Seventh Edition

PRINCIPLES OF BIOCHEMISTRY: Mammalian Biochemistry

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Contents of *General Aspects* (companion text)

Preface

The publication of the seven editions of this book over the last thirty years has paralleled an explosive growth of biochemistry. During this time we have witnessed not only an increase in knowledge of the traditional subjects of biochemistry, but also an understanding of the molecular basis of various biological phenomena previously inaccessible to study. Moreover, biochemistry has become the language of much of biology, as evident from the diversity of subjects considered in Chapter 1, "The Scope of Biochemistry." The principles and methods of biochemistry now provide the underpinnings of all of the basic biological sciences and are the rational language for discourse in such diverse areas as ecology, clinical medicine, and agriculture. Indeed, the boundaries between biochemistry and much of the rest of biology have become blurred. Consequently, the preparation of this edition has been a formidable task since it has become necessary more than ever before to limit or even omit certain subjects considered in past editions in favor of the inclusion of new developments.

Our goal continues to be not only an exposition of the well-established principles that are generally acknowledged as the subject matter of biochemistry, but also an introduction to the new knowledge of the numerous biological structures and processes that has emerged in recent years. As in the past, the primary emphasis is on mammalian biochemistry, particularly of human beings. We have, however, been unwilling to omit large and important areas of fundamental biochemical interest and have decided for the first time to present the subject in two distinct but related books, each of which can stand by itself. We have retained the name, *Principles of Biochemistry* for both books, with one subtitled *General Aspects,* and its companion subtitled *Mammalian Biochemistry.* Clearly, *General Aspects* contains material essential for the beginning student and encompasses the subjects that are usually considered in an introductory course in biochemistry. The material in *Mammalian Biochemistry* requires some previous

exposure to basic biochemical principles, but also illustrates how these principles have been applied to gain great insight into the molecular functions of diverse mammalian organ systems. Although each book is separately indexed for the convenience of the reader, each also contains numerous cross-references denoted by G for general and by M for mammalian aspects, so that the reader can correlate the relevant subject matter in different parts of the two texts.

The text of *Principles of Biochemistry: General Aspects* is divided into four parts: (I) "The Major Constituents of Cells," (II) "Catalysis," (III) "Metabolism," and (IV) "Molecular Genetics." The chapters in each part were largely rewritten, and in many cases shortened considerably by omission of material that has been judged to be less essential for the beginning student interested in mammalian biochemistry. Such important processes, however, as photosynthesis (Chapter 19) and nitrogen fixation by microorganisms (Chapter 22) have been retained since they are of such significance to all of biology.

Part I, "The Major Constituents of Cells," considers the chemistry of carbohydrates, lipids, proteins, and nucleic acids, as in past editions. Two new chapters, however, are included. Chapter 2 introduces the reader to the general nature of cellular constituents, including water, the solvent for all biological processes. Chapter 9, "Isolation of Compounds of Biological Interest," presents the principles which underlie the highly selective methods for analysis and preparation of various cellular constituents. Some of the subject material of these chapters was included in several other chapters in earlier editions; however, the current unified presentation permits better focus on the essential concepts. Among the most important revisions in this Part are those in Chapter 8, "The Nucleic Acids," which includes a description of the rapid micromethods that have been developed recently for sequence analysis of DNA, and which have provided information beyond the imagination of the authors of the first edition.

Part II, "Catalysis," considers the nature and properties of enzymes, that large class of proteins that catalyzes biochemical reactions. The mechanisms of action of a large number of enzymes have now been elucidated, but limitations of space permit only a few to be considered in detail. Nevertheless, from the examples given, the beginning student will be able to glean the important principles necessary for understanding the behavior of the many other enzymes to be encountered in subsequent parts of the text.

Part III, "Metabolism," has been extensively revised and reorganized, especially the introductory chapters. Thus, Chapter 13, "Membranes and Subcellular Organelles," is a new chapter written in response to the recent advances in our knowledge of the molecular basis of many aspects of cellular action, including membrane structure and function. In addition, Chapter 14, "Receptors and Transport," treats systematically the biochemical principles required to understand these important phenomena. Indeed, if we were to hazard a choice of one area of biochemistry that has had a greater impact than any other since the sixth edition was published, it is the biochemistry of receptors. This is reflected in the fact that new knowledge of membrane receptor function pervades the remaining chapters in Part III on carbohydrate and lipid metabolism to an extent not possible in earlier editions, and it is at the heart of many chapters in *Mammalian Biochemistry,* especially in Part III, "Biochemistry of the Endocrine Systems."

