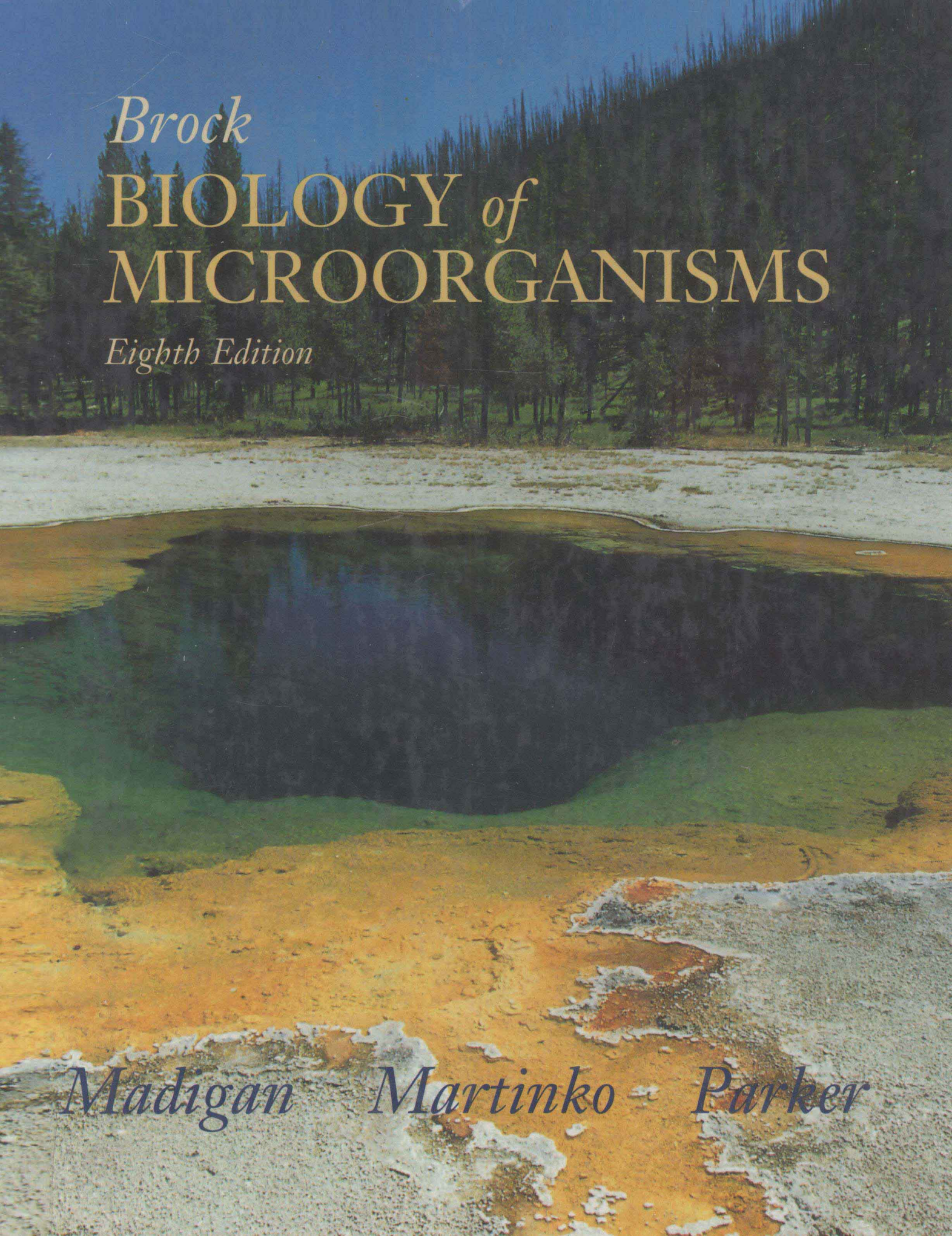

Brock BIOLOGY *of* MICROORGANISMS

Eighth Edition

Madigan Martinko Parker

Brock

Biology of Microorganisms

EIGHTH EDITION

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Biology of Microorganisms

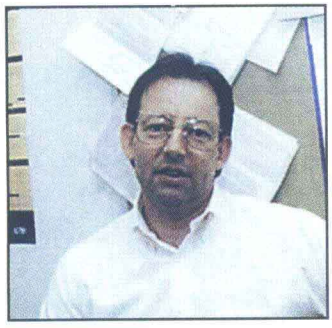
MICHAEL T. MADIGAN dedicates this book to the memory of Andy and Marcy (Yorg and Pedder or "The Feeders")—the two best friends he ever had.

JOHN M. MARTINKO dedicates this book to his wife Judy and to his family. Thanks for your unending patience, good humor, and support during the seemingly unending process of getting this finished!

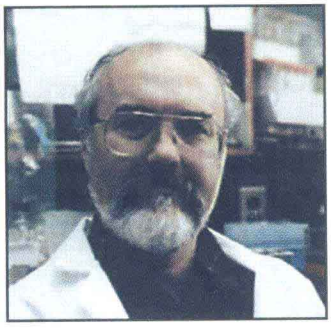
JACK PARKER dedicates this book to Justine, D'Arcy, and Grant Parker: three of the best and brightest.

About the Authors

MICHAEL T. MADIGAN (in photo with Andy) received a bachelor's degree in biology and education from Wisconsin State University at Stevens Point in 1971 and M.S. and Ph.D. degrees in 1974 and 1976, respectively, from the University of Wisconsin, Madison, Department of Bacteriology. His graduate work involved study of the biology of hot spring photosynthetic bacteria under the direction of Thomas D. Brock. Following three years of postdoctoral training in the Department of Microbiology, Indiana University, where he worked on photosynthetic bacteria with Howard Gest, he moved to Southern Illinois University at Carbondale, where he is now Professor of Microbiology. He has been a coauthor of *Biology of Microorganisms* since the fourth edition (1984) and teaches courses in introductory microbiology and bacterial diversity. In 1988 he was selected as the outstanding teacher in the College of Science, and in 1993 its outstanding researcher. His research has dealt almost exclusively with anoxygenic phototrophic bacteria, especially those representatives that inhabit extreme environments, and has focused on the nitrogen-fixing and major photosynthetic properties of these organisms. He has published nearly 75 research papers and has coedited a major treatise on photosynthetic bacteria. His nonscientific interests include reading, hiking, tree planting, and caring for his dogs and horses. He lives on a quiet lake about five miles from the SIU campus with his wife, Nancy, two dogs, Willie and Plum, and King, Peggy, and Silas (horses).



