中国科学院研究生教学丛书

生物化学导论（第二版）

BIOCHEMISTRY: AN INTRODUCTION (Second Edition)

（影印版）

著者 Trudy McKee
Thomas Jefferson University
James R. McKee
University of the Sciences in Philadelphia

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内 容 简 介

本书属于中国科学院推荐的研究生用原版教材。本书作者资深生物化学教授 Trudy McKee，以逻辑性强和易于理解的编写风格使得学生能够非常清楚地掌握 21 世纪生命科学最重要的研究工具——生物化学的概念和技术，并且始终将生化步骤和生物体结构间的相互关系贯穿全书，达到了理论和实际相结合教学，是一本学习效果相当好的教科书。本书配有大量的背景资料、图片资料和参考资料，使研究生能够扩大进一步阅读的范围。本书英文清晰、简练、准确，非常有利于研究生直接掌握最新的专业知识和提高外语能力。本书是一本非常有特色和适合研究生使用的生物化学教材。

本书还可供生命科学相关专业的科研、教学人员参考。

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《中国科学院研究生教学丛书》序

在21世纪曙光初露，中国科技、教育面临重大改革和蓬勃发展之际，《中国科学院研究生教学丛书》——这套凝聚了中国科学院新老科学家、研究生导师们多年心血的研究生教材面世了。相信这套丛书的出版，会在一定程度上缓解研究生教材不足的困难，对提高研究生教育质量起着积极的推动作用。

21世纪将是科学技术日新月异，迅猛发展的新世纪，科学技术将成为经济发展的最重要的资源和不竭的动力，成为经济和社会发展的首要推动力量。世界各国之间综合国力的竞争，实质上是科技实力的竞争。而一个国家科技实力的决定因素是它所拥有的科技人才的数量和质量。我国要想在21世纪顺利地实施“科教兴国”和“可持续发展”战略，实现邓小平同志规划的第三步战略目标——把我国建设成中等发达国家，关键在于培养造就一支数量宏大、素质优良、结构合理、有能力参与国际竞争与合作的科技大军。这是摆在我国高等教育面前的一项十分繁重而光荣的战略任务。

中国科学院作为我国自然科学与高新技术的综合研究与发展中心，在建院之初就明确了出成果出人才并举的办院宗旨，长期坚持走科研与教育相结合的道路，发挥了高级科技专家多、科研条件好、科研水平高的优势，结合科研工作，积极培养研究生；在出成果的同时，为国家培养了数以万计的研究生。当前，中国科学院正在按照江泽民同志关于中国科学院要努力建设好“三个基地”的指示，在建设具有国际先进水平的科学研究基地和促进高新技术产业发展基地的同时，加强研究生教育，努力建设好高级人才培养基地，在肩负起发展我国科学技术及促进高新技术产业发展重任的同时，为国家源源不断地培养输送大批高级科技人才。

质量是研究生教育的生命，全面提高研究生培养质量是当前我国研究生教育的首要任务。研究生教材建设是提高研究生培养质量的一项重要的基础性工作。由于各种原因，目前我国研究生教材的建设滞后于研究生教育的发展。为了改变这种情况，中国科学院组织了一批在科学前沿工作，同时又具有相当教学经验的科学家撰写研究生教材，并以专项资金资助优秀的研究生教材的出版。希望通过数年努力，出版一套面向21世纪科技发展、体现中国科学院特色的高水平的研究生教学丛书。本丛书内容力求具有科学性、系统性和基础性，同时也兼顾前沿性，使阅读者不仅能获得相关学科的比较系统的科学基础知识，也能被引导进入当代科学研究的前沿。这套研究生教学丛书，不仅适合于在校研究生学习使用，也可以作为高校教师和专业研究人员工作和学习的参考书。

“桃李不言，下自成蹊。”我相信，通过中国科学院一批科学家的辛勤耕耘，《中国科学院研究生教学丛书》将成为我国研究生教育园地的一丛鲜花，也将似润物春雨，滋养莘莘学子的心田，把他们引向科学的殿堂，不仅为科学院，也为全国研究生教育的发展作出重要贡献。

This book is dedicated to our son

James Adrian McKee

Preface

Life is a mystery with the power to enchant or terrify. This is no less true for biochemists than it is for poets and artists. While many humans appreciate the visual beauty and the majesty of the natural world, biochemists seek to discover the underlying mechanisms of living processes. As life's secrets have been probed, researchers have often been both awed and humbled by the intricacy, sophistication, and resilience of living organisms. In this textbook we have attempted to convey to students the excitement and pleasure we have experienced in our search for knowledge about life.

ORGANIZATION AND APPROACH

This textbook is designed for use by chemistry majors and students in the life sciences. Few assumptions have been made about the chemistry and biology backgrounds the students have. To ensure that all students are sufficiently prepared for acquiring a meaningful understanding of biochemistry, the first four chapters review the principles of relevant topics, such as organic functional groups, noncovalent bonding, thermodynamics, and cell structure. In our experience, students retain new information more efficiently if they can readily see its applications. Therefore, in the remaining chapters of the book, discussions of biomolecules are usually followed immediately by descriptions of their roles in metabolism. For example, chapters devoted to carbohydrate and lipid structure are followed by chapters describing their metabolic functions. A notable theme that begins in the early chapters and continues throughout the book is the relationship between biochemical processes and biological structure. We believe that this approach affords students an interesting holistic view of a subject that so often has been treated as if biochemical reactions occur in some dimension isolated from biology.

During the past 50 years, scientific investigation has increasingly deepened and expanded human understanding of life. In the waning years of the twentieth century, the pace of discovery has become explosive. The continuing avalanche of information, made possible by technological innovations in biochemistry and molecular biology, now allows previously unimaginable insights into the inner workings of living organisms and the causes of disease. The challenge to life sciences educators is how to prepare students for a new century when revolutionary changes created by scientific discovery will affect both their personal and professional lives. The most important tool for students is a clear understanding of biochemistry. The purpose of the second edition of *Biochemistry: An Introduction* remains unchanged from that of the first edition, that is, to present a logical and accessible description of essential biochemical principles.

