HELLENIC REPUBLIC

UNIVERSITY OF CRETE

Academic English

Section: Proteins and Amino Acids

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Proteins and Amino Acids

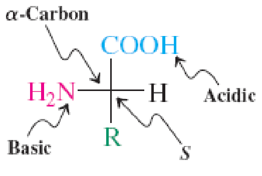
Pre-text Quiz: True or False

1. Amino acids are built from proteins
2. There are twenty essential amino acids
3. Proteins are large polypeptides (> 50 amino acids)
4. In biochemistry and molecular biology, a residue refers to a specific monomer within the polymeric chain of a polysaccharide, protein or nucleic acid; hence, an amino acid residue is a monomer.
5. To understand protein behaviour you need to look at how the amino acid residues join together in chains.
6. Polypeptides are poly(amino acids) linked by amide bonds. Most natural polypeptides are made from only 19 different l-amino acids and glycine, all of which have common names and three- and one-letter abbreviations.
7. Amino acids are amphoteric; they can be protonated and deprotonated.
8. The structures of polypeptides are varied; they can be linear, cyclic, disulfide bridged, pleated sheet, a-helical or super helical, or disordered, depending on size, composition, hydrogen bonding, and electrostatic and London forces.
9. Proteins can also be classed as fibrous and globular.
10. In globular proteins, several a helices are coiled together to form a superhelix.
11. Denaturation is another name for disruption, loss or destruction of protein structure and function.

Proteins and Amino Acids

Proteins have an astounding diversity of functions in living systems. As enzymes, they catalyze transformations ranging in complexity from the simple **hydration** of carbon dioxide to the **replication** of entire chromosomes — great **coiled** strands of DNA, the genetic material in living cells. Enzymes can accelerate certain reactions many **millionfold**.

Some proteins serve for transport and storage. Thus, **hemoglobin** carries oxygen; iron is transported in the blood by transferrin and stored in the liver by ferritin. Proteins play a crucial role in coordinated motion, such as muscle **contraction**. They give mechanical support to skin and bone; they are the antibodies responsible for our immune protection; and they control **growth** and differentiation — that is, which part of the information stored in DNA is to be used at any given time.



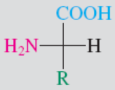
α-Amino acid

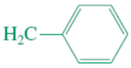
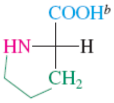
Amino acids are carboxylic acids that bear an amine group. The most common of these in nature are the **2-amino acids,** or ***α*-amino acids,** which have the general formula $RCH(NH_2)COOH$; that is, the amino function is located at C2, the α-carbon. The R group can be alkyl or aryl, and it can contain hydroxy, amino, mercapto, sulfide, carboxy, guanidino, or imidazolyl groups. Because of the presence of both amino and carboxy functions, amino acids are both acidic and basic.

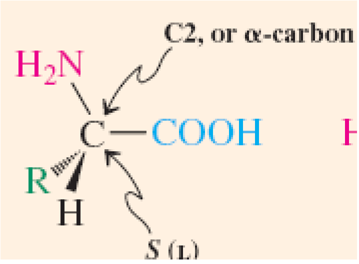
The stereocenter of common 2-amino acids has the *S* configuration

More than 500 amino acids exist in nature, but the proteins in all species, from bacteria to humans, consist mainly of only 20. Adult humans can synthesize all but eight, and two only in insufficient quantities. This group is often called the **essential amino acids** because they must be included in our diet. Although amino acids can be named in a systematic manner, they rarely are; so we shall use their common names. Table 26-1 lists the 20 most common amino acids, along with their structures, their pK_a values, and the three- and (the newer) one-letter codes that abbreviate their names. We shall see later how to use these codes to describe peptides conveniently.