JOHN M. MARTINKO attended The Cleveland State University and majored in biology with a chemistry minor. As an undergraduate student he participated in a unique cooperative education program gaining research experience in several microbiology and immunology laboratories. He then worked for two years at Case Western Reserve University as a Laboratory Manager, continuing his cooperative education research on the structure and serology of *Streptococcus pyogenes* cell wall antigens and on the epidemiology of streptococcal infections. He next went to the State University of New York (SUNY) at Buffalo where he did research on antibody specificity for his M.A. and Ph.D. (1978) in Microbiology. As a postdoctoral fellow, he worked at Albert Einstein College of Medicine in New York on the structure of major histocompatibility complex proteins. Since 1981, he has been in the Department of Microbiology at Southern Illinois University at Carbondale where he is currently the Chair and an Associate Professor. His research interests include the structure, genetics, and evolution of histocompatibility complex proteins and T-cell receptors, the molecular evolution of blood group antigens, and the effects of stress on the immune response. His teaching interests include undergraduate and graduate courses in immunology and a team-taught general microbiology course, where he is responsible for immunology, host defense, and infectious diseases. He lives with his wife, Judy, a junior high school science teacher, and their daughters, Martha and Helen, in Carbondale where he coaches his daughters soccer teams.



JACK PARKER received his bachelor's degree in biology and also received his doctoral degree in a biology program (Ph.D., Purdue University, 1973). However, his research project dealt with bacterial physiology and he completed his Ph.D. research while in the microbiology department at the University of Michigan. Following this he spent four years studying bacterial genetics at York University in Toronto, Ontario. He has taught courses in bacterial genetics, general genetics, molecular biology, and molecular genetics, and has participated in courses in introductory microbiology, medical microbiology, and virology primarily at Southern Illinois University at Carbondale, where he is now a Professor in the Department of Microbiology and Dean of the College of Science. His research has been in the broad area of molecular genetics and gene expression and for the last 15 years has been focused most specifically on studies of how cells control the accuracy of protein synthesis. He is the author of approximately 50 research papers. His home is on the edge of the Shawnee National Forest in deep southern Illinois where he lives with his wife, Beth, and three children, Justine, D'Arcy, and Grant.

Overview

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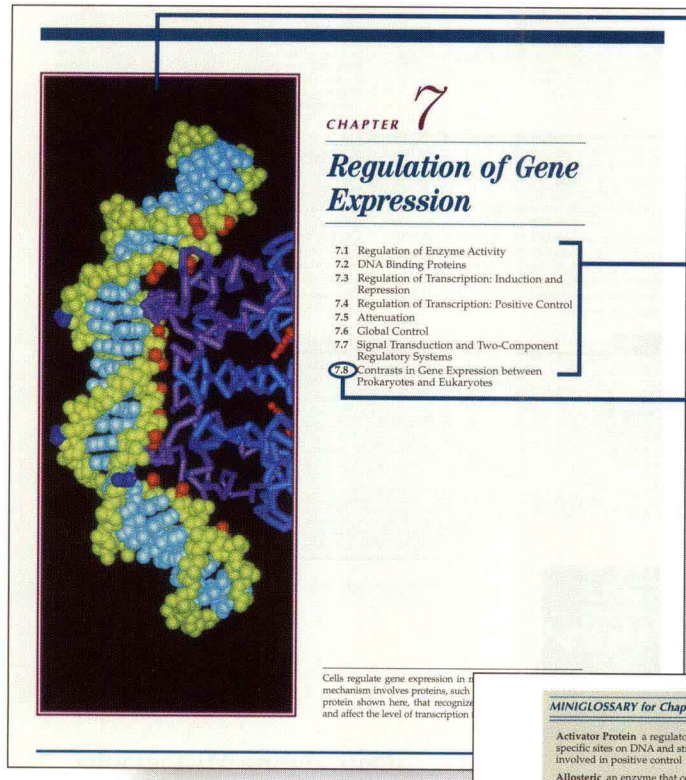

CHAPTER 7

Regulation of Gene Expression

7.1 Regulation of Enzyme Activity
7.2 DNA Binding Proteins
7.3 Regulation of Transcription: Induction and Repression
7.4 Regulation of Transcription: Positive Control
7.5 Attenuation
7.6 Global Control
7.7 Signal Transduction and Two-Component Regulatory Systems
7.8 Contrasts in Gene Expression between Prokaryotes and Eukaryotes

Cells regulate gene expression in r
mechanism involves proteins, such
protein shown here, that recogniz
and affect the level of transcription

Colorful Visuals

full-color photographs throughout the book

Chapter Outline

provides a sketch of the chapter content

Section Numbers

used for convenient reference

MINIGLOSSARY for Chapter 7

Activator Protein a regulatory protein that binds to specific sites on DNA and stimulates transcription; involved in positive control

Allosteric an enzyme that contains two combining sites, the active site (where the substrate binds) and the allosteric site (where an effector molecule binds)

Attenuation a mechanism for controlling gene expression; typically transcription is terminated after initiation but before a full-length mRNA is produced

Feedback Inhibition a decrease in the activity of the first enzyme of a pathway caused by the final product of the pathway

Kinase an enzyme that adds a phosphoryl group to a compound

Repressor Protein a regulatory protein that binds to specific sites on DNA and blocks transcription; involved in negative control

Response Regulator Protein one of the members of a two-component system; a regulatory protein that is phosphorylated by a sensor protein (see Sensor Protein)

Sensor Protein one of the members of a two-component system; a kinase that is found in the cell membrane and that phosphorylates itself in response to an external signal and then passes the phosphoryl group to a response regulator protein (see Response Regulator Protein)

Two-Component System a regulatory system containing a sensor protein and a response regulator protein (see Sensor Protein and Response Regulator Protein)

Miniglossary

provides definitions of important key words found in the chapter

The mechanism of feedback inhibition is of more than just academic interest. We will see in Chapter 12 how an understanding of the biochemistry of feedback inhibition has allowed industrial microbiologists to isolate mutants that have lost the ability to feedback inhibit the production of specific amino acids. These mutants are then used for the large scale commercial production of amino acids as a food supplement (∞ Section 12.7 and Figure 12.17).

Covalent modification

Several examples are known in bacteria in which an enzyme is regulated by being *covalently modified*, usually by addition or deletion of some small organic molecule.

