discussions and opportunities for student participation in active learning.

FYIs Each chapter contains sidebars that provide brief descriptive highlights of points of interest. The sidebars supplement the text and provide starting points for class discussion.

REFERENCES Two key references for each major section are included at the end of each chapter. Comprehensive lists of references are provided as an online supplement. Review articles and primary papers are distinguished by [R] and [P] designations, respectively.

ANIMATION AND VIDEO REFERENCES Boxes in the margin and end-of-chapter descriptions and a Web link (URL) direct students to the website's animations and videos.

Media and Supplements to Accompany *The Cell*, Eighth Edition

eBook (ISBN 9-781-60535-771-3)

The Cell, Eighth Edition, is available as an eBook in several formats, including RedShelf and VitalSource. All major mobile devices are supported.

For Students

Companion Website (www.oup.com/us/cooper8e)

The Companion Website for *The Cell,* Eighth Edition, provides students with a wide range of study and review materials and rich multimedia resources. The site, which is available free of charge (no access code required), includes the following resources:

- *Chapter Overviews*: Brief introductions to each chapter's content
- *Videos*: Online videos (referenced throughout the book) to help students understand complex cellular and molecular structures and processes
- *Animations*: Narrated animations (referenced throughout the book) of key concepts and processes
- *Micrographs*: Interactive micrographs illustrating cellular structure
- *Flashcards*: Study aids to help students learn the key terminology introduced in each chapter
- *In-book Reviews*: End-of-section questions to reinforce understanding of chapter material
- *References*: A comprehensive list of additional reference material for every chapter
- *Online Quizzes*: Two sets of questions for each chapter, assignable by the instructor (Adopting instructors must register online for their students to access the quizzes.)
    - Multiple-choice quizzes test comprehension of the chapter's key material.
    - Free-response questions ask students to apply what they have learned from the chapter.

- *Web Links*: Links that provide additional information about selected textbook topics
- *Complete Glossary*: Easily searchable guide to textbook terminology

Dashboard (www.oup.com/us/dashboard)

Dashboard delivers a wealth of automatically graded quizzes and study resources for *The Cell,* along with an interactive eBook, all in an intuitive, web-based learning environment.

For Instructors (available to qualified adopters)

Ancillary Resource Center (www.oup.com/us/cooper8e)

The Ancillary Resource Center includes a wide range of digital resources to aid in planning your course, presenting your lectures, and assessing your students. Contents include the following:

- *Instructor's Manual*:
    - **Active Learning Guide** with in-class exercises, references to relevant media resources, clicker questions, and more, all structured around the in-text Learning Objectives and designed to help you create a dynamic learning environment in the classroom
    - **Data Analysis Problems** to challenge students by working with experimental data
    - **Chapter overviews, reviews, and key terms**
- *Textbook Figures and Tables*: All available in PowerPoint slides and as both high- and low-resolution JPEGs
- *Animations*: The collection of animations from the Companion Website, for use in lectures
- *Online Quiz Questions*: *The Cell*'s Companion Website features prebuilt chapter quizzes that report into an online gradebook. Adopting instructors have access to these quizzes and can choose to either assign them or let students use them for review. (Instructors must register in order for their students to be able to take the quizzes.) Instructors also have the ability to add their own questions and create their own quizzes.
- *Test Bank*: Revised and updated for the Eighth Edition, the Test Bank includes more than 1,300 multiple-choice, fill-in-the-blank, true/false, and short-answer questions covering the full range of content in every chapter. All questions are referenced to Bloom's Taxonomy, making it easier to select the right balance of questions when building assessments.
- *Computerized Test Bank*: The entire test bank plus all of the online quiz questions are provided in Blackboard's Diploma software. Diploma makes it easy to assemble quizzes and exams from any combination of publisher-provided questions and instructor-created questions. In addition, quizzes and exams can be exported to many different course management systems, such as Blackboard and Moodle.

