Biochemistry

Biochemistry

J. Stenesh

Western Michigan University
Kalamazoo, Michigan

PLENUM PRESS • NEW YORK AND LONDON

Library of Congress Cataloging-in-Publication Data

Stenesh, Jochanan.
Biochemistry / Jochanan Stenesh.
p. cm.
Includes bibliographical references and index.
ISBN 0-306-45732-6 (hardcover). -- ISBN 0-306-45733-4 (pbk.)
1. Biochemistry. I. Title.
QP514.2.S635 1998
572--dc21 97-41014
CIP

ISBN 0-306-45732-6 (Hardbound)
ISBN 0-306-45733-4 (Paperback)

A Division of Plenum Publishing Corporation
233 Spring Street, New York, N.Y. 10013

http://www.plenum.com

10 9 8 7 6 5 4 3 2 1

Printed in the United States in America

Biochemistry

Preface

This text is intended for an introductory course in biochemistry. While such a course draws students from various curricula, all students are presumed to have had at least general chemistry and one semester of organic chemistry.

My main goal in writing this book was to provide students with a basic body of biochemical knowledge and a thorough exposition of fundamental biochemical concepts, including full definitions of key terms. My aim has been to present this material in a reasonably balanced form by neither deluging central topics with excessive detail nor slighting secondary topics by extreme brevity.

Every author of an introductory text struggles with the problem of what to include in the coverage. My guideline has been to make sure first that the essentials are covered in sufficient depth to give students a firm basis on which to build further. Beyond that, material is covered to varying extents. More tangential material is frequently collected in the final sections of a chapter so that it can be omitted at the discretion of the instructor.

Following an introduction, which outlines the scope of biochemistry, the book is organized into four parts along traditional lines. Part I, FOUNDATION OF BIOCHEMISTRY, covers four general "frameworks" of biochemistry—the origin of life, the living cell, water, and noncovalent interactions. Part II, BIOMOLECULES, surveys structures and properties of the different classes of molecules that occur in living systems. Part III, METABOLISM, opens with an introductory chapter, followed by a study of the essential reactions, interconversions, and pathways of biomolecules. For cohesiveness, anabolism (synthesis) and catabolism (degradation) of a given class of biomolecules are covered in a single chapter. The discussion of metabolism concludes with photosynthesis. The last section of the book, Part IV, TRANSFER OF GENETIC INFORMATION, also opens with an introductory chapter and then explores the expression of genetic information. Replication, transcription, and translation are covered in this order. To allow for varying student backgrounds and for possible needed refreshers, a number of topics are included as four appendixes. These cover acid–base calculations, principles of organic chemistry, tools of biochemistry, and oxidation–reduction reactions.

Each chapter includes a summary, a list of selected readings, and a comprehensive study section that consists of three types of review questions and a large number of problems. Asterisks mark more difficult problems, and answers to all problems are given.

A solutions manual, providing step-by-step solutions of the problems, is available separately, as is a set of overhead transparencies.

The text has been extensively reviewed to eliminate all errors in fact. I thank the following reviewers who critically read portions of the manuscript and made valuable comments:

Richard Amasino, University of Wisconsin at Madison
Gary D. Anderson, Marshall University
Linda Atwood, California Polytechnic State University at San Luis Obispo
Katherine A. Bichler, Carthage College
Veronica C. Blasquez, University of Notre Dame
Ronald W. Brosemer, Washington State University
Larry Byers, Tulane University
Stephen W. Carper, University of Nevada

