

ENGLISH

生物学英语 与论文写作

于湘晖 吴永革 马俊锋 编

The Second Edition

第二版

化学工业出版社

生物学英语 与论文写作

于湘晖 吴永革 马俊锋 编



化学工业出版社

· 北京 ·

图书在版编目 (CIP) 数据

生物学英语与论文写作/于湘晖, 吴永革, 马俊锋
编. —2 版. —北京: 化学工业出版社, 2018. 8
ISBN 978-7-122-32333-0

I. ①生… II. ①于… ②吴… ③马… III. ①生物学-
英语-论文-写作 IV. ①Q1

中国版本图书馆 CIP 数据核字 (2018) 第 123705 号

责任编辑: 傅四周 郎红旗
责任校对: 边 涛

装帧设计: 王晓宇

出版发行: 化学工业出版社 (北京市东城区青年湖南街 13 号 邮政编码 100011)
印 装: 三河市延风印装有限公司
787mm×1092mm 1/16 印张 20 字数 540 千字 2018 年 10 月北京第 2 版第 1 次印刷

购书咨询: 010-64518888 (传真: 010-64519686) 售后服务: 010-64518899
网 址: <http://www.cip.com.cn>
凡购买本书, 如有缺损质量问题, 本社销售中心负责调换。

定 价: 59.80 元

版权所有 违者必究

前言

随着生命科学的迅猛发展和国际学术交流、学生国际化培养等的日益加强,生物学专业英语的教和学越来越重要。许多高校要求专业课程采用英文原版教材,用双语或英语讲授,这都极大促进了专业英语的教学工作。为了学生们能够熟练地阅读英文文献、书籍,将研究成果整理成英文科研论文在期刊杂志上发表;为了学生们能够进入国际高水平的大学研修,编写高水平的、内容前沿的生物学专业英语教材就显得十分重要。

吉林大学从1980年以来开设“生物学专业英语”课程至今,先后编写并出版了两部教材——《生物化学与分子生物学英语》(1993年)和《生物学英语与写作》(2008年)。近几年生物学的发展日新月异,专业英语教材的内容需要不断更新补充,才能适应新的知识体系。因此,本书编者在对近几年的实际教学经验总结基础上,对2008年版教材进行修订和再版。本教材对英文科技论文写作进行了系统讲述,第二版书名相应更名为《生物学英语与论文写作》。

全书共分为两部分内容,第一部分是课文,内容涵盖生物化学、酶工程、分子生物学、动物学、微生物学、遗传学、细胞生物学、基因组学、生物信息学、系统发育生物学和基因编辑等学科领域,力求扩大专业覆盖面和单词量。在素材的选择方面既注意内容的广泛性,又注意技术的新颖性,特别是较前一版增加了在生物学研究领域的新研究方向和技术,使学生既学习了英文语言又能了解专业知识的前沿,例如二代基因测序和CRISPR/Cas9基因编辑等。为了便于学习,课文后附有单词表(注明音标)和难句分析。第二部分是英语学术论文写作,全面介绍英文科技文章的写作知识,这也是本书的一个特色。本书不仅可以作为生命科学各学科本科生的专业英语教材,并且可供研究生专业阅读和写作学习,也可以作为青年教师和生物学专业相关人员的专业英语学习材料。

参加本书编写的于湘晖教授、吴永革教授和马俊锋副教授是吉林大学生命科学学院双语课程《生物化学》教学第一线的老师,都有国外的学习或工作经历,具有丰富的教学经验。李青山教授虽然已经退休,但长期从事生物学专业英语的教学,经验十分丰富,为本书把好质量关。编写英语写作部分的刘永新教授多年来担任英文版专业杂志的总编辑工作,英文文字能力强,文风严谨。

由于时间、水平有限,书中可能存在疏漏和不足,敬请广大读者批评指正,以便进一步完善和提高。

在本书的设计、编写和出版过程中,化学工业出版社编辑给予了认真、细致和耐心的指导,在此表示衷心的感谢。

编者

2018年5月于长春

第一版前言

随着大学英语教学质量的不断提高和四、六级考试不断普及,我国大学本科学生的基础英语水平越来越好,这为进一步提高英语的运用能力奠定了坚实的基础。近年来,各学校在加强基础英语教学的同时,十分重视基础英语之后的专业英语的教学,这对于学生提高英语语言运用能力,适应专业教材和文献的阅读、写作和翻译是十分重要的。为了适应教育和科学技术国际化的需要,许多学校要求专业课采用原版教材,用英语或双语讲授,这就更促进了专业英语的教学工作。

