高等医药院校双语教材

供临床医学、口腔医学、药学与制药工程专业用

生物化学

BIOCHEMISTRY

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INTRODUCTION TO BIOCHEMISTRY

Biochemistry (生物化学) may be defined as the study of the molecular basis of life. Scientists have long struggled to provide a coherent and accurate view of living processes. In the late nineteenth century, significant progress was made as investigators in the newly emerging science of biochemistry used the concepts of biology, chemistry, physics, and mathematics. Biochemistry is the science concerned with studying the various molecules that occur in living cells and organisms and with their chemical reactions. Because life depends on biochemical reactions, biochemistry has become the basic language of all biologic sciences. The cell is the structural unit of living systems. Consideration of this concept leads to a functional definition of biochemistry as the science concerned with the chemical constituents of living cells and with the reactions and processes that they undergo. By this definition, biochemistry encompasses large areas of cell biology, of molecular biology, and of molecular genetics. The ultimate goal of biochemistry is to explain all life processes in molecular detail. Because life processes are performed by organic molecules and other basic sciences, biochemistry is to describe and explain, in molecular term, all chemical processes of living cells.

One of the objectives of biochemistry is the complete understanding at the molecular level of all of the chemical processes associated with living cells. To achieve this objective, biochemists have sought to isolate numerous molecules found in cells, determine their structures, and analyze how they function. For example, the efforts of many biochemists to understand the molecular basis of contractility—a process associated primarily, but not exclusively, with muscle cells—have entailed purification of many molecules, both simple and complex, followed by detailed structure-function studies. Through these efforts, some of the features of the molecular basis of muscle contraction have been revealed.

The scope of biochemistry is as wide as life itself. Wherever there is life, chemical processes are occurring. Biochemists study the chemical processes that occur in microorganisms, plants, insects, fish, birds, mammals, and human beings.

Another objective of biochemistry is to attempt to understand how life began. Knowledge of this fascinating subject is still embryonic.

Advances in biochemical knowledge have illuminated many areas of medicine. Conversely, the study of disease has often revealed previously unsuspected aspects of biochemistry.

A sound knowledge of biochemistry and other related basic disciplines is essential for the rational practice of medical and related health sciences. The World Health Organization (WHO) defines health as a state of "complete physical, mental and social well-being and not merely the absence of disease or infirmity". All diseases are manifestations of abnormalities of molecules, chemical reactions, or processes. There is a wealth of documentations of the uses of biochemistry in prevention, diagnosis and treatment of diseases; many cases will be cited throughout this text.

The overall objective of this book is to provide concise yet authoritative coverage of the principles of biochemistry and molecular biology. The text offers numerous examples of how knowledge of biochemistry is essential for understanding the maintenance of health and the cause and rational treatment of many diseases. The goals of the authors in preparing this latest edition were, firstly, to provide both medical students and other students of the health sciences with a book that not only describes the basics of biochemistry but also is user-friendly and interesting and secondly, to reflect the latest advances in biochemistry that are important to medicine.

The text is divided into four parts:

Part Ⅰ: Structure and function of biomacromolecule Describes the structures and functions of the proteins, nucleic acids and enzymes. This section also describes the principles of enzyme.

Part Ⅱ: Metabolism Explains how various cellular reactions either utilize or produce energy and traces the pathway by which carbohydrates and lipids are synthesized and degraded. Metabolism is a basic characteristic of life. It has been divided into two major categories: catabolism and anabolism. The energy required by anabolic processes is provided by catabolic processes. So, the content of this part deals with the catabolic processes of amino acid, the metabolism of carbohydrates, nucleotides and lipids. It also relates to the biological oxidation.

Part Ⅲ: Gene expressing Describes the representation of DNA →RNA→ proteins. In the section, explanations of DNA replication and DNA repair have been updated. RNA synthesis is delineated. Discussions of the assembly of the preinitiation complex are explained in detail.

Part Ⅳ: Special topics Deals with the hepatic biochemistry and blood biochemistry.

WEI Xiao-dong
December 2008

CONTENTS

PART I

STRUCTURE AND FUNCTION OF BIOMACROMOLECULE

Chapter 1

Structure and Function of Protein

Proteins are very important. They provide structure, and organic catalysts are mostly made of proteins. They can also be used to store energy. They are produced by the ribosome in our cells. As with almost everything else in the world, the function of anything depends on its structure.

