Proteins—Natural Polyamides 2.4

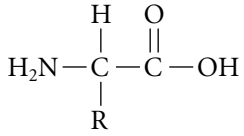
Living systems produce a large variety of molecules whose properties fulfill many different functions in the organism. Some substances need to be mobile and water soluble in order to be transported throughout the system. Other substances serve a structural function, providing support or motion; so the properties of strength, flexibility, and insolubility in water are desirable in these molecules.

Many of the substances that make up living organisms are large molecules of high molecular mass, and are polymers of functionally similar subunits. We will be looking at four groups of these biological **macromolecules**: proteins, carbohydrates, nucleic acids, and fats and lipids.

Proteins make up about half of the dry mass of our bodies. Our muscles, skin, cartilage, tendons, and nails are all made up of protein molecules. We also produce thousands of different enzymes, all proteins, to catalyze specific reactions, and many other protein molecules such as hemoglobin and some hormones. Although these proteins appear so diverse in function and in structure, they are made from the same set of monomers: a group of 20 molecules called **amino acids**.

macromolecule a large molecule composed of several subunits

amino acid a compound in which an amino group and a carboxyl group are attached to the same carbon atom



amino acid

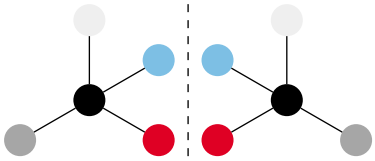
Amino Acids

Just as their name suggests, amino acids contain two functional groups—an amine group and a carboxylic acid group—attached to a central carbon atom. The central carbon atom completes its bonding with a hydrogen atom and a substituted group, shown in the margin as R.

Each of the 20 natural amino acids has a different R group. The simplest amino acid, glycine, has a hydrogen atom for its R group. Some of the R groups are acidic, others basic; some are polar and others nonpolar. Each protein molecule is a polymer of these amino acids, linked together in a sequence that is specific to the protein, each monomer contributing its characteristics to the overall molecule.

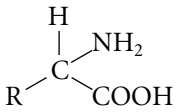
Let us consider the diversity possible in this construction. Using the alphabet as an analogy, consider the number of words that exist with an alphabet of 26 letters—enough to fill a dictionary. Now imagine the number of words that we can make up if each word may be hundreds of letters long, and any sequence of letters is permissible. This limitless number of combinations of amino acids affords the diversity of structure and properties that we find in the proteins of living organisms.

chiral able to exist in two forms that are mirror images of each other



L (from the Latin, *laevus*) for left

D (from the Latin, *dexter*) for right



amino acid

Figure 1
Chiral molecules

Chiral Molecules

Any molecule containing a carbon with four different attached groups is capable of existing as two different isomers that (like our two hands) are mirror images of each other. These are known as **chiral** molecules (**Figure 1**). All the amino acids, with the exception of glycine, can therefore exist in two different configurations: L and D. In fact, natural amino acids appear in only one configuration, designated by convention as "L."

TRY THIS activity

Making Chiral Molecules

Any molecule that contains a carbon atom bonded to four different atoms or groups is a chiral molecule. Prove it to yourself!
Materials: molecular model kit; mirror

- Join four different atoms or groups to a single carbon atom. Hold the model next to the mirror and observe the reflection.
  (a) What is the correct name for your molecule?
- Now take a duplicate set of atoms and create a model of the image you can see in the mirror. Compare it to the original.
  (b) What is the correct name for your second molecule?
  (c) Would you expect the two molecules to have the same properties? Explain.