吉林大学从1980年以来,开设“生物学专业英语”课,编写了讲义;又于1993年编写出版了《生物化学与分子生物学英语》教材。这次的编写是在多年教学经验基础上的总结。本书分为两部分,第一部分是课文,内容包括生物化学、分子生物学、细胞生物学、微生物学、免疫学、生理学和生态学等,力求扩大专业覆盖面,扩大单词量。为了便于学习,课文后有单词表(并注明音标)和难句分析。第二部分是科技英语写作,全面介绍英文科技文章的写作知识。这部分也是本书的一个特点。在素材的选择方面既注意内容的广泛性又注意新颖性,特别是选择那些代表目前生物学新发展的材料,使学生既学习了语言又能得到专业知识的前沿内容,例如基因组学、蛋白质组学、基因治疗等。因此,本书不仅可以作为生物学各学科本科生的专业英语教材,而且适合于研究生的专业阅读和写作的需要,也可以作为青年教师和从事生物学相关人员的专业英语学习材料。

参加本书编写的于湘晖教授、吴永革教授是我院专业英语教学第一线的老师,他们都有国外的工作经历,具有丰富的教学经验。编写英语写作的刘永新教授多年来从事英文版专业杂志的总编辑工作,英文文字能力强,文风严谨。他们为本书的问世做了大量的工作,保证了本书的质量。但是,由于时间、水平有限,书中可能存有疏漏和不足,敬请广大读者批评指正,以便进一步完善和提高。

在本书的设计、编写和出版过程中,化学工业出版社编辑给予了认真、细致和耐心的指导,在此表示衷心的感谢。

吉林大学生命科学学院

李青山

2008年1月于长春

Contents

Section I Lessons	001
The Structure and Function of Protein	001
The Structure and Function of Enzymes	013
Polysaccharides and Glycoconjugates	021
The Structure of DNA	032
Cells—Discovery and Basic Structure	045
The Origins of Genetics and Molecular Biology	058
The Genome Jigsaw	063
Functions of Cell Membranes	073
General Properties of Immune Responses	084
Cytokines	097
The Science of Virology	105
A Review of Pathway-Based Analysis Tools That Visualize Genetic Variants	119
From Genomics to Proteomics: Techniques and Applications in Cancer Research	127
Gene Therapy	136
The Molecular Basis of Cancer—Cell Behavior	152
The Basic Principles of Recombinant DNA Technology	169
Laboratory Techniques Commonly Used in Immunology	176
Viable Offspring Derived from Fetal and Adult Mammalian Cells	191
CRISPR/Cas9 for Genome Editing: Progress, Implications and Challenges	196
Epigenetics in Humans: An Overview	204
Making New Bodies Mechanisms of Developmental Organization	214
Neuropathological Alterations in Alzheimer Disease	222
Section II How to Write a Scientific Paper (英语学术论文写作)	243
1 Introduction (序论)	243
2 How to Write the Title (论文题目的写法)	246
3 How to List the Authors and Addresses (作者及其工作单位的写法)	249
4 How to Write the Abstract (摘要的写法)	251
5 How to Choose the Key Words (关键词的选择)	255
6 How to Write the Introduction (引言的写法)	256
7 How to Write the Main Body (正文的写法)	261
8 Acknowledgments (致谢)	275
9 Reference Citation and Reference Lists (参考文献及其著录)	276
10 Appendix (附录)	280
11 Grammar (英语科技论文写作中的几个语法问题)	280
12 Quantities and Units (科技英语表述中的物理量及其单位)	287
13 Numeral Usage (数字的使用)	289

14 Capitalization and Lower Case of English Letters (英文字母的大写和小写)	294
15 Roman Type and Italic Type of English Letters (西文字母的正体和斜体)	295
16 Usage of Punctuation (科技英语论文中标点符号的用法)	297
17 Submitting the Manuscripts and Publication (投稿与发表)	302
参考文献	314

Section I Lessons

The Structure and Function of Protein

Proteins are the most abundant macromolecules in living cells and constitute 50 percent or more of their dry weight. They are found in all cells and all parts of cells. Proteins also occur in great variety; hundreds of different kinds may be found in a single cell. Moreover, proteins have many different biological roles since they are the molecular instruments through which genetic information is expressed. It is therefore appropriate to begin the study of biological macromolecules with the proteins, whose name means "first" or "foremost".

The key to the structure of the thousands of different proteins is the group of relatively simple building-block molecules from which proteins are built. All proteins whether from the most ancient lines of bacteria or from the highest forms of life, are constructed from the same basic set of 20 amino acids, covalently linked in characteristic sequences. Because each of these amino acids has a distinctive side chain which lends it chemical individuality, this group of 20 building-block molecules may be regarded as the alphabet of protein structure.

In this paper we shall also examine peptides, short chains of two or more amino acids joined by covalent bonds. What is most remarkable is that cells can join the 20 amino acids in many different combinations and sequences, yielding peptides and proteins having strikingly different properties and activities. From these building blocks different organisms can make such widely diverse products as enzymes, hormones, the lens protein of the eye, feathers, spider webs, tortoise shell, nutritive milk proteins, enkephalins (the body's own opiates), antibiotics, mushroom poisons, and many other substances having specific biological activity.