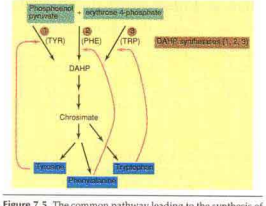

Figure 7.5 The common pathway leading to the synthesis of the aromatic amino acids contains three isozymes of DAHP synthetase. (DAHP is 3-deoxy-*D-arabino*-heptulosonate 7-phosphate.) Each of these enzymes is specifically feedback-inhibited by one of the aromatic amino acids. Note how an excess of all three amino acids is required to completely shut off the synthesis of DAHP.

As in the case of allosteric proteins, the covalent binding of the modifying group changes the conformation of the protein and can dramatically affect its catalytic activity. Removal of the modifying group returns the enzyme to an active state. Many examples of covalent modification regulatory systems are known, but the best characterized are enzymes whose activity is affected by attachment of the nucleotide adenosine monophosphate (AMP) or adenosine diphosphate (ADP), by attachment of inorganic phosphate, or by methylation.

These examples are representative of the major regulatory patterns observed; there are other, rather elegant examples of regulation now known. The phenomenon of enzyme regulation may have evolved because efficient control of the rate of enzyme *activity* enables an organism to quickly adapt to changing environments.

CONCEPT CHECK 7.1

The vast array of metabolic reactions do not all occur in the cell at the same rate. Metabolic reactions can be regulated through control of the activities of the enzymes that catalyze these reactions. An important type of regulation of enzyme activity is feedback inhibition, in which the final product of a biosynthetic pathway feeds back and inhibits the first enzyme unique to that pathway. Covalent modification is a regulatory mechanism for temporarily inactivating a specific enzyme.

✔ *How does* feedback inhibition *differ from* product inhibition?

✔ *What is an* allosteric enzyme?

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reiterates key concepts and provides "quick quiz" for students

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Tables

summarize important information for easy reference

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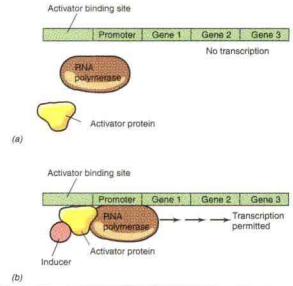


Figure 7.13 Positive control of enzyme induction. (a) In the absence of an inducer, neither the activator protein nor the RNA polymerase can bind to the DNA. (b) An inducer molecule binds to the activator protein, which in turn binds to the activator binding site. This allows RNA polymerase to bind to the promoter and begin transcription.

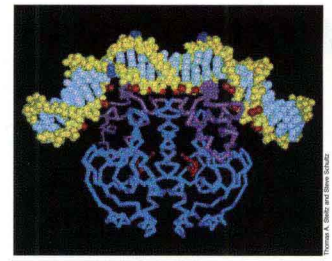


Figure 7.14 Computer model of the interaction of a positive regulatory protein with DNA. This figure shows the cyclic AMP binding protein, a regulatory protein involved in the control of several operons (see Section 7.6). The α-carbon backbone of this protein is shown in blue and purple. The protein is shown binding to a DNA double helix, which is shown in yellow and light blue. Note that binding of this protein to DNA has caused the DNA to be bent by almost 90°. Reprinted with permission from Science 253:1001–1007 (1991), © AAAS.

regulation may have evolved because efficient control of the rate of enzyme activity. However, working together, these mechanisms result in an efficient regulation of cell metabolism so energy is not wasted carrying out unnecessary reactions.

Control systems that vary the level of *expression* of particular genes are the main subject of this chapter. However, the actual number of different regulatory mechanisms is vast, and most genes seem to be regulated by more than one. We begin by briefly discussing the processes involved in regulating the *activity* of preformed enzymes before considering how the synthesis of enzymes is controlled.

7.1 Regulation of Enzyme Activity

There are a large number of mechanisms of posttranslational regulation. In some cases an enzyme is synthesized as part of a larger inactive precursor protein, and the enzyme must be activated by removing a portion of the precursor protein. Another mechanism is to reduce the level of activity by actually degrading the enzyme molecules. However, we discuss here a reversible and temporary form of regulation involving less drastic changes to the enzyme molecule.

TABLE 7.1 A few of the global control systems known in *Escherichia coli*[a]

System	Signal	Primary activity of regulatory protein	Number of genes regulated
Aerobic respiration	Presence of O_2	Repressor	20
Anaerobic respiration	Lack of O_2	Activator	20+
Catabolite repression	Cyclic AMP concentration	Activator	300+
Heat shock	Temperature	Alternative sigma	17
Nitrogen utilization	NH_3 limitation	Activator/alternative sigma	12+
Oxidative stress	Oxidizing agent	Activator	12+
SOS response	Damaged DNA	Repressor	17

[a]For many of the global control systems, regulation is complex. A single regulatory protein can play more than one role. For instance, the regulatory protein for anaerobic respiration, FNR, is an activator protein for many promoters but a repressor for others. Regulation can also be indirect or ... the activator for the nitrogen utilization system activates promoters recognized by an alterna... proteins involved are members of two-component systems (see Section 7.7). Many genes are ... for a discussion of the SOS response, see Section 9.3.)

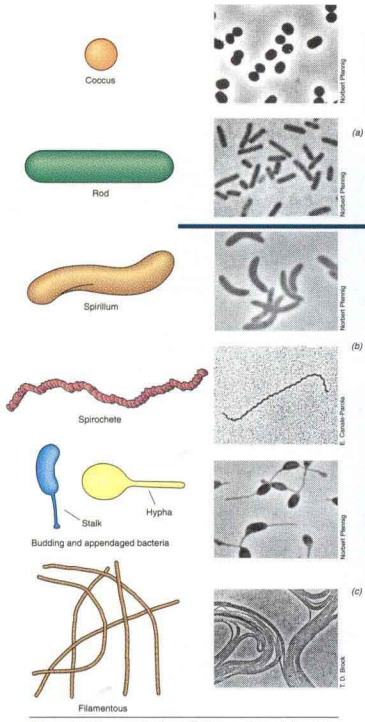


Figure 3.9 Representative cell shapes (morphology) in prokaryotes. Next to each drawing is a phase photomicrograph showing an example of that morphology. Organisms are coccus, *Thiocapsa roseopersicina* (diameter of a single cell = 1.5 μm); rod, *Desulfuromonas acetoxidans* (diameter = 1 μm); spirillum, *Rhodospirillum rubrum* (diameter = 1 μm); spirochete, *Spirochaeta stenostrepta* (diameter = 0.25 μm); budding and appendaged, *Rhodomicrobium vannielii* (diameter = 1.2 μm); filamentous, *Chloroflexus aurantiacus* (diameter = 0.8 μm).