Part IV, "Molecular Genetics," has been almost entirely rewritten to reflect the rapid pace of discovery in this area in recent years. The differences in the structure and the expression of the genomes of prokaryotes and eukaryotes have necessitated treating these two subjects separately (Chapters 28 and 29). Indeed, the rapid advances in sequence analysis of genes and the ability to examine eukaryotic genes in the laboratory have brought not only unexpected insights into eukaryotic molecular genetics, but also enormous opportunities for gene manipulation with potentially great benefit to humanity.

Although we expect that the subject matter in *General Aspects* will suffice for many students whose interests may lie in other scientific disciplines, we recognize that many of the topics covered cannot be included in all university courses. It is our hope, however, that students will subsequently seek to broaden and deepen their knowledge of other areas of biochemistry, including the substance of *Mammalian Biochemistry*.

The companion text, *Principles of Biochemistry: Mammalian Biochemistry* is also divided into four parts: (I) "Body Fluids and Their Constituents," (II) "Specialized Tissues," (III) "Biochemistry of the Endocrine Systems," and (IV) "Nutrition." This book will be of special interest to students of human biology and medicine, although the subjects considered illuminate behavior of molecules and cells of great general importance to all students of biology. Most chapters in Parts I and II have been extensively revised as required by the continuing important progress in many of the subjects treated, for example, blood coagulation, the complement system, erythrocytes and leukocytes, and the control of body fluids. Chapter 2, "The Immune System," has been extensively revised to incorporate the rapidly accumulating advances in molecular and cellular immunology. Perhaps no other chapter better illustrates how the approaches of molecular and cellular biology have impinged to give great insight into the functions of a specialized organ system. Chapter 10, "The Gastrointestinal Tract," is a new chapter that systematically treats the many advances in our knowledge of this organ system, especially its hormonal control by peptides, several of which may also function as neurotransmitters in the brain (Chapter 8).

Part III, "Biochemistry of the Endocrine System," has been completely reorganized and rewritten, and several new chapters introduced. These focus on the general principles of endocrine biochemistry (Chapter 11) and the mechanisms of hormone action (Chapter 12). Since its beginnings as a physiological science, endocrinology has advanced to a remarkable extent into the realm of biochemistry. Although diverse in their actions, all hormones are now recognized as acting by receptor-mediated mechanisms with similar principles underlying their functions.

Part IV, "Nutrition," remains central to all of biochemistry. Few areas of science have been applied more triumphantly to the benefit of humankind than the principles of nutrition. Failure to nourish adequately the human population results from inadequate production and distribution of food, rather than an incomplete knowledge of the nutritional requirements of human beings.

Although the separation into two distinct books has permitted introduction of new information, there have had to be many painful omissions. Regretfully, we have had to omit presentation of the historical developments of biochemistry and the names of the untold cadre of scientists who have contributed to our

knowledge. Few descriptions of actual experiments could be included. The serious student will have to go beyond these texts to gather an appreciation of the arduous process by which knowledge has been gained, bit by bit, in countless laboratories utilizing a remarkable panoply of biological materials, techniques, instruments, and experimental approaches. References have been limited to more recent monographs and reviews that can help the student find additional information, as well as the relevant details of the experimental findings and the historical background.

In the presentation of this edition, we acknowledge our great loss in the deaths of two of our coauthors. Abraham White was the initiator of this book and its senior author through six editions. While this edition was in its first phases of preparation, Philip Handler was struck by the difficult illness which terminated his life. In dedicating this edition to them and retaining their names as coauthors, we acknowledge the large residue of their scholarship, wisdom, and perspective that remains in this seventh edition. Their contributions as scientists and teachers will not be forgotten. It is painful to accept the termination of a happy collaboration and friendship with them during which we shared the joy of interpreting and presenting the ever-accelerating growth of our science; for the present senior author (E.L.S.), this began more than thirty years ago.

One of us (R. J. L.) is a new coauthor for this edition, but as in past editions, we continue to take collective responsibility for the content of the entire work. Although each chapter was the primary responsibility of one author, all chapters were circulated among, criticized by, and even rewritten by one or more of the other authors.