Amino acids have common structural features

When proteins are boiled with strong acid or base, their amino acid building blocks are released from the covalent linkages that join them into chains. The free amino acids so formed are relatively small molecules, and their structures are all known. The first amino acid to be discovered was asparagines, in 1806. The last of the 20 to be found, threonine, was not identified until 1938. All the amino acids have trivial or common names, sometimes derived from the source from which they were first isolated. Asparagines was first found in asparagus, as one might guess; glutamic acid was found in wheat gluten; and glycine (Greek, glykos, "sweet") was so named because of its sweet taste.

All of the 20 amino acids found in proteins have as common denominators a carboxyl group and an amino group bonded to the same carbon atom. They differ from each other in their side chains, or R groups, which vary in structure, size, electric charge, and solubility in water. The 20 amino acids of proteins are often referred to as the standard, primary, or normal amino acids, to distinguish them from other kinds of amino acids present in living or-

ganisms but not in proteins. The standard amino acids have been assigned three-letter abbreviations and one-letter symbols, which are used as shorthand to indicate to composition and sequence of amino acids in polypeptide chains.

General structure of an amino acid. This structure is common to all but one of the α -amino acid (proline, a cyclic amino acid, is the exception). The R group or side chain attached

to the α carbon is different in each amino acid.

$$\begin{array}{c} \text{R} \\ | \\ \text{H}_3\text{N}^+ - \text{CH} - \text{COOH} \\ | \\ \alpha \end{array}$$

Nearly all amino acids have an asymmetric carbon atom

We note that all the standard amino acids except one have an asymmetric carbon atom, the α carbon, to which are bonded four different substituent groups, i.e., a carboxyl group, an amino group, a R group, and a hydrogen atom. The asymmetric α carbon atom is thus a chiral center. As we have seen, compounds with a chiral center occur in two different isomeric forms, which are identical in all chemical and physical properties except one, the direction in which they can cause the rotation of plane-polarized light in a polarimeter. With the single exception of glycine, which has no asymmetric carbon atom, all of the 20 amino acids obtained from the hydrolysis of proteins under sufficiently mild conditions are optically active. i.e., they can rotate the plane-polarized light in one direction or the other. Because of the tetrahedral arrangement of the valence bonds around the α carbon atom of amino acids the four different substituent groups can occupy two different arrangements in space, which are nonsuperimposable, mirror images of each other. These two forms are called optical isomers, enantiomers, or stereoisomers. A solution of one stereoisomer of a given amino acid will rotate plane-polarized light to the left (counterclockwise) and is called the levorotatory isomer [designated $(-)$]; the other stereoisomer will rotate plane-polarized light to the same extent but to the right (clockwise) and is called the dextrorotatory isomer [designated $(+)$]. An equimolar mixture of the $(+)$ and $(-)$ forms will not rotate plane-polarized light. Because all the amino acids (except glycine) when carefully isolated from proteins do rotate plane-polarized light, they evidently occur in only one of their stereoisomeric forms in protein molecules.

Optical activity of a stereoisomer is expressed quantitatively by its specific rotation, determined from measurements of the degree of rotation of a solution of the pure stereoisomer at a given concentration in a tube of a given length in a polarimeter:

$$[\alpha]_D^{25} = \frac{\text{observed rotation, deg}}{\text{length of tube, dm} \times \text{concentration, g/mL}}$$

the abbreviation dm stands for decimeters (0.1m).

The temperature and the wavelength of the light employed (usually the D line of sodium, 589nm) must be specified. For the specific rotation of several amino acids, some are levorotatory and others dextrorotatory.

Periodic structures: the alpha helix, beta pleated sheet, and collagen helix

Can a polypeptide chain fold into a regularly repeating structure? To answer this question, Pauling and Corey evaluated a variety of potential polypeptide conformations by building precise molecular models of them. They adhered closely to the experimentally observed bond angles and distances for amino acids and small peptides. In 1951, they proposed two

periodic polypeptide structures, called α helix and β pleated sheet.

The α helix is a rod-like structure. The tightly coiled polypeptide main chain forms the inner part of the rod, and the side chains extend outward in a helical array. The α helix is stabilized by hydrogen bonds between the NH and CO groups of the main chain. The CO group of each amino acid is hydrogen bonded to the NH group of the amino acid that is situated four residues ahead in the linear sequence. Thus, all the main-chain CO and NH groups are hydrogen bonded. Each residue is related to the next one by a translation of $1.5 \text{ \AA}$ ^① along the helix axis and a rotation of 100° , which gives 3.6 amino acid residues per turn of helix. Thus, amino acids spaced three and four apart in the linear sequence are spatially quite close to one another in an α helix. In contrast, amino acids two apart in the linear sequence are situated on opposite sides of the helix and so are unlikely to make contact. The pitch of the α helix is $5.4 \text{ \AA}$, the product of the translation ($1.5 \text{ \AA}$) and the number of residues per turn (3.6). The screw-sense of α helix can be right-handed (clockwise) or left-handed (counterclockwise); the α helices found in proteins are right-handed.