peptide bond the bond formed when the amine group of one amino acid reacts with the acid group of the next

polypeptide a polymer made up of amino acids joined together with peptide bonds

dipeptide two amino acids joined together with a peptide bond

Polypeptides from Amino Acids

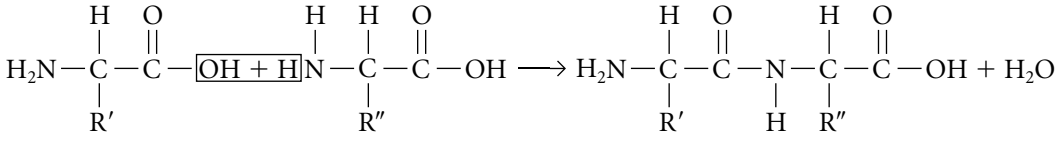
The difference between chiral isomers is dramatic in biological systems. For example, in the late 1950s the L-isomer of the drug thalidomide was found to be an effective treatment for "morning sickness" in pregnant women. However, the drug that was sold contained a mixture of both isomers. The other isomer turned out to cause "errors" in fetus development and suppress natural abortions. As a result, the use of the drug led to a significant increase in physical deformities among newborns. Synthetic processes often produce a mixture of the two possible isomers, and the pharmaceutical industry has to take great care to market only the isomer with the desired effect.

A list of the names and condensed structural formulas of the 20 amino acids is shown in **Figure 2**. Let us look at how these amino acids are linked together. In the previous section, we discussed the formation of polyamides; the same reaction occurs here. The amine group of one amino acid reacts with the acid group of the next amino acid in the sequence, with the elimination of a water molecule. The bond formed in this reaction between amino acids is given a special name—a **peptide bond**. These biological polyamides are accordingly called **polypeptides**.

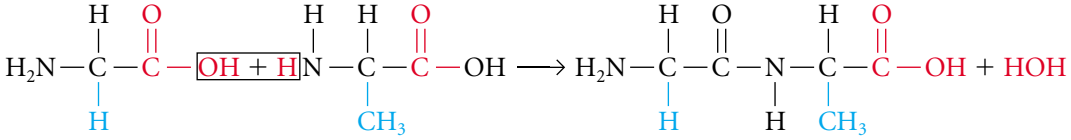
How is a polypeptide different from a protein? Proteins may consist of several polypeptide chains, and may also have other components, such as the "heme unit" in hemoglobin.

Protein molecules are long and flexible, and can form bonds and links with themselves or with other protein molecules.

The diagram below shows two amino acids reacting to form a **dipeptide**.



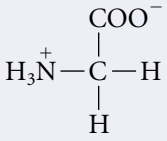
amino acid 1 amino acid 2 dipeptide



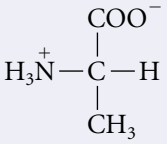
glycine alanine glycyl alanine (gly-ala)

