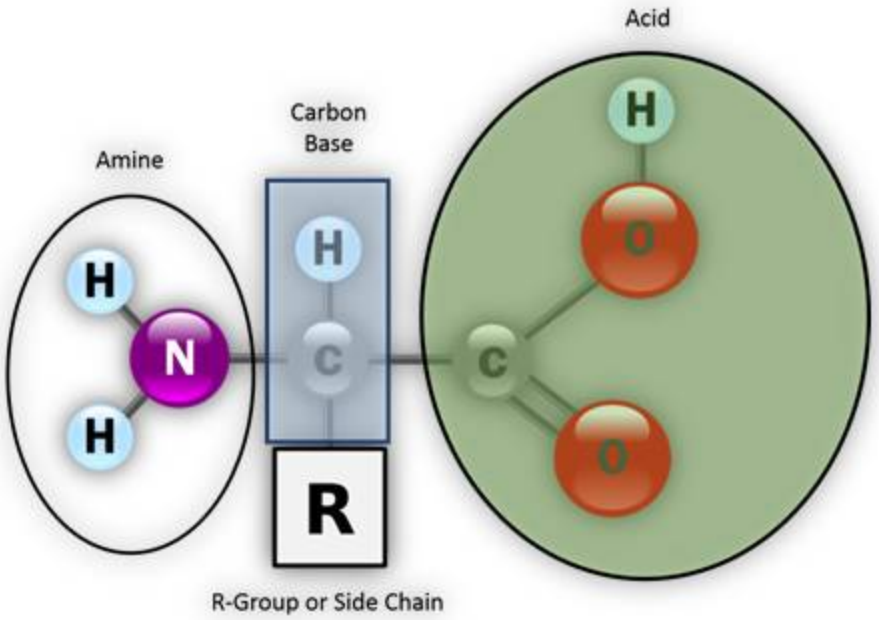
BIOCHEMISTRY - YEAR 2



Amino Acids
Protein structure
Lecture No: 5

Assistant Professor
Dr Ali Taha Yassen

College of Dentistry
University of Basrah

Objectives

At the end of this lecture we will understand the following points.

- The difference between Symmetry and asymmetry molecules .
- The chemical structure of amino acids and types.
- Peptide bond formation.

Function of Proteins

- Proteins are built as chains of amino acids, which then fold into unique three-dimensional shapes. Bonding within protein molecules helps stabilize their structure, and the final folded forms of proteins are well-adapted for their functions.

- Protein has many roles in your body. It helps repair and build your body's tissues, allows metabolic reactions to take place, and coordinates bodily functions. In addition to providing your body with a structural framework, proteins also maintain proper pH and fluid balance.

