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# Prescott's MICROBIOLOGY

TWELFTH EDITION

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Kathleen SANDMAN

Dorothy WOOD

Mc Graw Hill

twelfth edition

# Prescott's Microbiology

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EDUCATION & TRAINING SYSTEMS INTERNATIONAL

Mc Graw Hill

PRESCOTT'S MICROBIOLOGY



This book is printed on acid-free paper.

1 2 3 4 5 6 7 8 9 LWI 27 26 25 24 23 22

ISBN 978-1-265-12303-1
MHID 1-265-12303-9

Cover Image: *National Institute of Allergy and Infectious Diseases (NIAID)/CDC*



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# Brief Contents

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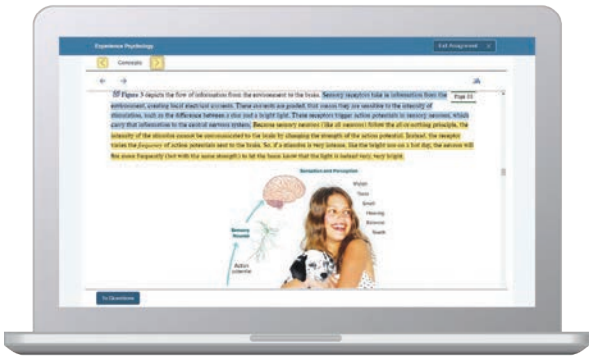

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These simulations help each student learn the practical and conceptual skills needed, then check for understanding and provide feedback. With adaptive pre-lab and post-lab assessment available, instructors can customize each assignment.

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Test Builder allows you to:

- access all test bank content from a particular title.
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- manipulate the order of questions or scramble questions and/or answers.
- pin questions to a specific location within a test.
- determine your preferred treatment of algorithmic questions.
- choose the layout and spacing.
- add instructions and configure default settings.

Test Builder provides a secure interface for better protection of content and allows for just-in-time updates to flow directly into assessments.

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# A Modern Approach to Microbiology

## Evolution as a Framework

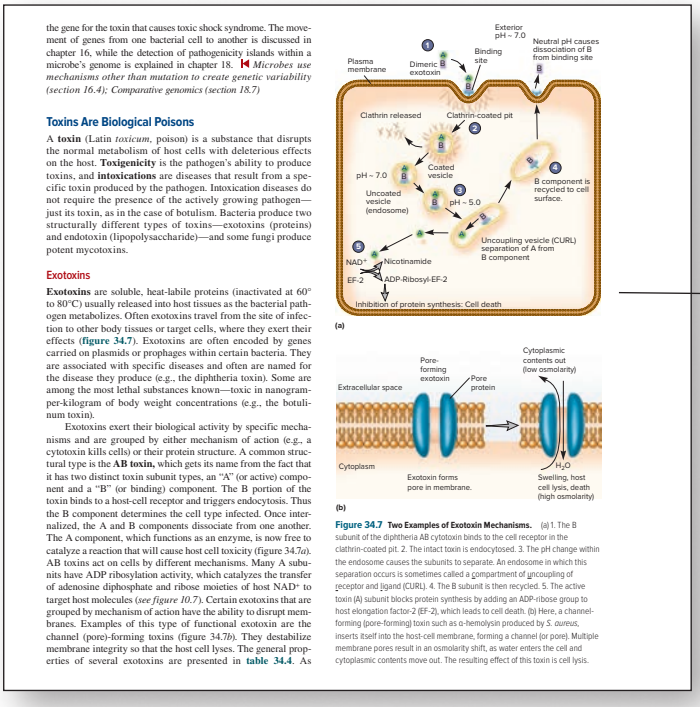
Introduced immediately in chapter 1 and used as an overarching theme throughout, evolution helps unite microbiological concepts and provides a framework upon which students can build their knowledge.

## An Introduction to the Entire Microbial World

Covered in chapters 3–6, separate chapters on the structure and function of bacteria and archaea are followed by the discussion of eukaryotic cells and viruses.

## Broad Coverage of Microbial Ecology

The importance and multidisciplinary nature of microbial ecology are demonstrated by content that ranges from global climate change to the human microbiome.



the gene for the toxin that causes toxic shock syndrome. The movement of genes from one bacterial cell to another is discussed in chapter 16, while the detection of pathogenicity islands within a microbe's genome is explained in chapter 18. ◀ *Microbes use mechanisms other than mutation to create genetic variability (section 16.4); Comparative genomics (section 18.7)*

### Toxins Are Biological Poisons

A **toxin** (Latin *toxicum*, poison) is a substance that disrupts the normal metabolism of host cells with deleterious effects on the host. **Toxigenicity** is the pathogen's ability to produce toxins, and **intoxications** are diseases that result from a specific toxin produced by the pathogen. Intoxication diseases do not require the presence of the actively growing pathogen—just its toxin, as in the case of botulism. Bacteria produce two structurally different types of toxins—exotoxins (proteins) and endotoxin (lipopolysaccharide)—and some fungi produce potent mycotoxins.

### Exotoxins

**Exotoxins** are soluble, heat-labile proteins (inactivated at 60° to 80°C) usually released into host tissues as the bacterial pathogen metabolizes. Often exotoxins travel from the site of infection to other body tissues or target cells, where they exert their effects (**figure 34.7**). Exotoxins are often encoded by genes carried on plasmids or prophages within certain bacteria. They are associated with specific diseases and often are named for the disease they produce (e.g., the diphtheria toxin). Some are among the most lethal substances known—toxic in nanogram-per-kilogram of body weight concentrations (e.g., the botulinum toxin).

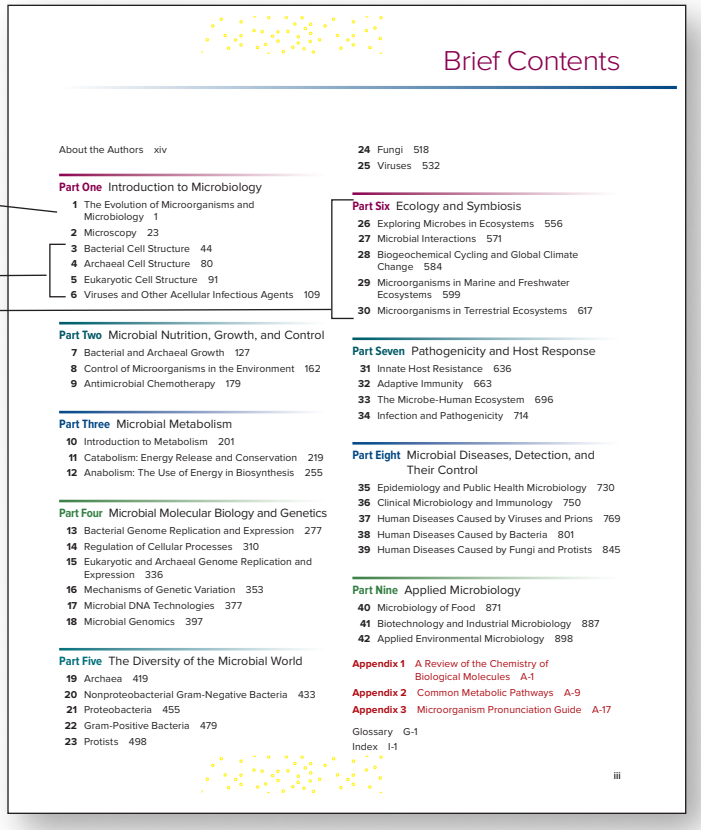
Exotoxins exert their biological activity by specific mechanisms and are grouped by either mechanism of action (e.g., a cytotoxin kills cells) or their protein structure. A common structural type is the **AB toxin,** which gets its name from the fact that it has two distinct toxin subunit types, an "A" (or active) component and a "B" (or binding) component. The B portion of the toxin binds to a host-cell receptor and triggers endocytosis. Thus the B component determines the cell type infected. Once internalized, the A and B components dissociate from one another. The A component, which functions as an enzyme, is now free to catalyze a reaction that will cause host cell toxicity (figure 34.7*a*). AB toxins act on cells by different mechanisms. Many A subunits have ADP ribosylation activity, which catalyzes the transfer of adenosine diphosphate and ribose moieties of host $NAD^+$ to target host molecules (*see figure 10.7*). Certain exotoxins that are grouped by mechanism of action have the ability to disrupt membranes. Examples of this type of functional exotoxin are the channel (pore)-forming toxins (figure 34.7*b*). They destabilize membrane integrity so that the host cell lyses. The general properties of several exotoxins are presented in **table 34.4**. As



**Figure 34.7 Two Examples of Exotoxin Mechanisms.** (*a*) 1. The B subunit of the diphtheria AB cytotoxin binds to the cell receptor in the clathrin-coated pit. 2. The intact toxin is endocytosed. 3. The pH change within the endosome causes the subunits to separate. An endosome in which this separation occurs is sometimes called a compartment of uncoupling of receptor and ligand (CURL). 4. The B subunit is then recycled. 5. The active toxin (A) subunit blocks protein synthesis by adding an ADP-ribose group to host elongation factor-2 (EF-2), which leads to cell death. (*b*) Here, a channel-forming (pore-forming) toxin such as α-hemolysin produced by *S. aureus*, inserts itself into the host-cell membrane, forming a channel (or pore). Multiple membrane pores result in an osmolarity shift, as water enters the cell and cytoplasmic contents move out. The resulting effect of this toxin is cell lysis.

## SARS-CoV-2 and the Impact of COVID-19

Students are introduced to the virology of SARS-CoV-2 and the pathobiology of COVID-19 in chapters 25 and 37, respectively. Throughout the text, the relevance of concepts to the pandemic are noted as easy-to-find text boxes.



## Brief Contents



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## Molecular Microbiology and Immunology

The twelfth edition includes updates on genetics, biotechnology, genomics and metagenomics, immunology, and the human microbiome. An up-to-date discussion of immunity, with enhanced detail between innate and adaptive linkages, helps students grasp the complexity and specificity of immune responses. The microbiome and its impact on human homeostasis is introduced in chapter 33, The Microbe-Human Ecosystem.

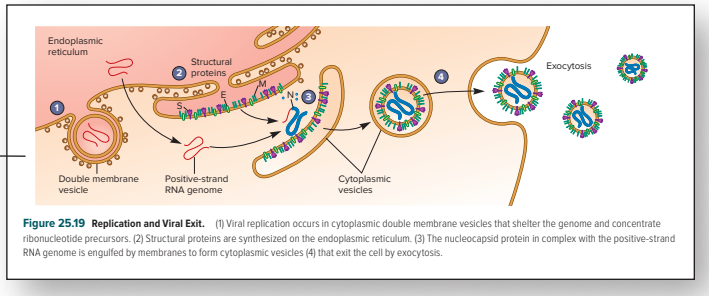




**Figure 25.19 Replication and Viral Exit.** (1) Viral replication occurs in cytoplasmic double membrane vesicles that shelter the genome and concentrate ribonucleotide precursors. (2) Structural proteins are synthesized on the endoplasmic reticulum. (3) The nucleocapsid protein in complex with the positive-strand RNA genome is engulfed by membranes to form cytoplasmic vesicles (4) that exit the cell by exocytosis.