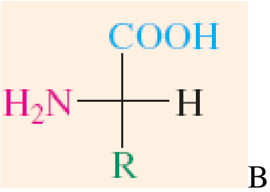
Table 26-1 Natural (2*S*)-Amino Acids



R	Name	Three-letter code	One-letter code	pK_a of α-COOH	pK_a of α-$^+NH_3$	pK_a of acidic function in R	Isoelectric point, p*I*
H	Glycine	Gly	G	2.3	9.6	—	6.0
Alkyl group							
CH_3	Alanine	Ala	A	2.3	9.7	—	6.0
$CH(CH_3)_2$	Valine[a]	Val	V	2.3	9.6	—	6.0
$CH_2CH(CH_3)_2$	Leucine[a]	Leu	L	2.4	9.6	—	6.0
 $\underset{\displaystyle CH_3}{\underset{\vert}{C}}HCH_2CH_3$ (*S*)	Isoleucine[a]	Ile	I	2.4	9.6	—	6.0
	Phenylalanine[a]	Phe	F	1.8	9.1	—	5.5
	Proline	Pro	P	2.0	10.6	—	6.3



A.



B.

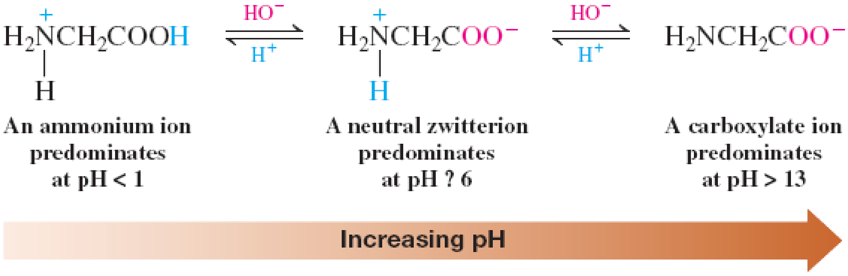
Amino acids may be depicted by either hashed-wedged line structures or by Fischer projections. (Look at the pervious models built and identify them!)

In all but glycine, the simplest of the amino acids, C2 is a stereocenter and usually adoptsthe *S* configuration. Other stereocenters located in the substituent R may have either *R* (as in threonine) or *S* configuration (as in isoleucine).

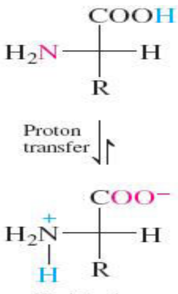
Amino acids are acidic and basic: zwitterions

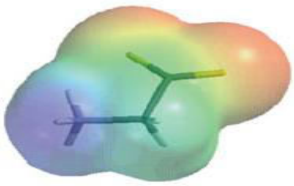
Because of their two functional groups, the amino acids are both acidic and basic; that is, they are **amphoteric** (Section 8-3). The carboxylic acid group protonates the amine function, thus forming a **zwitterion.** This ammonium carboxylate form is favored because an ammonium ion is much less acidic ($pK_a \approx 10–11$) than a carboxylic acid ($pK_a \approx 2–5$). The highly polar zwitterionic structure allows amino acids to form particularly strong crystal lattices. Most of them therefore are fairly insoluble in organic solvents, and they decompose rather than melt when heated. The electrostatic potential map of glycine in the margin depicts its highly dipolar nature, originating from the juxtaposition of the electron-rich (red) carboxylate function with the electron-poor (blue) ammonium group.

The structure of an amino acid in aqueous solution depends on the pH. Consider, for example, the simplest member of the series, glycine. The major form in neutral solution is the zwitterion. However, in strong acid (pH < 1), glycine exists predominantly as the cationic ammonium carboxylic acid, whereas strongly basic solutions (pH > 13) contain mainly the deprotonated 2-aminocarboxylate ion. These forms interconvert by acid-base equilibria (Section 2-2).



$$H_3\overset{+}{N}CH_2COOH \underset{H^+}{\overset{HO^-}{\rightleftharpoons}} H_3\overset{+}{N}CH_2COO^- \underset{H^+}{\overset{HO^-}{\rightleftharpoons}} H_2NCH_2COO^-$$