Dashboard (*www.oup.com/us/dashboard*)

Dashboard delivers an abundance of study resources and automatically graded quizzes for *The Cell* in an intuitive, web-based learning environment. A built-in, color-coded gradebook allows instructors to track student progress. Dashboard includes:

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PART I

Fundamentals and Foundations

Chapter 1 Introduction to Cells and Cell Research
Chapter 2 Molecules and Membranes
Chapter 3 Bioenergetics and Metabolism
Chapter 4 Fundamentals of Molecular Biology
Chapter 5 Genomics, Proteomics, and Systems Biology

CHAPTER

1

Introduction to Cells and Cell Research

Understanding the molecular biology of cells is one of the most active and fundamental areas of research in the biological sciences. This is true not only from the standpoint of basic science, but also with respect to the numerous applications of cell and molecular biology to medicine, biotechnology, and agriculture. Especially with the ability to obtain rapid sequences of complete genomes, progress in cell and molecular biology is opening new horizons in the practice of medicine. Striking examples include genome editing; the identification of genes that contribute to susceptibility to a variety of common diseases, such as heart disease, rheumatoid arthritis, and diabetes; the development of new drugs specifically targeted to interfere with the growth of cancer cells; and the potential use of stem cells to replace damaged tissues and treat patients suffering from conditions like diabetes, Parkinson's disease, Alzheimer's disease, and spinal cord injuries.

Because cell and molecular biology is such a rapidly growing field of research, it is important to understand its experimental basis as well as the current state of our knowledge. This chapter will therefore focus on how cells are studied, as well as review some of their basic properties. Appreciating the similarities and differences between cells is particularly important to understanding cell biology. The first section of this chapter discusses both the unity and the diversity of present-day cells in terms of their evolution from a common ancestor. On the one hand, all cells share common fundamental properties that have been conserved throughout evolution. For example, all cells employ DNA as their genetic material, are surrounded by plasma membranes, and use the same basic mechanisms for energy metabolism. On the other hand, present-day cells have evolved a variety of different lifestyles. Many organisms, such as bacteria, amoebas, and yeasts, consist of single cells that are capable of independent self-replication. More complex organisms are composed of collections of cells that function in a coordinated manner, with different cells specialized to perform particular tasks. The human body, for example, is composed of more than 200 different kinds of cells, each specialized for such distinctive functions as memory, sight, movement, and digestion. The diversity exhibited by the many different kinds of cells is striking; for example, consider the differences between bacteria and the cells of the human brain.

The fundamental similarities between different types of cells provide a unifying theme to cell biology, allowing the basic principles learned from experiments with one kind of cell to be extrapolated and generalized to other cell types. Several kinds of cells and organisms are widely used to study different aspects of cell and molecular biology; the second section of this chapter discusses some of the properties of these cells that make them particularly valuable as experimental models. Finally, it is important to recognize that progress in cell biology depends heavily on the availability of experimental tools that allow scientists to make new observations or conduct novel kinds of experiments. This introductory chapter therefore concludes with a discussion of some of the experimental approaches used to study cells, as well as a review of some of the major historical developments that have led to our current understanding of cell structure and function.

1.1 The Origin and Evolution of Cells

Learning Objectives

You should be able to:

- **Explain how the first cell originated.**
- **Describe the major steps in evolution of metabolism.**
- **Illustrate the structures of eukaryotic and prokaryotic cells.**
- **Outline the evolution of eukaryotic cells and multicellular organisms.**

Cells are divided into two main classes, initially defined by whether they contain a nucleus. Prokaryotic cells, such as bacteria, lack a nuclear envelope and are generally smaller and simpler than eukaryotic cells, which include the highly specialized cells of multicellular organisms. In spite of these differences, the same basic molecular mechanisms govern the lives of both prokaryotes and eukaryotes, indicating that all present-day cells are descended from a single primordial ancestor. How did this first cell develop? And how did the complexity and diversity exhibited by present-day cells evolve?

How did the first cell arise?