# A Modern Approach to Microbiology

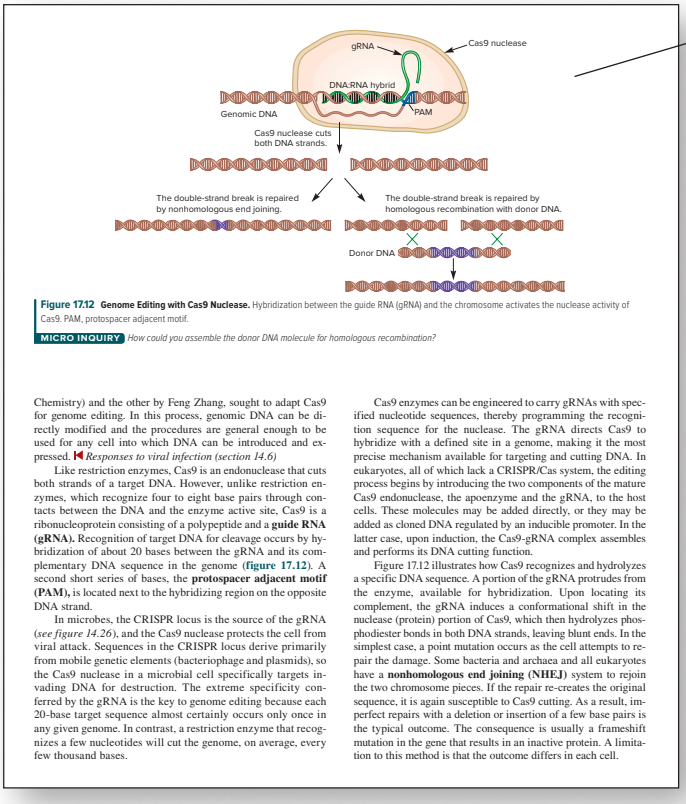



**Figure 17.12 Genome Editing with Cas9 Nuclease.** Hybridization between the guide RNA (gRNA) and the chromosome activates the nuclease activity of Cas9. PAM, protospacer adjacent motif.

**MICRO INQUIRY** *How could you assemble the donor DNA molecule for homologous recombination?*

Chemistry) and the other by Feng Zhang, sought to adapt Cas9 for genome editing. In this process, genomic DNA can be directly modified and the procedures are general enough to be used for any cell into which DNA can be introduced and expressed. ◀ *Responses to viral infection (section 14.6)*

Like restriction enzymes, Cas9 is an endonuclease that cuts both strands of a target DNA. However, unlike restriction enzymes, which recognize four to eight base pairs through contacts between the DNA and the enzyme active site, Cas9 is a ribonucleoprotein consisting of a polypeptide and a **guide RNA (gRNA).** Recognition of target DNA for cleavage occurs by hybridization of about 20 bases between the gRNA and its complementary DNA sequence in the genome (**figure 17.12**). A second short series of bases, the **protospacer adjacent motif (PAM),** is located next to the hybridizing region on the opposite DNA strand.

In microbes, the CRISPR locus is the source of the gRNA (*see figure 14.26*), and the Cas9 nuclease protects the cell from viral attack. Sequences in the CRISPR locus derive primarily from mobile genetic elements (bacteriophage and plasmids), so the Cas9 nuclease in a microbial cell specifically targets invading DNA for destruction. The extreme specificity conferred by the gRNA is the key to genome editing because each 20-base target sequence almost certainly occurs only once in any given genome. In contrast, a restriction enzyme that recognizes a few nucleotides will cut the genome, on average, every few thousand bases.

Cas9 enzymes can be engineered to carry gRNAs with specified nucleotide sequences, thereby programming the recognition sequence for the nuclease. The gRNA directs Cas9 to hybridize with a defined site in a genome, making it the most precise mechanism available for targeting and cutting DNA. In eukaryotes, all of which lack a CRISPR/Cas system, the editing process begins by introducing the two components of the mature Cas9 endonuclease, the apoenzyme and the gRNA, to the host cells. These molecules may be added directly, or they may be added as cloned DNA regulated by an inducible promoter. In the latter case, upon induction, the Cas9-gRNA complex assembles and performs its DNA cutting function.

Figure 17.12 illustrates how Cas9 recognizes and hydrolyzes a specific DNA sequence. A portion of the gRNA protrudes from the enzyme, available for hybridization. Upon locating its complement, the gRNA induces a conformational shift in the nuclease (protein) portion of Cas9, which then hydrolyzes phosphodiester bonds in both DNA strands, leaving blunt ends. In the simplest case, a point mutation occurs as the cell attempts to repair the damage. Some bacteria and archaea and all eukaryotes have a **nonhomologous end joining (NHEJ)** system to rejoin the two chromosome pieces. If the repair re-creates the original sequence, it is again susceptible to Cas9 cutting. As a result, imperfect repairs with a deletion or insertion of a few base pairs is the typical outcome. The consequence is usually a frameshift mutation in the gene that results in an inactive protein. A limitation to this method is that the outcome differs in each cell.

## 21st-Century Microbiology

*Prescott's Microbiology* leads the way with text devoted to CRISPR genome engineering, global climate change, and microbial fuel cells. For more, see chapters 17, 28, and 42.

## Metagenomics and the Human Microbiome

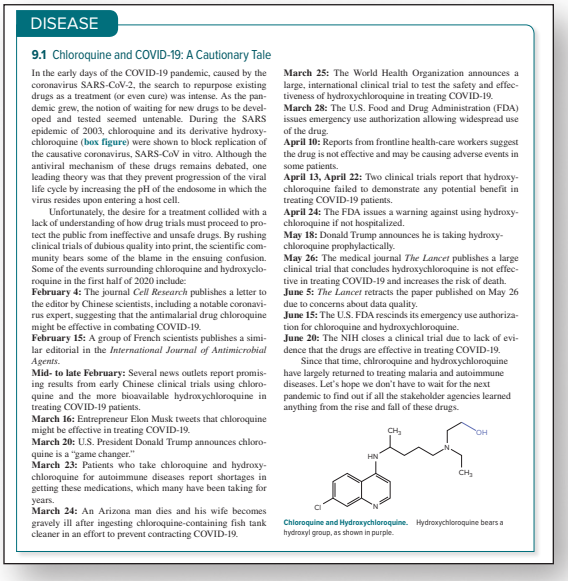
Expanded coverage of metagenomics and its importance in understanding the role of microbes in all environments and in exploring symbionts of invertebrates is threaded throughout the text. Chapter 33, The Microbe-Human Ecosystem, explores the human microbiome and its role in health and disease.

## Laboratory Safety

Reflecting recommendations from the Centers for Disease Control and Prevention, along with the American Society for Microbiology, chapter 36 provides specific guidance for laboratory best practices to help instructors provide safe conditions during the teaching of laboratory exercises.

## Special Interest Essays

Organized into four themes—Microbial Diversity & Ecology, Techniques & Applications, Historical Highlights, and Disease—these focused and interesting essays provide additional insight into relevant topics.



DISEASE

**9.1** Chloroquine and COVID-19: A Cautionary Tale

In the early days of the COVID-19 pandemic, caused by the coronavirus SARS-CoV-2, the search to repurpose existing drugs as a treatment (or even cure) was intense. As the pandemic grew, the notion of waiting for new drugs to be developed and tested seemed untenable. During the SARS epidemic of 2003, chloroquine and its derivative hydroxychloroquine (**box figure**) were shown to block replication of the causative coronavirus, SARS-CoV in vitro. Although the antiviral mechanism of these drugs remains debated, one leading theory was that they prevent progression of the viral life cycle by increasing the pH of the endosome in which the virus resides upon entering a host cell.

Unfortunately, the desire for a treatment collided with a lack of understanding of how drug trials must proceed to protect the public from ineffective and unsafe drugs. By rushing clinical trials of dubious quality into print, the scientific community bears some of the blame in the ensuing confusion. Some of the events surrounding chloroquine and hydroxychloroquine in the first half of 2020 include:

**February 4:** The journal *Cell Research* publishes a letter to the editor by Chinese scientists, including a notable coronavirus expert, suggesting that the antimalarial drug chloroquine might be effective in combating COVID-19.

**February 15:** A group of French scientists publishes a similar editorial in the *International Journal of Antimicrobial Agents*.

**Mid- to late February:** Several news outlets report promising results from early Chinese clinical trials using chloroquine and the more bioavailable hydroxychloroquine in treating COVID-19 patients.

**March 16:** Entrepreneur Elon Musk tweets that chloroquine might be effective in treating COVID-19.

**March 20:** U.S. President Donald Trump announces chloroquine is a "game changer."

**March 23:** Patients who take chloroquine and hydroxychloroquine for autoimmune diseases report shortages in getting these medications, which many have been taking for years.

**March 24:** An Arizona man dies and his wife becomes gravely ill after ingesting chloroquine-containing fish tank cleaner in an effort to prevent contracting COVID-19.

**March 25:** The World Health Organization announces a large, international clinical trial to test the safety and effectiveness of hydroxychloroquine in treating COVID-19.

**March 28:** The U.S. Food and Drug Administration (FDA) issues emergency use authorization allowing widespread use of the drug.

**April 10:** Reports from frontline health-care workers suggest the drug is not effective and may be causing adverse events in some patients.

**April 13, April 22:** Two clinical trials report that hydroxychloroquine failed to demonstrate any potential benefit in treating COVID-19 patients.

**April 24:** The FDA issues a warning against using hydroxychloroquine if not hospitalized.

**May 18:** Donald Trump announces he is taking hydroxychloroquine prophylactically.

**May 26:** The medical journal *The Lancet* publishes a large clinical trial that concludes hydroxychloroquine is not effective in treating COVID-19 and increases the risk of death.

**June 5:** *The Lancet* retracts the paper published on May 26 due to concerns about data quality.

**June 15:** The U.S. FDA rescinds its emergency use authorization for chloroquine and hydroxychloroquine.

**June 20:** The NIH closes a clinical trial due to lack of evidence that the drugs are effective in treating COVID-19.

Since that time, chloroquine and hydroxychloroquine have largely returned to treating malaria and autoimmune diseases. Let's hope we don't have to wait for the next pandemic to find out if all the stakeholder agencies learned anything from the rise and fall of these drugs.

**Chloroquine and Hydroxychloroquine.** Hydroxychloroquine bears a hydroxyl group, as shown in purple.

MICROBIAL DIVERSITY & ECOLOGY

**1.1** Hydrothermal Vents: Did Life Begin Under the Sea?

Whether or not early life was RNA-based, one thing is clear: the origin of life needed energy to synthesize biomolecules. So, perhaps the most fundamental evolutionary question is "Where did biomolecules and the energy needed to build them come from?" Three hypotheses have been suggested. First, the *panspermia theory* speculates that meteorites bombarded our planet, bringing with them other-worldly biomolecules. Second, the more familiar *primordial soup theory* suggests that organic molecules were spontaneously assembled by an input of energy, such as lightning strikes. The last theory, which has gained evidence in recent years, hypothesizes that both the energy and the molecules originated in hydrothermal vents. Let's explore the *hydrothermal vent theory*.

Hydrothermal vents are geothermally active deep-sea chasms thousands of meters below the surface of the ocean. Their discovery in 1977 sparked tremendous excitement as images of entirely new ecosystems with mysterious organisms captured the attention of scientists and the public (*see section 27.2*). These vents pump 400°C sulfide-rich water into cold ambient water, causing the sulfide to instantly precipitate, so these chimneylike structures are dubbed "black smokers." In 2000, scientists made yet another deep-sea discovery with a different kind of vent system. These are cooler (45–90°C) and alkaline (pH 9–11). When these waters mix with the surrounding seawater (pH about 8.0), calcium carbonate precipitates, forming white chimneys, as seen in the Lost City vents (**box figure**).

This pH gradient is critical to the hypothesis that a vent system, such as Lost City, could be the origin of biomolecules. As you may have learned when studying mitochondria or batteries, the separation of positive and negative charges captures potential energy (remember that energy can't be created). In Lost City vents, the thin walls of the chimneys serve

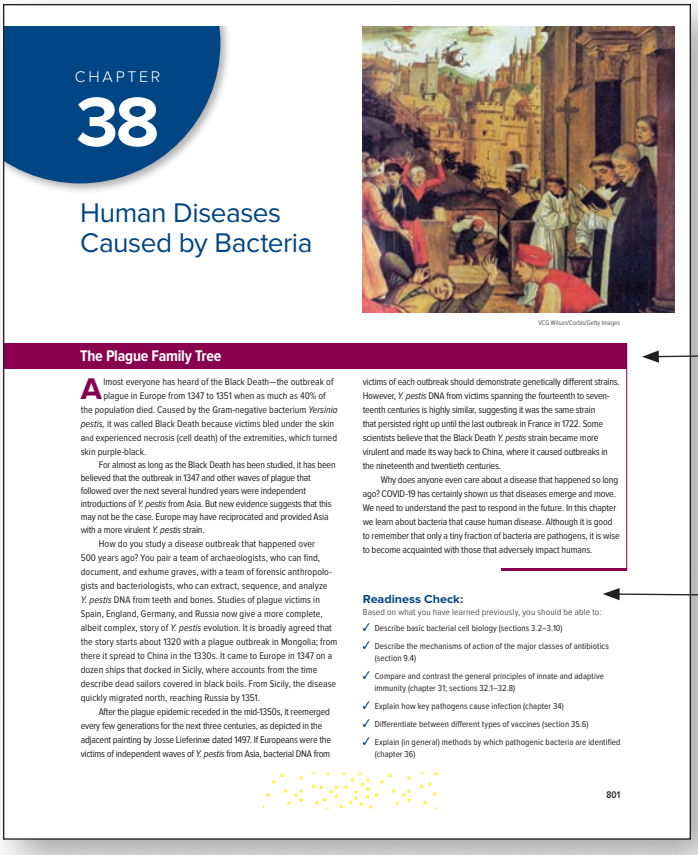


D.Kelley, University of Washington.

to separate these fluids with as much as a 3-unit pH difference. The question now being asked is "Was this potential energy tapped to convert $CO_2$ in seawater to simple carbon-based molecules, such as amino acids, short hydrocarbons, and others?"