This chapter discusses the function and structure, including primary, secondary, tertiary and quaternary structures of proteins. Major topics include the α-helix, β-sheet, β-turn and loop, how the structure features. The close linkage between protein structure and biologic function is illustrated for proteins that serve structural roles. Proteins play crucial roles in almost every biological process. They are responsible in one form or another for a variety of physiological functions including:

1. Enzymatic catalysis   Almost all biological reactions are enzyme catalyzed. Enzymes are known to increase the rate of a biological reaction by a factor of 10 to the 6th power. There are several thousand enzymes, which have been identified to date.

2. Transportation and storage   Small molecules are often carried by proteins in the physiological setting (for example, the protein hemoglobin is responsible for the transportation of oxygen to tissues). Many drug molecules are partially bound to serum albumins in the plasma.

3. Coordinated motion   Muscle is mostly protein, and the sliding motion of two protein

filaments, actin and myosin, mediates muscle contraction.

4. Mechanical support Skin and bone are strengthened by the protein collagen.

5. Immune protection Antibodies are protein structures that are responsible for reacting with specific foreign substances in the body.

6. Generation and transmission of nerve impulses Some amino acids act as neurotransmitters, which transmit electrical signals from one nerve cell to another. In addition, receptors for neurotransmitters, drugs, etc. are proteins in nature. An example of this is the acetylcholine receptor, which is a protein structure that is embedded in postsynaptic neurons.

7. Control of growth and differentiation Proteins can be critical to the control of growth, cell differentiation and expression of DNA. For example, repressor proteins may bind to specific segments of DNA, preventing expression and thus the formation of the product of that DNA segment. Likewise, many hormones and growth factors that regulate cell function, such as insulin or thyroid stimulating hormone are proteins.

SECTION 1 THE COMPOSITION OF PROTEIN

Tab.1-1 gives the elementary composition of protein. There is phosphorus, zinc, manganese or copper in some of protein. It is important that the nitrogen composition average is approaching 16 percent in all kinds of proteins. So we can calculate the content of protein by nitrogen quantity.

Tab.1-1 Normal elementary composition of protein

element	percent	element	percent
carbon	50%-55%	nitrogen	13%-19%
hydrogen	6%-7%	sulfur	0%-4%
oxygen	19%-24%	minerals	0%-0.1%

Protein=quantity of nitrogen×6.25

There are two kinds of proteins, and they both serve different purposes:

(1) Fibrous proteins: They usually provide structures and are usually long and thin. Examples include muscles, hair, cartilage, veins, ducts, and other structures.

(2) Globular proteins: The name describes their structures. These proteins usually do things other than providing structures. They transport oxygen and nutrients, fight invasions by foreign objects, help maintain homeostasis in the body, transport electrons, and catalyze reactions that would take too long in their absence. Most hormones are proteins. Enzymes are very important globular proteins, so we will get to that section in a bit.

1.1 Amino acid

Like most biological macromolecules, proteins are made up of simple building blocks; in the case of proteins, these building blocks are called amino acids (Fig.1-1). The amino and carboxyl moieties in an amino acid are alpha to one another; also located on the alpha carbon is an "R" group. The nature of this R-group (called the side chain) determines the identity of a particular amino acid. They differ from each other in their side chains, or R-groups, which vary in structure, size and electric charge, and influence the solubility of amino acids in water. There are a total of 20 amino acids, which are used to make up proteins (some modified or otherwise unusual amino acids exist that we will discuss later in the course). In solution at physiological pH (7.4), amino acids undergo an acid-base reaction to form zwitterions. In a zwitterion, the positive and negative charges cancel to give a molecule with a net charge of zero. However, the p*K*a values for a typical amino acid (glycine, for example) are 9.6 and 2.3 for the amino and carboxyl groups, respectively. If the pH of an amino acid solution is lowered significantly from 7.4, a species results in which the amino group has a positive charge, while the carboxyl is neutral. Likewise, if the pH is raised from 7.4, a species results in which the amino group is neutral, while the carboxyl has a negative charge. Thus, the ionization state of amino acids is pH dependent. Amino acids are the monomers of proteins. The basic parts of an amino acid are an amino group, a carboxylic group, and a side chain, all attached to an alpha-carbon (central carbon). There are only 20 R-groups, and therefore only 20 kinds of amino acids are found in nature, 12 of which can be produced by humans. The rest we have to obtain by eating stuff, and these are called essential amino acids.