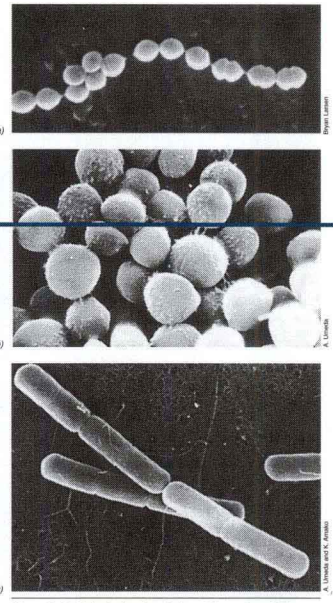


Figure 3.10 Spherical and rod-shaped bacteria, which associate in characteristically different ways as viewed by scanning electron microscopy. (a) *Streptococcus*, a chain-forming organism that divides only in one plane. (b) *Staphylococcus*, a coccus that divides in more than one plane. Cells of both organisms are about 1 μm in diameter. (c) Chains of the rod-shaped bacterium *Bacillus*. Cells are about 0.8 μm in diame-

which is a complex but highly organized process. Two identical daughter cells result from the division of one parent cell; each daughter cell receives a nucleus with an identical set of chromosomes.

Eukaryotic cells also contain distinct structures called **organelles,** within which important cellular functions occur (Figure 3.11). Organelles are absent from prokaryotes, although major physiological processes that take place in organelles, such as respiration and photosyn-

TECHNIQUES & APPLICATIONS

Working with Nucleic Acids: The Tools

Our knowledge of molecular biology and genetics has depended on the development of adequate research tools. Advances in knowledge of how nucleic acids work have generally been tied to the development of new methods. We discuss here some of these methods.

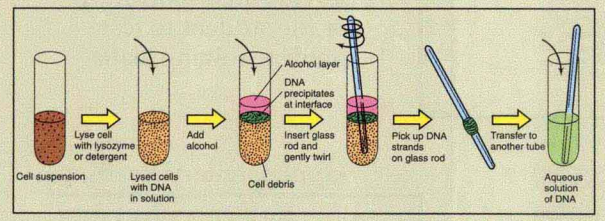
1. Extraction and purification of DNA The first requirement is a sample of DNA free of other cellular chemicals. The steps in the purification of DNA are shown here. The aqueous solution in the final step is treated with RNAse to remove RNA. Proteins are then removed by use of denaturing solvents (usually phenol). By repeating the purification steps a number of times, a solution can be obtained that is virtually free of any components other than DNA.

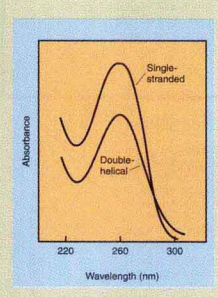
Note that the solution of DNA obtained never consists of native DNA molecules of the length found in the cell. The purification process causes the DNA to be broken into fragments of various (random) lengths. If the DNA has been handled gently during purification, the lengths of the fragments will be about one-hundredth of the length of the whole chromosome.

2. Detecting the presence of DNA There are several methods for detecting the presence of DNA in a solution. One of the most widely used is by its absorption of ultraviolet radiation. DNA strongly absorbs ultraviolet radiation at a wavelength of 260 nm. The absorption is due to the purine and pyrimidine bases. As seen in the figure, double-stranded DNA absorbs less strongly than single-stranded DNA. This is because the interaction between the bases on the opposite strands of the double-stranded DNA (hydrogen bonding) reduces the ultraviolet absorbance.

3. Density-gradient centrifugation of DNA DNA molecules vary in density, depending on their exact chemical composition. DNA molecules with a higher content of guanine plus cytosine (GC) are denser than molecules with low GC. The density of DNA can be determined by centrifugation at very high speed in a *gradient* of cesium chloride (CsCl). The DNA solution is added to a solution of CsCl and centrifuged at high speed for several hours until equilibrium is reached. The CsCl forms a density gradient from the top to bottom of the tube, and DNA molecules form bands at appropriate densities. At equilibrium, the DNA molecules become positioned in the gradient at positions corresponding to their densities. If ethidium bromide has been added, observation of the centrifuge tube with ultraviolet radiation after the centrifugation reveals bands of DNA by fluorescence (see later). This method is called the *buoyant density method* and permits both determination of density and separation of molecules of differing density.

4. Gel electrophoresis One of the most widespread methods of





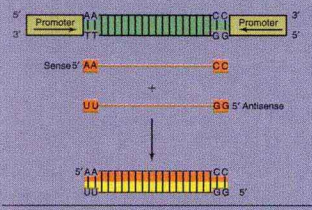
A FOCUS ON . . .

Antisense Nucleic Acid

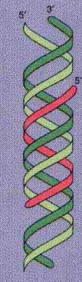
Regulation of the synthesis of proteins often involves transcriptional control. Less often, genes are controlled at the level of translation. Most control networks, whether they are transcriptional or translational, utilize regulatory proteins. However, it is now clear that in some cases it is a regulatory *RNA*, not a regulatory *protein*, that is involved. One type of regulatory RNA, called **antisense RNA,** is known to be used in the regulation of several different bacterial genes. Antisense RNA acts by forming base pairs with a complementary, or sense, strand of RNA. When the sense RNA is mRNA, the resulting double-stranded structure can prevent translation. Antisense RNA can be synthesized from the same gene as the sense RNA by having a second promoter oriented in the direction opposite that of the first or by having a second gene with the promoter at the other end. Antisense RNA does not have to be used only to regulate the synthesis of a protein. In some plasmids, it controls the initiation of DNA synthesis.

Antisense nucleic acids can be specifically designed and synthesized by scientists in the laboratory and delivered directly to cells. These short (15–25 nucleotides) synthetic chains (oligonucleotides) are usually made of DNA rather than RNA. Their sequence can be made to allow them to bind to a specific mRNA and prevent translation (or allow the molecule to be recognized by nucleases). Antisense nucleic acid can also bind to the DNA in the nucleus and prevent transcription. The latter is possible because some DNA can form a *triple* helix! The "extra" strand (the oligonucleotide) forms specific interactions with those parts of the bases that are in the major groove of a normal double helix to give **triplex DNA.** (Not all DNA sequences can form triple helices, at least not without the aid of special enzymes.)