If the answer is yes, a 2019 study shows that a mixture of molecules called single-chain amphiphiles (SCAs), which are simpler versions of more familiar phospholipids, can form vesicles in hot, alkaline pH seawater that mimics that of Lost City. Putting this together, we can hypothesize a series of events that occurred 3.7–4.0 billion years ago. First, the presence of the pH gradient across geological barriers in the Lost City drove the formation of random organic molecules, some of which were SCAs. These SCAs accumulated and formed vesicles that entrapped fluids preserving the pH gradient. These vesicles had the energy to test the formation of different molecules. Was one of them RNA?

# Student-Friendly Organization



CHAPTER
38

Human Diseases Caused by Bacteria



VCG Wilson/Corbis/Getty Images

**The Plague Family Tree**

Almost everyone has heard of the Black Death—the outbreak of plague in Europe from 1347 to 1351 when as much as 40% of the population died. Caused by the Gram-negative bacterium *Yersinia pestis*, it was called Black Death because victims bled under the skin and experienced necrosis (cell death) of the extremities, which turned skin purple-black.

For almost as long as the Black Death has been studied, it has been believed that the outbreak in 1347 and other waves of plague that followed over the next several hundred years were independent introductions of *Y. pestis* from Asia. But new evidence suggests that this may not be the case. Europe may have reciprocated and provided Asia with a more virulent *Y. pestis* strain.

How do you study a disease outbreak that happened over 500 years ago? You pair a team of archaeologists, who can find, document, and exhume graves, with a team of forensic anthropologists and bacteriologists, who can extract, sequence, and analyze *Y. pestis* DNA from teeth and bones. Studies of plague victims in Spain, England, Germany, and Russia now give a more complete, albeit complex, story of *Y. pestis* evolution. It is broadly agreed that the story starts about 1320 with a plague outbreak in Mongolia; from there it spread to China in the 1330s. It came to Europe in 1347 on a dozen ships that docked in Sicily, where accounts from the time describe dead sailors covered in black boils. From Sicily, the disease quickly migrated north, reaching Russia by 1351.

After the plague epidemic receded in the mid-1350s, it reemerged every few generations for the next three centuries, as depicted in the adjacent painting by Josse Lieferinxe dated 1497. If Europeans were the victims of independent waves of *Y. pestis* from Asia, bacterial DNA from victims of each outbreak should demonstrate genetically different strains. However, *Y. pestis* DNA from victims spanning the fourteenth to seventeenth centuries is highly similar, suggesting it was the same strain that persisted right up until the last outbreak in France in 1722. Some scientists believe that the Black Death *Y. pestis* strain became more virulent and made its way back to China, where it caused outbreaks in the nineteenth and twentieth centuries.

Why does anyone even care about a disease that happened so long ago? COVID-19 has certainly shown us that diseases emerge and move. We need to understand the past to respond in the future. In this chapter we learn about bacteria that cause human disease. Although it is good to remember that only a tiny fraction of bacteria are pathogens, it is wise to become acquainted with those that adversely impact humans.

**Readiness Check:**

Based on what you have learned previously, you should be able to:

- ✓ Describe basic bacterial cell biology (sections 3.2–3.10)
- ✓ Describe the mechanisms of action of the major classes of antibiotics (section 9.4)
- ✓ Compare and contrast the general principles of innate and adaptive immunity (chapter 31; sections 32.1–32.8)
- ✓ Explain how key pathogens cause infection (chapter 34)
- ✓ Differentiate between different types of vaccines (section 35.6)
- ✓ Explain (in general) methods by which pathogenic bacteria are identified (chapter 36)

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**Micro Focus**—Each chapter begins with a real-life story illustrating the relevance of the content covered in the upcoming text.

**Readiness Check**—The introduction to each chapter includes a skills checklist that defines the prior knowledge students need to understand the material that follows.

**Comprehension Check**—Questions within the narrative of each chapter help students master section concepts before moving on to other topics.

**Cross-Referenced Notes**—In-text references refer students to other parts of the book to review.

**Animation Icon**—This symbol indicates that material presented in the text is accompanied by an animation within Instructor Resources in Connect. Create a file attachment assignment in Connect to have your students view the animation, or post it to your Learning Management System for students.

**Learning Outcomes**—Every section in each chapter begins with a list of content-based activities students should be able to perform after reading.

excises incorrectly to generate a specialized transducing particle, these bacterial genes are most often present (**figure 16.24**).
▶| *Bacteriophage lambda: a temperate bacteriophage (section 25.2)* ❁ *Specialized Transduction*

**Comprehension Check**

1. Describe generalized transduction and how it occurs. What is an abortive transductant?
2. What is specialized transduction and how does it come about?
3. How might one tell whether horizontal gene transfer was mediated by generalized or specialized transduction?
4. Why doesn't a cell lyse after successful transduction with a temperate phage?
5. How are conjugation, transformation, and transduction similar? How are they different?

## 16.9 Evolution in Action: The Development of Antibiotic Resistance in Bacteria

**After reading this section, you should be able to:**

a. Describe an R plasmid and its associated genetic elements
b. Distinguish integrative conjugative elements, transposons, and conjugative plasmids
c. Describe how genetic elements mobilize portions of chromosomes

Within 3 years after the widespread use of penicillin began in the 1940s, penicillin-resistant bacteria were found in clinical speci-

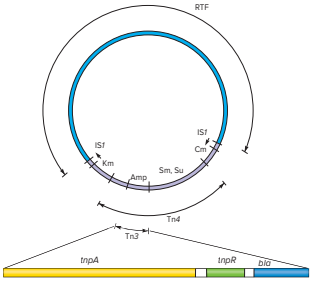


**Figure 16.25 An R Plasmid.** Plasmid R1 is an R plasmid that contains the replicative transposon Tn*3*. Tn*3* contains the gene for β-lactamase (*bla*), an enzyme that confers resistance to ampicillin (Amp). Note that Tn*3* is inserted into another transposable element, Tn*4*. Tn*4* carries genes that provide resistance to streptomycin (Sm) and sulfonamide (Su). The R1 plasmid also carries resistance genes for kanamycin (Km) and chloramphenicol (Cm). The RTF region of R1 codes for proteins needed for plasmid replication and transfer. Transposase and resolvase are encoded by *tnpA* and *tnpR*, respectively.

**MICRO INQUIRY** *As a replicative transposon, what would happen if Tn3 hopped from this R1 plasmid into a different plasmid?*

**Micro Inquiry**—Selected figures in every chapter contain probing questions, adding another assessment opportunity for the student.

# Student-Friendly Organization

**Vivid Instructional Art**—Three-dimensional renditions and bright, attractive colors enhance learning.

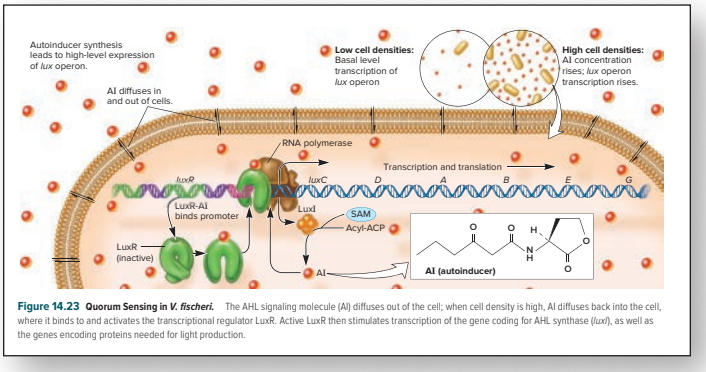


**Figure 14.23** **Quorum Sensing in *V. fischeri*.** The AHL signaling molecule (AI) diffuses out of the cell; when cell density is high, AI diffuses back into the cell, where it binds to and activates the transcriptional regulator LuxR. Active LuxR then stimulates transcription of the gene coding for AHL synthase (*luxI*), as well as the genes encoding proteins needed for light production.

**Annotated Figures**—All key metabolic pathways and molecular processes are annotated, so each step is clearly illustrated and explained.

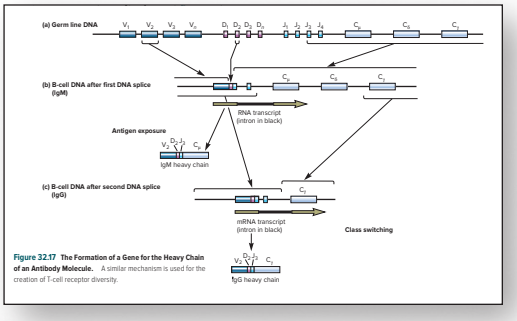


**Figure 32.17** **The Formation of a Gene for the Heavy Chain of an Antibody Molecule.** A similar mechanism is used for the creation of T-cell receptor diversity.

## Key Concepts

### 2.1 Lenses Create Images by Bending Light

- A light ray moving from air to glass or vice versa is bent in a process known as refraction (**figure 2.1**).
- Lenses focus light rays at a focal point and magnify images (**figure 2.2**).

### 2.2 There Are Several Types of Light Microscopes

- In a compound microscope such as the bright-field microscope, the primary image is an enlarged image formed by the objective lens. The primary image is further enlarged by the ocular lens to yield the final image (**figure 2.3**).
- Microscope resolution increases as the wavelength of radiation used to illuminate the specimen decreases and as the numerical aperture increases. The maximum resolution of a light microscope is about 0.2 µm (**figure 2.4**).
- The dark-field microscope uses only refracted light to form an image, and objects appear light against a black background (**figure 2.6**).
- The phase-contrast microscope converts variations in the refractive index into changes in light intensity and thus makes colorless, unstained, live cells visible (**figures 2.8–2.10**).
- The differential interference contrast microscope uses two beams of light to create high-contrast images of live specimens (**figure 2.11**).
- The fluorescence microscope illuminates a fluorochrome-labeled specimen and forms an image from its fluorescence (**figures 2.12–2.14**).
- The confocal microscope is used to study thick, complex specimens. It creates an image by using only the light emanating from the plane of focus, while blocking out light from above and below the plane of focus (**figure 2.15**).

### 2.3 Staining Helps to Visualize and Identify Microbes

- Specimens are often fixed and stained before viewing in the bright-field microscope. There are two fixation methods: heat fixation and chemical fixation.
- Most dyes are either positively charged basic dyes or negatively charged acidic dyes that bind to ionized parts of cells.
- In simple staining, a single dye is used to stain microorganisms (**figure 2.16**).
- Differential staining procedures such as Gram and acid-fast staining distinguish between microbial groups by staining them differently (**figures 2.17** and **2.18*a, b***). Other differential staining techniques are specific for particular structures such as bacterial capsules and flagella (**figure 2.18*c, d***).

### 2.4 Electron Microscopes Use Beams of Electrons to Create Highly Magnified Images

- The transmission electron microscope (TEM) uses magnetic lenses to form an image from electrons that have passed through a very thin section of a specimen (**figure 2.21**). Resolution is high because the wavelength of a beam of electrons is very short.
- Specimens for TEM are usually prepared by methods that increase contrast. Specimens can be stained by treatment with solutions of heavy metals such as osmium, uranium, and lead. They can also be prepared for TEM by negative staining, shadowing with metal, or freeze-etching (**figures 2.23** and **2.24**).
- The scanning electron microscope is used to study external surface features of microorganisms (**figures 2.25** and **2.26**).
- Cryo-EM enables visualization of single molecules and complex molecular structures. Samples are flash frozen and when examined, a series of images are captured that when combined and processed form a three-dimensional reconstruction of the specimen (**figure 2.27**).