Nonpolar, Aliphatic R Groups

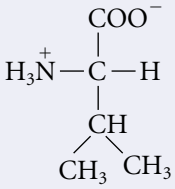
glycine



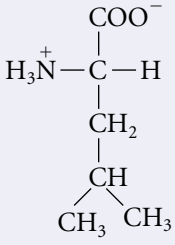
alanine



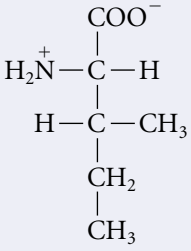
valine



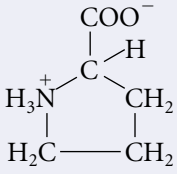
leucine



isoleucine

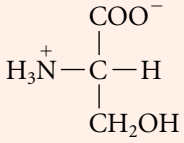


proline

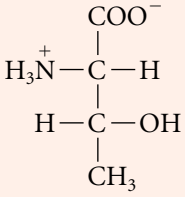


Polar, Uncharged R Groups

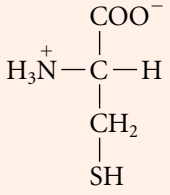
serine



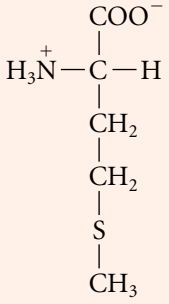
threonine



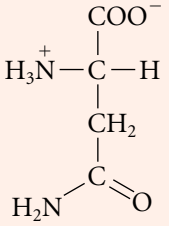
cysteine



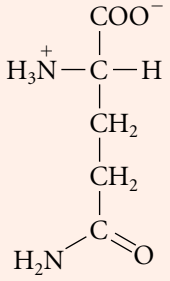
methionine



asparagine

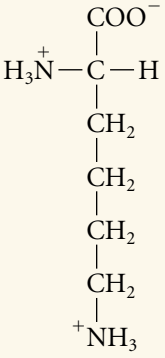


glutamine

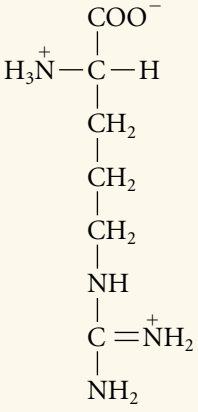


Positively Charged R Groups

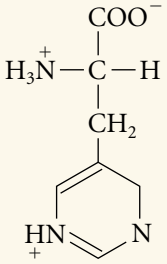
lysine



arginine

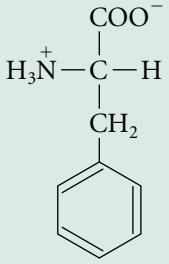


histidine

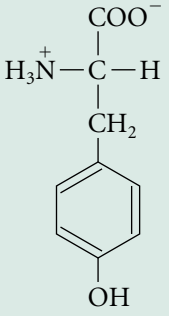


Aromatic R Groups

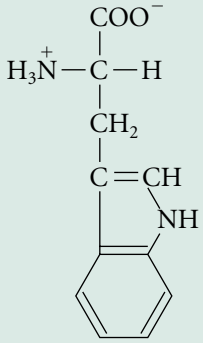
phenylalanine



tyrosine

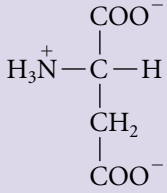


tryptophan



Negatively Charged R Groups

aspartate



glutamate

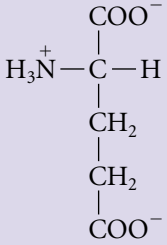


Figure 2
The 20 amino acids used by living things

EXPLORE an issue

Take a Stand: Will That Be "Regular" or "Diet"?

Decision-Making Skills

○ Define the Issue	○ Identify Alternatives	● Research
● Analyze the Issue	● Defend the Position	○ Evaluate

You have probably seen its name on cans of "diet" soft drinks. You might also have tasted its flavour, which is not quite the same as that of sugar. Aspartame, sold as NutraSweet and Equal, is probably the most widely used sugar substitute in North America. More than 200 studies have been done on the safety of the use of aspartame, some claiming that it produces side effects ranging from headaches to brain tumours, others claiming that there is no evidence of any harmful effects.

(a) Research some of these studies, writing brief summaries of the arguments for and against the use of aspartame or another food substitute or additive (e.g., artificial flavour, food colour).

(b) In a small group discuss the factors that you would consider in reviewing any such scientific study to determine the validity of the results.

(c) Analyze the risks and benefits of the use of your chosen food substitute or additive. Write a report on the results of your analysis, and make a recommendation on its use, with supporting arguments.

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Protein Structure

While some proteins provide the structure and support in a living system, others are transported throughout the organism, serving as carriers of oxygen or regulators of biological processes. If all proteins are long strands of polypeptides, how do they show such variation in function? The answer can be found in the sequence of amino acids, which is determined genetically and is unique to each protein. The complex structure of giant protein molecules (**Figure 3**) all depends on the electronic attractions and repulsions that develop between the functional groups on the component amino acids.

primary structure the sequence of the monomers in a polymer chain; in polypeptides and proteins, it is the sequence of amino acid subunits