The α helix content of proteins of known three-dimensional structure is highly variable. In some, such as myoglobin and hemoglobin, the α helix is the major structural motif. Other proteins, such as the digestive enzyme chymotrypsin, are virtually devoid of α helix. The single-stranded α helix discussed above is usually a rather short rod, typically less than $40 \text{ \AA}$ in length. A variation of the α helical theme is used to construct much longer rods, extending to $1000 \text{ \AA}$ or more. Two or more α helices can entwine around each other to form a cable. Such α helical coiled coils are found in several proteins; keratin in hair, myosin and tropomyosin in muscle, epidermin in skin, and fibrin in blood clots. The helical cables in these proteins serve a mechanical role in forming stiff bundles of fibers.

The structure of the α helix was deduced by Pauling and Corey six years before it was actually to be seen in the X-ray reconstruction of the structure of myoglobin. The elucidation of the structure of the α helix is a landmark in molecular biology because it demonstrated that the conformation of a polypeptide chain can be predicted if the properties of its components are rigorously and precisely known.

In the same year, Pauling and Corey discovered another periodic structural motif, which they named the β pleated sheet (β because it was the second structure they elucidated, the α helix having been the first). The β pleated sheet differs markedly from the α helix in that it is a sheet rather than a rod. The polypeptide chain in the β pleated sheet is almost fully extended rather than being tightly coiled as in the α helix. The axial distance between adjacent amino acids is $3.5 \text{ \AA}$ in contrast with $1.5 \text{ \AA}$ for the α helix. Another difference is that the β pleated sheet is stabilized by hydrogen bonds between NH and CO groups in different polypeptide strands, whereas in the α helix the hydrogen bonds are between NH and CO groups in the same polypeptide chain. Adjacent strands in a β pleated sheet can run in the same direction (parallel β sheet) or in opposite directions (antiparallel β sheet). For example, silk fibroin consists almost entirely of stacks of antiparallel β sheets. Such β sheet regions are a recurring structural motif in many proteins. Structural units comprising from two to five parallel or antiparallel β strands are especially common.

① $1 \text{ \AA} = 0.1 \text{ nm}$.

The collagen helix, a third periodic structure, will be discussed in detail. This specialized structure is responsible for the high tensile strength of collagen, the major component of skin, bone, and tendon.

Polypeptide chains can reverse direction by making β turn

Most proteins have compact, globular shapes due to frequent reversals of the direction of their polypeptide chains. Analyses of the three-dimensional structures of numerous proteins have revealed that many of these chain reversals are accomplished by a common structural element called the β turn. The essence of this hairpin turn is that the CO group of residue n of a polypeptide is hydrogen bonded to the NH group of residue $(n+3)$. Thus, a polypeptide chain can abruptly reverse its direction.

Levels of structure in protein architecture

In discussing the architecture of proteins, it is convenient to refer to four levels of structure (Fig. 1.1). Primary structure is simply the sequence of amino acids and location of disulfide bridges, if there are any. The primary structure is thus a complete description of the covalent connections of a protein. Secondary structure refers to the steric relationship of amino acid residues that are close to one another in the linear sequence. Some of these steric relationships are of a regular kind, giving rise to a periodic structure. The α helix, the β pleated sheet, and the collagen helix are examples of secondary structure. Tertiary structure refers to the steric relationship of amino acid residues that are far apart in the linear sequence. It should be noted that the dividing line between secondary and tertiary structure is arbitrary. Proteins that contain more than one polypeptide chain display an additional level of structural organization, namely quaternary structure, which refers to the way in which the