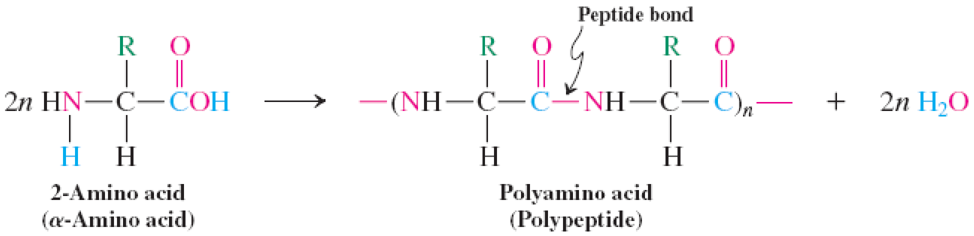
Glycine zwitterion

26-4 Peptides and Proteins: Amino Acid Oligomers and Polymers

Amino acids are very versatile biologically because they can be polymerized. In this section, we describe the structure and properties of such **polypeptide** chains. Long polypeptide chains are called proteins (somewhat arbitrarily defined as >50 amino acids) and are one of the major constituents of biological structures. Proteins serve an enormous variety of biological functions; these functions are often facilitated by the twists and folds of the component chains.

Amino acids form peptide bonds

2-Amino acids are the monomer units in polypeptides. The polymer forms by repeated reaction of the carboxylic acid function of one amino acid with the amine group in another to make a chain of amides (Section 20-6). The amide linkage joining amino acids is also called a **peptide bond.**

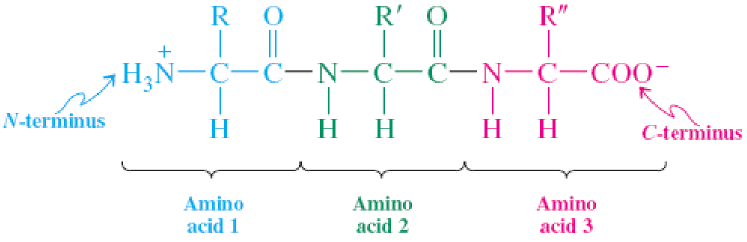


The oligomers formed by linking amino acids in this way are called **peptides.** For example, two amino acids give rise to a **dipeptide,** three to a **tripeptide,** and so forth. The individual amino acid units forming the peptide are referred to as **residues.** In some proteins, two or more polypeptide chains are linked by disulfide bridges (Sections 9-10 and 26-1).

Polypeptides are characterized by their sequence of amino acid residues

In drawing a polypeptide chain, the **amino end,** or ***N*-terminal amino acid,** is placed at the left. The **carboxy end,** or ***C*-terminal amino acid,** appears at the right. The configuration at the C2 stereocenters is usually presumed to be *S*.

How to Draw the Structure of a Tripeptide



The chain incorporating the amide (peptide) bonds is called the **main chain,** the substituents R, R′, and so forth, are the **side chains.**

The naming of peptides is straightforward. Starting from the amino end, the names of the individual residues are simply connected in sequence, each regarded as a substituent to the next amino acid, ending with the *C*-terminal residue. Because this procedure rapidly becomes cumbersome, the three-letter abbreviations listed in Table 26-1 are used for larger peptides.