### 2.5 Scanning Probe Microscopy Can Visualize Molecules and Atoms

- Scanning probe microscopes reach very high magnifications that allow scientists to observe biological molecules (**figures 2.28** and **2.30**).
- Scanning tunneling microscopy enables the visualization of molecular surfaces using electron interaction between the probe and the specimen, whereas atomic force microscopy can scan the surface of molecules that do not conduct electricity well (**figure 2.29**).

## Active Learning

1. You have prepared a specimen for light microscopy, stained it using the Gram-staining procedure, but failed to see anything when you looked through your light microscope. Discuss the things you may have done incorrectly.
2. Which type of microscopy and stain (if appropriate) would you use to visualize each of the following? (There may be more than one correct answer.) Be sure to explain your answer. *Mycobacterium tuberculosis* (which causes tuberculosis), microbes in pond scum, *Staphylococcus*

**Key Concepts**—At the end of each chapter, organized by numbered headings, this feature distills the content to its essential components with cross-references to figures and tables.

**Active Learning**—Includes questions taken from current literature; designed to stimulate analytical problem-solving skills.

# List of Content Changes

Each chapter has been thoroughly reviewed.

**Part One**

**Chapter 1**—We open the text with a new emphasis on the fundamentals of microbial evolution, thereby setting the stage for weaving this theme throughout the text.

**Chapter 2**—A new section has been added that describes exciting advances in cryo-electron microscopy and the visualization of biomolecules.

**Chapter 3**—In this discussion of the bacterial cell, the two main types of cell walls have been reframed as monoderm and diderm, reflecting their structural differences. A new section describes the structure and function of extracellular vesicles. Membraneless organelles and liquid-liquid phase separation are introduced in a Microbial Diversity & Ecology box. New figures complement an expanded discussion of nucleoid-associated proteins and nucleoid structure.

**Chapter 4**—The discussion of the archaeal cell features an enhanced comparison of bacterial and archaeal cells, and an expanded diagram of archaeal lipids. Extracellular vesicles, nanotubes, and nanopods are described and illustrated.

**Chapter 5**—An updated discussion of endocytic pathways and extracellular vesicles has been added.

**Chapter 6**—This introduction to the morphological, physiological, and genetic elements of viruses has been streamlined with new images and figures and an updated discussion of prions.

**Part Two**

**Chapter 7**—This discussion of microbial growth highlights recent advances in Z ring and divisome formation. New figures complement discussions of the archaeal cell cycle, biofilm development, and quorum sensing. A new Microbial Diversity & Ecology box illustrates how some microbes can form bioconcrete.

**Chapter 8**—Microbial control is reorganized into physical, chemical, and biological methods, with information on destruction of the SARS-CoV-2 virus.

**Chapter 9**—In addition to reviewing the structure and mechanism of action of antimicrobial classes, the growing threat of antimicrobial resistance is emphasized.

**Part Three**

**Chapter 10**—This chapter provides the foundation for understanding energy conservation and biosynthesis.

**Chapter 11**—Catabolic pathways and energy conservation have been refocused in this chapter to emphasize bacterial and archaeal processes. A new art program uses concept maps to provide overviews of microbial catabolic strategies such as aerobic versus anaerobic respiration.

**Chapter 12**—Biosynthetic pathways are illustrated in detail in this chapter, and several have been expanded to include archaeal variations. Lipopolysaccharide biosynthesis is elaborated and illustrated in a new figure.

**Part Four**

**Chapter 13**—Revisions to this chapter on the basic molecular biology of the cell include expanded discussion and images for the origin of replication and the replisome. A new section describes the physical constraints on DNA and RNA polymerases acting on the same chromosomal template.

**Chapter 14**—The regulation of cellular processes has been expanded to include control by RNA secondary structures such as RNA thermometers and T box riboswitches. The importance of secondary messengers is highlighted in the updated discussion of cyclic-di-GMP regulation.

**Chapter 15**—This chapter focuses on a discussion of eukaryotic and archaeal molecular biology, including an introduction to biomolecular condensates for eukaryotic processes. Recent research on gene regulation in archaea is presented, as well as an updated discussion of transcription from a chromatin template.

**Chapter 16**—This focus on mutation and repair features new figures and an updated description of DNA repair mechanisms. Recent research on mobile genetic elements and mechanisms of gene transfer is included.

**Chapter 17**—This chapter introduces students to the common laboratory techniques for manipulating DNA, including gene cloning, PCR, heterologous gene expression, and CRISPR/Cas9 gene editing. A section on synthetic biology is now included.

**Chapter 18**—Essential genomic techniques, including single-cell genomic sequencing and metagenomics, are introduced with real-world applications, including those related to SARS-CoV-2.

**Part Five**

**Chapter 19**—Archaeal taxonomy now reflects the formalism established in the Genome Taxonomy Database. Microbial dark matter is described, as many archaea are known only from metagenomic sequences. The discussion of archaeal carbon pathways has been streamlined, and the Wolfe cycle of hydrogenotrophic methanogenesis has been carefully annotated.

**Chapter 20**—Bacterial taxonomy now also reflects the formalism derived in the Genome Taxonomy Database. As a consequence, organisms previously classified as delta- and epsilonproteobacteria are now included in this chapter. Variations on the diderm cell envelope are discussed. Cable bacteria and extracellular electron transport are introduced, and discussions of radiation resistance in *Deinococcus* and chromatic acclimation in cyanobacteria have been updated.

# List of Content Changes

**Chapter 21**—This chapter on the proteobacteria contains a new section describing *Acinetobacter*. In addition, the β-hydroxyaspartate cycle linking autotrophs and heterotrophs in the open ocean is included.

**Chapter 22**—This chapter surveying the Gram-positive bacteria now includes *Mycoplasma* spp. The section on *Streptomyces* presents a discussion of biosynthetic gene clusters.

**Chapter 23**—Updated protist classification based on recent phylogenomic analysis is provided as clades of protists of medical and environmental importance are reviewed.

**Chapter 24**—This chapter has been reorganized based on recent phylogenomic evidence. The six major fungal groups are presented.

**Chapter 25**—Viral taxonomy has been revised, and this chapter reflects the classification used by the International Committee on the Taxonomy of Viruses. The detailed life cycle of a coronavirus serves as an example of positive-strand RNA viruses, thereby presenting the replication cycle of SARS-CoV-2. This is accompanied by new figures.

**Part Six**

**Chapter 26**—This chapter presents a discussion of key techniques used for assessing microbial populations and communities and includes an expanded discussion on metagenomics. Applications to environmental and microbiome research are included.

**Chapter 27**—This chapter on microbial interactions has been extensively revised, grouping interactions as mutualism, cooperation, or antagonism. Multiple new examples are detailed, with emphasis on metabolic interdependence.

**Chapter 28**—An expanded introduction to nutrient cycling and biogeochemical cycling precedes the review of major elemental cycles. New art brings these cycles to life. The chapter builds upon these concepts to explain the role of microbes in an updated discussion of climate change.

**Chapter 29**—Discussions of microbial adaptation to the marine environment and the importance of the oceans in global climate change have been updated. Coverage of freshwater microbiology has also been revised, emphasizing anthropogenic impacts.

**Chapter 30**—This chapter complements chapter 27 with discussions of mycorrhizal fungi and nitrogen-fixing bacteria. The role of metagenomics in advancing our understanding of soil microbiology is stressed. Coverage of plant pathogens has been expanded.

**Part Seven**

**Chapter 31**—This chapter has been updated and its organization refined to provide a concise introduction of innate immunity, including advances in our understanding of the role of the inflammasome and innate lymphoid cells.

**Chapter 32**—Revised and updated, this discussion of adaptive immunity and immunopathologies provides a current overview to introduce students to the dynamics of human immunity. Many figures have been revised for clarity.

**Chapter 33**—The rapidly expanding field of the human microbiome is introduced. This chapter follows those on immunology for a complete discussion of the role of human microbiota in immune function, as well as their role in maintaining system homeostasis.

**Chapter 34**—This chapter provides a broad overview of infectious disease from pathogen transmission to pathogenicity.

**Part Eight**

**Chapter 35**—This chapter has been revised to reflect recent epidemiological data, a discussion of $R_0$ and herd immunity, and an updated vaccine section to include mRNA vaccines. The epidemiology of SARS-CoV-2 is highlighted, as well as pandemic management.

**Chapter 36**—This chapter provides students with an overview of key microbiological and immunological techniques enabling the identification of clinical samples.

**Chapter 37**—This chapter now includes a complete discussion of our current understanding of the pathobiology of SARS-CoV-2. The genomics and evolution of the virus is emphasized, as well as the clinical manifestations of COVID-19.

**Chapter 38**—Students are introduced to bacterial diseases, including pathogenesis, prevalence, and clinical presentation. Where applicable, the importance of vaccine prevention is stressed.

**Chapter 39**—This chapter provides an overview of fungal and protozoan diseases of local and global significance. The global burden of key diseases such as Chagas and malaria is emphasized.

**Part Nine**

**Chapter 40**—The essentials of food safety now include a discussion of hazards and safety measures at all stages from farm to market. Methods for food testing have been updated to reflect the use of molecular methods and whole-genome sequencing.

**Chapter 41**—The growing reach of biotechnology is illustrated in several examples, including an expanded discussion of industrial enzymes derived from microbes, rational vaccine design strategies, microbial biosensors, and diatoms as nanotechnology platforms.

**Chapter 42**—The discussion of water safety has been expanded to include a discussion of microbial source tracking, and a COVID box notes the importance of monitoring sewage for SARS-CoV-2 as an aspect of public health. The section on biodegradation has been expanded to include petroleum hydrocarbons, halogenated organic molecules, and a description of the plastisphere.

# About the Authors

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**Joanne M. Willey** has been a professor at Hofstra University on Long Island, New York, since 1993, where she is the Leo A. Guthart Professor of Biomedical Science and Chair of the Department of Science Education at the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell. Dr. Willey received her B.A. in Biology from the University of Pennsylvania, where her interest in microbiology began with work on cyanobacterial growth in eutrophic streams. She earned her Ph.D. in biological oceanography (specializing in marine microbiology) from the Massachusetts Institute of Technology–Woods Hole Oceanographic Institution Joint Program in 1987. She then went to Harvard University, where she spent her postdoctoral fellowship studying the filamentous soil bacterium *Streptomyces coelicolor*. Dr. Willey has coauthored a number of publications that focus on its complex developmental cycle. She is an active member of the American Society for Microbiology (ASM), and served on the editorial board of the journal *Applied and Environmental Microbiology* for nine years and as Chair of the Division of General Microbiology. Dr. Willey taught microbiology to biology majors for 20 years and now teaches microbiology and infectious disease to medical students. She has taught courses in cell biology, marine microbiology, and laboratory techniques in molecular genetics. Dr. Willey lives on the north shore of Long Island and has two grown sons. She is an avid runner and enjoys skiing, hiking, rock climbing, and reading. She can be reached at joanne.m.willey@hofstra.edu.

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**Kathleen M. Sandman** received her B.A. in Biology from La Salle University and her Ph.D. in Cellular and Developmental Biology from Harvard University. She was inspired to a career in science by her older brother's experience as an organic chemist and by the developing technology in recombinant DNA in the 1970s. Her graduate work used a transposable element as a mutagen in *Bacillus subtilis* to study gene expression during endospore formation. She continued in the genetics of Gram-positive bacteria with a postdoctoral year studying *Bacillus thuringiensis* at the University of Cambridge in the United Kingdom. Another postdoctoral opportunity at The Ohio State University provided an introduction to the emerging field of archaeal molecular biology, where Dr. Sandman discovered archaeal histones and continued research in the structural biology of archaeal chromatin for about 20 years. She served the National Science Foundation as a research grant reviewer and panelist for the Life in Extreme Environments program, and has organized conference sessions on archaeal molecular biology and proteins from extremophiles. Dr. Sandman has taught microbiology to hundreds of students, at both the introductory level and in an advanced molecular microbiology laboratory. Dr. Sandman has worked as a consultant in a variety of industries, including industrial microbiology, environmental geomicrobiology, and technical publishing. She lives with her husband in Columbus, Ohio, and has two grown daughters. She enjoys biking, fabric arts, reading, and genealogy, and can be reached at kathleenmsandman@gmail.com.