Synthetic antisense oligonucleotides can be designed to be extremely specific, whether they bind to a message or to the regulatory region of a gene. The specificity arises because a sequence of only 20 bases should occur no more often than once in 10^{12} bases of "random" DNA. Therefore, it is unlikely that the antisense RNA would bind to anything other than its known target in any cell. This specificity might allow antisense nucleic acids to become an important new type of antibiotic, and this possibility is being pursued by a number of pharmaceutical companies. Antisense nucleic acids could be designed to be used against specific viruses or to regulate particular genes in either disease-causing (pathogenic) organisms or human tumor cells. The possible utility of these molecules is just one example of how understanding the structure of a gene may have very practical applications (☞ Chapter 10). ■



A gene with promoters at either end. If the RNA made by the promoter on the left is the *sense* RNA, then the RNA made by the promoter on the right is the *antisense* RNA. If both RNA molecules are made, they will form a duplex. Only a relatively short region of overlap is necessary for strong base pairing. Usually the antisense RNA is shorter than the sense RNA, and therefore the second promoter is actually within the gene.



A triple helix. The "extra" strand is shown in red and is in the major groove of a double helix.

Boxed Features
provide additional information on relevant topics

Techniques & Applications:
microbiologists' methods and the ways in which microbioloby is useful in the "real" world

Learning from the Past:
historical developments in microbiology

A Focus On...:
more in-depth discussions of important text topics

Boldfaced Key Terms
also defined in the Glossary

Concept Links
cue the student that new material is related to or builds on an earlier discussion

Material for Review

REVIEW QUESTIONS

1. If an enzyme can be effectively inhibited by feedback inhibition, why would cells also have mechanisms to regulate its synthesis?
2. Describe why a protein that binds to a specific sequence of double-stranded DNA is unlikely to bind to the same sequence if the DNA is single-stranded.
3. Describe the regulation of two different operons, one having an effector that is an *inducer* and the other having an effector that is a *corepressor.*
4. The maltose regulon is inducible and is regulated by an activator protein. The lactose operon is inducible but is regulated by a repressor protein. Explain how induction can be brought about by either positive control (activator protein) or negative control (repressor protein).
5. In most cases operators are very close to the promoters they control, while activator binding sites can be some distance away. Explain why this should be so.
6. Describe how transcriptional attenuation works. What is actually being "attenuated"? Why hasn't the type of attenuation that controls several different amino acid biosynthetic pathways in *Escherichia coli* also been found in eukaryotes?
7. Describe the mechanism by which catabolic activator protein (CAP), the regulatory protein for catabolite repression, functions using the lactose operon as an example. For this operon the CAP protein is not a repressor. Describe the regulatory region of a gene for which the CAP protein *is* a repressor. (*Hint:* Think about your answer to Question 5.)
8. What are the two components that give the name to signal transduction regulation in prokaryotes? What is the function of each of the components?
9. One of the members of a two-component system is typically located in the cell membrane. What reason can you think of why this might be so?
10. Many genes are under multiple control systems. In the lactose operon, there is lactose-specific regulation and regulation by a global control system. Describe how each of the controls on the lactose operon actually functions. Why do you think both systems are necessary?

APPLICATION QUESTIONS

1. The amino acids isoleucine and valine share a common pathway for most steps in their biosynthesis. In *Escherichia coli* the first common step can be subject to feedback inhibition by valine but not by isoleucine. In most strains, though, the addition of valine does not cause isoleucine deprivation. However, in other strains it does (that is, adding valine causes isoleucine starvation and the cells stop growing). What explanation can you give for the difference between the normal "valine-resistant" strains and those whose growth is sensitive to valine?
2. What would happen to regulation from a promoter under negative control if the region where the regulatory protein binds were deleted? What if the promoter were under positive control?
3. Promoters from *Escherichia coli* under positive control are not close matches to the DNA consensus sequence for *E. coli* (CO Section 6.6). Why?
4. Interestingly, the attenuation control of some of the pyrimidine biosynthetic pathway genes in *Escherichia coli* actually involves coupled transcription and translation. Can you describe a mechanism whereby the cell could somehow make use of translation to help it measure the level of pyrimidine nucleotides?

SUPPLEMENTARY READINGS

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On-line resources for this chapter are on the World Wide Web a
http://www.prenhall.com/~brock (click on the table of contents li

Review Questions

challenge the student's mastery of chapter concepts

Application Questions

provide an opportunity for the student to test problem-solving skills

Supplementary Readings

offer further sources for in-depth pursuit of a topic

Appendices

provide useful tutorial and reference information

Website Icon

links students and instructors to resources on the Web including an interactive microbiology study guide, links to "hot" micro sites, and teaching strategies using the Web.

APPENDIX 2 Advanced Mathematics of Microbial Growth and Chemostat Operation

Exponential Growth

Although analyses of microbial growth can be done graphically or algebraically, as discussed in Chapter 5, for some purposes it is necessary to use a differential equation to express the quantitative relationships of growth:

$$\frac{dX}{dt} = \mu X \qquad (1)$$

where X may be cell number or some specific cellular component such as protein and μ is the *instantaneous growth-rate constant.* When this equation is integrated, we obtain a form that reflects the activities of a typical microbial population in batch culture:

$$\ln X = \ln X_0 + \mu(t) \qquad (2)$$

where ln refers to the natural logarithm (logarithm base e), X_0 is cell number at time 0, X is cell number at time t, and t is elapsed time during which growth is measured. This equation fits experimental data from the exponential phase of bacterial cultures very well, such as those in Figure 5.2. Taking the antilogarithm of each side gives

$$X = X_0 e^{\mu t} \qquad (3)$$

This equation is useful because it allows prediction of population density at a future time from the present value and μ, the growth-rate constant. As discussed in Section 5.2, an important constant parameter for an exponentially growing population is the doubling (or generation) time. Doubling of the population has occurred when $X/X_0 = 2$. Rearranging and substituting this value into Equation (3) gives

$$2 = e^{\mu(t_{gen})} \qquad (4)$$

Taking the natural logarithm of each side and rearranging gives

$$\mu = \frac{\ln 2}{t_{gen}} = \frac{0.693}{t_{gen}} \qquad (5)$$

The generation time, t_{gen}, may be used to define another growth parameter, k, as follows:

$$k = \frac{1}{t_{gen}} \qquad (6)$$

where k is the growth-rate constant for a batch culture. Combining Equations (5) and (6) shows that the two growth-rate constants, μ and k, are related:

$$\mu = 0.693k$$

It is important to understand that μ and k are both reflections of the same growth process of an exponentially increasing population. The difference between them may be seen in their derivation: μ is the *instantaneous rate constant,* and k is an *average* value for the population over a finite period of time. (See Table A2.1 for calculation of k values from experimental results.) This distinction is more than a mathematical point. As was emphasized in Chapter 5, microbial growth studies must deal with *population* phenomena, not the activities of individual cells. The constant k reflects this averaging assumption. However, the constant μ, being instantaneous, is a closer approximation of the rate at which individual activities are occurring. Further, the instantaneous constant μ allows us to consider bacterial growth dynamics in a theoretical framework separate from the traditional batch culture.