We are grateful to the colleagues and friends too numerous to mention, who have generously contributed information and suggestions for the preparation of this edition. We acknowledge with thanks those teachers and students who have made valuable comments and have noted our occasional past errors. We wish also to recognize and thank Richard S. Laufer, Ellen J. Warren, Editors; Donna McIvor, Editing Supervisor; and other members of the staff of the McGraw-Hill Book Company for their pleasant cooperation and help in the task of preparing and publishing these books.

Emil L. Smith
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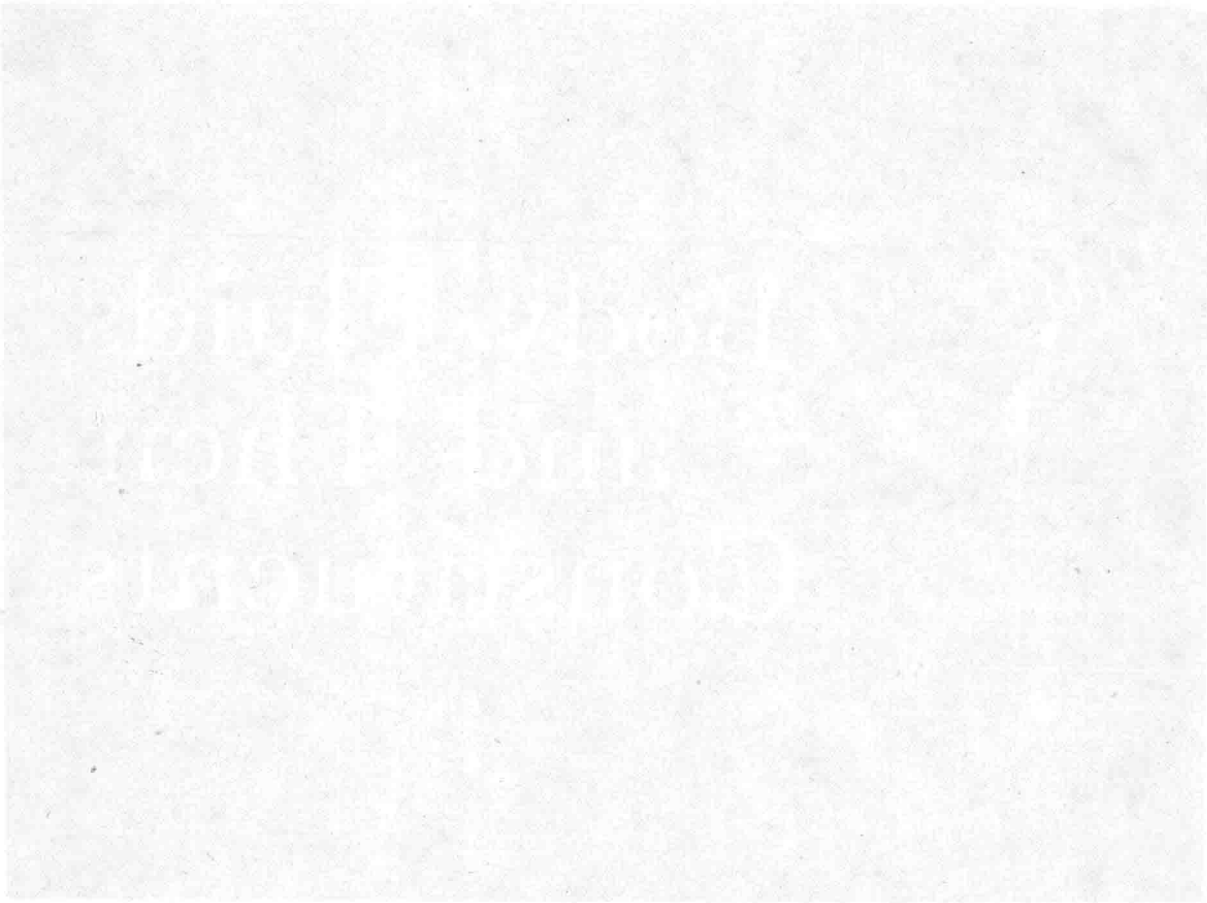
Contents

Part Four Nutrition

Part 1

Body Fluids and Their Constituents



Chapter 1

Blood

Composition of blood plasma. Plasma proteins. Blood clotting.