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**Dorothy H. Wood** taught microbiology and general biology at Durham Technical Community College in North Carolina for 17 years. Dr. Wood received her B.A. in Biology from Rhode Island College where her love of microbes began, nurtured by Dr. Charles Owens. She earned her Ph.D. in Cell and Molecular Pathology from the University of North Carolina at Chapel Hill, focusing on pancreatic damage caused by antimicrobial drugs, and investigated alternative therapies based on receptor binding by novel compounds. After three years as Assistant Professor at NC Central University, Dr. Wood made the move to the NC Community College System to focus her attention on her primary interest of teaching. Throughout her career she developed additional courses, including graduate bacteriology, pathophysiology, and biotechnology. Dr. Wood is a digital faculty consultant for McGraw Hill and has worked on several textbooks in a variety of disciplines, developing and editing digital content to accompany the texts. Dr. Wood is a curriculum design consultant for Education & Training Systems International based in Chapel Hill, NC. She is a fitness professional, leads health and wellness seminars, and has been the treasurer of a nonprofit organization for the past 10 years. She enjoys life in North Carolina with her husband and two grown children, and can be reached at dorothywood241@gmail.com.

# Acknowledgements

In the preparation of each edition, we are guided by the collective wisdom of reviewers who are expert microbiologists and excellent teachers. They represent experience in community colleges, liberal arts colleges, comprehensive institutions, and research universities. We have followed their recommendations, while remaining true to our overriding goal of writing readable, student-centered content. Each feature incorporated into this edition has been carefully considered in terms of how it may be used to support student learning in both the traditional and the flipped learning environment.

Also in this edition, we are very excited to incorporate real student data points and input, derived from thousands of our LearnSmart users, to help guide our revision. With this information, we were able to hone both book and digital content.

The authors wish to extend their gratitude to our team at McGraw Hill, including Lauren Vondra, Darlene Schueller, Tami Hodge, Vicki Krug, David Hash, Beth Cray, and Tammy Juran. Thanks to Rebecca E. Steiner, Shonteria L. Johnson, Rita Mary King, Jonathan A. Miller, Brittany Gasper, and Mary Colavito for your assistance with this edition. Finally, we thank our spouses and children, who provided support and tolerated our absences (mental, if not physical) while we completed this demanding project.

We offer our sincere thanks to the following reviewers and/or focus group participants who provided valuable input. Your suggestions and recommendations helped shape and guide this revision.

Chris Allen, *Lone Star College-University Park*
Daniel Aruscavage, *Kutztown University*
Paul Babitzke, *Pennsylvania State University*
R. Berlemont, *California State University, Long Beach*
Linda D. Bruslind, *Oregon State University*
Becky Buckley, *Metropolitan State University of Denver*
Hildamarie Caceres-Velazquez, *Coastal Carolina Community College*
Kathleen L. Campbell, *Emory University*
Daniel N. Clark, *Weber State University*
Laszlo Csonka, *Purdue University*
Deborah Dardis, *Southeastern Louisiana University*
Ellen B. Duffy, *Siena College*
Dale Emeagwali, *Excelsior College*
Jed A. Fuhrman, *University of Southern California*
Melanie C. Griffin, *Kennesaw State University*
Judyth Gulden, *Northeastern State University*
Isaac M. Hagenbuch, *University of South Carolina, Columbia*
Cecily L. Haley, *San Jacinto College North Campus*
Andrew F. Herbig, *Washburn University*
Timothy Hoover, *University of Georgia*
Amy G. Hurst, *Rose State College*
Mark Kainz, *Ripon College*
Bessie W. Kebaara, *Baylor University*
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Yong Jin Lee, *Albany State University*
Cynthia Littlejohn, *The University of Southern Mississippi*
Danielle M. McGrath, *San Jacinto College*
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Roderick M. Morgan, *Grand Valley State University*
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Kaustubha Qanungo, *Clemson University*
Shawna Reed, *Quinnipiac University*
Rebecca D. Riggs, *Auburn University*
Janet Rinehart-Kim, *Old Dominion University*
Paul G. Rudenberg, *Southern Maine Community College*
Pratibha Saxena, *University of Texas at Austin*
Sarah Sidiropoulos, *Oakland Community College*
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Fanxiu Zhu, *Florida State University*

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twelfth edition

# Prescott's Microbiology

CHAPTER

# 1

# The Evolution of Microorganisms and Microbiology

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## Microbiology's Reach

How does it feel to witness history? The COVID-19 pandemic will be studied for years to come by scientists, clinicians, and politicians. However, as the COVID-19 pandemic exploded, we had the tools to address many of the questions that needed answers in real time. Each of these questions also illustrates the reach of microbiology. Let's explore five of them:

- *What is the nature of the virus that causes COVID-19, SARS-CoV-2?* It is easy to see that virologists—those who study viruses—helped answer this question. But they were supported by many others. For example, electron microscopists were needed to visualize the virus, and the work of molecular biologists and geneticists was critical. The ability to rapidly sequence the first isolated SARS-CoV-2 genome, followed by new many new isolates cultured from patients, illustrates the importance of bioinformaticists (people who analyze large biological data sets), computer scientists, and clinical microbiologists.
- *How does SARS-CoV-2 cause disease?* This turned out to be much more complicated than anyone initially anticipated. To answer this question, immunologists, physiologists, infectious disease specialists, pathologists, and every manner of clinician-scientist conducted studies.
- *How do we best treat patients with COVID-19?* The process of repurposing existing drugs and developing new drugs required the coordinated efforts of virologists, molecular biologists, biochemists, chemists, and immunologists to identify and design new drugs. Meanwhile, clinicians—including physicians, nurses, pharmacists, and public health officials—tested new therapies on patients. Data scientists and statisticians were needed to interpret the outcomes of trials.
- *How do we prevent the spread of COVID-19?* The world got a crash course on the role of epidemiologists and disease modelers in tracking, tracing, and predicting the spread of disease. Geographic information scientists helped figure out where the virus was spreading. As it became clear that vaccines take time for microbiologists, biochemists, and immunologists to develop, the design and deployment of cheaper and easier testing by industrial microbiologists and bioengineers was critical.

These are only some of the questions wrought by COVID-19. The goal of this textbook is to introduce you to the microbial world—the magnitude of its diversity, the elegance of its biology, and the many subdisciplines within microbiology. Unfortunately, COVID-19 has probably already convinced you of microbiology's importance.

Our goal in this chapter is to introduce you to this amazing world of microorganisms and outline their evolution and history of discovery. Much of microbiology is similar to what you have learned in other biology classes that focus on large organisms. But microbes have unique properties that often require unique approaches to understand them. But before you delve into this chapter, check to see if you have the background needed to get the most from it.

### Readiness Check:

Based on what you have learned previously, you should be able to:

- ✓ List the features of eukaryotic cells that distinguish them from other cell types
- ✓ Understand the basic structure of the macromolecules, nucleic acids, proteins, carbohydrates, and lipids (*see appendix I*)
- ✓ Explain the terms *genome, genotype,* and *mutation*

## 1.1 Members of the Microbial World

**After reading this section, you should be able to:**

- **a.** Define the term *microbiology*
- **b.** Explain Carl Woese's contributions in establishing the three-domain system for classifying cellular life
- **c.** Determine the type of microbe (bacterium, fungus, etc.) when given a description of a microorganism
- **d.** Provide an example of the importance to humans of each of the major types of microbes

**Microorganisms**—those organisms too small to be seen clearly by the unaided eye (**figure 1.1**) are fabulously diverse and unimaginably abundant. It is difficult to count the number of microbes on Earth, but estimates are about $10^{30}$ microbial cells in habitats as diverse as termite guts and sediments deep beneath the seafloor (**figure 1.2**). There are more microbes on Earth than stars in the known universe.

Although microbes are generally 1 millimeter or less in diameter, some, such as bread molds, are visible without microscopes. Some macroscopic microorganisms are multicellular. They are distinguished from other multicellular life forms such as plants and animals by their lack of highly differentiated tissues. In addition, a variety of acellular biological entities, including viruses and subviral agents, are also called *microorganisms* and *microbes*. This is not without controversy because these agents cannot reproduce independently.

The diversity of microorganisms has always presented a challenge to microbial taxonomists. Early descriptions of cellular microbes as either plants or animals were too simple. For instance, some microbes are motile like animals but also have cell walls and are photosynthetic like plants. An important breakthrough in microbial taxonomy arose from studies of their cellular architecture, when it was discovered that cells exhibited one of two possible "floor plans." Cells that came to be called **prokaryotic cells** (Greek *pro,* before; *karyon,* nut or kernel) have an open floor plan. That is, their contents are not divided into compartments by membranes. Only **eukaryotic cells** (Greek *eu,* true) have a nucleus and other membrane-bound organelles (e.g., mitochondria, chloroplasts) that separate some cellular materials and processes from others.

These observations eventually led to the development of a classification scheme that divided organisms into five kingdoms: Monera, Protista, Fungi, Animalia, and Plantae. Microorganisms (except for viruses and other acellular infectious agents) were placed in the first three kingdoms. In this scheme, all organisms with prokaryotic cell structure were placed in Monera. However, the five-kingdom system is no longer accepted by microbiologists. This is because prokaryotes are too diverse to be grouped together in a single kingdom. ▶| *Use of the term prokaryote is controversial (section 3.1)*

Classifying microbes has benefited from progress in three areas. First, the development of electron microscopy techniques reveals the detailed structure of microbial cells. Second, methods that measure the biochemical and physiological characteristics of many different microorganisms demonstrate

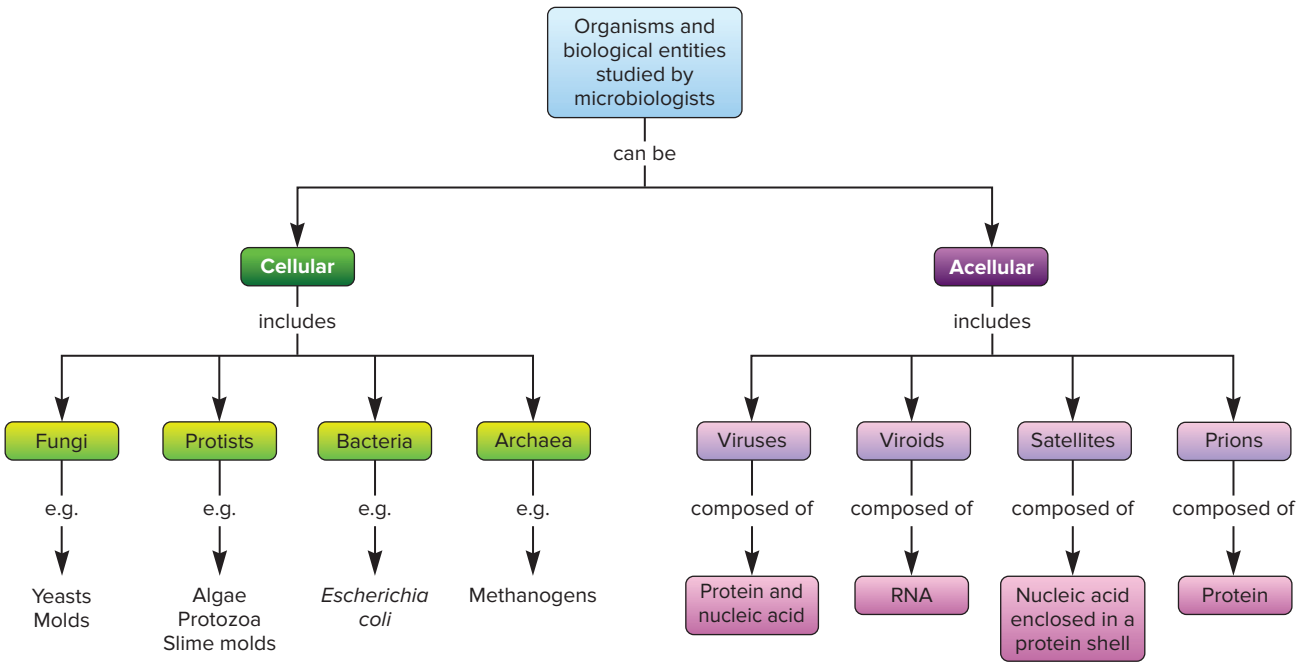


**Figure 1.1 Concept Map Showing the Types of Biological Entities Studied by Microbiologists.**

**MICRO INQUIRY** *How would you alter this concept map so that cellular organisms are differentiated by their key features?*