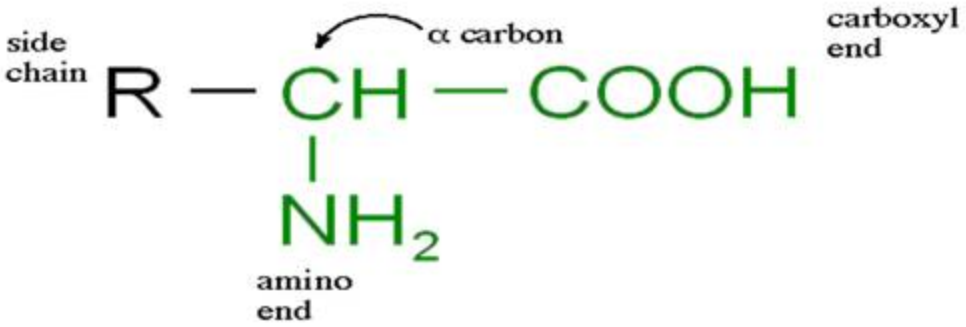
Biochemistry - Year 2

Classification of some proteins and their functions

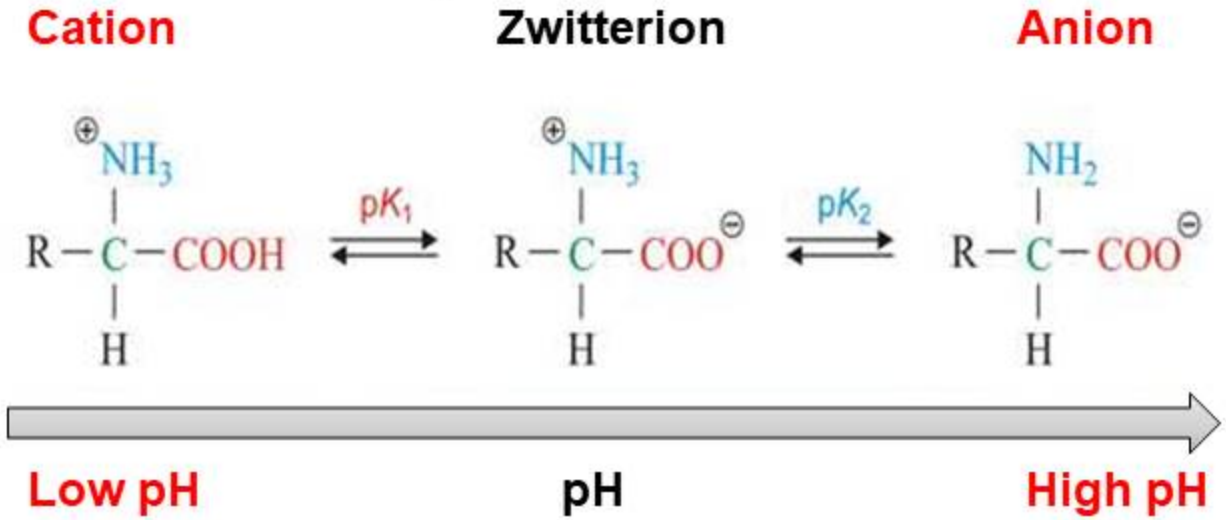
Class of Protein	Function	Example
Structural	Provide structural components	Collagen is in tendons and cartilage. Keratin is in hair, skin, wool, and nails.
Contractile	Movement of muscles	Myosin and actin contract muscle fibers.
Transport	Carry essential substances throughout the body	Hemoglobin transports oxygen. Lipoproteins transport lipids.
Storage	Store nutrients	Stores iron in the spleen and liver.
Hormone	Regulate body metabolism and nervous system	Insulin regulates blood glucose level. Growth hormone regulates body growth.
Enzyme	Catalyze biochemical reactions in the cells	Sucrase catalyzes the hydrolysis of sucrose. Trypsin catalyzes the hydrolysis of proteins.
Protection	Recognize and destroy foreign substances	Immunoglobulins stimulate immune responses.

General properties

- Amino acids are derivatives of carboxylic acids.
- Each amino acid contains a central C atom, an amino group (NH_2), a carboxyl group (COOH), and a specific R group.
- The R group determines the characteristics (size, polarity, and pH) for each type of amino acid.
- Peptide bonds form between the carboxyl group of one amino acid and the amino group of another through dehydration synthesis.



Amino acids are **amphoteric**, which means they have **acidic** and **basic** groups. The carboxyl group is able to lose a proton and the amine group is able to accept a proton.

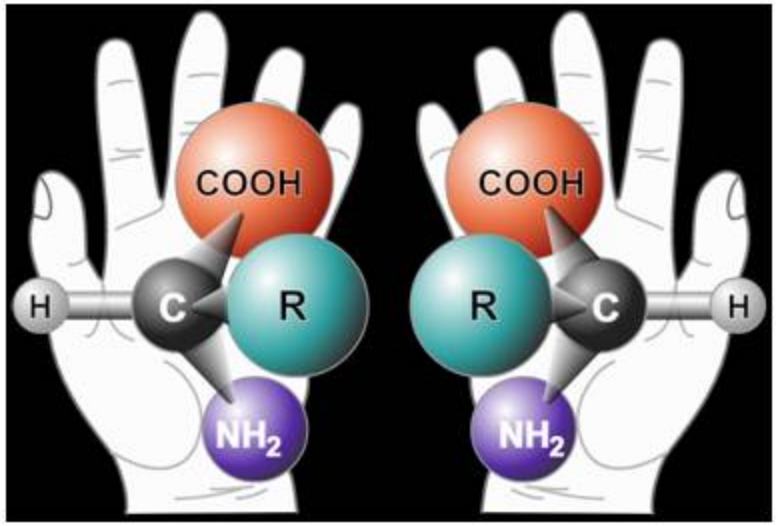


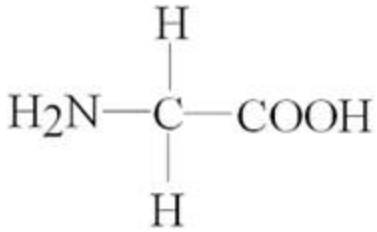
Symmetry and asymmetry molecules

A compound capable of optical rotation is said to be optically active. All pure chiral compounds are optically active. eg: (R)-Lactic acid (1) is chiral and rotates the plane of plane-polarized light.