BLOOD, LYMPH, AND THE CIRCULATORY SYSTEM

Unicellular organisms that live in immediate contact with the external environment obtain nutrients directly from that environment and eliminate unused or unwanted materials directly into the external milieu. As organisms evolved into more complex structures, special means of communication were established that permitted a continuing integration of various tissues and organs as well as facilitating contact with the external environment. The blood and the lymph are the important fluids connecting the diverse anatomical structures of the mammalian organism. Although lymph contains large numbers of leukocytes, or white cells, there are very few erythrocytes.

The specific gravity of blood is 1.055 to 1.065; its viscosity is approximately five to six times that of water. If blood is drawn from a vein and measures are taken to prevent clotting, the suspended cellular elements can be separated by centrifugation. The normally clear, slightly yellow supernatant fluid is termed *blood plasma*. Should the blood be allowed to clot, there separates from the clot a clear yellowish fluid, the *blood serum*. The yellow color is due to the presence of small quantities of bilirubin, a bile pigment, and of carotenoids. The clot consists of cellular elements, enmeshed in a network of fibrous strands of *fibrin*. Thus blood plasma represents blood minus its cellular elements; blood serum also lacks fibrinogen, the precursor of fibrin. Lymph also clots, although somewhat more slowly than blood. The composition of lymph is discussed in Chap. 5.

Any cross-references coded G refer to the companion text, *Principles of Biochemistry: General Aspects*.

COMPOSITION OF BLOOD PLASMA

The total volume of blood in the vascular system approximates 8 percent of the body weight, about 5 or 6 liters of blood in an adult. Infants have a larger blood volume in proportion to their body weight than adults.

The solutes of the blood plasma constitute approximately 10 percent of the volume: proteins, approximately 7 percent; inorganic salts, approximately 0.9 percent; the remainder consisting of diverse organic compounds other than protein. Tables 1.1 and 1.2 indicate the concentrations of the principal nonprotein organic and inorganic components, respectively, of human blood plasma, with

TABLE 1.1

Approximate Ranges of Values for Certain of the Principal Nonprotein Organic Constituents of Human Blood Plasma

Constituent	Normal range, mg/dl	Constituent	Normal range, mg/dl
Nonprotein N	25–40	Creatinine	1–2
Urea	20–30	Uric acid	2–6
Urea N	10–20	Carbohydrates:	
Amino acid N	4–8	Glucose	65–90
Amino acids	35–65	Fructose	6–8
Alanine	2.5–7.5	Glycogen	5–6
α-Aminobutyric acid	0.1–0.3	Polysaccharides (as	
Arginine	1.2–3.0	hexose)	70–105
Asparagine	0.5–1.4	Glucosamine (as	
Aspartic acid	0.01–0.3	polysaccharide)	60–105
Citrulline	0.5	Hexuronates (as	
Cystine	0.8–5.0	glucuronic acid)	0.4–1.4
Glutamic acid	0.4–4.4	Pentose, total	2–4
Glutamine	4.5–10.0	Organic acids:	
Glycine	0.8–5.4	Citric acid	1.4–3.0
Histidine	0.8–3.8	α-Ketoglutaric acid	0.2–1.0
Isoleucine	0.7–4.2	Malic acid	0.1–0.9
Leucine	1.0–5.2	Succinic acid	0.1–0.6
Lysine	1.4–5.8	Acetoacetic acid	0.8–2.8
Methionine	0.2–1.0	Lactic acid	8–17
N^1-Methylhistidine	0.1	Pyruvic acid	0.4–2.0
N^3-Methylhistidine	0.1	Lipids:	
Ornithine	0.6–0.8	Total lipids	285–675
Phenylalanine	0.7–4.0	Neutral fat	80–240
Proline	1.5–5.7	Cholesterol, total	130–260
Serine	0.3–2.0	Esters	90–190
Taurine	0.2–0.8	Free	40–70
Threonine	0.9–3.6	Phosphoglycerides	
Tryptophan	0.4–3.0	Total	150–250
Tyrosine	0.8–2.5	Phosphatidylcholine	100–200
Valine	1.9–4.2	Phosphatidylethanolamine	0–30
Bilirubin	0.2–1.4	Plasmalogens	7–8
Creatine	0.2–0.9	Sphingomyelin	10–50
		Total fatty acids	150–500
		Unesterified fatty acids	8–30