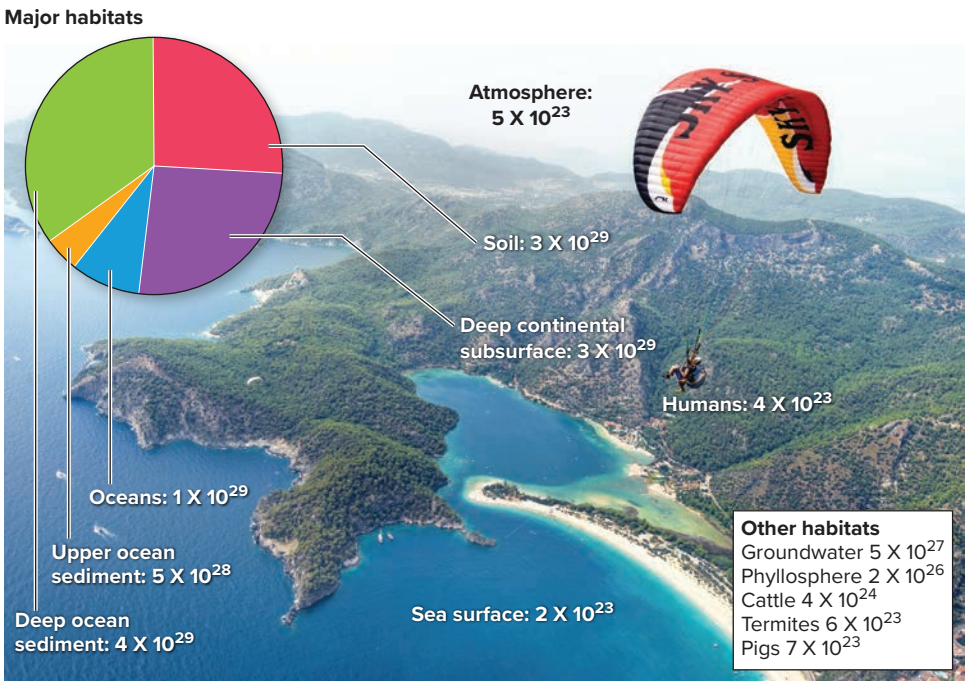


**Figure 1.2 Bacterial and Archaeal Habitats and Abundance.** Numbers indicate the number of microbial cells in each habitat. The majority of bacteria and archaea live in oceans and sediments, either within the Earth's crust or deep below the crust (subsurface). The discovery of viable microbes so deep within our planet is a recent and exciting development. Other habitats include the phyllopshere (above ground portions of plants), livestock, and humans.

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many similarities and differences. Third, the genomic revolution enabled the analysis of nucleic acid and protein sequences from a wide variety of organisms. The comparison of ribosomal RNA (rRNA) nucleic acid sequences, begun by Carl Woese (1928–2012) in the 1970s, transformed our understanding of the term *prokaryote*. It was discovered that there are two very different groups of organisms with prokaryotic cell morphology: Bacteria and Archaea. Among eukaryotic microbes, later studies showed that Protista is not a cohesive taxonomic unit (i.e., taxon) and that it should be divided into three or more kingdoms. These studies and others led many taxonomists to reject the five-kingdom system in favor of one that divides cellular organisms into three domains: Bacteria, Archaea, and Eukarya (all eukaryotic organisms) (**figure 1.3**). ▶| *Nucleic acids (appendix I); Proteins (appendix I)*

Members of domain **Bacteria** are usually single-celled organisms.[1] Most have cell walls that contain the structural molecule peptidoglycan. Despite popular belief, most bacteria do not cause disease. In fact, bacteria are major inhabitants of our bodies, forming the human **microbiome.** Indeed, at least as many microbial cells are found in and on the human body as there are human cells. These microbes contribute to the development of the body's immune system. Microbes that inhabit the large intestine help the body digest food and produce vitamins. In these and many other ways, the human microbiome helps maintain our health and well-being. ▶| *Overview of bacterial cell wall structure (section 3.4); Human microbiome and host interactions (chapter 33)*

Unfortunately some bacteria do cause disease, and some of these diseases can have a huge impact. In 1347 the plague (Black Death), a disease caused by bacteria living in fleas, struck Europe with brutal force, killing one-third of the population within 4 years. Over the next 80 years, the disease struck repeatedly, eventually wiping out roughly half of the European population. The resulting labor shortage gave workers more power, ultimately eliminating serfdom, and preparing the way for the Renaissance.

Members of domain **Archaea** are distinguished from bacteria by many features, most notably their distinctive rRNA sequences, cell walls, and membrane lipids. Some have unique metabolic characteristics, such as the ability to generate methane (natural) gas. Some archaea are found in extreme environments, including those with high temperatures (thermophiles) and high concentrations of salt (extreme halophiles). Archaea do not appear to directly cause disease in humans.

Domain **Eukarya** includes plants, animals, and microorganisms classified as protists or fungi. **Protists** are generally unicellular but larger than most bacteria and archaea. They have traditionally been divided into **protozoa,** which have an animal-like metabolism, and **algae,** which are photosynthetic. However, these terms lack taxonomic value because protists, algae, and protozoa do not form three groups, each with a single evolutionary history. Nonetheless, for convenience, we use these terms here. ▶| *Protist diversity reflects broad phylogeny (section 23.1)*

**Fungi** are a diverse group of microorganisms that range from unicellular forms (yeasts) to multicellular molds and mushrooms. Because of their metabolic capabilities, many fungi play beneficial roles, including making bread dough rise, producing antibiotics, and decomposing dead organisms. Some fungi associate with plant roots to form mycorrhizae. Mycorrhizal fungi transfer nutrients to the roots, improving growth of the plants, especially in poor soils. Other fungi cause plant diseases (e.g., rusts, powdery mildews, and smuts) and diseases in humans and other animals. ▶| *Fungal biology reflects vast diversity (section 24.1)*

1 In this text, the term *bacteria* (s., *bacterium*) is used to refer to those microbes belonging to domain Bacteria, and the term *archaea* (s., *archaeon*) is used to refer to those that belong to domain Archaea. In some publications, the term *bacteria* is used to refer to all cells having prokaryotic cell structure. That is not the case in this text.

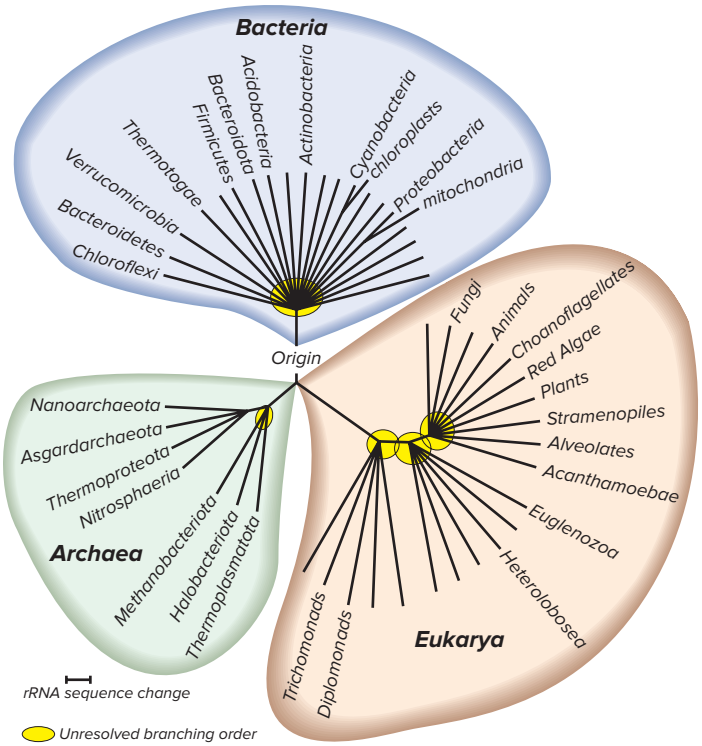



**Figure 1.3 Universal Phylogenetic Tree.** Only representative lineages have been identified.

**MICRO INQUIRY** *How many of the taxa listed in the figure include microbes?*

The microbial world also includes numerous acellular infectious agents. **Viruses** are acellular entities that must invade a host cell to multiply. The simplest virus particles (also called virions) are composed only of proteins and a nucleic acid, and can be extremely small (the smallest is 10,000 times smaller than a typical bacterium). However, their small size belies their power. They cause many animal and plant diseases and, as we saw most recently with COVID-19, can trigger epidemics and pandemics that shape human history. In addition to COVID-19, viral diseases include rabies, influenza, AIDS, the common cold, and some cancers. Viruses are also important in aquatic environments, where they play a critical role in shaping microbial communities. **Viroids** are infectious agents composed only of ribonucleic acid (RNA). They cause numerous plant diseases. **Satellites** are composed of a nucleic acid enclosed in a protein shell. They must coinfect a host cell with a virus, called a helper virus, to complete their life cycle. Satellites and their helper viruses cause both plant and animal diseases. Finally, **prions,** infectious agents composed only of protein, are responsible for causing neurological diseases such as scrapie and "mad cow disease." ▶| *Viruses and other acellular infectious agents (chapter 25)*

### Comprehension Check

1. How did the methods used to classify microbes change, particularly in the last half of the twentieth century? What was the result of these technological advances?
2. Identify one characteristic for each of these types of microbes that distinguishes it from the other types: bacteria, archaea, protists, fungi, viruses, viroids, satellites, and prions.
3. Describe one interaction with microbes you had yesterday.

## 1.2 Microbes Have Evolved and Diversified for Billions of Years

**After reading this section, you should be able to:**

- **a.** Explain the RNA world hypothesis and the evidence that supports it
- **b.** Design a set of experiments that could be used to place a newly discovered cellular microbe on a phylogenetic tree based on small subunit (SSU) rRNA sequences
- **c.** Compare and contrast the evolution of mitochondria and chloroplasts

A review of figure 1.3 reminds us that microbes are the dominant organisms on Earth. How has microbial life been able to radiate to such an astonishing level of diversity? To answer this question, we must consider microbial evolution. The field of microbial evolution, like any other scientific endeavor, is based on the formulation of hypotheses, the gathering and analysis of data, and the reformation of hypotheses based on newly acquired evidence. That is to say, the study of microbial evolution is based on the scientific method. To be sure, it is difficult to amass evidence when considering events that occurred millions, and often billions, of years ago, but the application of molecular methods has revealed a living record of life's ancient history. This section describes the outcome of this scientific research.

### Theories of the Origin of Life Depend Primarily on Indirect Evidence

Dating meteorites through the use of radioisotopes places our planet at an estimated 4.5 to 4.6 billion years old. However, conditions on Earth for the first 100 million years or so were far too harsh to sustain any type of life. Eventually bombardment by meteorites decreased, water appeared on the planet in liquid form, and gases were released by geological activity to form Earth's atmosphere. These conditions were amenable to the origin of the first life forms. But how did this occur, and what did these life forms look like?

To find evidence of life and develop hypotheses about its origin and subsequent evolution, scientists must be able to define life. Although even very young children can examine an object

and correctly determine whether it is living or not, defining life succinctly is actually not that easy. Most definitions of life consist of a set of attributes. The attributes of particular importance to paleobiologists are an orderly structure, the ability to obtain and use energy (i.e., metabolism), and the ability to reproduce. Just as NASA scientists are using the characteristics of microbes on Earth today to search for life elsewhere, so too are scientists examining **extant organisms,** those organisms present today, to explore the origin of life. Some extant organisms have structures and molecules that represent relics of ancient life forms. These can provide scientists with ideas about the type of evidence to seek when testing hypotheses.