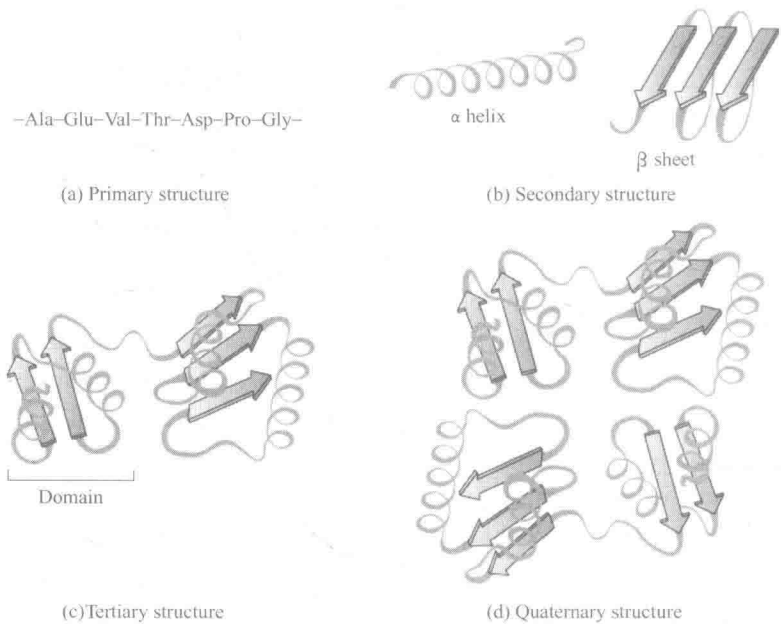


Fig. 1.1 Protein structure
From primary to quaternary structure

chains are packed together. Each polypeptide chain in such a protein is called a subunit. Another useful term is domain, which refers to a compact, globular unit of protein structure. Many proteins fold into domains having masses that range from 10 to 20 kD. The domains of large proteins are usually connected by relatively flexible regions of polypeptide chain.

Amino acid sequence specifies three-dimensional structure

Insight into the relation between the amino acid sequence of a protein and its conformation came from the work of Christian Anfinsen on ribonuclease, an enzyme that hydrolyzes RNA. Ribonuclease is a single polypeptide chain consisting of 124 amino acid residues. It contains four disulfide bonds, which can be irreversibly oxidized by performic acid to give cysteic acid residues. Alternatively, these disulfide bonds can be cleaved reversibly by reducing them with a reagent such as β -mercaptoethanol, which forms mixed disulfides with cysteine side chains. In the presence of a large excess of β -mercaptoethanol, the mixed disulfides also are reduced, so that the final product is a protein in which the disulfides (cystines) are fully converted into sulfhydryls (cysteines). However, it was found that ribonuclease at 37°C and pH7 cannot be readily reduced by β -mercaptoethanol unless the protein is partially unfolded by denaturing agents such as urea or guanidine hydrochloride. Although the mechanism of action of these denaturing agents is not fully understood, it is evident that they disrupt noncovalent interactions. Polypeptide chains devoid of cross-links usually assume a random-coil conformation in 8 mol/L urea or 6 mol/L guanidine HCl, as evidenced by physical properties such as viscosity and optical rotary spectra. When ribonuclease was treated with β -mercaptoethanol in 8 mol/L urea, the product was a fully reduced, randomly coiled polypeptide chain devoid of enzymatic activity. In other words, ribonuclease was denatured by this treatment.

Anfinsen then made the critical observation that the denatured ribonuclease, freed of urea and β -mercaptoethanol by dialysis, slowly regained enzymatic activity. He immediately perceived the significance of this chance finding: the sulfhydryls of the denatured enzyme became oxidized by air and the enzyme spontaneously refolded into a catalytically active form. Detailed studies then showed that nearly all of the original enzymatic activity was regained if the sulfhydryls were oxidized under suitable conditions. All of the measured physical and chemical properties of the refolded enzyme were virtually identical with those of the native enzyme. These experiments showed that the information needed to specify the complex three-dimensional structure of ribonuclease is contained in its amino acid sequence. Subsequent studies of other proteins have established the generality of this principle, which is a central one in molecular biology: sequence specifies conformation.

A quite different result was obtained when reduced ribonuclease was reoxidized while it was still in 8 mol/L urea, this preparation was then dialyzed to remove the urea. Ribonuclease reoxidized in this way had only 1% of the enzymatic activity of the native protein. Why was the outcome of the experiment different from the one in which reduced ribonuclease was reoxidized in a solution free of urea? The reason is that wrong disulfide pairings were formed when the random-coil form of the reduced molecule was reoxidized. There are 105 different ways of pairing eight cysteines to form four disulfides; only one of these combinations is enzymatically active. The 104 wrong pairings have been picturesquely termed "scrambled" ribonuclease spontaneously converted into fully active, native ribonuclease when trace amounts

of β -mercaptoethanol were added to the aqueous solution of the reoxidized protein. The added β -mercaptoethanol catalyzed the rearrangement of disulfide pairings until the native structure was regained, which took about the hours. This process was driven entirely by the decrease in free energy as the “scrambled” conformations were converted into the stable, native conformation of the enzyme. Thus, the native form of ribonucleases appears to be the thermodynamically most stable structure.