WHAT IS NEW IN THIS EDITION

As a result of our teaching experience, the suggestions of many students and biochemistry instructors who have used the text, and numerous advances in biochemical research, many changes and improvements have been made, including the following:

The design of the book has been completely revised to make it easier to read and comprehend.

Each chapter has been revised and updated. Examples of topics with improved coverage include protein structure, nucleotide chemistry, DNA synthesis, and DNA repair mechanisms. The art program has also been reevaluated. Some figures have been altered and others have been rerendered to improve clarity.

The sequence of coverage of some topics has been modified to improve comprehension. For example, the chapters devoted to discussions of lipid and membrane structure and metabolism now precede the discussion of energy generation in the aerobic metabolism chapter.

Each paragraph, table, worked problem, and illustration has been reviewed for accuracy.

SUPPLEMENTARY AIDS

1. **Instructors Manual/Test Item File:** Written by the authors, this manual is designed to assist instructors plan and prepare for classes using *Biochemistry: An Introduction.* For each chapter in the text, this manual provides a chapter outline, key words, an extended lecture outline, and enrichment ideas. The test item file contains approximately thirty-five multiple choice, true/false, critical thinking, and mathematical problems per chapter. Suggested answers for the problems appear at the end of each part.
2. **Student Study Guide/Solutions Manual:** This guide accompanies the text and was written by Bruce Morimoto of Purdue University. For each text chapter, a corresponding study guide chapter offers comprehensive reviews, study tips, and additional questions for biochemistry students.
3. **Transparencies:** Accompanying this text, 140 transparencies of key illustrations in the text help the instructor coordinate the lecture to the text.
4. **Microtest:** This computerized classroom management system/service includes a database of test questions, reproducible student self-quizzes, and a grade-recording program. Disks are available for IBM and Macintosh computers and require no program.

5. **Laboratory Manual in Biochemistry (0-697-16735-6):** Written by Dr. Henry Zeiden and Dr. William Dashek, this laboratory manual stresses the theory behind the biochemical and molecular biology techniques and uses an investigative laboratory approach. This manual contains 12 modules, each containing several exercises. Traditional topics such as enzymology, cutting-edge topics, such as molecular biology, and applied topics, such as analysis of carbohydrates, are covered in this laboratory manual.
6. **McGraw-Hill 3D Library of Biomolecules:** Developed by McGraw-Hill, this browser-based CD-Rom takes advantage of virtual reality technology. Instructors and students can view and manipulate three-dimensional animations of more than 100 of the most commonly studied molecules in biochemistry. The library can be accessed via the Netscape Navigator or Internet Explorer browsers on both Windows and Macintosh computers.
7. **How to Study Science:** Written by Fred Drewes of Suffolk County Community College, this excellent workbook offers students helpful suggestions for meeting the considerable challenges of a science course. It offers tips on how to overcome science anxiety. This book's unique design helps to stir students' critical thinking skills and help them develop careful note taking.

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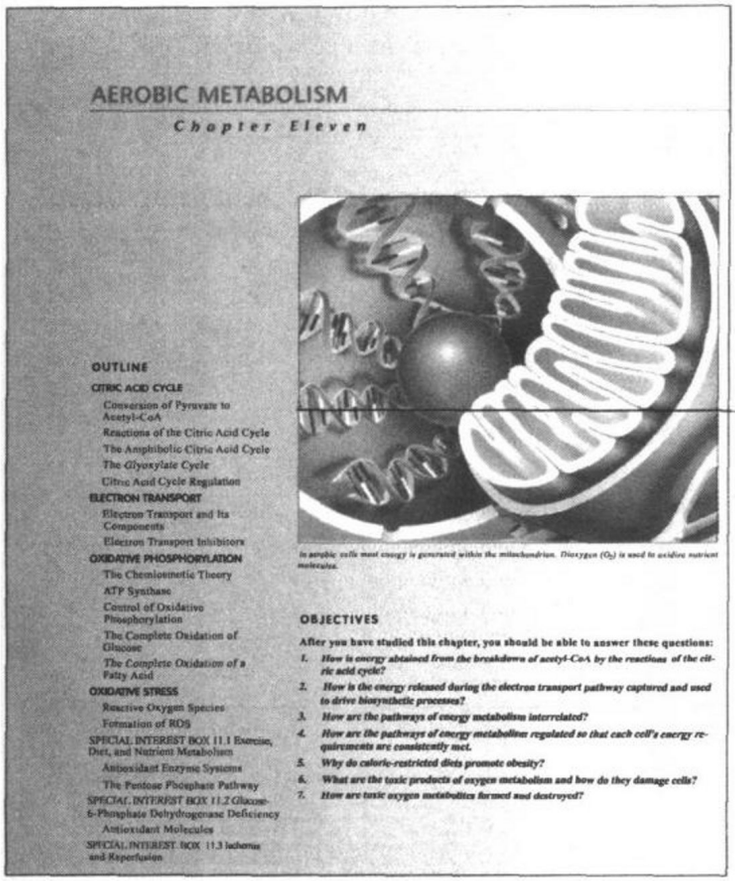
Finally, we wish to extend our deep appreciation to those individuals who have helped and encouraged us and made this project possible: Nicholas Rosa, Ira Cantor, Joseph and Josephine Rabinowitz, and William and Barbara Morris. To James R. McKee, Sr., and Margaret McKee and our son James Adrian McKee we extend our appreciation for their unfailing patience and encouragement.