The best direct evidence for the nature of primitive life would be a fossil record. There have been reports of microbial fossil discoveries since 1977. These have always met with skepticism because some objects that look like cells can be formed by geological forces that occurred as the rock was formed. The result is that the fossil record for microbes is sparse and always open to reinterpretation.

Despite these problems, most scientists agree that life was present on Earth about 3.5 to 3.8 billion years ago (**figure 1.4**). To reach this conclusion, biologists rely on indirect evidence. Among the indirect evidence used are molecular fossils. These are chemicals found in rock or sediment that are chemically related to biological molecules. For instance, the presence of molecules called hopanes in a rock indicates that bacteria were present when the rock was formed. This conclusion is reached because hopanes are formed from hopanoids, which are found in the plasma membranes of extant bacteria. As you can see, no single piece of evidence can stand alone. Instead many pieces of evidence are put together in an attempt to get a coherent picture to emerge, as with a jigsaw puzzle.

## Early Life Was Probably RNA-based

Before there was life, most evidence suggests that Earth was a very different place: hot and anoxic, with an atmosphere rich in water vapor, carbon dioxide, and nitrogen. In the oceans, hydrogen, methane, and carboxylic acids were formed by geological and chemical processes. Areas near hydrothermal vents may have provided the conditions that allowed chemicals to react with one another, randomly testing the usefulness of the reaction and the stability of its products. Some reactions generated molecules that functioned as catalysts, some aggregated with other molecules to form the predecessors of modern cell structures, and others were able to replicate and act as units of hereditary information (**Microbial Diversity & Ecology 1.1**).

How did early cells, sometimes called *probionts*, arise? In modern cells, three different molecules fulfill the roles of catalysts, structural molecules, and hereditary molecules. Proteins have two major roles in modern cells: catalytic and structural. Catalytic proteins are **enzymes** and structural proteins serve myriad functions, such as transport, attachment, and motility. DNA stores hereditary information that is replicated and passed on to the next generation. RNA converts the information stored in DNA into protein. Any hypothesis about the origin of life must account for the evolution of these molecules, but their relationships to each other in modern cells complicates attempts to imagine how they evolved. Proteins can do cellular work, but their synthesis involves other proteins and RNA, and uses information stored in DNA. DNA cannot do cellular work, and proteins are needed for its replication. RNA synthesis requires both DNA as the template and proteins as catalysts.

Based on these considerations, it is hypothesized that at some time in the evolution of probionts, there must have been a single molecule that could do both cellular work and replicate. This idea was supported in 1981 when Thomas Cech discovered an RNA molecule in a protist (*Tetrahymena* sp.) that also had catalytic activity. Since then, other catalytic RNA molecules have been discovered, including an RNA found in ribosomes that is responsible for forming peptide bonds—the bonds that hold together amino acids, the building blocks of proteins. Catalytic RNA molecules are now called **ribozymes.**

The discovery of ribozymes suggested that RNA at some time was capable of storing, copying, and expressing genetic information, as well as catalyzing other chemical reactions. In 1986 Nobel laureate Walter Gilbert coined the term **RNA world** to describe this precellular stage in the evolution of life. However, for this precellular RNA-based stage to proceed to the evolution of cellular life forms, a lipid membrane must have formed around the RNA (**figure 1.5**). This important evolutionary step is easier to imagine than other events in the origin of cellular life forms because lipids, major structural components of the membranes of modern organisms, spontaneously form liposomes—vesicles bounded by a lipid bilayer. The notion of an RNA world has caused some scientists to look for evidence on Mars, where conditions are thought to have been frozen in the prebiotic era.

▶| *Lipids (appendix I)*

Back here on Earth, Jack Szostak, also a Noble laureate, is a leader in experimentally simulating how protobionts containing only RNA may have formed. When his group created liposomes using simpler fatty acids than those found in membranes today, the liposomes were leaky. These leaky liposomes allowed single RNA nucleotides to move into the liposome, but prevented large RNA chains from moving out. Furthermore, researchers could prod the liposomes into growing and dividing. Dr. Szostak's group has also been able to create conditions in which an RNA molecule could serve as a template for synthesis of a complementary RNA strand. These experiments may have recapitulated early steps in the evolution of cells. As seen in figure 1.5, several other processes need to occur to reach the level of complexity found in extant cells.

Apart from its ability to perform catalytic activities, the function of RNA suggests its ancient origin. Consider that much of the cellular pool of RNA in modern cells exists in the ribosome, a structure that consists largely of ribosomal RNA (rRNA) and uses messenger RNA (mRNA) and transfer RNA

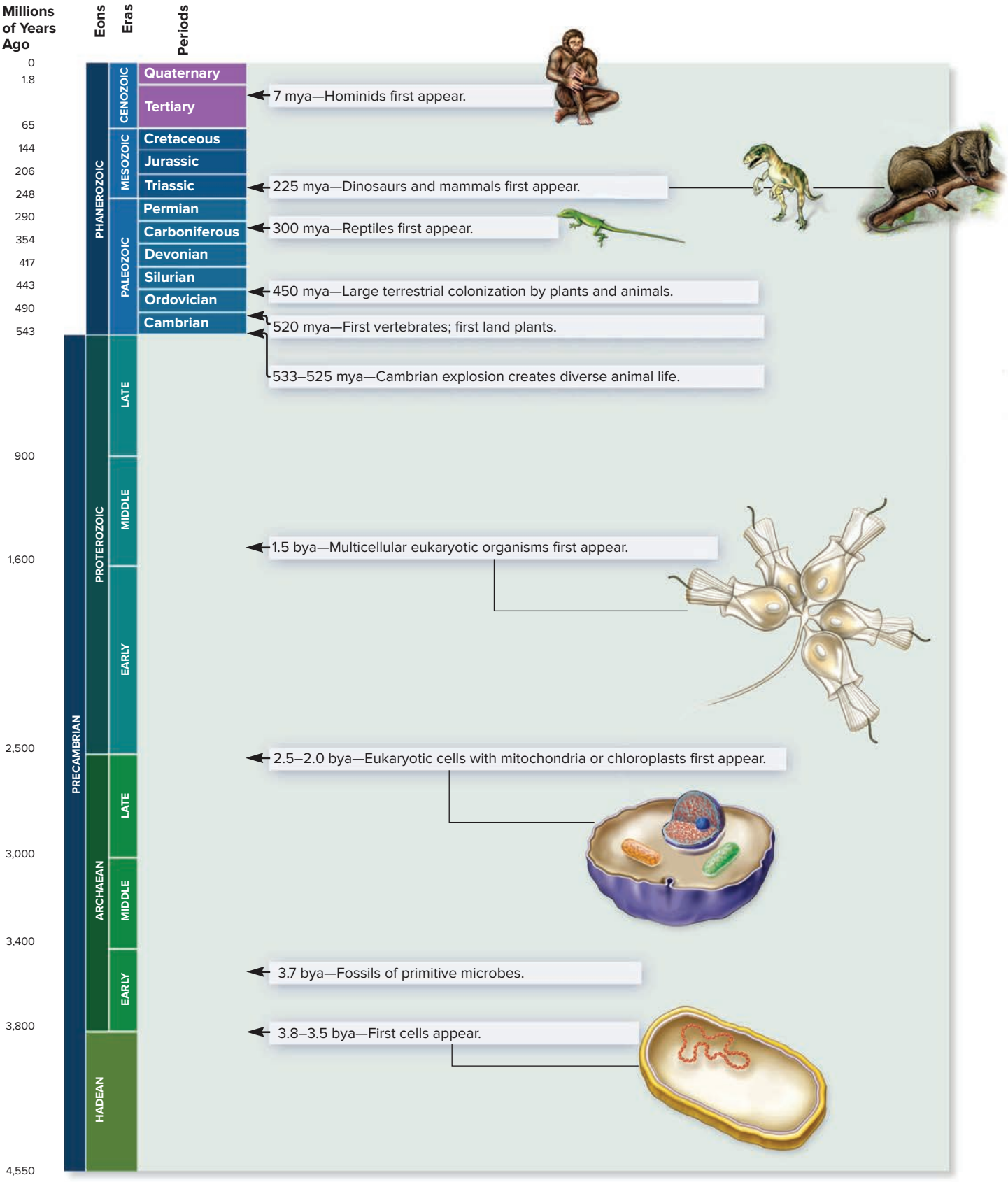



**Figure 1.4 An Overview of the History of Life on Earth.** mya = million years ago; bya = billion years ago.

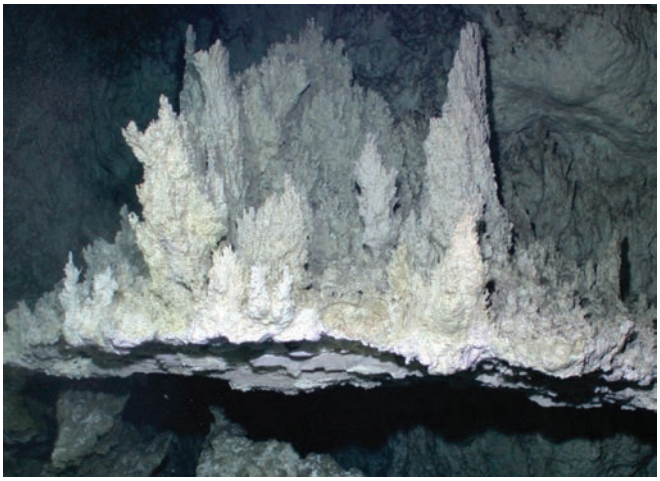
# MICROBIAL DIVERSITY & ECOLOGY

## 1.1 Hydrothermal Vents: Did Life Begin Under the Sea?

Whether or not early life was RNA-based, one thing is clear: the origin of life needed energy to synthesize biomolecules. So, perhaps the most fundamental evolutionary question is "Where did biomolecules and the energy needed to build them come from?" Three hypotheses have been suggested. First, the *panspermia theory* speculates that meteorites bombarded our planet, bringing with them other-worldly biomolecules. Second, the more familiar *primordial soup theory* suggests that organic molecules were spontaneously assembled by an input of energy, such as lightning strikes. The last theory, which has gained evidence in recent years, hypothesizes that both the energy and the molecules originated in hydrothermal vents. Let's explore the *hydrothermal vent theory.*

Hydrothermal vents are geothermally active deep-sea chasms thousands of meters below the surface of the ocean. Their discovery in 1977 sparked tremendous excitement as images of entirely new ecosystems with mysterious organisms captured the attention of scientists and the public (*see section 27.2*). These vents pump 400°C sulfide-rich water into cold ambient water, causing the sulfide to instantly precipitate, so these chimneylike structures are dubbed "black smokers." In 2000, scientists made yet another deep-sea discovery with a different kind of vent system. These are cooler (45–90°C) and alkaline (pH 9–11). When these waters mix with the surrounding seawater (pH about 8.0), calcium carbonate precipitates, forming white chimneys, as seen in the Lost City vents (**box figure**).

This pH gradient is critical to the hypothesis that a vent system, such as Lost City, could be the origin of biomolecules. As you may have learned when studying mitochondria or batteries, the separation of positive and negative charges captures potential energy (remember that energy can't be created). In Lost City vents, the thin walls of the chimneys serve to separate these fluids with as much as a 3-unit pH difference. The question now being asked is "Was this potential energy tapped to convert $CO_2$ in seawater to simple carbon-based molecules, such as amino acids, short hydrocarbons, and others?"



D.Kelley, University of Washington.

If the answer is yes, a 2019 study shows that a mixture of molecules called single-chain amphiphiles (SCAs), which are simpler versions of more familiar phospholipids, can form vesicles in hot, alkaline pH seawater that mimics that of Lost City. Putting this together, we can hypothesize a series of events that occurred 3.7–4.0 billion years ago. First, the presence of the pH gradient across geological barriers in the Lost City drove the formation of random organic molecules, some of which were SCAs. These SCAs accumulated and formed vesicles that entrapped fluids preserving the pH gradient. These vesicles had the energy to test the formation of different molecules. Was one of them RNA?