Functions of proteins

Proteins are undoubtedly the most functionally diverse of biomolecules. In general, globular proteins function by recognizing other molecules to which they specifically bind. Such precise binding is possible because the protein molecule has a site that is complementary to a site on the molecule recognized. However, this binding is not fixed and rigid but, rather, exists in a dynamic equilibrium with recognition, binding and release occurring continuously. At any moment the proportion of bound molecules depends upon (a) the relative concentrations of the protein and the molecule to which it binds, and (b) the strength of association between them. The latter depends on how well the complementary sites fit together and the types of interactions involved, for example, hydrophobic, ionic, hydrogen bonding, which occurs between the sites. Once binding does occur, there is a conformational change in the protein-bound molecule, or in the complex of protein and protein-bound molecule. This change is the signal that initiates the biochemical activity associated with the protein and forms the basis for the remarkable range of biological roles exhibited by proteins.

The formation of proteins is under the direct control of DNA. The growth and differentiation of cells, organs and organisms result from the orderly expression of information contained in the DNA molecules. However a chicken and egg situation exists, since the formation of proteins, and indeed the replication of DNA, requires the activity of pre-existing proteins.

Much of biochemistry is concerned with the remarkable protein catalysts called enzymes. Many reactions that normally proceed at barely measurable rates are typically accelerated by a factor of 10^8 - 10^{11} by the presence of the appropriate enzyme. In comparison with chemical catalysts, enzymes are also amazingly specific; a given enzyme catalyses only a single transformation or group of similar reactions. Their catalytic power, their specificity and the fact that their activity can be regulated, mean that enzymes ensure that metabolism proceeds in an orderly fashion.

Specific transport proteins are a feature of living systems. The well-known blood protein, haemoglobin, transports O_2 in the blood of vertebrates. Examples of transport proteins in the serum are albumin, which can transport fatty acids; lipoproteins, which carry cholesterol and other lipids; and transferrin, which transports iron. Invertebrates have copper-containing proteins called haemocyanins, which have O_2 -carrying roles parallel to those of the vertebrate haemoglobins.

Other transport proteins have a different function. They are situated in biological membranes and allow materials to be transported across the membrane. For example, the Na^+ , K^+ -ATPase is a protein that pumps Na^+ , out of cells and K^+ into cells, at the expense of metabolic energy.

Proteins play a key role in the co-ordination of metabolism. For example, neurons respond to specific signals via protein receptors on their surfaces. Indeed, many of these “signals” are chemical ones, consisting of peptides or small proteins. Co-ordination in multicellular types is often mediated by hormonal signals; and in animals the hormone receptors and, indeed, some hormones themselves are proteins.

The movement of organisms is achieved by a dynamic function of protein molecules. Some bacteria are motile using extended appendages called flagella. Eukaryotic cells use cilia and flagella in locomotion, but multicellular animals move using skeletal muscle. All of these locomotory activities depend upon the co-ordinated movements of sets of fibrous proteins.

Protein molecules are responsible for the mechanisms by which organisms protect themselves against parasites and toxins. Scavenging white blood corpuscles, called leukocytes, recognize invading microorganisms by means of protein receptor molecules on their surfaces, and then engulf them. Antibodies are serum proteins that can combine with antigens such as bacterial toxins, leading to their neutralization. Other proteins such as fibrinogen, circulate in the blood and are able to form fibrous mats to seal wounds.

Mechanical support is given by several types of fibrous proteins both inside and outside cells. Tubulin forms extended microtubules within the cytoplasm, which help determine the shape of the cell. Other proteins are found extracellularly and help organize the matrix that surrounds the cell. Collagen is a widely distributed extracellular protein, which imparts a high tensile strength to tissues such as cartilage, bone and the skin.

Haemoglobinopathies

Survival of vertebrates is not possible without haemoglobin. However, many humans survive with partially defective haemoglobins. One such condition is sickle cell anaemia where because of mutation, an amino acid on the surface of the protein molecule is altered producing a haemoglobin that precipitates in the deoxygenated state and therefore does not transport O_2 effectively. This condition leads to deformation of the red cells (“sickling”) which become trapped in the capillaries and haemolysis occurs, resulting in anaemia.

Sickle cell disease is fairly common, especially amongst the North American black population, but it is rather unusual as a “haemoglobinopathy” or haemoglobin disease. The amino acid change results in there being a “sticky patch” on the β -polypeptide chain of deoxyhaemoglobin, leading to the aggregation and precipitation described above. The mutation arose by chance at some time in the past. Much more likely events to occur (and many hundreds of haemoglobin mutations are now known) are ones in which the haem pocket is modified so that haem does not bind or function properly, or ones in which the α or the β chains are not constructed properly.