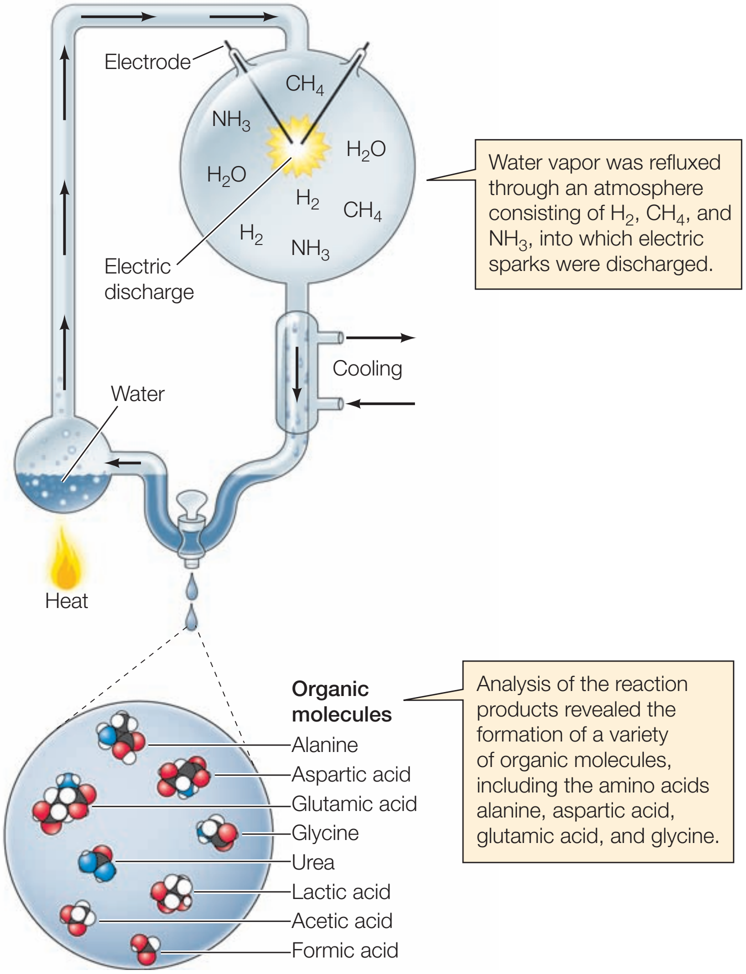
It appears that life first emerged at least 3.8 billion years ago, approximately 750 million years after Earth was formed. How life originated and how the first cell came into being are matters of speculation, since these events cannot be reproduced in the laboratory. Nonetheless, several types of experiments provide important evidence bearing on some steps of the process.

Organic molecules formed spontaneously in primitive Earth's atmosphere.

It was first suggested in the 1920s that simple organic molecules could form and spontaneously polymerize into macromolecules under the conditions thought to exist in primitive Earth's atmosphere. At the time life arose, the atmosphere of Earth is thought to have contained little or no free oxygen, instead consisting principally of CO_2 and N_2 in addition to smaller amounts of gases such as H_2, H_2S, and CO. Such an atmosphere provides reducing conditions in which organic molecules, given a source of energy such as sunlight or electrical discharge, can form spontaneously. The spontaneous formation of organic molecules was first demonstrated experimentally in the 1950s when Stanley Miller (then a graduate student) showed that the discharge of electric sparks into a mixture of H_2, CH_4, and NH_3, in the presence of water, leads to the formation of a variety of organic molecules, including several amino acids (**Figure 1.1**). Although Miller's experiments did not precisely reproduce the conditions of primitive Earth, they clearly demonstrated the plausibility of the spontaneous synthesis of organic molecules, providing the basic materials from which the first living organisms arose.

The next step in evolution was the formation of macromolecules. The monomeric building blocks of macromolecules have been demonstrated to polymerize spontaneously under plausible prebiotic conditions. Heating dry mixtures of amino acids, for example, results in their polymerization to form polypeptides. But the critical characteristic of the macromolecule from which life evolved must have been the ability to replicate itself. Only a macromolecule capable of directing the synthesis of new copies of itself would have been capable of reproduction and further evolution.

Of the two major classes of informational macromolecules in present-day cells (nucleic acids and proteins), only the nucleic acids are capable of directing their own self-replication. Nucleic acids can serve as templates for their own synthesis as a result of specific base pairing between complementary nucleotides (**Figure 1.2**). A critical step in understanding molecular evolution was thus reached in the early 1980s, when it was discovered in the laboratories of Sid Altman and Tom Cech that RNA is capable of catalyzing a number of chemical reactions, including the polymerization of nucleotides. Further studies have extended the known catalytic activities of RNA, including the description of RNA molecules that direct the synthesis of a new RNA strand from an RNA template. RNA is thus uniquely able to both serve as a template and to catalyze its own replication. Consequently, RNA is generally believed to have been the initial genetic system, and an early stage of chemical evolution is thought to have been based on self-replicating



Water vapor was refluxed through an atmosphere consisting of H_2, CH_4, and NH_3, into which electric sparks were discharged.