Trudy McKee
James R. McKee

Guided Tour Through the Biochemistry Learning System



AEROBIC METABOLISM

Chapter Eleven

OUTLINE

CITRIC ACID CYCLE
- Conversion of Pyruvate to Acetyl-CoA
- Reactions of the Citric Acid Cycle
- The Amphibolic Citric Acid Cycle
- The Glyoxylate Cycle
- Citric Acid Cycle Regulation

ELECTRON TRANSPORT
- Electron Transport and Its Components
- Electron Transport Inhibitors

OXIDATIVE PHOSPHORYLATION
- The Chemiosmotic Theory
- ATP Synthase
- Control of Oxidative Phosphorylation
- The Complete Oxidation of Glucose
- The Complete Oxidation of a Fatty Acid

OXIDATIVE STRESS
- Reactive Oxygen Species
- Formation of ROS

SPECIAL INTEREST BOX 11.1 Exercise, Diet, and Nutrient Metabolism
- Antioxidant Enzyme Systems
- The Pentose Phosphate Pathway

SPECIAL INTEREST BOX 11.2 Glucose-6-Phosphate Dehydrogenase Deficiency
- Antioxidant Molecules

SPECIAL INTEREST BOX 11.3 Ischemia and Reperfusion

In aerobic cells most energy is generated within the mitochondrion. Dioxygen (O_2) is used to oxidize nutrient molecules.

OBJECTIVES

After you have studied this chapter, you should be able to answer these questions:

1. *How is energy obtained from the breakdown of acetyl-CoA by the reactions of the citric acid cycle?*
2. *How is the energy released during the electron transport pathway captured and used to drive biosynthetic processes?*
3. *How are the pathways of energy metabolism interrelated?*
4. *How are the pathways of energy metabolism regulated so that each cell's energy requirements are consistently met.*
5. *Why do caloric-restricted diets promote obesity?*
6. *What are the toxic products of oxygen metabolism and how do they damage cells?*
7. *How are toxic oxygen metabolites formed and destroyed?*

CHAPTER OUTLINES AND OBJECTIVES

Each chapter begins with an outline that introduces students to the topics to be presented. This outline also provides the instructor with a quick topic summary and help to organize lecture material. A list of objectives, based on major concepts covered in the chapter, enables students to preview the material and become aware of the topics they are expected to master.

DRAMATIC VISUAL PROGRAM

Colorful and informative photographs, illustrations, and tables enhance the learning program. Each chapter begins with an attractive opening photograph or illustration that visually introduces the topics to be discussed.

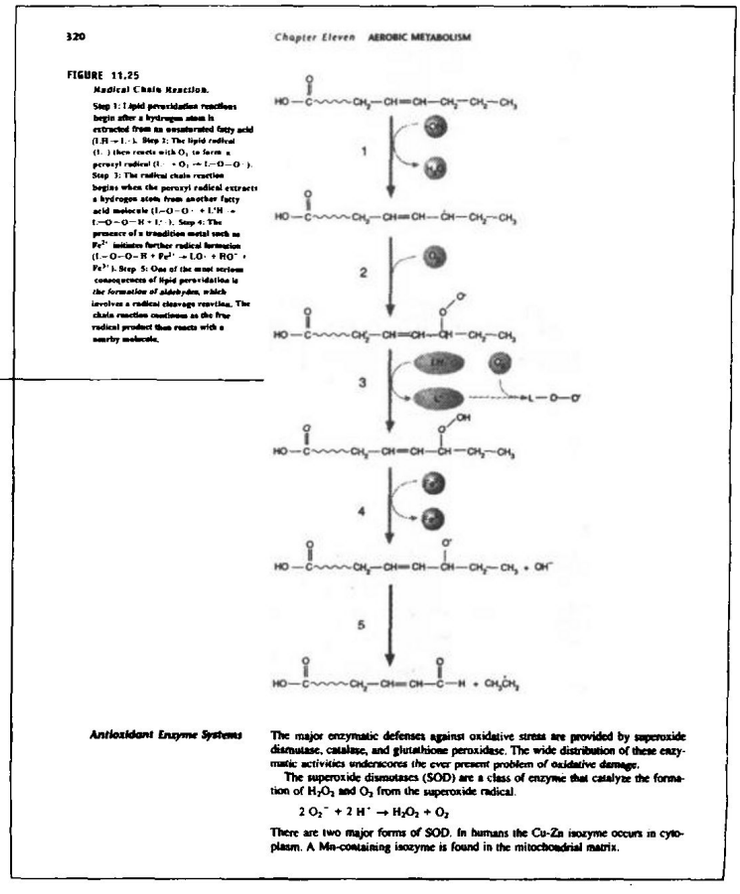


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FIGURE 11.25
Radical Chain Reaction.

Step 1: *Lipid peroxidation reactions* begin after a hydrogen atom is extracted from an unsaturated fatty acid (L–H → L· + H·). **Step 2:** The *lipid radical* (L·) then reacts with O_2 to form a *peroxyl radical* (L· + O_2 → L–O–O·). **Step 3:** The radical chain reaction begins when the peroxyl radical extracts a hydrogen atom from another fatty acid molecule (L–O–O· + L'H → L'· + L–O–O–H). **Step 4:** The presence of a transition metal such as Fe^{2+} initiates further radical formation (L–O–O–H + Fe^{2+} → LO· + HO^- + Fe^{3+}). **Step 5:** One of the most serious consequences of lipid peroxidation is *the formation of aldehydes*, which involves a radical cleavage reaction. The chain reaction continues as the free radical product then reacts with a nearby molecule.