The various parts of the haemoglobin, like all quaternary proteins, fit and stay together because they are complementary in shape, charge, hydrophobicity, etc. In particular, the Fe^{2+} -containing haem group is a highly hydrophobic molecule and requires to be placed in a hydrophobic pocket in the molecule, where it is held and carries out its function of binding oxygen reversibly. Mutations that result in the amino acid residues lining the haem pocket being replaced by ones that are less hydrophobic or more bulky may result in a failure to bind haem or failure to bind oxygen properly (i. e. not at all or irreversibly). Many such muta-

tions are known and characterized. In the majority of cases only one type of subunit is affected. Thus, although the remaining unmutated subunits can potentially bind haem and oxygen normally, they often do not do so. Having only two oxygen-binding centers in the molecule, instead of four, does not allow for the usual subunit interactions which influence the binding and release of O_2 , instead of behaving in the required way generating a sigmoidal binding curve, the oxygen-binding curve may be much more like that of myoglobin. Consequently, oxygen is not transported successfully.

Many patients with haemoglobinopathies are heterozygotic for the haemoglobinopathy in question; they have both a defective and a normal gene, so that effectively 50% of the haemoglobin they synthesize is normal. There may be a high rate of destruction of the abnormal haemoglobin which further lessens the problem. Also several of the genes for the polypeptide chains of haemoglobin are present in multiple copies. Consequently, only one of the genes may have mutated, while the others, even in homozygotes, still produce normal polypeptides.

In some individuals the results of the mutation may be slight and not noticed until sensitive blood screening is carried out. In others, it may be sufficiently severe as to cause debilitating anemia and other conditions. Many individuals probably do not survive because they are homozygous for the condition. However, this depends partly on how severe the defect is.

Haemoglobin variants are commonly detected by electrophoresis of a solution of the protein. When amino acids are changed as a result of a mutation, there may be a modification of the charge on the molecule, which may then display a higher or lower mobility than that of normal haemoglobin. Such screening may be done cheaply. Obviously, to determine which amino acid is altered requires a more extensive study, including peptide mapping and partial sequencing. Haemoglobin variants are usually named from the town/hospital where the case was first detected (e. g. Hb "Memphis"), although this gives the uninitiated little useful information. Hb Memphis is actually a rather unusual variant in which there are mutations in both the α and the β chains. It might more helpfully be described as:



Obviously, mutations do not necessarily have to be single amino acid substitutions, and do not have only to affect the haem pocket. Many mutations on the surface of the molecule are known, which have almost no effect on the properties of the molecule (sickle cell haemoglobin is the exception to this rule).

As well as single amino acid changes, there may be double changes, changes in both α and β chains, deletions resulting in a failure to make chains, mutations that change a stop codon so that a much larger than normal polypeptide is produced, and so on. It is probably true to say that almost all variations have been encountered. The present-day distribution of defective haemoglobins has arisen from the accumulation of harmless mutations, early death of individuals with harmful mutations, and survival of some individuals because although they have a harmful mutation, this confers a selective survival advantage such as increased resistance to malaria, as is the case with sickle cell disease.

As a result of a great deal of experimental work (protein sequencing and, later DNA sequencing), an enormous amount is known about the haemoglobinopathies called thalassaemias. Almost all the possibilities that potentially could occur, do so. These include; deletion of one or more α chain genes per haploid genome; deletion of the β chain genes (unbalanced

synthesis of chains may result in the production of homotetrameric molecules such as Hb α_4 in β -thalassaemia, which are unstable and precipitate or oxidize very rapidly); chain-termination mutation (e. g. Hb "Seal Rock"); absent, reduced or inactive mRNA; gene fusion; and increased globin chain degradation.

Haemoglobin variants may now be detected in the fetus by molecular biology techniques and parents may be counselled about abortion. Although sickle cell disease may confer resistance to malaria, and consequently a selective survival advantage, there is usually little that can be done in any of the haemoglobinopathies in terms of medical treatment, other than to cope with crises and pain. Because there is anaemia, blood transfusions may be used, but in the longer term, repeated blood transfusion is not helpful.