Analysis of the reaction products revealed the formation of a variety of organic molecules, including the amino acids alanine, aspartic acid, glutamic acid, and glycine.

Figure 1.1 Spontaneous formation of organic molecules

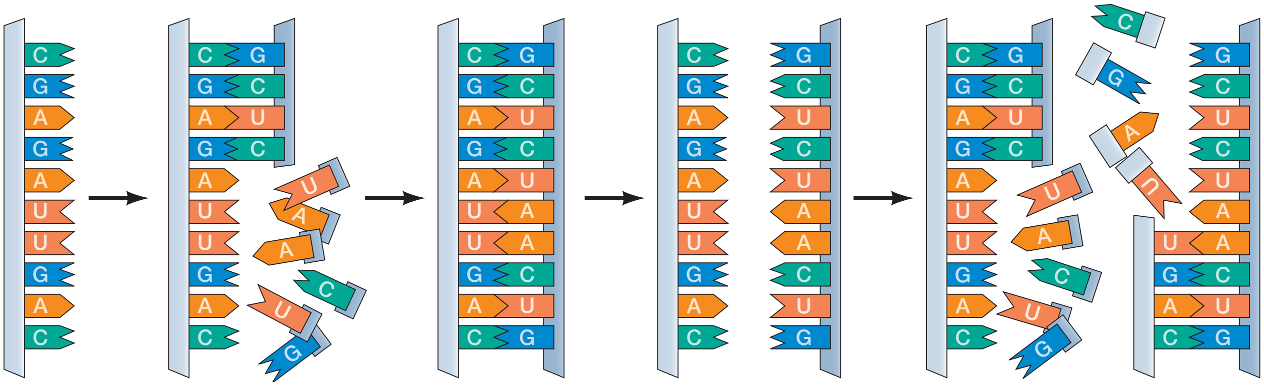


Figure 1.2 Self-replication of RNA Complementary pairing between nucleotides (adenine [A] with uracil [U] and guanine [G] with cytosine [C]) allows one strand of RNA to serve as a template for the synthesis of a new strand with the complementary sequence.

RNA can catalyze its own replication.

All present-day cells use the same genetic mechanisms.

Phospholipids are the basic components of biological membranes.

RNA molecules—a period of evolution known as the **RNA world**. Ordered interactions between RNA and amino acids then evolved into the present-day genetic code, and DNA eventually replaced RNA as the genetic material.

As discussed further in Chapter 4, all present-day cells use DNA as the genetic material and employ the same basic mechanisms for DNA replication and expression of the genetic information. **Genes** are the functional units of inheritance, corresponding to segments of DNA that encode proteins or RNA molecules. The nucleotide sequence of a gene is copied into RNA by a process called **transcription**. For RNAs that encode proteins, their nucleotide sequence is then used to specify the order of amino acids in a protein by a process called **translation**.

The first cell is presumed to have arisen by the enclosure of self-replicating RNA in a membrane composed of **phospholipids** (**Figure 1.3**). As discussed in detail in the next chapter, phospholipids are the basic components of all present-day biological membranes, including the plasma membranes of both prokaryotic and eukaryotic cells. The key characteristic of the phospholipids that form membranes is that they are **amphipathic** molecules, meaning that one portion of the molecule is soluble in water and another portion is not. Phospholipids have long, water-insoluble (**hydrophobic**) hydrocarbon chains joined to water-soluble (**hydrophilic**) head groups that contain phosphate. When placed in water, phospholipids spontaneously aggregate into a bilayer with their phosphate-containing head groups on the outside in contact with water and their hydrocarbon tails in the interior in contact with each other. Such a phospholipid bilayer forms a stable barrier between two aqueous compartments—for example, separating the interior of the cell from its external environment.