Mathematical relationships of chemostats

An especially important application of the instantaneous growth-rate constant, μ, is the chemostat, a culture device (CO Section 5.5) in which population size and growth rate may be maintained at constant values of the experimenter's choosing over a wide range of values. As we saw in Section 5.5, the rate of bacterial growth is a function of nutrient concentration. This function represents a saturation process that may be described by the equation

TABLE A2.1 Calculation of k values

Bacterial population densities are expressed in scientific notation with powers of 10, and so Equation (3) may be converted to terms of logarithm base 10 and k substituted for the instantaneous constant μ:

$$k = \frac{\log_{10} X_t - \log_{10} X_0}{0.301t}$$

Example 1:
X_0 = 1000 (= 10^3) $\log_{10}$ of 1000 = 3
X_t = 100,000 (= 10^5) $\log_{10}$ of 100,000 = 5
t = 4 hr
$k = \frac{5-3}{(0.301)4} = \frac{2}{1.204}$
k = 1.66 doublings/hr
t_{gen} = 0.60 hr (36 min) for population to double

Example 2:
X_0 = 1000 (= 10^3) $\log_{10}$ of 1000 = 3
X_t = 100,000,000 (= 10^8) $\log_{10}$ of 10^8 = 8
t = 120 hr
$k = \frac{8-3}{(0.301)120} = \frac{5}{36.12}$
k = 0.138 doubling/hr
t_{gen} = 7.2 hr (430 min) for population to double

Preface

A new Golden Age of Microbiology is upon us! An entire bacterial genome can be sequenced in a few months' time, our understanding of the molecular bases of microbial diseases has blossomed, we have developed keen insight into the inner workings and evolutionary history of microorganisms, and career opportunities in the biomedical sciences are unprecedented. What a great time to learn microbiology! We therefore take great pride in introducing students to the field of microbiology as it exists today through our book, *Brock Biology of Microorganisms 8/e.*

Like previous editions of *Biology of Microorganisms, Brock Biology of Microorganisms 8/e (BBOM 8/e)* clearly presents the essential concepts of microbiology and illustrates them with the latest information available from the scientific literature. However, our main goal remains the same as it has always been: to explain the basic science and applications of microbiology at a level that the introductory student can readily appreciate and master but in a way that generates excitement about this fundamental area of biology.

With this new edition, the title of our book has changed, as Thomas D. Brock—the architect of the previous seven editions of *Biology of Microorganisms*—has passed the torch to his co-authors. However, the reader can be assured that we are firmly committed to maintaining the outstanding reputation this book has enjoyed for over a quarter of a century. It is thus fitting and proper that the name *Brock* be incorporated into the title because although he is no longer a co-author, *Brock Biology of Microorganisms 8/e* continues to emphasize strong, well-documented science, a philosophy that made Thomas Brock one of the premier scientists and educators of the last half of this century. The current co-authors of *BBOM 8/e* have integrated this philosophy into their own coverage of the three major areas of microbiology today: general/organismal (Madigan), molecular/genetic (Parker), and medical/immunological (Martinko).

Changes from the 7th Edition

Users of previous editions of *Biology of Microorganisms* will note some organizational changes in this book. The medical/immunology block of chapters, previously placed in the middle of the book, has been moved to the end. From the examination of over 75 lecture outlines for introductory microbiology courses and from discussions with several users of the book, the authors were convinced that this move made good pedagogical sense and was consistent with the mainstream of introductory microbiology courses. As a result of this change, the chapters on metabolic diversity, ecology, evolution, and the major microbial groups have been moved forward and now closely follow the introductory and genetics chapters. We have also moved the chapter on microbial growth forward to immediately follow the chapter on nutrition and metabolism. This is the point in introductory microbiology courses where the concepts of exponential growth are usually taught and frequently illustrated with laboratory experiments; thus, the new edition places the growth material where it should be most useful for tying together lecture concepts with laboratory practice. The sequence of chapters in *BBOM 8/e* also closely follows the guidelines established by the Education Division of the American Society for Microbiology (ASM) for teaching introductory microbiology courses.

Two new chapters appear in *Brock Biology of Microorganisms 8/e.* The first, Chapter 7, is entitled "Regulation of Gene Expression." This chapter, whose foundation was previously present in the chapter entitled "Macromolecules and Molecular Genetics," focuses on how genes are controlled in prokaryotes. This material has been strengthened by the addition of new information on "two-component regulatory systems" (using chemotaxis as a molecular model) and other examples of the exciting area of bacterial gene regulation. The second new chapter, Chapter 11, is entitled "Microbial Control Agents." In this chapter we have consolidated discussion of the basic science and mode of action of antibiotics and chemotherapeutic agents, as well as other antimicrobial agents. Instructors who wish to cover this material as a unit will now find it logically organized and in one place. The chapter on industrial microbiology also contains some material on antibiotics, but the focus here is on *industrial production* rather than on the characteristics of the agents themselves.

Besides these organizational changes and new chapters, *Brock Biology of Microorganism 8/e* has undergone extensive revision in every chapter. The genetics revolution of the past 20 years has spawned new and powerful research tools that have impacted virtually every area of microbiology; as a result, bacterial genetics now offers solutions to applied problems in medicine, agriculture, and the environment. All these areas are covered here, stressing real-life examples that join the theoretical with the practical and make the material come alive.

Despite these changes, however, users of previous editions of this book can rest assured that *Brock Biology of Microorganisms 8/e* retains its emphasis on the microorganisms themselves. Although important research tools, microorganisms are significant in their own right and their basic biology and ecological activities remain the focus of this book. In addition, we have made every effort to produce an up-to-date book that maintains the authority, clarity, and breadth of coverage that instruc-

tors expect from *Biology of Microorganisms*. We trust that users will agree and we welcome comments from students and instructors alike on any aspect of our book.