Glossary

- abortion [ə'bo:ʃən] n. 流产, 堕胎, 失败, 夭折, 中止, 早产
 albumin [æl'bju:mɪn] n. 清蛋白, 白蛋白
 amino acid n. 氨基酸, 胺
 amino group 氨基
 appendage [ə'pendɪdʒ] n. 附属物, 附肢, 附属丝
 aqueous [eɪkwɪəs] n. 水的, 眼房水的
 asparagine [æs'pærədʒi:n] n. 天(门)冬素, 天冬酰胺酸
 asymmetric [æsi'metrik] adj. 不均匀的, 不对称的
 axis [æksɪs] n. 轴
 carboxyl group 羧基
 chiral ['tʃɪrəl] adj. (化)手(征)性的
 cholesterol [kəlestəʊl,-rɔl] n. 胆固醇
 chymotrypsin [kaɪmə'tripsɪn] n. (生化①)胰凝乳蛋白酶, 糜蛋白酶
 cilia ['sɪliə] n. 睫, 纤毛
 codon ['kəʊdən] n. (遗②)密码子
 coil [kɔɪl] v. 盘绕, 卷
 collagen ['kɒlədʒən] n. 胶原质, 胶原
 corpuscle ['kɔ:pʌs(ə)] n. 血细胞
 covalent [kəu'veɪlənt] adj. (化③)共有原子价的, 共价的
 cysteic acid 半胱氨酸
 cystine ['sɪstɪ:n,-tɪn] n. (生化)胱氨酸, 双硫丙氨酸
 decimeter ['desɪ,mɪ:tə(r)] n. 分米
 denominator [dɪ'nəmineɪtə] n. (数)分母, 命名者
 dextrorotatory isomer 右旋异构体
 dialysis [daɪ'æləsɪs] n. (化)透析, 分离
 disulfide bridge 二硫键
 domain [dəu'meɪn] n. 结构域
 dynamic [daɪ'næmɪk] adj. 动力的, 动力学的, 动态的
 enantiomer [ɪ'næntiəmə] n. (化)对映(结构)体
 enkephalin [enkefəli:n] n. 脑啡肽
 enzyme ['enzaim] n. (生化)酶

① “生化”表示“生物化学”, 后同。

② “遗”表示“遗传学”, 后同。

③ “化”表示“化学”, 后同。

- epidermin [ˈepɪdərmin] n. 表皮素 (一种构成表皮主要成分的纤维蛋白)
- fiber [ˈfaɪbə] n. 纤维
- fibrin [ˈfaɪbrɪn] n. (生化) (血) 纤维蛋白, (血) 纤维
- flagella [ˈflæɡzələ] n. 鞭节, 鞭毛
- glutamic acid [ˈɡluːtæmɪk æsɪd] n. 谷氨酸
- gluten [ˈɡluːtən] n. 谷蛋白, 黏菌膜, 黏胶质
- guanidine hydrochloride n. 盐酸胍
- haemocyanin [ˈhiːməʊˈsaɪənɪn] n. 血清蛋白, 血细胞, 血蓝蛋白
- haemoglobinopathy [ˈhiːməʊˌɡleʊbɪˈnɒpəθi] n. (医①) 血红蛋白病
- haemoglobin [ˈhiːməʊˌɡleʊbɪn] n. 血色素, 血红蛋白
- hairpin [ˈheəpɪn] n. 发夹
- hydrogen bond 氢键
- hydrogen [ˈhaɪdrədʒən] n. 氢
- hydrophobicity n. 疏水性
- hydrophobic [ˌhaɪdrəʊˈfəʊbɪk] adj. 疏水的, 狂犬病的, 恐水病的, 患恐水病的
- ionic [aɪˈɒnɪk] adj. 离子的
- irreversible [ˌɪrɪˈvəːsəbl̩, -sɪb-] adj. 不能撤回的, 不能取消的
- isomeric form 同分异构
- keratin [ˈkerətɪn] n. (生化) 角蛋白
- levorotatory isomer 左旋异构体
- macromolecule [ˌmækroʊˈmɒlɪkjʊːl] n. 大分子, 高分子
- malaria [məˈleəriə] n. 疟疾, 瘴气
- matrix [ˈmeɪtrɪks] n. 矩阵; 基质, 衬质, 间质
- mercaptoethanol [məˌkæptəʊˈeθənɒl] n. (化) 巯基乙醇
- metabolism [meˈtæbəlaɪzəm] n. 新陈代谢, 代谢作用
- opiate [ˈəʊpiət] n. 鸦片剂; adj. 安眠的; v. 缓和
- optical isomer n. 旋光异构体, 旋光异构物
- organism [ˈɔːɡənɪzəm] n. 生物体, 有机体
- peptide [ˈpeptaid] n. 多肽
- performic acid 过氧甲酸
- pitch [pɪtʃ] n. 螺距
- plane-polarized light 平面偏振光
- polarimeter [ˌpəʊləˈrɪmɪtə] n. 偏光计
- primary structure (免疫②) 一级结构
- protein [ˈprəʊtiːn] n. (生化) 蛋白质; adj. 蛋白质的
- quaternary structure 四级结构
- reversal [rɪˈvəːsəl] n. 颠倒, 反转, 反向, 逆转
- ribonuclease [ˌraɪbəʊˈnjuːkleɪs] n. (生化) 核糖核酸酶
- secondary structure 二级结构
- sickle cell anaemia n. 镰刀形红细胞贫血症
- side chain 侧链, (聚合物中) 支链
- sigmoidal n. S形曲线; adj. S形的
- silk fibroin 蚕丝蛋白
- sodium [ˈsəʊdʒəm, -diəm] n. (化) 钠
- solubility [ˌsɒljʊˈbɪlɪti] n. 溶度, 溶性, 溶解性

① “医”表示“医学”, 后同。

② “免疫”表示免疫学, 后同。