(tRNA) to construct proteins. Also rRNA itself catalyzes peptide bond formation during protein synthesis. Thus RNA seems to be well poised for its importance in the development of proteins (figure 1.5). Because RNA and DNA are structurally similar, RNA could have given rise to double-stranded DNA. It is suggested that once DNA evolved, it became the storage facility for genetic information because it provides a more chemically stable structure. Two other pieces of evidence support the RNA world hypothesis: the fact that the energy currency of cells, ATP, is a ribonucleotide and the discovery that RNA can regulate gene expression. ▶| *ATP: the major energy currency of cells (section 10.2); Riboswitches: effector-mRNA interactions regulate transcription (section 14.3); Translational riboswitches (section 14.4)*

However, the RNA world hypothesis is not without problems, and more recent experiments suggest the first nucleic acids may have been a mix of DNA and RNA molecules. Another area of research also fraught with considerable debate is the evolution of metabolism. The early Earth was a hot environment that lacked oxygen. Thus cells that arose there must have been able to use the available energy sources under these harsh conditions. Today there are heat-loving archaea capable of using inorganic molecules such as FeS as a source of energy. Some suggest that this interesting metabolic capability is a remnant of

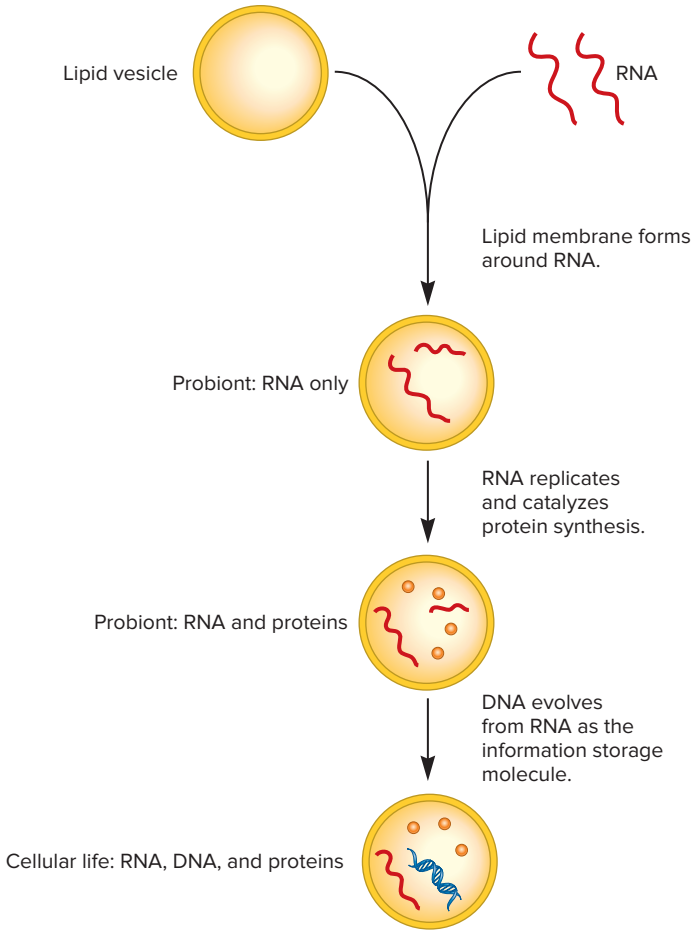



**Figure 1.5 The RNA World Hypothesis for the Origin of Life.**

**MICRO INQUIRY** *Why are the probionts pictured above not considered cellular life?*

the first form of energy metabolism. Another metabolic strategy, oxygen-releasing photosynthesis (oxygenic photosynthesis), appears to have evolved perhaps as early as 2.7 billion years ago. This is supported by the discovery of ancient stromatolites (**figure 1.6**). Stromatolites are layered rocks formed by the incorporation of mineral sediments into layers of cyanobacteria growing in thick mats on surfaces. The oxygen released by these early cyanobacteria is thought to have altered Earth's atmosphere to its current oxygen-rich state, allowing the evolution of additional energy-capturing strategies such as aerobic respiration, the oxygen-consuming metabolic process used by many microbes and animals.

## Evolution of the Three Domains of Life

Look closely at figure 1.3 and find a line labeled "Origin." This is where data indicate the ***l*ast *u*niversal *c*ommon *a*ncestor (LUCA)** to all three domains should be placed. LUCA is the most recent organism from which all three types of life—bacterial, archaeal, and eukaryotic—arose. On this tree of life,

**Figure 1.6 Stromatolites.** Modern stromatolites from Western Australia. Each stromatolite is a rocklike structure, typically 1 m in diameter, containing layers of cyanobacteria.

Horst Mahr/imagebroker/age fotostock

LUCA is on the bacterial branch, which means that Archaea and Eukarya evolved independently, separate from Bacteria.

The evolutionary relationship of Archaea and Eukarya is still a matter of considerable debate. According to the **universal phylogenetic tree** (figure 1.3), Archaea and Eukarya shared common ancestry but diverged and became separate domains. Recent evidence supports the notion that Eukarya evolved from Archaea *(see Microbial Diversity & Ecology 26.1)*. The close evolutionary relationship of these two forms of life is still evident in the manner in which they process genetic information. For instance, certain protein subunits of archaeal and eukaryotic RNA polymerases, the enzymes that catalyze RNA synthesis, resemble each other to the exclusion of those of bacteria. However, archaea have other features that are most similar to their counterparts in bacteria (e.g., mechanisms for conserving energy). This has further complicated and fueled the debate. The evolution of the nucleus and endoplasmic reticulum is also controversial. However, hypotheses regarding the evolution of other membrane-bound organelles are more widely accepted and are considered next.

## Mitochondria, Mitochondria-Like Organelles, and Chloroplasts Evolved from Endosymbionts

The **endosymbiotic hypothesis** is generally accepted as the origin of several eukaryotic organelles, including mitochondria, chloroplasts, and hydrogenosomes. **Endosymbiosis** is an interaction between two organisms in which one organism lives inside the other. The original endosymbiotic hypothesis proposed that over time a bacterial endosymbiont of an ancestral cell in the eukaryotic lineage lost its ability to live independently. If the intracellular bacterium used aerobic respiration, it became a mitochondrion. If the endosymbiont was a cyanobacterium and therefore performed photosynthesis, it became a chloroplast (**figure 1.7**).

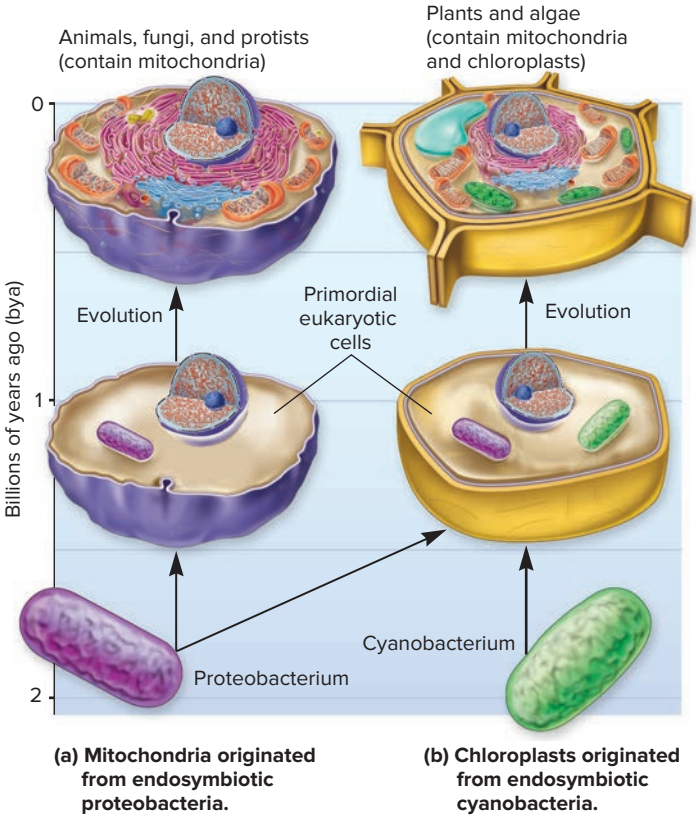



**Figure 1.7 The Endosymbiotic Theory.** (a) According to this hypothesis, mitochondria derived from a bacterium in the phylum Proteobacteria. (b) A similar phenomenon occurred for chloroplasts, which derived from cyanobacteria.

Although the mechanism by which the endosymbiotic relationship was established is unknown, there is considerable evidence to support this hypothesis. Mitochondria and chloroplasts contain DNA and ribosomes; both are similar to bacterial DNA and ribosomes. Peptidoglycan, the unique bacterial cell wall molecule, has even been found between the two membranes that enclose the chloroplasts of some algae. Indeed, inspection of figure 1.3 shows that both organelles belong to the bacterial lineage. More specifically, mitochondria are most closely related to bacteria called proteobacteria. The chloroplasts of plants and green algae are thought to have descended from an ancestor of the cyanobacterial genus *Prochloron,* which contains species that live within marine invertebrates. ▶| *Phylum Cyanobacteria: oxygenic photosynthetic bacteria (section 20.4); The proteobacterial origin of mitochondria (section 21.1)*

The endosymbiotic hypothesis for mitochondria has been refined by the **hydrogen hypothesis.** This asserts that the endosymbiont was an anaerobic bacterium that produced $H_2$ and $CO_2$ as end products of its metabolism. Over time, the host became dependent on the $H_2$ produced by the endosymbiont. Ultimately the endosymbiont evolved into one of several organelles (*see figure 5.13*). Some endosymbionts evolved into organelles such as a hydrogenosome—an organelle found in some extant protists that produces ATP by a process called fermentation *(see figure 5.15).*

## Evolution of Cellular Microbes

Although the history of early cellular life forms may never be known, we know that once microbial cells arose, they were subjected to the same evolutionary processes as modern organisms. The ancestral bacteria, archaea, and eukaryotes possessed genetic information that could be duplicated, lost, or mutated in other ways. Mutations could have many outcomes. Some led to the death of the microbe, but others allowed new functions and characteristics to evolve. Mutations that allowed the organism to increase its rate of reproduction or survival were selected and passed on to subsequent generations. In addition to selective forces, geographic isolation of populations allowed some groups to evolve separately from others. Thus selection and isolation led to the eventual development of new collections of genes (i.e., genotypes) and new species.

In addition to mutation, other mechanisms exist for reconfiguring genomes and therefore creating genetic diversity. Most eukaryotic species increase their genetic diversity by reproducing sexually, whereby each offspring has a mixture of parental genes and a unique genotype. Bacteria and archaea do not reproduce sexually. They increase their genetic diversity by mutation and horizontal gene transfer (HGT). During HGT, genetic information from a donor organism is transferred to a recipient, creating a new genotype in the recipient. In this way genetic information is passed between individuals of the same generation and even between species found in different domains of life. Genome sequencing has revealed that HGT has played an important role in the evolution of all microbial species. Importantly, HGT still occurs in bacteria and archaea leading to the rapid evolution of microorganisms with antibiotic resistance, new virulence properties, and novel metabolic capabilities. The outcome of HGT is that most microbes have mosaic genomes composed of bits and pieces of the genomes of other organisms. ▶| *Horizontal gene transfer: creating genetic variation the asexual way (section 16.4)*

**Phylogenetic** or **phyletic classification systems** compare organisms on the basis of evolutionary relationships. The term **phylogeny** (Greek *phylon,* tribe or race; *genesis,* generation or origin) refers to the evolutionary development of organisms. As discussed, microbial phylogeny relies on comparisons of multiple features found in extant organisms. These include cell wall structure, biomolecules such as fatty acids, and certain housekeeping proteins (proteins used to maintain cellular life, therefore found in many different organisms), and nucleotide sequences, particularly of small subunit rRNA molecules (SSU rRNA) (**table 1.1**). ▶| *Bacterial ribosomes (section 3.7); Archaeal ribosomes (section 4.3); Eukaryotic ribosomes (section 5.5)*

## Phylogenetic Trees

Figure 1.3 is an example of a **phylogenetic tree.** The goal of phylogenetic tree construction is to display the evolutionary