The enclosure of self-replicating RNA and associated molecules in a phospholipid membrane would thus have maintained them as a unit, capable of self-reproduction and further evolution. RNA-directed protein synthesis

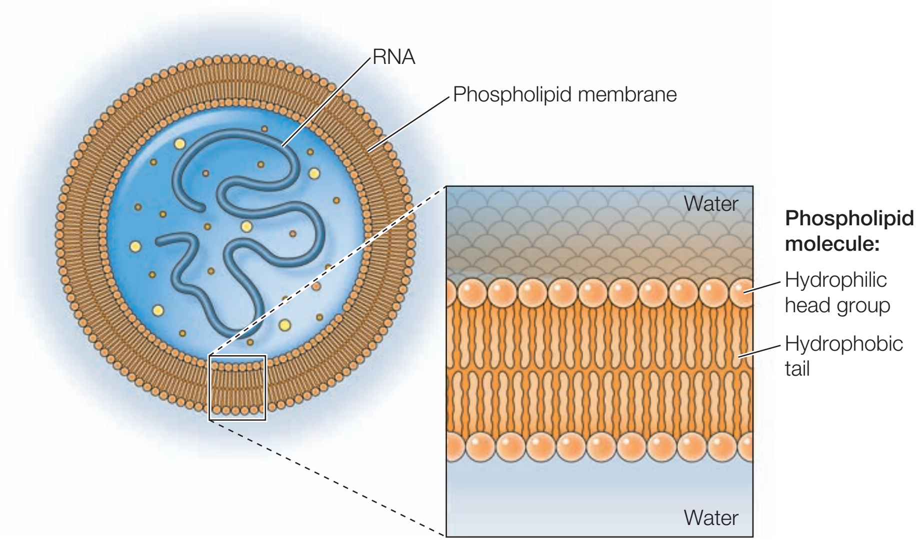


Figure 1.3 Enclosure of self-replicating RNA in a phospholipid membrane The first cell is thought to have arisen by the enclosure of self-replicating RNA and associated molecules in a membrane composed of phospholipids. Each phospholipid molecule has two long hydrophobic tails attached to a hydrophilic head group. The hydrophobic tails are buried in the lipid bilayer; the hydrophilic heads are exposed to water on both sides of the membrane.

may already have evolved by this time, in which case the first cell would have consisted of self-replicating RNA and its encoded proteins.

The evolution of metabolism

Because cells originated in a sea of organic molecules, they were able to obtain food and energy directly from their environment. But such a situation is self-limiting, so cells needed to evolve their own mechanisms for generating energy and synthesizing the molecules necessary for their replication. The generation and controlled utilization of metabolic energy is central to all cell activities, and the principal pathways of energy metabolism (discussed in detail in Chapter 3) are highly conserved in present-day cells. All cells use **adenosine 5′-triphosphate (ATP)** as their source of metabolic energy to drive the synthesis of cell constituents and carry out other energy-requiring activities, such as movement (e.g., muscle contraction). The mechanisms used by cells for the generation of ATP are thought to have evolved in three stages, corresponding to the evolution of glycolysis, photosynthesis, and oxidative metabolism (**Figure 1.4**). The development of these metabolic pathways changed Earth's atmosphere, thereby altering the course of further evolution.

The first cells obtained energy by glycolysis.

In the initially anaerobic atmosphere of Earth, the first energy-generating reactions presumably involved the breakdown of organic molecules in the absence of oxygen. These reactions are likely to have been a form of present-day **glycolysis**—the anaerobic breakdown of glucose to lactic acid, with the net energy gain of two molecules of ATP. In addition to using ATP as their source of intracellular chemical energy, all present-day cells carry out glycolysis, consistent with the notion that these reactions arose very early in evolution.

Photosynthesis made cells independent of organic molecules in the environment.

Glycolysis provided a mechanism by which the energy in preformed organic molecules (e.g., glucose) could be converted to ATP, which could then be used as a source of energy to drive other metabolic reactions. The development of **photosynthesis** is generally thought to have been the next major evolutionary step, which allowed the cell to harness energy from sunlight and provided independence from the utilization of preformed organic molecules. The first photosynthetic bacteria probably utilized H_2S to convert CO_2 to organic