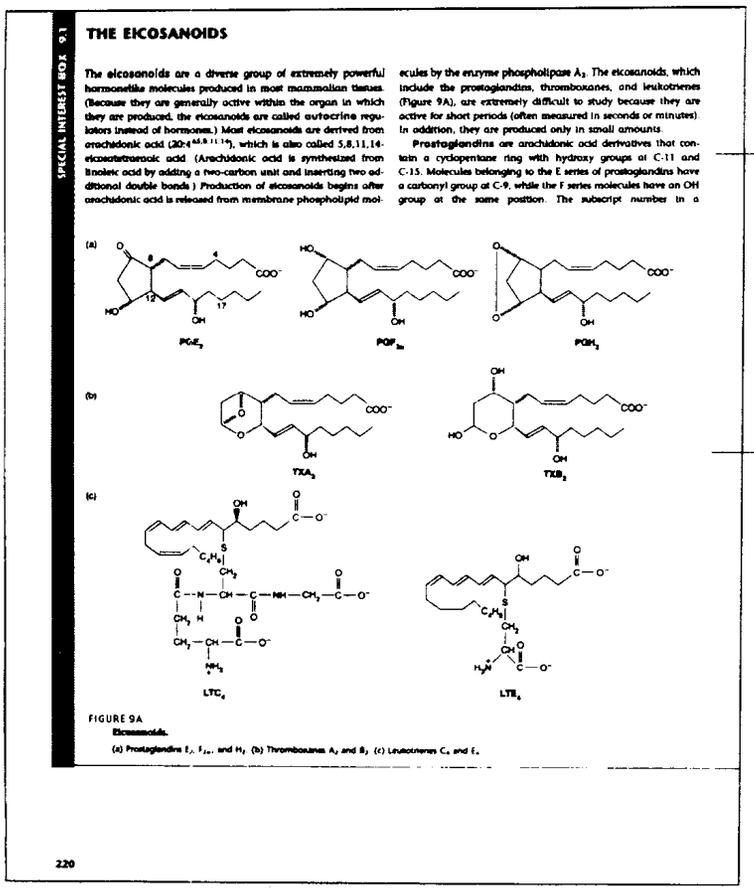
Antioxidant Enzyme Systems

The major enzymatic defenses against oxidative stress are provided by superoxide dismutase, catalase, and glutathione peroxidase. The wide distribution of these enzymatic activities underscores the ever present problem of oxidative damage.

The superoxide dismutases (SOD) are a class of enzyme that catalyze the formation of H_2O_2 and O_2 from the superoxide radical.

$$2\ O_2^- + 2\ H^+ \rightarrow H_2O_2 + O_2$$

There are two major forms of SOD. In humans the Cu-Zn isozyme occurs in cytoplasm. A Mn-containing isozyme is found in the mitochondrial matrix.



SPECIAL INTEREST BOX 9.1

THE EICOSANOIDS

The eicosanoids are a diverse group of extremely powerful hormonelike molecules produced in most mammalian tissues. (Because they are generally active within the organ in which they are produced, the eicosanoids are called autocrine regulators instead of hormones.) Most eicosanoids are derived from arachidonic acid ($20{:}4^{5,8,11,14}$), which is also called 5,8,11,14-eicosatetraenoic acid (Arachidonic acid is synthesized from linoleic acid by adding a two-carbon unit and inserting two additional double bonds.) Production of eicosanoids begins after arachidonic acid is released from membrane phospholipid molecules by the enzyme phospholipase A_2. The eicosanoids, which include the prostaglandins, thromboxanes, and leukotrienes (Figure 9A), are extremely difficult to study because they are active for short periods (often measured in seconds or minutes). In addition, they are produced only in small amounts.

Prostaglandins are arachidonic acid derivatives that contain a cyclopentane ring with hydroxy groups at C-11 and C-15. Molecules belonging to the E series of prostaglandins have a carbonyl group at C-9, while the F series molecules have an OH group at the same position. The subscript number in a

(a) PGE_2 $PGF_{2\alpha}$ PGH_2

(b) TXA_2 TXB_2

(c) LTC_4 LTE_4

FIGURE 9A
Eicosanoids.
(a) Prostaglandins E_2, $F_{2\alpha}$, and H_2 (b) Thromboxanes A_2 and B_2 (c) Leukotrienes C_4 and E_4

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BOLDFACED KEY WORDS

Key words appear in boldface when they are introduced within the text and are immediately defined by the context. All key words are also defined in the glossary.

SPECIAL INTEREST BOXES

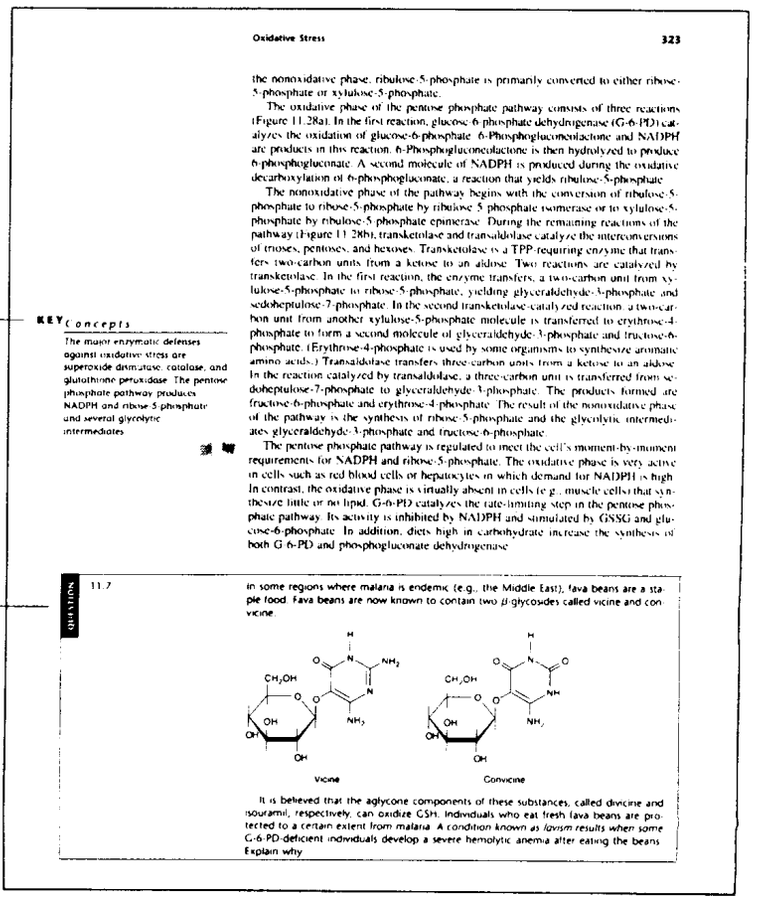
These essays which appear throughout the text, help students connect biochemical principles and everyday applications.