Proteins fold into pleated sheets and helices: secondary and tertiary structure

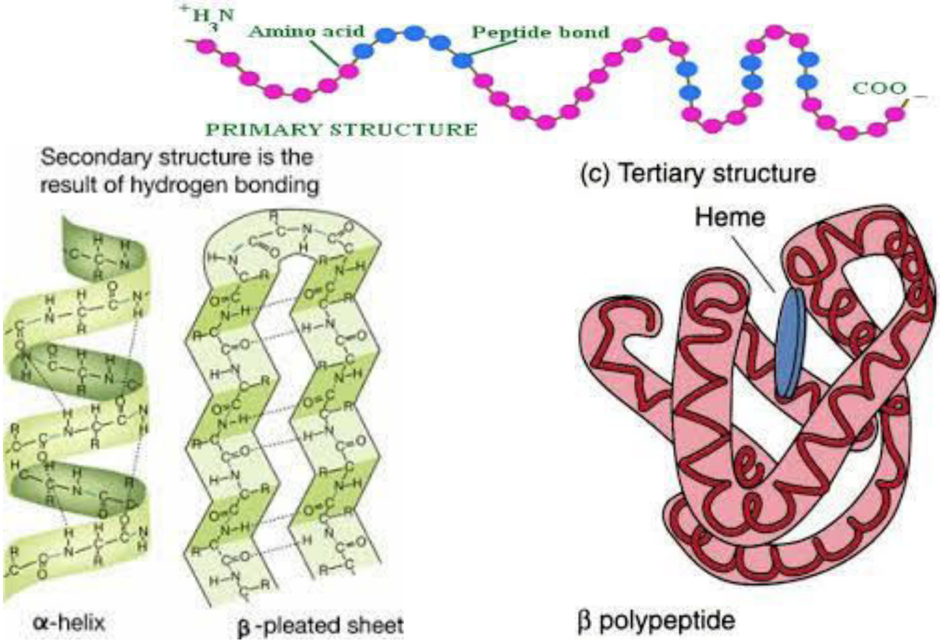
Insulin and other polypeptide chains adopt well-defined three-dimensional structures. Whereas the sequence of amino acids in the chain defines the **primary structure,** the folding pattern of the chain induced by the spatial arrangement of close-lying amino acid residues gives rise to the **secondary structure** of the polypeptide. The secondary structure results mainly from the rigidity of the amide bond and from hydrogen (and other noncovalent) bonding (margin) along the chain(s). Two important arrangements are the pleated sheet, or β configuration, and the α helix.

In the **pleated sheet** (also called β sheet; Figure 26-3), two chains line up with the amino groups of one peptide opposite the carbonyl groups of a second, thereby allowing hydrogen bonds to form. Such bonds can also develop within a single chain if it loops back on itself. Multiple hydrogen bonding of this type can impart considerable rigidity to a system. The planes of adjacent amide linkages form a specific angle, a geometry that produces the observed pleated-sheet structure, in which the R groups protrude above and below at each kink.

The **α helix,** as shown in Figure 26-4, allows for intramolecular hydrogen bonding between nearby amino acids in the chain: The carbonyl oxygen of each amino acid is interacting with the amide hydrogen four residues ahead. There are 3.6 amino acids per turn of the helix, two equivalent points in neighboring turns being about 5.4 Å apart. The C=O and N—H bonds point in opposite directions and are roughly aligned with the helical axis. On the other hand, the (hydrophobic) R groups point away from the helix.

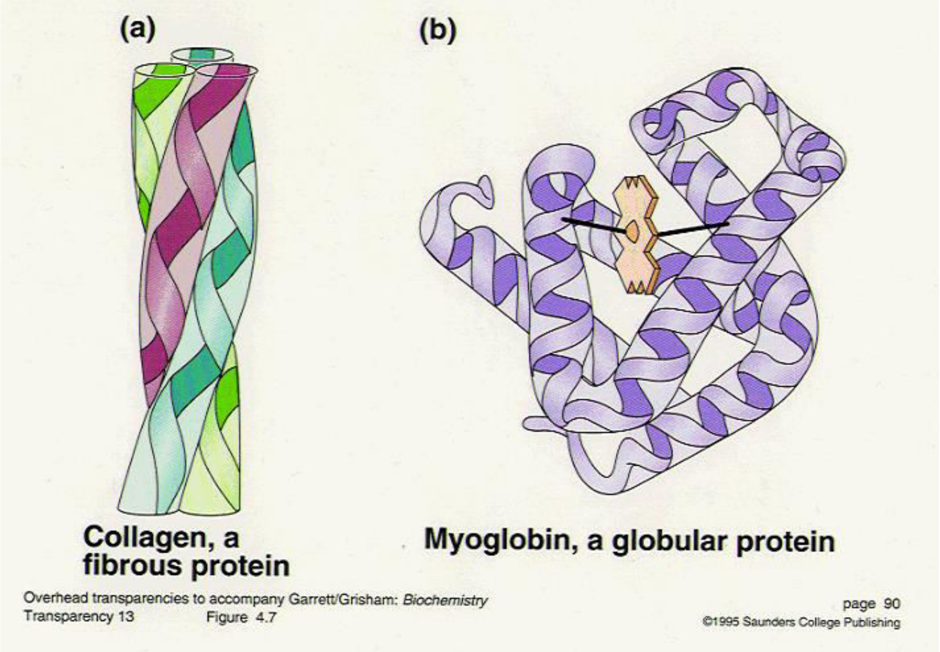
Not all polypeptides adopt idealized structures such as these. If too much charge of the same kind builds up along the chain, charge repulsion will enforce a more random orientation. In addition, the rigid proline, because its amino nitrogen is part of the substituent ring and has no N−H available for hydrogen bonding, can cause a kink or bend in an α helix.