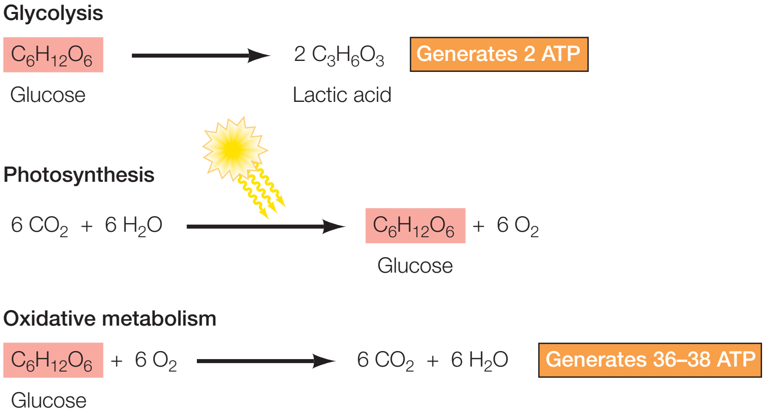


Figure 1.4 Generation of metabolic energy Glycolysis is the anaerobic breakdown of glucose to lactic acid. Photosynthesis utilizes energy from sunlight to drive the synthesis of glucose from CO_2 and H_2O, with the release of O_2 as a by-product. The O_2 released by photosynthesis is used in oxidative metabolism, in which glucose is broken down to CO_2 and H_2O, releasing much more energy than can be obtained from glycolysis.

FYI

Existence of organisms in extreme conditions has led to the hypothesis that life could exist in similar environments elsewhere in the solar system. The field of astrobiology (or exobiology) seeks to find signs of this extraterrestrial life.

molecules—a pathway of photosynthesis still used by some bacteria. The use of H_2O as a donor of electrons and hydrogen for the conversion of CO_2 to organic compounds evolved later and had the important consequence of changing Earth's atmosphere. The use of H_2O in photosynthetic reactions produces the by-product free O_2; this mechanism is thought to have been responsible for making O_2 abundant in Earth's atmosphere, which occurred about 2.4 billion years ago.

The oxidation of glucose to carbon dioxide and water yields much more energy than glycolysis.

The release of O_2 as a consequence of photosynthesis changed the environment in which cells evolved and is commonly thought to have led to the development of **oxidative metabolism**. Alternatively, oxidative metabolism may have evolved before photosynthesis, with the increase in atmospheric O_2 then providing a strong selective advantage for organisms capable of using O_2 in energy-producing reactions. In either case, O_2 is a highly reactive molecule, and oxidative metabolism, utilizing this reactivity, has provided a mechanism for generating energy from organic molecules that is much more efficient than anaerobic glycolysis. For example, the complete oxidative breakdown of glucose to CO_2 and H_2O yields energy equivalent to that of 36 to 38 molecules of ATP, in contrast to the 2 ATP molecules formed by anaerobic glycolysis (see Figure 1.4). With few exceptions, present-day cells use oxidative reactions as their principal source of energy.

Prokaryotes

Prokaryotes include cells of two domains, the **Archaea** and the **Bacteria**, which diverged early in evolution. The Archaea include cells that live in extreme environments that are unusual today but may have been prevalent in primitive Earth. For example, thermoacidophiles live in hot sulfur springs with temperatures as high as 80°C and pH values as low as 2. The Bacteria include the common forms of present-day prokaryotes—a large group of organisms that live in a wide range of environments, including soil, water, and other organisms (e.g., human pathogens).

Prokaryotic cells are smaller and simpler than most eukaryotic cells, their genomes are less complex, and they do not contain nuclei or cytoplasmic organelles (**Table 1.1**). Most prokaryotic cells are spherical, rod-shaped, or spiral, with diameters of 1 to 10 μm. Their DNA contents range from about 0.6 million to 5 million base pairs, an amount sufficient to encode about 5000 different proteins. The largest and most complex prokaryotes are the **cyanobacteria**—bacteria in which photosynthesis evolved.

The structure of a typical bacterial cell is illustrated by ***Escherichia coli (E. coli)***, a common inhabitant of the human intestinal tract (**Figure 1.5**). The cell is rod-shaped, about 1 μm in diameter and about 2 μm long. Like most other prokaryotes, *E. coli* is surrounded by a rigid **cell wall** composed of polysaccharides and peptides. Beneath the cell wall is the **plasma membrane**, which is a bilayer of phospholipids and associated proteins. Whereas the cell wall is porous and readily penetrated by a variety of molecules, the plasma membrane provides the functional separation between the inside of the cell and its external environment. The DNA of *E. coli* is a single circular molecule in the **nucleoid**, which, in contrast to the nucleus of eukaryotes,