KEY CONCEPTS

At the end of sections is a brief summary to help students understand the essential ideas in the section.

IN-CHAPTER PROBLEMS, SOLUTIONS, AND QUESTIONS

Because problem solving is most easily learned by studying examples and practicing, problems with solutions are provided wherever appropriate. In chapter questions help students integrate newly learned material with timely and interesting related information.



Oxidative Stress 323

the nonoxidative phase, ribulose-5-phosphate is primarily converted to either ribose-5-phosphate or xylulose-5-phosphate.

The oxidative phase of the pentose phosphate pathway consists of three reactions (Figure 11.28a). In the first reaction, glucose-6-phosphate dehydrogenase (G-6-PD) catalyzes the oxidation of glucose-6-phosphate. 6-Phosphogluconolactone and NADPH are products in this reaction. 6-Phosphogluconolactone is then hydrolyzed to produce 6-phosphogluconate. A second molecule of NADPH is produced during the oxidative decarboxylation of 6-phosphogluconate, a reaction that yields ribulose-5-phosphate.

The nonoxidative phase of the pathway begins with the conversion of ribulose-5-phosphate to ribose-5-phosphate by ribulose 5 phosphate isomerase or to xylulose-5-phosphate by ribulose-5 phosphate epimerase. During the remaining reactions of the pathway (Figure 11.28b), transketolase and transaldolase catalyze the interconversions of trioses, pentoses, and hexoses. Transketolase is a TPP-requiring enzyme that transfers two-carbon units from a ketose to an aldose. Two reactions are catalyzed by transketolase. In the first reaction, the enzyme transfers a two-carbon unit from xylulose-5-phosphate to ribose-5-phosphate, yielding glyceraldehyde-3-phosphate and sedoheptulose-7-phosphate. In the second transketolase-catalyzed reaction, a two-carbon unit from another xylulose-5-phosphate molecule is transferred to erythrose-4-phosphate to form a second molecule of glyceraldehyde-3-phosphate and fructose-6-phosphate. (Erythrose-4-phosphate is used by some organisms to synthesize aromatic amino acids.) Transaldolase transfers three-carbon units from a ketose to an aldose. In the reaction catalyzed by transaldolase, a three-carbon unit is transferred from sedoheptulose-7-phosphate to glyceraldehyde-3-phosphate. The products formed are fructose-6-phosphate and erythrose-4-phosphate. The result of the nonoxidative phase of the pathway is the synthesis of ribose-5-phosphate and the glycolytic intermediates glyceraldehyde-3-phosphate and fructose-6-phosphate.

The pentose phosphate pathway is regulated to meet the cell's moment-by-moment requirements for NADPH and ribose-5-phosphate. The oxidative phase is very active in cells such as red blood cells or hepatocytes in which demand for NADPH is high. In contrast, the oxidative phase is virtually absent in cells (e.g., muscle cells) that synthesize little or no lipid. G-6-PD catalyzes the rate-limiting step in the pentose phosphate pathway. Its activity is inhibited by NADPH and stimulated by GSSG and glucose-6-phosphate. In addition, diets high in carbohydrate increase the synthesis of both G-6-PD and phosphogluconate dehydrogenase.

KEY *Concepts*

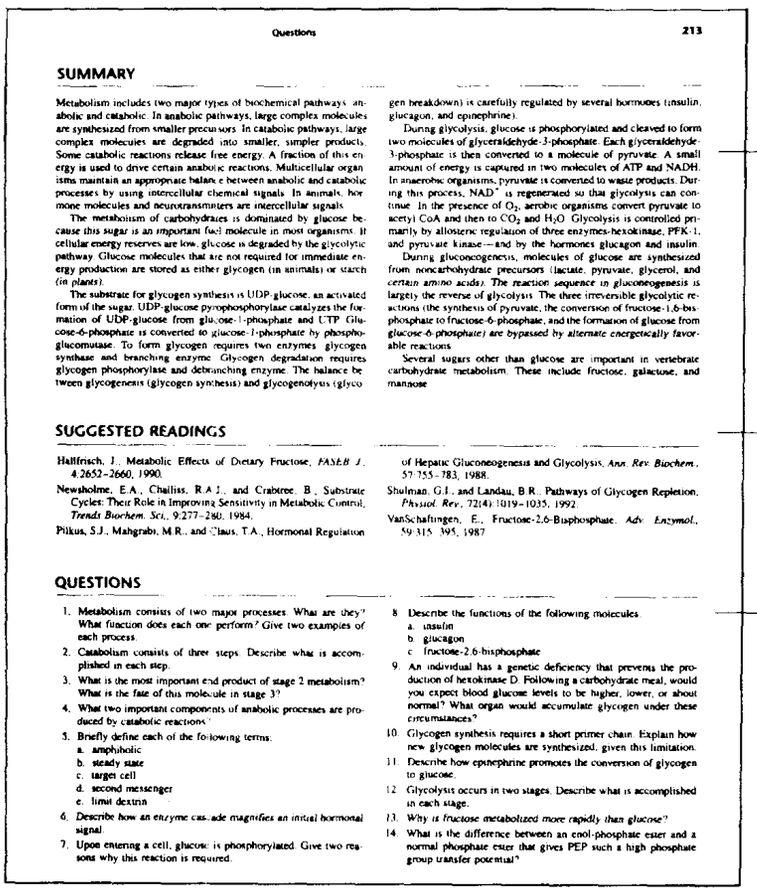
The major enzymatic defenses against oxidative stress are superoxide dismutase, catalase, and glutathione peroxidase. The pentose phosphate pathway produces NADPH and ribose-5-phosphate and several glycolytic intermediates.