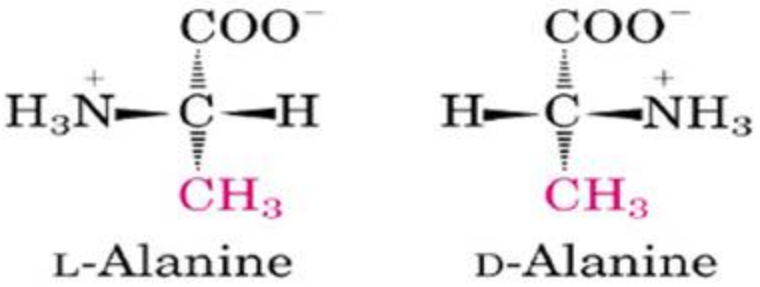
Symmetry and asymmetry molecules

Amino acids are optically active molecules and asymmetry of their mirror images is not superimposable (except in the case of glycine where the R-group is hydrogen)





glycine



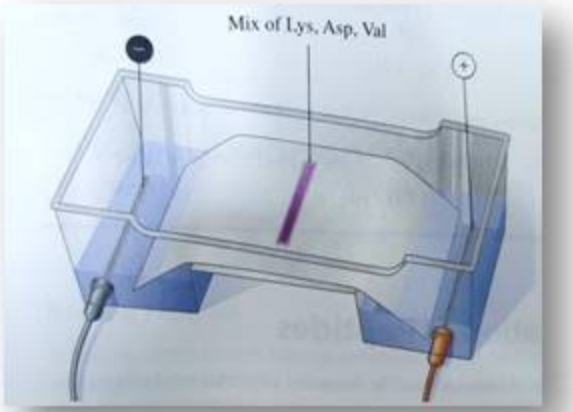
L-Alanine D-Alanine

Electrophoresis

It is possible to separate a mixture of amino acids by their isoelectric points using a laboratory method called electrophoresis. A buffered amino acid mixture is applied to a gel on a thin plate or piece of filter paper, which is connected to two electrodes. A voltage applied to the electrodes causes the positively charged amino acids to move toward the negative electrode and the negatively charged amino acids to move toward the positive electrode. Any amino acid at its isoelectric point with zero net charge would not move. After several hours, the sample is removed. It can be sprayed with a dye such as ninhydrin to make the amino acids visible. They are identified by their direction and rate of migration toward the electrodes. They are recovered separately by cutting up the filter paper or removing the amino acids from the gel.

Electrophoresis

Suppose we have a mixture of valine (pI 6.0), aspartic acid (pI 2.8), and lysine (pI 9.7) in a buffer of pH 6.0. When the mixture is placed between two electrodes at a high voltage, the aspartic acid, which would have a negative charge at pH 6.0, would move to the positive electrode (anode). The lysine, which would be positively charged at a pH of 6.0, would move toward the negative electrode. Valine, which is a zwitterion at pH 6.0, would be neutral and not move in the presence of an electric field. Electrophoresis is a method used in medicine to screen for the sickle cell trait in newborn infants.



Separation of amino acids

Position of amino group – α-amino acids exist in two enantiomeric forms. Only L-(S-) acids are found in nature.

Essential (unexpendable) – organism is not able to synthesize these AA but accept from food.

Nonessential (expendable) – organism produced from essential AA by transamination.