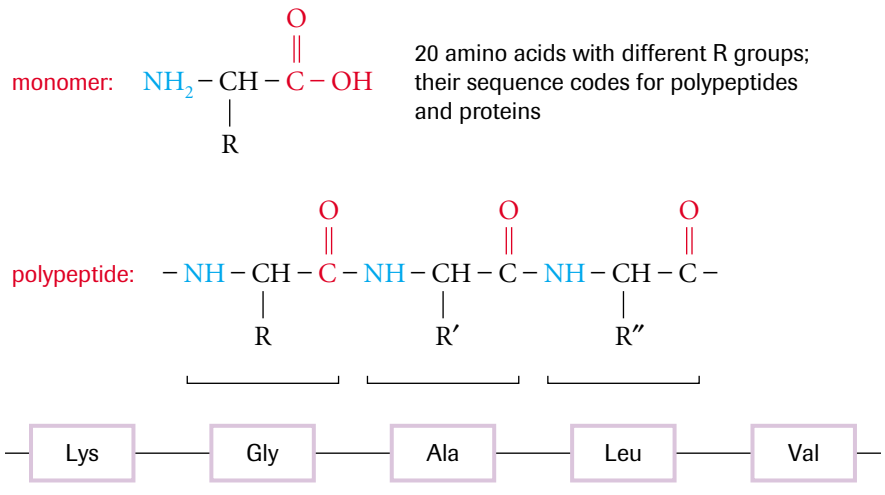
secondary structure the three-dimensional organization of segments of a polymer chain, such as alpha-helices and pleated-sheet structures

alpha-helix a right-handed spiraling structure held by intramolecular hydrogen bonding between groups along a polymer chain

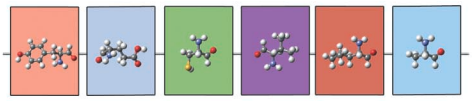
pleated-sheet conformation a folded sheetlike structure held by intramolecular or intermolecular hydrogen bonding between polymer chains

Primary Structure of Proteins

As you know, all proteins are polypeptides: long strings of amino acids arranged in a very specific order. This is the primary structure of the protein. It can be altered by changes (mutations) in the DNA. A change in primary structure can cause a "ripple effect," interfering with all the other levels of structure, and so possibly making the protein completely useless for its "intended" task.

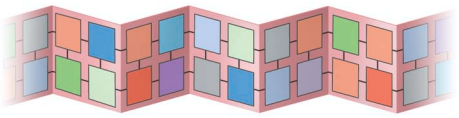


Primary structure, 1°
The sequence of amino acids in the polypeptide chain determines which protein is created.



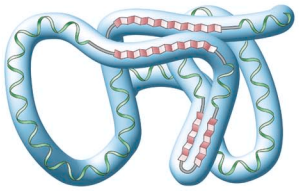
Secondary structure, 2°
Polar and nonpolar amino acids at different locations within the long polypeptide chain interact with each other, forming coils or pleated sheets. The interactions may be van der Waals forces, hydrogen bonding, or other attractions.

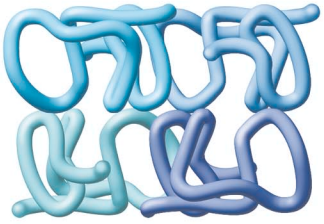
Alpha-helix This coiled secondary structure results from hydrogen bonds between the amine group in a peptide linkage and the carbonyl group of an amino acid further along on the same chain. The R groups of the amino acids protrude outward from the coil.



Pleated-sheet (or beta-pleated sheet) This folded secondary structure results from the zigzag shape of the backbone of the polypeptide chain forming a series of pleated sheets. Hydrogen bonds form between the amine groups and the carbonyl groups on adjacent pleated sheets.

Tertiary structure, 3°
Proteins may have helical sections and pleated-sheet sections within the same molecule. These sections attract each other, within the molecule, folding a long, twisted ribbon into a specific shape. Proteins such as enzymes, hemoglobin, and hormones tend to have a spherical or globular tertiary structure, to travel easily through narrow vessels.





Quaternary structure, 4°
Some proteins are complexes formed from two or more protein subunits, joined by van der Waals forces and hydrogen bonding between protein subunits. For example, hemoglobin has four subunits held together in a roughly tetrahedral arrangement.

Figure 3
Proteins are very complicated compounds, with up to four levels of organization giving each protein a unique physical shape with unique physical characteristics.