QUESTION 11.7

In some regions where malaria is endemic (e.g., the Middle East), fava beans are a staple food. Fava beans are now known to contain two β-glycosides called vicine and convicine.

Vicine Convicine

It is believed that the aglycone components of these substances, called divicine and isouramil, respectively, can oxidize GSH. Individuals who eat fresh fava beans are protected to a certain extent from malaria. A condition known as *lavism* results when some G-6-PD-deficient individuals develop a severe hemolytic anemia after eating the beans. Explain why.



Questions 213

SUMMARY

Metabolism includes two major types of biochemical pathways: anabolic and catabolic. In anabolic pathways, large complex molecules are synthesized from smaller precursors. In catabolic pathways, large complex molecules are degraded into smaller, simpler products. Some catabolic reactions release free energy. A fraction of this energy is used to drive certain anabolic reactions. Multicellular organisms maintain an appropriate balance between anabolic and catabolic processes by using intercellular chemical signals. In animals, hormone molecules and neurotransmitters are intercellular signals.

The metabolism of carbohydrates is dominated by glucose because this sugar is an important fuel molecule in most organisms. If cellular energy reserves are low, glucose is degraded by the glycolytic pathway. Glucose molecules that are not required for immediate energy production are stored as either glycogen (in animals) or starch (in plants).

The substrate for glycogen synthesis is UDP-glucose, an activated form of the sugar. UDP-glucose pyrophosphorylase catalyzes the formation of UDP-glucose from glucose-1-phosphate and UTP. Glucose-6-phosphate is converted to glucose-1-phosphate by phosphoglucomutase. To form glycogen requires two enzymes: glycogen synthase and branching enzyme. Glycogen degradation requires glycogen phosphorylase and debranching enzyme. The balance between glycogenesis (glycogen synthesis) and glycogenolysis (glycogen breakdown) is carefully regulated by several hormones (insulin, glucagon, and epinephrine).

During glycolysis, glucose is phosphorylated and cleaved to form two molecules of glyceraldehyde-3-phosphate. Each glyceraldehyde-3-phosphate is then converted to a molecule of pyruvate. A small amount of energy is captured in two molecules of ATP and NADH. In anaerobic organisms, pyruvate is converted to waste products. During this process, NAD^+ is regenerated so that glycolysis can continue. In the presence of O_2, aerobic organisms convert pyruvate to acetyl CoA and then to CO_2 and H_2O. Glycolysis is controlled primarily by allosteric regulation of three enzymes-hexokinase, PFK-1, and pyruvate kinase—and by the hormones glucagon and insulin.

During gluconeogenesis, molecules of glucose are synthesized from noncarbohydrate precursors (lactate, pyruvate, glycerol, and certain amino acids). The reaction sequence in gluconeogenesis is largely the reverse of glycolysis. The three irreversible glycolytic reactions (the synthesis of pyruvate, the conversion of fructose-1,6-bisphosphate to fructose-6-phosphate, and the formation of glucose from glucose-6-phosphate) are bypassed by alternate energetically favorable reactions.

Several sugars other than glucose are important in vertebrate carbohydrate metabolism. These include fructose, galactose, and mannose.

SUGGESTED READINGS

Halffrisch, J., Metabolic Effects of Dietary Fructose, *FASEB J.*, 4:2652–2660, 1990.

Newsholme, E.A., Challiss, R.A.J., and Crabtree, B., Substrate Cycles: Their Role in Improving Sensitivity in Metabolic Control, *Trends Biochem. Sci.*, 9:277–280, 1984.

Pilkus, S.J., Mahgrabi, M.R., and Claus, T.A., Hormonal Regulation of Hepatic Gluconeogenesis and Glycolysis, *Ann. Rev. Biochem.*, 57:755–783, 1988.

Shulman, G.I., and Landau, B.R., Pathways of Glycogen Repletion, *Physiol. Rev.*, 72(4):1019–1035, 1992.

VanSchaftingen, E., Fructose-2,6-Bisphosphate, *Adv. Enzymol.*, 59:315–395, 1987.

QUESTIONS

1. Metabolism consists of two major processes. What are they? What function does each one perform? Give two examples of each process.
2. Catabolism consists of three steps. Describe what is accomplished in each step.
3. What is the most important end product of stage 2 metabolism? What is the fate of this molecule in stage 3?
4. What two important components of anabolic processes are produced by catabolic reactions?
5. Briefly define each of the following terms:
   a. amphibiotic
   b. steady state
   c. target cell
   d. second messenger
   e. limit dextrin
6. Describe how an enzyme cascade magnifies an initial hormonal signal.
7. Upon entering a cell, glucose is phosphorylated. Give two reasons why this reaction is required.
8. Describe the functions of the following molecules:
   a. insulin
   b. glucagon
   c. fructose-2,6-bisphosphate
9. An individual has a genetic deficiency that prevents the production of hexokinase D. Following a carbohydrate meal, would you expect blood glucose levels to be higher, lower, or about normal? What organ would accumulate glycogen under these circumstances?
10. Glycogen synthesis requires a short primer chain. Explain how new glycogen molecules are synthesized, given this limitation.
11. Describe how epinephrine promotes the conversion of glycogen to glucose.
12. Glycolysis occurs in two stages. Describe what is accomplished in each stage.
13. Why is fructose metabolized more rapidly than glucose?
14. What is the difference between an enol-phosphate ester and a normal phosphate ester that gives PEP such a high phosphate group transfer potential?