Further folding, coiling, and aggregation of polypeptides is induced by distant residues in the chain end and give rise to their **tertiary structure.** A variety of forces, all arising from the R group, come into play to stabilize such molecules, including disulfide bridges, hydrogen bonds, London Forces and electrostatic attraction and repulsion. There are also micellar effects: The polymer adopts a structure that maximizes exposure of polar



groups to the aqueous environment while minimizing exposure of hydrophobic groups (e.g. alkyl or phenyl), the hydrophobic effect. Pronounced folding is observed in the globular proeteins, many of which perform a chemical transport and catalysis (e.g. myoglobin and hemoglobin). In the **fibrous proteins,** such as myosin (in muscle), fibrin (in blood clots), and α-keratin (in hair, nails, and wool), several α helices are coiled to produce a **superhelix** (Figure 26-5).

Properties	Fibrous Protein	Globular Protein
Shape	Long and narrow	Rounded / spherical
Role	Structural (strength and support)	Functional (catalytic, transport, etc.)
Solubility	(Generally) insoluble in water	(Generally) soluble in water
Sequence	Repetitive amino acid sequence	Irregular amino acid sequence
Stability	Less sensitive to changes in heat, pH, etc.	More sensitive to changes in heat, pH, etc.
Examples	Collagen, myosin, fibrin, actin, keratin, elastin	Catalase, haemoglobin, insulin, immunoglobulin



Collagen, a fibrous protein

Myoglobin, a globular protein

Overhead transparencies to accompany Garrett/Grisham: *Biochemistry*
Transparency 13 Figure 4.7
page 90
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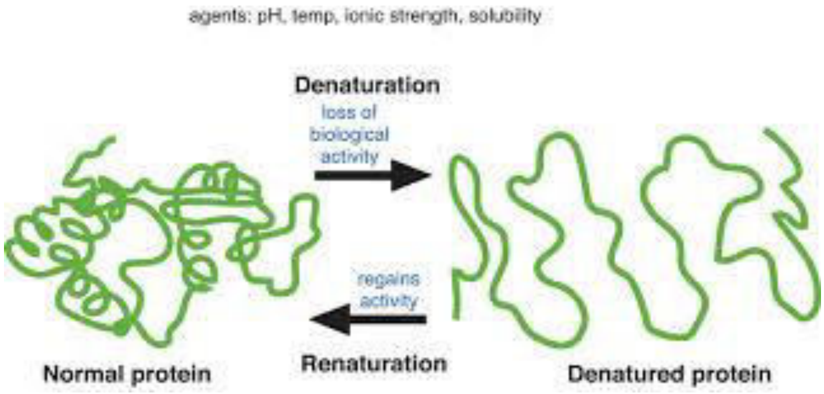
The tertiary structures of enzymes and transport proteins (proteins that carry molecules from place to place) usually give rise to three-dimensional pockets, called **active sites** or **binding sites.** The size and shape of the active site provide a highly specific "fit" for the **substrate** or **ligand,** the molecule on which the protein carries out its intended function. The inner surface of the pocket typically contains a specific arrangement of the side chains of polar amino acids that attracts functional groups in the substrate by hydrogen bonding or ionic interactions. In enzymes, the active site aligns functional groups and additional molecules in a way that promotes their reactions with the substrate.

Protein Denaturation

Denaturation, or breakdown of the tertiary structure of a protein, usually causes precipitation of the protein and destroys its catalytic activity. Denaturation is caused by exposure to excessive heat or extreme pH values. Think, for example, of what happens to clear egg white when it is poured into a hot frying pan or to milk when it is added to lemon tea. Some molecules, such as hemoglobin, also adopt a quaternary structure, in which two or more polypeptide chains, each with its own tertiary structure, combine to form a larger assembly. A simplified picture of the progression from primary to quaternary structures is given below.