A. J. Clark, Auburn University
Rick H. Cote, University of New Hampshire
Richard C. Crain, University of Connecticut
Dorothy E. Croall, University of Maine
John Cronin, Arizona State University
John R. Edwards, Villanova University
Jeffrey A. Evans, University of Southern Mississippi
William Fordham, Fairleigh Dickinson University
Edward A. Funkhouser, Texas A & M University
Mina L. Hector, California State University at Chico
John L. Hess, Virginia Polytechnic Institute
Ken Hilt, University of California at Davis
Mahendra Jain, University of Delaware
Jerry P. Jasinski, Keene State College
Marjorie A. Jones, Illinois State University
Ivan I. Kaiser, University of Wyoming
Michael R. Kanost, Kansas State University
Herman W. Knoche, University of Nebraska
Roger E. Koeppe II, University of Arkansas
Glenn D. Kuehn, New Mexico State University
Michael Mendenhall, University of Kentucky
Robert Oberlender, University of the Pacific
Robert S. Orr, Delaware Valley College
R. Steven Pappas, Georgia State University
Samuel J. Rogers, Montana State University
D. L. Rohlfing, University of South Carolina
Laura Silberstein, San Jose State University
Thomas W. Sneider, Colorado State University
Ming Tien, Pennsylvania State University
Anthony P. Toste, Southwest Missouri State University
Martin Tuck, Ohio University
Ron Utecht, South Dakota State University
Thomas G. Waddell, University of Tennessee
Edward B. Walker, Weber State University
Daniel Weeks, University of Iowa
James H. Yuan, Old Dominion University

I am very grateful to John Dunigan who was responsible for producing most of the artwork. The excellent quality of the illustrations are a reflection of his tireless effort and careful attention to detail. Last, but not least, I want to express my sincere appreciation to the individuals at Plenum Publishing Corporation involved in this project: Amelia McNamara, Ken Howell, and Jacqueline Sedman, my editors, for their guidance and input, and Mary Curioli and Robert Maged for their supervision of the book's production.

J. Stenesh

Introduction
The Scope of Biochemistry

Biochemistry—the chemistry of life—deals with the chemical and physical properties of molecules and processes of living organisms. This relatively new science had its origin in the 1700s, emerged as an independent scientific discipline at the beginning of the 20th century, and erupted into unprecedented growth some 50 years ago.

For a long time, many people believed that reactions in living organisms (as distinct from those in nonliving systems) required a special "vital" force. Only when this theory of "vitalism" was discarded could development of biochemistry proceed. One of the earliest scientists whose work helped bring about the downfall of vitalism was Antoine Lavoisier. In 1777, Lavoisier conducted experiments on respiration and combustion and showed that both processes converted organic matter to carbon dioxide and water. He concluded that cellular respiration was slower than combustion but not essentially different from it.

Half a century later, in 1828, Friedrich Wöhler succeeded in synthesizing urea by heating ammonium cyanate in the laboratory. Until then, scientists had assumed that urea, like other organic compounds of living matter, could be synthesized only by and in a living organism. Two other important developments followed in short succession. In 1838, Matthias Schleiden and Theodor Schwann proposed that a membrane-bound structure—the cell—is the fundamental unit of all living organisms. In 1862, Louis Pasteur proved that living organisms arise only from other living organisms and not by "spontaneous generation." Pasteur showed that microorganisms did not form in a sterilized solution of organic matter unless that solution was exposed to air and other microorganisms.

Vitalism was finally rejected as a scientific theory when Eduard Buchner (1896) obtained a cell-free extract from yeast that was capable of carrying out fermentation and when J. B. Sumner (1926) crystallized the enzyme urease from jack beans.

The model of the double helix of DNA, proposed by James Watson and Francis Crick in 1953, revolutionized both biochemistry and biology. The proposal opened up countless avenues for studying life sciences at the molecular level. In particular, the concept of the double helix led to an ever-increasing interweaving of the sciences of biochemistry, cell biology, and genetics. This resulted in formation of a separate discipline called molecular genetics or molecular biology, which has mushroomed into a very active research area with major implications for medicine and other fields.

In the course of its development, at least four central themes have come to characterize biochemistry.

1. *Reactions carried out by living organisms obey the laws of chemistry and physics that describe reactions in the laboratory.* Physical properties of molecules, chemical reaction mechanisms of inorganic and organic compounds, energy relationships of products and reactants—all these apply to biochemical reactions proceeding *in vivo* in precisely the same manner as they apply to *in vitro* reactions carried out in the laboratory. No special forces such as "vitalism," or special processes like "spontaneous generation," play a role in the synthesis, degradation, and interconversions of compounds found in living cells.