TRY THIS activity — Identifying Fibres by Odour

Fibre artists, such as weavers and felters, need to know the composition of the fibres or textiles they are thinking of using. Are they cellulose fibres (e.g., linen, cotton, hemp), protein fibres (e.g., silk, wool, fur, mohair), or synthetics (e.g., nylon or polyester)? Sometimes the fibres aren't labelled, so the artists use a burn test to narrow down their identification. Wool, hair, and fur smell of sulfur when exposed to flame, and don't burn well. Cellulose fibres have a "burning wood" smell and burn very readily. Synthetic fibres have an acrid smell.
Materials: eye protection; small pieces (1 cm × 1 cm) of several fabrics, including wool, cotton, polyester, and a few strands of hair or fur; a similar sample of unknown composition; laboratory burner; metal tweezers or forceps; fume hood or well-ventilated room

- Take a small piece of several known fabrics.
  (a) Classify the fibres as protein, cellulose, or synthetic.
- Over a nonflammable surface, burn each sample by passing it slowly through the flame of the laboratory burner. Carefully smell the odour by wafting the smoke toward your nose.
- Repeat the test with the unknown fabric sample.
  (b) Classify the unknown sample as protein, cellulose, or synthetic.

Secondary Structure of Proteins

The alpha-helical secondary structure accounts for the strength of fibrous proteins such as alpha-keratin in hair and nails (**Figure 4**), and collagen in tendons and cartilage. In these proteins, alpha-helical chains are coiled in groups of three, into a "rope" structure; these ropes are further bundled into thicker fibres. The strength of these fibres is increased by crosslinking between polypeptide chains, provided by disulfide (–S–S–) bonds.

X-ray analysis has revealed that the pleated-sheet secondary structure is indeed found in fibroin, the protein in silk, and in a similar protein in spider webs. These proteins are rich in Ala and Gly, the amino acids with the two smallest R groups, allowing the pleated sheets to be closely packed into layers. The pleated-sheet structure affords the protein added strength—the strength of silk and spider webs is well respected—so pleated-sheet proteins are used in products ranging from parachutes to the cross hairs of rifles.

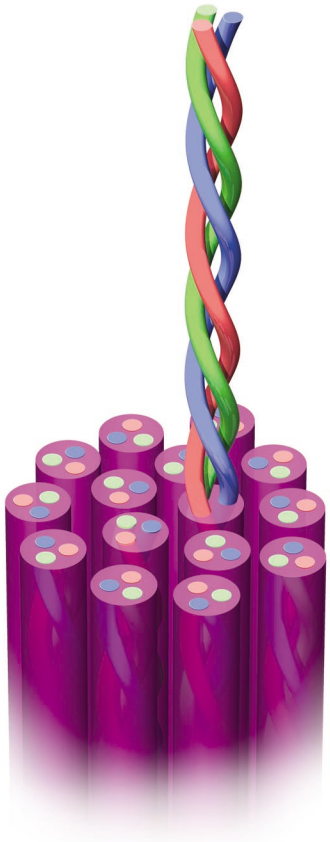


Figure 4
Keratin is structurally strong and smooth because of the way the molecules pack together and form crosslinkages.

Tertiary Structure of Proteins

The tertiary structure of proteins is highly specific and is closely related to its role in the organism. The winter flounder (**Figure 5**), a fish found off the coast of Newfoundland, is able to lower its own freezing point sufficiently to survive the winter without migrating to warmer climes. (The formation of ice crystals in tissue fluids causes irreparable damage to cell membranes.) Canadian scientists have found that these fish, when stimulated with the appropriate trigger, produce an "antifreeze protein" whose three-dimensional structure fits well into the surface of a developing ice crystal, inhibiting further ice growth. Similar antifreeze mechanisms exist in other organisms, such as insects, each using different structural features of the proteins and ice surfaces.

tertiary structure a description of the three-dimensional folding of the alpha-helices and pleated-sheet structures of polypeptide chains

Figure 5
The winter flounder produces its own antifreeze protein.