CHAPTER SUMMARIES

At the end of each chapter is a summary designed to help students more easily identify important concepts and help them review for quizzes and tests.

SUGGESTED READINGS

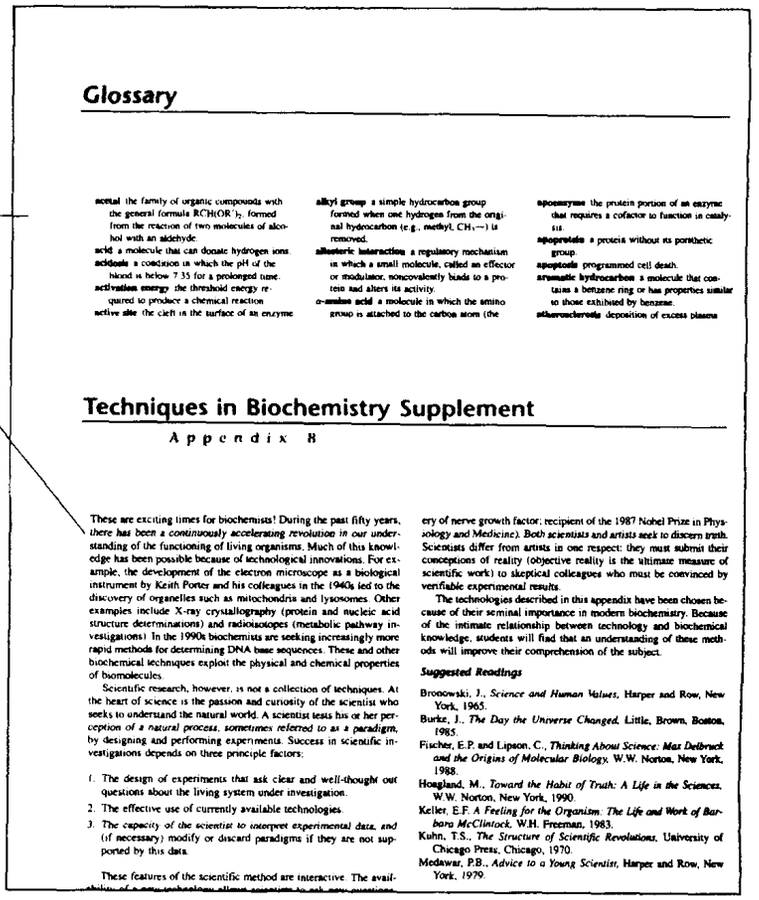
At the end of each chapter are suggested references for further study of topics in the text or timely related topics.

END-OF-CHAPTER QUESTIONS

A variety of questions and problems that range in level of difficulty help students measure their mastery of the chapter.

END-OF-BOOK GLOSSARY OF KEY WORDS

All key words in boldface in the text are defined in the glossary at the end of the textbook.



Glossary

acetal the family of organic compounds with the general formula $RCH(OR')_2$, formed from the reaction of two molecules of alcohol with an aldehyde.
acid a molecule that can donate hydrogen ions.
acidosis a condition in which the pH of the blood is below 7.35 for a prolonged time.
activation energy the threshold energy required to produce a chemical reaction.
active site the cleft in the surface of an enzyme
alkyl group a simple hydrocarbon group formed when one hydrogen from the original hydrocarbon (e.g., methyl, CH_3—) is removed.
allosteric interaction a regulatory mechanism in which a small molecule, called an effector or modulator, noncovalently binds to a protein and alters its activity.
α-amino acid a molecule in which the amino group is attached to the carbon atom (the
apoenzyme the protein portion of an enzyme that requires a cofactor to function in catalysis.
apoprotein a protein without its prosthetic group.
apoptosis programmed cell death.
aromatic hydrocarbon a molecule that contains a benzene ring or has properties similar to those exhibited by benzene.
atherosclerosis deposition of excess plasma

TECHNIQUES IN BIOCHEMISTRY SUPPLEMENT

From this review of the principle research techniques used to investigate living processes, students can appreciate the relationship between technology and scientific knowledge. Information in this supplement (Appendix B) helps students answer some in-chapter and end-of-chapter questions.

Techniques in Biochemistry Supplement

Appendix B

These are exciting times for biochemists! During the past fifty years, there has been a continuously accelerating revolution in our understanding of the functioning of living organisms. Much of this knowledge has been possible because of technological innovations. For example, the development of the electron microscope as a biological instrument by Keith Porter and his colleagues in the 1940s led to the discovery of organelles such as mitochondria and lysosomes. Other examples include X-ray crystallography (protein and nucleic acid structure determinations) and radioisotopes (metabolic pathway investigations). In the 1990s biochemists are seeking increasingly more rapid methods for determining DNA base sequences. These and other biochemical techniques exploit the physical and chemical properties of biomolecules.

Scientific research, however, is not a collection of techniques. At the heart of science is the passion and curiosity of the scientist who seeks to understand the natural world. A scientist tests his or her perception of a natural process, sometimes referred to as a paradigm, by designing and performing experiments. Success in scientific investigations depends on three principle factors:

1. The design of experiments that ask clear and well-thought out questions about the living system under investigation.
2. The effective use of currently available technologies.
3. The capacity of the scientist to interpret experimental data, and (if necessary) modify or discard paradigms if they are not supported by this data.

These features of the scientific method are interactive. The avail-

ery of nerve growth factor; recipient of the 1987 Nobel Prize in Physiology and Medicine). Both scientists and artists seek to discern truth. Scientists differ from artists in one respect: they must submit their conceptions of reality (objective reality is the ultimate measure of scientific work) to skeptical colleagues who must be convinced by verifiable experimental results.