Summary

Polypeptides are polymers of amino acids linked by amide bonds. Their amino acid sequences can be described in a shorthand notation using the three- or one-letter abbreviations compiled in Table 26-1. The amino end group is placed at the left, the carboxy end at the right. Polypeptides can be cyclic and can also be linked by disulfide and hydrogen bonds. The sequence of amino acids is the primary structure of a polypeptide, folding gives rise to its secondary structure, further folding and coiling produce its tertiary structure, and aggregation of several polypeptides results in the quaternary structure

A. Match the terms and their definitions

1. twisted into a continuous circular or spiral shape
2. becoming tighter or narrower
3. having; displaying
4. having various functions and uses
5. slow and inefficient
6. monitor; control
7. pressed fold made (usually in a piece of clothing)
8. neighbouring
9. give (a quality of)
10. very noticeable

adjacent
coiled
pronounced
versatile
pleated
bearing
impart
contraction
cumbersome
regulate

B. Read the text carefully and define the following terms

1. Active sites
2. Amino acid
3. Alpha helix
4. Essential amino acid
5. Disulfide bridge
6. Denaturation
7. Protein
8. Protein Precipitation
9. Peptide
10. Residue

biologically important organic compounds composed of amine (-NH_2) and carboxylic acid (-COOH) functional groups, along with a side-chain specific to each amino acid

that cannot be synthesized *de novo (from scratch)*by the organism being considered, and therefore must be supplied in its diet

large biological molecules, or macromolecules, consisting of one or more long chains of amino acid residues

short chains of amino acid monomers linked by peptide (amide) bonds

a specific monomer within the polymeric chain of a polysaccharide, protein or nucleic acid

a covalent **bond**, usually derived by the coupling of two thiol groups

a small port in an enzyme where substrate molecules bind and undergo a chemical reaction

a common secondary structure of proteins and is a righthand-coiled or spiral conformation (helix) in which every backbone N-H group donates a hydrogen bond to the backbone C=O group of the amino acid four residues earlier ($i + 4 \rightarrow i$ hydrogen bonding)

when proteins or nucleic acids lose their quaternary tertiary and/or secondary structure which is present in their native state, due to external stress or compound such as a strong acid or base, a concentrated inorganic salt, an organic solvent (e.g., alcohol or chloroform), radiation or heat

C. Rephrase the following sentences:

1. As enzymes, they catalyse transformations ranging in complexity from the simple dehydration of carbon dioxide to the replication of entire chromosome-great coiled strands of DNA, the genetic material of living cells.

The reconstruction of

2. Amino-acids are carboxylic acids bearing an amino group.

Amino acids are molecules

3. More than 500 amino acids occur in nature but the proteins in all species, from bacteria to humans, consist mainly of only 20.

Regardless their biological activity,

4. Amino acids are very versatile biologically because they can be polymerised.

Amino acids exhibit

5. Gramicin S is a cyclic peptide antibiotic constructed out of two identical pentapeptides that have been joined head to tail.

A pair of

6. A second feature inducing rigidity is the strongly dipolar nature of the amide functional group, which cause an appreciable barrier to rotation around the relatively short carbonyl-nitrogen bond.

The rigidity of the dipolar

7. Denaturation or breakdown of the tertiary structure of a protein usually causes precipitation of protein and destroys its catalytic activity. It is caused by exposure to excessive heat or extreme ph values.

Destruction of catalytic activity (i.e. precipitation) of

Notes

Reference Note

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επένδυση στην κοινωνία της γνώσης
ΥΠΟΥΡΓΕΙΟ ΠΑΙΔΕΙΑΣ ΚΑΙ ΘΡΗΣΚΕΥΜΑΤΩΝ
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ΕΣΠΑ
2007-2013
πρόγραμμα για την ανάπτυξη
ΕΥΡΩΠΑΪΚΟ ΚΟΙΝΩΝΙΚΟ ΤΑΜΕΙΟ

Με τη συγχρηματοδότηση της Ελλάδας και της Ευρωπαϊκής Ένωσης