2. *Structure and function are interdependent.* Molecules and larger aggregates have particular structures that permit them to perform specific functions. Conversely, in order to be capable of performing specific functions, components must possess particular elements of structure. The structure–function interdependence exists at all levels of

organization. It occurs in low-molecular-weight compounds such as amino acids and fatty acids, in polymers such as proteins and nucleic acids, in supramolecular assemblies such as biological membranes, and in subcellular organelles such as mitochondria. Investigators have achieved many important breakthroughs in biochemistry, especially in molecular genetics, by focusing on the interdependence of structure and function.

3. *The cell is the basic unit of life.* The cell is the fundamental unit of living matter in both single-cell and multicellular organisms. Physical properties, the organization of chemical components, transport of substances in and out, and energy requirements and exchanges—all these play key roles in the functioning of a cell. Living cells are composed of lifeless molecules, but assembly, organization, and interactions of these molecules endow the cell with life. It is the goal of biochemistry to understand how cells accomplish this task.

Living cells exhibit an almost universal hierarchy of molecular organization (Figure 1). All the molecules that occur in living organisms (biomolecules) are formed from a small number of elements, primarily carbon, hydrogen, oxygen, nitrogen, phosphorus, and sulfur. Ultimately, all biomolecules are derived from low-molecular-weight precursors in the environment that contain these and several other elements. Precursors are converted by living matter via metabolic intermediates, or metabolites, into building blocks that become linked covalently to form macromolecules. Building blocks and/or macromolecules associate to form supramolecular assemblies and organelles.

4. *Living organisms exhibit both unity and diversity.* One of the outstanding phenomena of life is the existence of extensive biochemical similarities among diverse cells and organisms, despite significant morphological differences among them. This characteristic, known as the "principle of unity and diversity," describes a stunning paradox: The immense diversity of life at the cellular and organismal level is ultimately reducible to a surprising unity at the molecular level. The unity becomes evident not only in overall organization of cells (Figure 1), but also in properties of cellular components.

Major classes of biomolecules have identical functions in all types of cells. Nucleic acids store genetic information; proteins serve as structural components and as catalysts of metabolic reactions and have many other functions; lipids serve as a storage form of energy and as components of cell membranes; and carbohydrates represent a storage form of energy and, in prokaryotes, serve as components of the cell wall.

The biochemical unity of life, however, extends well beyond similarities among biomolecules. Proteins with the same function in different organisms have similar amino acid sequences. DNAs of closely related bacteria have similar molecular structures. Many of the same metabolic reactions and reaction sequences occur in a wide range of organisms. Fundamental cellular processes such as using nutrient energy, synthesizing proteins, respiring, transporting substances across cell membranes, and replicating genetic material involve identical or very similar mechanisms and components. Likewise, the genetic code used in the genes of nucleic acids is essentially universal. Based on such findings, most scientists today believe that all forms of life arose from a common ancestor and that, in the course of evolution, species diverged much as branches diverge from the trunk of a tree (see Section 1.1.2).