Pedagogical Aids

A variety of teaching and learning aids are built into *Brock Biology of Microorganisms 8/e*, some of them new to this edition.

Art and Photographs Virtually every piece of full color art has seen revision and several new pieces of art have been added to keep pace with the rapid developments occurring in the field of microbiology and to assist instructors in teaching the essential concepts of science. The color coding of macromolecules in all pieces of art remains the same as in previous editions: the two strands of DNA are in different shades of green, RNA is orange, and proteins are brown. From Chapter 1 through Chapter 23 this consistency in the use of color will help reinforce essential concepts and give students helpful visual feedback. As is a tradition with *Biology of Microorganisms*, this new edition contains superb photos obtained by the authors directly from researchers. Students and instructors alike will also appreciate how the electron micrographs in *BBOM 8/e* look just the way a scientist would see them in a research journal—as *black and white* photographs. The authors have resisted the practice of some microbiology textbooks to use false color to "enhance" electron micrographs; ironically, although admittedly adding color, such practice only decreases resolution. Thus, in *BBOM 8/e* the reader will be treated to electron micrographs that are crisp, clear, and as scientifically accurate as those published in the primary microbiological literature. Many of the light micrographs are in color, of course, because they were taken with color film to capture the natural colors of many microorganisms and microbial habitats.

Concept Checks and Concept Links The "In Brief" segments, first introduced in the 6th edition, have been blended into a new learning aid we call **Concept Checks.** A concept check consists of a brief overview of the material in the previous section followed by several short questions designed to ensure that students have gotten the "take-home" message from what they have just read. Concept Checks can be thought of as "speed bumps" along the road of text, figures, and tables in each chapter, and are intended to either reinforce what has just been learned or to signal that a key point has been missed.

In addition to Concept Checks, **Concept Links** are new to this edition. Concept Links, indicated by the chain link icon (∞), alert the reader to ties between what is being read and related material found elsewhere in the book. The section numbering system in *BBOM 8/e*, employed since the first edition and a unique organizational feature among microbiology textbooks, accompany Concept Links to direct the reader to the related material.

Study Questions, Supplementary Readings and Miniglossaries As usual, relevant and challenging **Study Questions,** many of them new to this edition, can be found at the end of each chapter. However, two levels of questions are now included. *Review Questions* emphasize factual material—the "database" necessary for an understanding of the concepts—while *Application Questions* require students to apply what they know, synthesize information, and solve a problem. The authors hope that the application questions will help build critical thinking skills in beginning microbiology students as they assimilate the basic information and master key microbiological concepts. As usual, the most recent **Supplementary Readings** will be found at the end of each chapter for students and instructors who wish to go beyond the textbook for a more detailed treatment of the material.

We maintain the popular **Miniglossaries** in the new edition. The old sports adage "You can't follow the *players* without a *program*," has a counterpart in microbiology: "You can't follow the *concepts* without the *language*." Thus, early in each chapter the key terms necessary to understand the ensuing material are succinctly defined and gathered together in one place for quick reference while reading the chapter. The authors feel that regular use of the miniglossaries will quickly build vocabulary and help reinforce critical concepts.

Boxes Boxes have become a popular means of focusing on particular issues in both textbooks and in the popular press. In *Brock Biology of Microorganisms 8/e* we have written a number of **new boxes** and have organized all of the boxes along three major themes: "Learning from the Past" (enrichment boxes placing a microbiological concept in historical context), "Techniques and Applications" (boxes that describe a particular method or application of a method central to the field of microbiology), and "A Focus On" (boxes that take an in-depth look at a particular aspect or issue in microbiology of both scientific and general interest). In addition, we have made considerable efforts to illustrate our boxes, either with photos or with art (or with both in some cases), in order for the reader to better visualize the points discussed.

All in all, we feel that the combination of learning aids and enrichment materials woven into *Brock Biology of Microorganisms 8/e* will make for a strong learning experience but will at the same time support, rather than detract from the main message—text, figures, and tables—that make up the core of the book.

Chapter Highlights in *Brock Biology of Microorganisms 8/e* include:

Chapter 1—Introduction: Overview of Microbiology and Cell Biology builds on the approach of previous editions as the introduction to the basic biology of the cell. New material on culturing methods and Koch's

postulates along with a new box on the development of solid culture media, enrich this chapter.

Chapter 2—Cell Chemistry maintains its important early position in the book as the chemical primer every student needs to master. The emphasis remains on understanding the *fundamental chemistry of macromolecules* and vivid illustrations help solidify this essential information. A new illustrated box on Pasteur and stereoisomerism enrich this chapter with historical perspective.

Chapter 3—Cell Biology emphasizes the structure of the prokaryotic cell with a completely rewritten section on the bacterial nucleoid and significant new material on cell wall structure. A new box discussing the possibility that bacterial endospores could survive for millions of years will be sure to stir controversy in both students and instructors alike.

Chapter 4—Nutrition and Metabolism has been reorganized to begin with an overview of basic nutrition and culture media from which it flows into concepts of enzymes, energetics, and metabolism. A new section on fatty acid biosynthesis completes the previous discussion of anabolic processes.

Chapter 5—Microbial Growth focuses on the concepts of exponential growth and population growth and flows from here into a discussion of environmental effects on microbial growth. Applied aspects (for example, control of microbial growth) have been moved to a new chapter (Chapter 11). New material on methods for measuring microbial growth bring the laboratory and the classroom closer together.

Chapter 6—Macromolecules and Molecular Genetics is shortened from the previous edition to maintain the focus on basic macromolecular syntheses and the key proteins and structures required to carry them out. Vivid and pedagogical use of color will guide the student through the central concepts of molecular biology as they occur in prokaryotes, contrasting them when appropriate with molecular processes in eukaryotes.

Chapter 7—Regulation of Gene Expression is a totally new chapter that blends discussion of both classical regulatory phenomena like induction and repression with new material on global control mechanisms. The hot topic of "signal transduction" involving two-component regulatory systems is introduced here using bacterial chemotaxis as a model of this complex regulatory process.

Chapter 8—Viruses has been streamlined somewhat to retain the focus on the essentials of viral replication. This chapter ends with an expanded section on viroids and prions—virus-like particles that are not viruses—comparing and contrasting these interesting genetic elements with viruses and emphasizing their unique replication features and pathogenic properties.