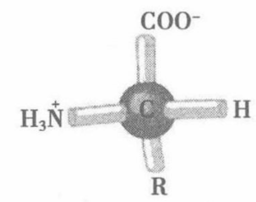


Fig.1-1 L-amino acid

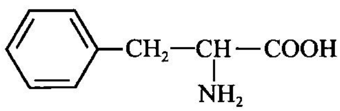
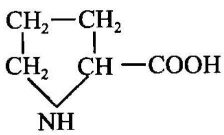
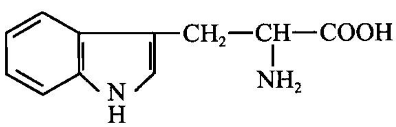
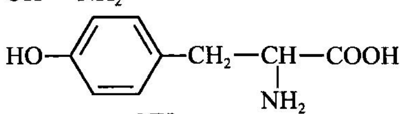
All amino acids except glycine (R=H) are chiral. Every amino acid in mammalian systems exists in the **L-configuration**, where "L" signifies that the amino acid in Fischer projection is similar to L-glyceraldehyde. This description of stereochemistry is outdated, and is seldom used except in trivial names.

As was mentioned above, there are 20 amino acids which are used to make up proteins in mammalian biological systems. The properties of each amino acid are dictated by the **side chain**, which can vary in **size, shape, charge, reactivity and ability to hydrogen bond**. The amino acids are grouped according to the properties of their side chains, as shown in the table below. Each amino acid has a standard three-letter abbreviation which is used in lieu of a full structure, as seen in Tab.1-2.

Tab.1-2 The classification and structure formula of amino acid

Structure formula	Chinese name	English name	Three letter name	One letter name	pI
1. nonpolar hydrophobic amino acid (非极性疏水性氨基酸)					
NH_2-CH_2-COOH	甘氨酸	glycine	Gly	G	5.97
$CH_3-\underset{NH_2}{\underset{\vert}{CH}}-COOH$	丙氨酸	alanine	Ala	A	6.00
$\begin{matrix}CH_3\\CH_3\end{matrix}\!>CH-\underset{NH_2}{\underset{\vert}{CH}}-COOH$	缬氨酸	valine	Val	V	5.96

Continued

Structure formula	Chinese name	English name	Three letter name	One letter name	pI
$(CH_3)_2CH-CH_2-CH(NH_2)-COOH$	亮氨酸	leucine	Leu	L	5.98
$(CH_3)(C_2H_5)CH-CH(NH_2)-COOH$	异亮氨酸	isoleucine	Ile	I	6.02
	苯丙氨酸	phenylalanine	Phe	F	5.48
	脯氨酸	proline	Pro	P	6.30
2. polar neutral amino acid (极性中性氨基酸)					
	色氨酸	tryptophan	Trp	W	5.89
$CH_2(OH)-CH(NH_2)-COOH$	丝氨酸	serine	Ser	S	5.68
	酪氨酸	tyrosine	Tyr	Y	5.66
$HS-CH_2-CH(NH_2)-COOH$	半胱氨酸	cysteine	Cys	C	5.07
$CH_3-S-CH_2-CH_2-CH(NH_2)-COOH$	甲硫氨酸	methionine	Met	M	5.74
$H_2NOC-CH_2-CH(NH_2)-COOH$	天冬酰胺	asparagine	Asn	N	5.41
$H_2NOC-CH_2-CH_2-CH(NH_2)-COOH$	谷氨酰胺	glutamine	Gln	Q	5.65
$CH_3-CH(OH)-CH(NH_2)-COOH$	苏氨酸	threonine	Thr	T	5.60
3. acidic amino acid (酸性氨基酸)					
$HOOC-CH_2-CH(NH_2)-COOH$	天冬氨酸	aspartic acid	Asp	D	2.97
$HOOC-CH_2-CH_2-CH(NH_2)-COOH$	谷氨酸	glutamic acid	Glu	E	3.22
4. basic amino acid (碱性氨基酸)					
$H_2N-CH_2-CH_2-CH_2-CH_2-CH(NH_2)-COOH$	赖氨酸	lysine	Lys	K	9.74