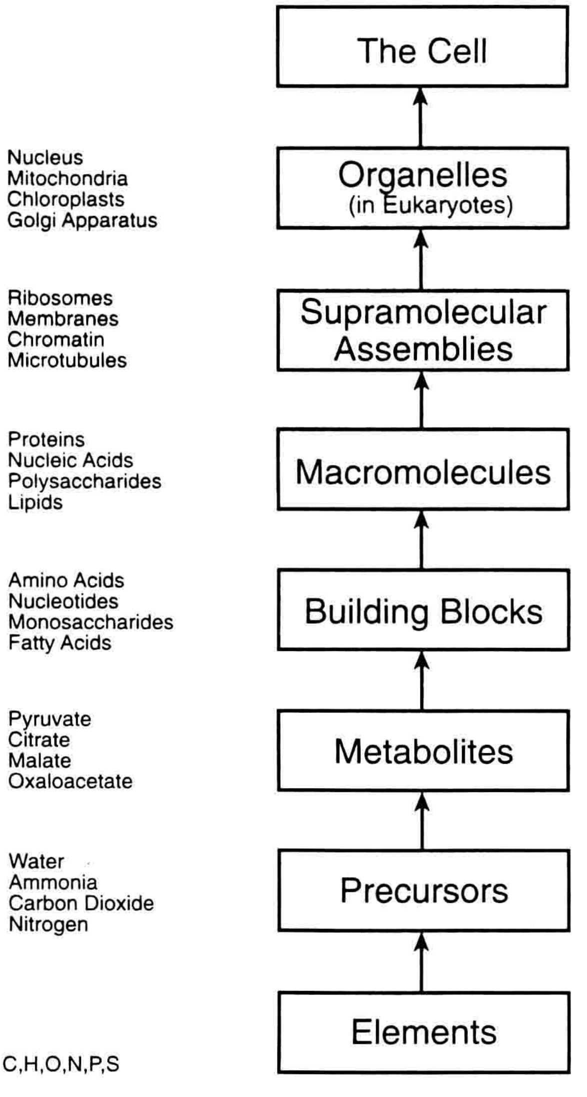

Figure 1. Hierarchy in the molecular organization of cells.

The biochemical unity of life makes it possible to apply information derived from one organism to the study of a different organism. A large body of biochemical knowledge comes from studies of prokaryotic microorganisms and has been found to apply, either directly or with some modifications, to eukaryotes, including humans. Similarly, researchers routinely use studies with laboratory animals to screen for potential hazards that drugs or toxic substances may pose for humans.

While many of life's mysteries still need to be unraveled, a few general characteristics consistently distinguish living organisms from nonliving matter.

All living organisms are complex and highly organized systems. Even the simplest unicellular organism contains many different components and constitutes a marvel of organization. Any single cell incorporates simultaneous control of multiple metabolic pathways and hundreds of different chemical reactions. Multicellular organisms have an even greater complexity of organization, and in higher animals and humans, the number of interrelationships and control systems must be truly staggering.

All living organisms contain many different kinds of biomolecules. Biomolecules can be small or large, simple or complex. They exist singly or form aggregates of varying sizes and intricacies. All forms of biomolecules have unique and specific functions.

Despite the occurrence of numerous types of biomolecules, living systems exhibit an underlying molecular economy. The complexity of biomolecules appears to be no greater than that required for molecular function. Likewise, the number of different types of biomolecules appears to be no greater than that needed to endow the cell with attributes of life in general and characteristics of the species in particular.

All living organisms require enzymes as catalysts for their metabolic reactions. Enzymes are protein molecules that catalyze most of the reactions of metabolism. These biomolecules are specially engineered for their catalytic function; they far exceed any human-made catalyst in both their selectivity and their efficiency. Life processes would not be feasible without the catalytic action of enzymes.

Enzyme reactions involve both changes of biomolecules and transformations of energy. Many of the hundreds of different enzyme reactions taking place within a single cell are linked into specific sequences of anywhere from 2 to over 20 steps. Intricate control systems regulate the resulting network of metabolic pathways. Enzyme reactions form the basis of the numerous processes characteristic of living organisms, such as vision, growth, nerve-impulse conduction, muscle contraction, and reproduction.

All living organisms require a supply of energy. The Sun is the ultimate source of energy for all life on Earth. Plants harness solar energy during photosynthesis and use it to synthesize carbohydrates. Many animals subsequently obtain their nutrients by feeding on plants. All living organisms extract energy from nutrients in the form of free energy and use it to drive life processes. Organisms return unused energy to the environment in the form of heat. Accumulating waste energy increases the disorder or entropy of the environment. Thus, living organisms maintain their organization at the expense of the environment, which they cause to become more random.

All living organisms have hereditary information encoded in genes. Life processes depend on the information contained within genes, which are structural components of nucleic acids. Because of the properties of their genetic material, living organisms can self-replicate and thereby transfer their genetic information to the next generation. Production of organisms identical in mass, shape, and internal structure constitutes the most extraordinary attribute of living systems.

Based on these characteristics of living matter, biochemistry can be divided into three main areas that deal with respectively, the chemistry of biomolecules, a study of metabolism, and molecular genetics. Biochemistry draws heavily on other life sciences and, in turn, provides key insights for related physical and biological disciplines. Chemistry, biology, nutrition, medicine, microbiology, physiology, agriculture, and biophysics are some of the sciences closely linked with biochemistry.

Contents