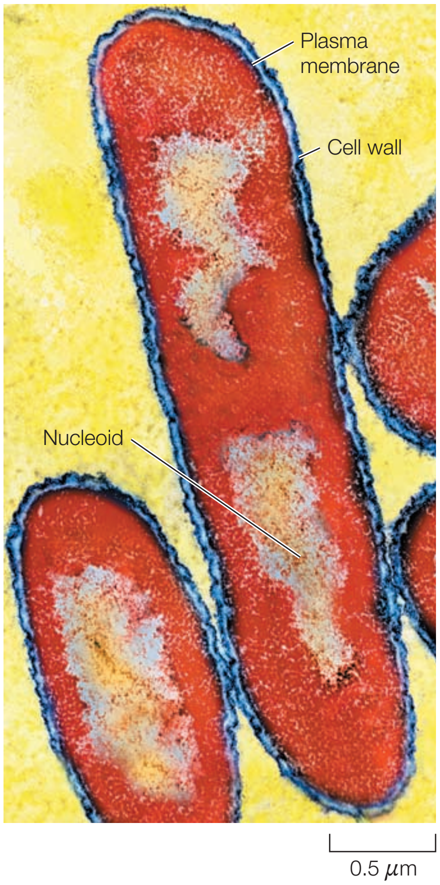


Figure 1.5 Electron micrograph of *E. coli* The cell is surrounded by a cell wall, beneath which is the plasma membrane. DNA is located in the nucleoid. Artificial color has been added. (© Biophoto Associates/Science Source.)

Table 1.1 Prokaryotic and Eukaryotic Cells

Characteristic	Prokaryote	Eukaryote
Nucleus	Absent	Present
Diameter of a typical cell	≈1 μm	10–100 μm
Cytoplasmic organelles	Absent	Present
DNA content (base pairs)	1×10^6 to 5×10^6	1.5×10^7 to 5×10^9
Chromosomes	Single circular DNA molecule	Multiple linear DNA molecules

Prokaryotes are smaller and simpler than eukaryotes.

is not surrounded by a membrane separating it from the cytoplasm. The cytoplasm contains approximately 30,000 **ribosomes** (the sites of protein synthesis), which account for its granular appearance.

Eukaryotic cells

Eukaryotic cells contain nuclei and cytoplasmic organelles.

Like prokaryotic cells, all **eukaryotic cells** are surrounded by a plasma membrane and contain ribosomes. However, eukaryotic cells are much more complex and contain a nucleus and a variety of cytoplasmic organelles (**Figure 1.6**). The largest and most prominent organelle of eukaryotic cells is the **nucleus**, with a diameter of approximately 5 μm. The nucleus contains the genetic information of the cell, which in eukaryotes is organized as linear rather than circular DNA molecules. The nucleus is the site of DNA replication and of RNA synthesis; the translation of RNA into proteins takes place on ribosomes in the cytoplasm.

In addition to a nucleus, eukaryotic cells contain a variety of membrane-enclosed organelles within their cytoplasm. These organelles provide compartments in which different metabolic activities are localized. Eukaryotic cells are generally much larger than prokaryotic cells, frequently having a cell volume at least a thousandfold greater. The compartmentalization provided by cytoplasmic organelles is what allows eukaryotic cells to function efficiently. Two of these organelles, **mitochondria** and **chloroplasts**, play critical roles in energy metabolism. Mitochondria, which are found in almost all eukaryotic cells, are the sites of oxidative metabolism and are thus responsible for generating most of the ATP derived from the breakdown of organic molecules. Chloroplasts are the sites of photosynthesis and are found only in the cells of plants and green algae. **Lysosomes** and **peroxisomes** also provide specialized metabolic compartments for the digestion of macromolecules and for various oxidative reactions, respectively. In addition, most plant cells contain large **vacuoles** that perform a variety of functions, including the digestion of macromolecules and the storage of both waste products and nutrients.

Because of the size and complexity of eukaryotic cells, the transport of proteins to their correct destinations within the cell is a formidable task. Two cytoplasmic organelles, the **endoplasmic reticulum (ER)** and the **Golgi apparatus**, are specifically devoted to the sorting and transport of proteins destined for secretion, incorporation into the plasma membrane, and incorporation into lysosomes and peroxisomes. The endoplasmic reticulum is an extensive network of intracellular membranes, extending from the nuclear envelope throughout the cytoplasm. It functions not only in the processing and transport of proteins (the **rough endoplasmic reticulum**, which is covered by ribosomes), but also in the synthesis of lipids (the **smooth endoplasmic reticulum**). From