Chapter 9—Microbial Genetics builds on the material in Chapters 6 through 8 to create a modern picture of genetics in prokaryotes. Coverage of both classical bacterial genetics and the molecular phenomena behind it is well supported by new art and illustrated boxes depicting the historical development of the field of bacterial genetics. New material on the bacterial genetic map and genomic sequencing reflect the enormous strides made in these areas in recent years. This chapter closes by contrasting prokaryotic and eukaryotic genetics using the highly studied *Saccharomyces cerevisiae* (baker's yeast) as a model eukaryote.

Chapter 10—Genetic Engineering and Biotechnology remains an up-to-the-minute chapter, discussing all the basic tools and methods of recombinant DNA technology and their latest applications in the field of biotechnology. The chapter has been greatly updated and strengthened with the addition of dramatic color photos illustrating new genetically engineered systems. But as always, the coverage in this chapter emphasizes the *basic science* behind the applications, tying it to the principles of molecular biology and genetics developed in Chapters 6–9.

Chapter 11—Microbial Growth Control is a new chapter consolidating coverage of material on chemical and physical agents used to prevent microbial growth. Discussion of major antibiotics of clinical significance highlight this chapter with the emphasis remaining on the structure and mode of action of antimicrobial agents and the basic principles behind microbial growth control.

Chapter 12—Industrial Microbiology focuses on large-scale microbial fermentations with antibiotic production remaining the driving force. However, several new pieces of art have been added to better illustrate the industrial production of important chemicals other than antibiotics, such as vitamins, amino acids and citric acid, and several new color photos of "industrial microbiology in action" will help students better grasp the variety and scale of industrial microbial processes. The "Home Brew" box, always a hit with students, is now illustrated with color photos to show the major steps in the small-scale brewing of beers and ales. Material on sewage and wastewater treatment round out this chapter, reminding students and instructors alike that this essential part of everyday life is a prime example of the large-scale use of microorganisms.

Chapter 13—Metabolic Diversity has been heavily revised to bring out the latest information on the nearly limitless ways in which microorganisms obtain the energy needed for growth. New material on syntrophic relationships among chemoorganotrophic bacteria and iron oxidation by phototrophic bacteria (an example of a totally new *concept* in microbiology), bring this chapter up to the minute.

Chapter 14—Microbial Ecology begins with new discussion of basic ecological principles underlying the activities of cells, cell populations, and communities of microorganisms in nature. New material has been added in virtually every section of this chapter and new boxes like "Microbial Life Deep Under-

ground" dramatically emphasize the old adage in microbiology that "bugs are everywhere".

Chapter 15—Microbial Evolution, Systematics, and Taxonomy has been shortened somewhat from the seventh edition by deletion of the detailed phylogenetic pictures of each major domain of life; the latter material has been updated and integrated as an introduction to each of the organisms chapters (Chapters 16–18). A more detailed treatment of classical bacterial taxonomy has been added to this chapter to better tie together phylogenetic and more traditional approaches of bacterial classification. New material on the "RNA world" and early life forms reflect the rapid advancements in our understanding of the origin of life.

Chapter 16–18—these "organisms" chapters remain the core of the traditional microbial diversity theme of *Biology of Microorganisms.* Each chapter (16–Prokaryotic Diversity: Bacteria; 17–Prokaryotic Diversity: Archaea; and 18–Eukarya: Eukaryotic Microorganisms) begins with a phylogenetic overview and then proceeds to a detailed description of the major microbial groups. Every section of these three chapters has seen updating as a result of the great strides made in understanding microbial diversity in recent years.

Chapter 19—Host–Parasite Relationships maintains the long tradition in this book of covering microbial interactions with humans. The focus remains on the struggle between the host and the parasite and the major weapons both possess to maintain health or to induce disease. To streamline this chapter coverage of cells involved in nonspecific immunity has been moved to Chapter 20 as part of an introduction to the immune system.

Chapter 20—Concepts of Immunology has been heavily updated to incorporate the latest concepts in probably the fastest moving field in all of biology. The focus here is on the *basic science* behind immunology; much of the material on applied and clinical microbiology has been moved to the next chapter. However, a new box on "Catalytic Antibodies" ties basic concepts to future applications and emphasizes how basic science frequently spawns exciting applications.

Chapter 21—Clinical and Diagnostic Microbiology and Immunology consolidates the microbiology and immunology applications of clinical significance. Several highly innovative clinical diagnostic methods have emerged from advances in microbiology and immunology and are described in detail in this chapter. Because these methods are rapidly changing the way hospital microbiology is done, this chapter will surely be important for courses with a health professions emphasis. Look for a number of new color photos here that show how clinical microbiology is done today.

Chapter 22—Epidemiology and Public Health Microbiology sets the stage for consideration of specific diseases in the following chapter by outlining the principles of disease transmission and the concepts of public health. An exciting new section on emerging and resurgent infectious diseases brings this chapter up-to-the-minute, describing how these diseases are so abruptly and successfully transmitted when conditions are right. New tables on epidemic diseases, immunization statistics, reportable diseases, resurgent and emerging diseases, and virulence factors help tie the concepts of disease transmission to real-life human situations and also lend reference value to this chapter.

Chapter 23—Major Microbiology Diseases maintains broad coverage of microbial diseases using an ecological approach of grouping individual diseases by their mode of transmission. As you would expect in such a chapter, every section has received updating, especially the coverage of AIDS. This chapter comes alive with excellent color photos and disease statistics that show human disease symptoms and reflect the worldwide prevalence and trends of these diseases.

Supplements

Several Supplements accompany this textbook. These include a **Student Study Guide,** which highlights key topics and contains a wealth of additional objective and subjective review questions. For the instructor, a valuable **Instructor's Manual** and **Test Item File** is available which describes various ways to structure an introductory microbiology course using *BBOM 8/e* as text, and gives answers to all the Study Questions. In addition, a set of **250 Color Transparencies** (containing over 350 individual pieces of art) will greatly assist instructors in organizing and presenting class lectures. In addition, a **CD-ROM** containing all art and tables from *Brock Biology of Microorganisms 8/e* is available to instructors for instant access to these materials in the classroom.

The **Contemporary View** program sponsored jointly by Prentice Hall and *The New York Times,* and initiated with the sixth edition of *Biology of Microorganisms,* complements the new edition as well. Through this program, core subject matter from the text is supplemented by articles describing microbiology in "real-life" situations pared from the pages of *The New York Times.* Contemporary View will strengthen the connection between the classroom and the real world, as students see how important an understanding of microbiology is to activities in their everyday lives.

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Brief Contents

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