The technologies described in this appendix have been chosen because of their seminal importance in modern biochemistry. Because of the intimate relationship between technology and biochemical knowledge, students will find that an understanding of these methods will improve their comprehension of the subject.

Suggested Readings

Bronowski, J., *Science and Human Values*, Harper and Row, New York, 1965.
Burke, J., *The Day the Universe Changed*, Little, Brown, Boston, 1985.
Fischer, E.P. and Lipson, C., *Thinking About Science: Max Delbruck and the Origins of Molecular Biology*, W.W. Norton, New York, 1988.
Hoagland, M., *Toward the Habit of Truth: A Life in the Sciences*, W.W. Norton, New York, 1990.
Keller, E.F. *A Feeling for the Organism: The Life and Work of Barbara McClintock*, W.H. Freeman, 1983.
Kuhn, T.S., *The Structure of Scientific Revolutions*, University of Chicago Press, Chicago, 1970.
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CONCEPT AND APPLICATION ICONS

Throughout the text, students find graphic devices that easily mark the following concepts and applications.

Plant Biochemistry

Biomedical Application

Metabolic Regulation Mechanism

A	adenine
ACTH	adrenocorticotropic hormone
ACP	acyl carrier protein
ADP	adenosine-5′-diphosphate
AIDS	acquired immune deficiency syndrome
ALA	δ-aminolevulinate
AMP	adenosine-5′-monophosphate
ATP	adenosine-5′-triphosphate
BCAA	branched chain amino acids
BH_2	dihydrobiopterin (oxidized form)
BH_4	tetrahydrobiopterin (reduced form)
bp	base pair
BPG	2,3-bisphosphoglycerate
C	cytosine
CAP	catabolite gene activator protein
CDP	cytidine-5′-diphosphate
CMP	cytidine-5′-monophosphate
CTP	cytidine-5′-triphosphate
CoA or CoASH	coenzyme A
cAMP	adenosine-3′,5′-cyclic monophosphate
cGMP	guanosine-3′,5′-cyclic monophosphate
cyt	cytochrome
DAG	diacylglycerol
DHAP	dihydroxyacetone phosphate
DNA	deoxyribonucleic acid
ssDNA	single-stranded DNA
dsDNA	double-stranded DNA
DNase	deoxyribonuclease
DNP	2,4-dinitrophenol
EAA	essential amino acids
EF	elongation factor
EGF	epidermal growth factor
ER	endoplasmic reticulum
ESR	electron spin resonance
FAD	flavin adenine dinucleotide (oxidized form)
$FADH_2$	flavin adenine dinucleotide (reduced form)
fMet	N-formylmethionine
FMN	flavin mononucleotide (oxidized form)
G	guanine or *Gibbs free energy*
G protein	guanine-nucleotide binding protein
GH	growth hormone
GDP	guanosine-5′-diphosphate
GMP	guanosine-5′-monophosphate
GSH	glutathione
GSSG	glutathione (oxidized form)
GTP	guanosine-5′-triphosphate
Hb	hemoglobin
HDL	high-density lipoprotein
HETPP	hydroxyethyl-thiamine pyrophosphate
HGPRT	hypoxanthine-guaninephosphoribosyltransferase
HIV	human immunodeficiency virus
HMG-CoA	β-hydroxy-β-methylglutaryl-CoA
HPLC	high pressure liquid chromatography
HRE	hormone response element
hsp	heat shock protein
IF	initiation factor
IGF	insulinlike growth factor
IgG	immunoglobulin G

IL	interleukin
IMP	inosine-5′-monophosphate
IP_3	inositol-1,4,5-triphosphate
K_m	Michaelis constant
kb	kilobases
kD	kilodalton
LDL	low-density lipoprotein
LHC	light harvesting complex
Man	mannose
NAA	nonessential amino acids
NAD^+	nicotinamide adenine dinucleotide (oxidized form)
NADH	nicotinamide adenine dinucleotide (reduced form)
$NADP^+$	nicotinamide adenine dinucleotide phosphate (oxidized form)
NADPH	nicotinamide adenine dinucleotide phosphate (reduced form)
NDP	nucleoside-5′-diphosphate
NMR	nuclear magnetic resonance
NO	nitric oxide
NTP	nucleoside-5′-triphosphate
P_i	orthophosphate (inorganic phosphate)
PAPS	3′-phosphoadenosine-5′-phosphosulfate
PC	plastocyanin
PDGF	platelet-derived growth factor
PEP	phosphoenolpyruvate
PFK	phosphofructokinase
PIP_2	phosphatidylinositol-4,5-bisphosphate
PP_i	pyrophosphate
PRPP	phosphoribosylpyrophosphate
PS	photosystem
PQ(Q)	plastoquinone (oxidized)
PQH_2 (QH_2)	plastoquinone (reduced)
RER	rough endoplasmic reticulum
RF	releasing factor
RFLP	restriction-frament length polymorphism
RNA	ribonucleic acid
dsRNA	double-stranded RNA
hnRNA	heterogenous nuclear RNA
mRNA	messenger RNA.
rRNA	ribosomal RNA
snRNA	small nuclear RNA
ssRNA	single-stranded RNA
tRNA	transfer RNA
snRNP	small ribonucleoprotein particles
RNase	ribonuclease
S	Svedberg unit
SAH	S-adenosylhomocysteine
SAM	S-adenosylmethionine
SDS	sodium dodecyl sulfate
SER	smooth endoplasmic reticulum
SRP	signal recognition particle
T	thymine
THF	tetrahydrofolate
TPP	thiamine pyrophosphate
U	uracil
UDP	uridine-5′-diphosphate
UMP	uridine-5′-monophosphate
UTP	uridine-5′-triphosphate
UQ	ubiquinone (coenzyme Q)(oxidized form)
UQH_2	ubiquinone (reduced form)
VLDL	very low density lipoprotein
XMP	xanthosine-5′ monophosphate

Brief Contents

Extended Contents