Quaternary Structure of Proteins

Quaternary structure, in which several protein subunits join together, is found in many proteins that serve a regulatory function, such as insulin, and the catalytic enzyme kinase. One of the best-known protein complexes is hemoglobin, which has four protein subunits. Interactions between subunits permit responses to changes in concentrations of the substance regulated, such as oxygen.

DID YOU KNOW ?

"Permanent" Bonding

When a permanent wave is applied to hair, it is the S–S bonds between amino acids that are sequentially broken and re-formed. The first chemical solution used in a permanent wave breaks the existing S–S bonds; the second solution enables new S–S bonds to form in the desired locations, leaving a new structure of the hair fibres and new curls.

Denaturation of Proteins

When the bonds responsible for the secondary and tertiary protein structures are broken, the protein loses its three-dimensional structure; this process is called *denaturation*. When fish is cooked, for example, no covalent bonds are broken by the mild heating, but the weaker forces of attraction such as van der Waals forces and hydrogen bonds are disrupted. Changing the pH affects electrostatic forces and disrupts hydrogen bonding, as witnessed in the curdling of milk in vinegar or orange juice. Organic solvents such as formaldehyde and acetone interact with the nonpolar components of the amino acids; these solvents denature the proteins in the specimens they are used to preserve. In all cases, even mild denaturation of a protein is accompanied by severe loss of function.

Practice

Understanding Concepts

4. Are proteins addition polymers or condensation polymers? Explain.
5. How do chiral molecules differ from each other?
6. Draw a structural diagram of the linkage between amino acids in a peptide chain.
7. Differentiate between the primary, secondary, tertiary, and quaternary structure of proteins. Sketch a simple diagram of each structure to illustrate your answer.
8. Give one example of a fibrous protein and one example of a globular protein. For each, describe its function in the organism and how its structure serves its function.

Section 2.4 Questions

Understanding Concepts

1. Explain why amino acids, with the exception of glycine, can occur in more than one chiral form.
2. Explain how it is possible to make millions of different proteins from only 20 amino acid monomers.
3. Describe the type of protein structure that gives fibrous proteins such as collagen their exceptional strength.
4. Explain why an alteration in the primary structure of a protein could result in a change in its tertiary structure.
5. What is meant by the quaternary structure of proteins? Give an example to illustrate your answer.
6. For each of the following types of chemical bonding, describe an example of its occurrence in protein molecules and its effect on the protein's structure:
   (a) covalent bonds
   (b) hydrogen bonds
   (c) van der Waals forces
   (d) disulfide bonds

Applying Inquiry Skills

7. In an experiment on the effects of artificial sweeteners on health, the sweetener saccharin was fed to lab rats. The experimenters reported an increase of 50% in the incidence of liver cancer in the saccharin-fed rats. You are asked to evaluate the experimental results with respect to any health risk of saccharin to humans.
   (a) List the missing information that you would require about the experimental design and conditions.
   (b) Describe essential experimental controls that must be incorporated.
   (c) Suggest any circumstances that might render the results of the experiment inconclusive.

Making Connections

8. When fresh vegetables are prepared for storage in the freezer, they are dipped momentarily in boiling water. This procedure, called blanching, stops the vegetables from further ripening through enzyme action. Give an explanation at the molecular level for the success of this technique.
9. Research the secondary and tertiary structures of one of the following proteins:
   (a) fibrinogen, the protein involved in blood clotting
   (b) collagen, a connective tissue
   (d) cytochrome c, used in electron transport
   (c) myoglobin, an oxygen-binding protein
   (d) myosin, a muscle protein

   Present your findings in a report that includes a description of the secondary and tertiary structures that make the protein ideally suited to its function.

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10. Thalidomide, so harmful when administered as a mix of L and D configurations, has been banned in many countries. However, it is a very versatile and inexpensive drug when the configurations are isolated and used selectively.
    (a) Research the current use of thalidomide (if any), and other pharmaceuticals (if any) that are used in its place.
    (b) Compare the costs of using thalidomide with the costs of developing alternative drugs or the costs of having no drugs available.
    (c) Write a brief report addressing the question, "Should thalidomide continue to be banned?" for use in a popular science magazine.

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