According R- functional group

- Nonpolar (hydrophobic)
- Polar (hydrophilic) – better soluble in water
- Basic – contains more atoms of nitrogen
- Acidic – contains more carboxyl groups

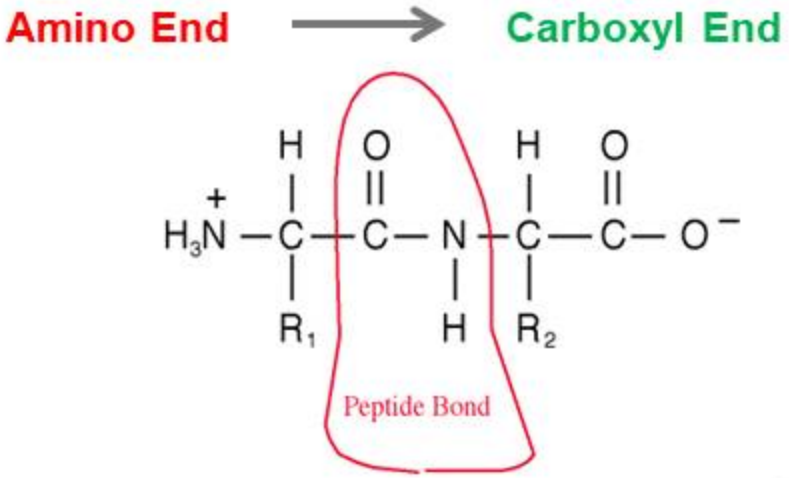
Reactions of amino acids

Polymerization - form peptides, proteins and enzymes
A condensation reaction between the carboxyl of one amino acid and the amino group of another forms a peptide bond.

Oligopeptides – condensation of 2 – 10 amino acids units

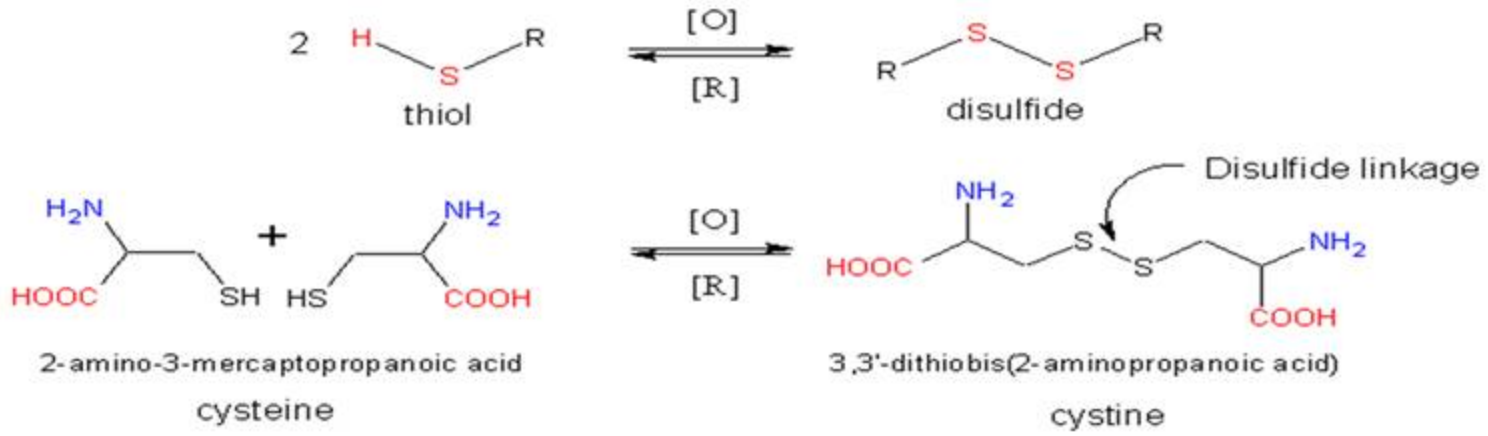
Polypeptides – condensation of 11 – 100 amino acids units

Proteins – more than 100 amino acids units



Disulfide linkage : conversion of cysteine to cystine is like a conversion of thiols to disulfides by mild oxidizing agents. This conversion can be reversed by mild reducing agents.

- Disulfide bonds stabilize protein structure by providing cross-link.

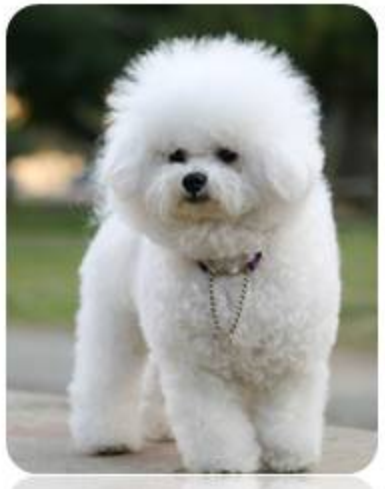


Protein in Human hair

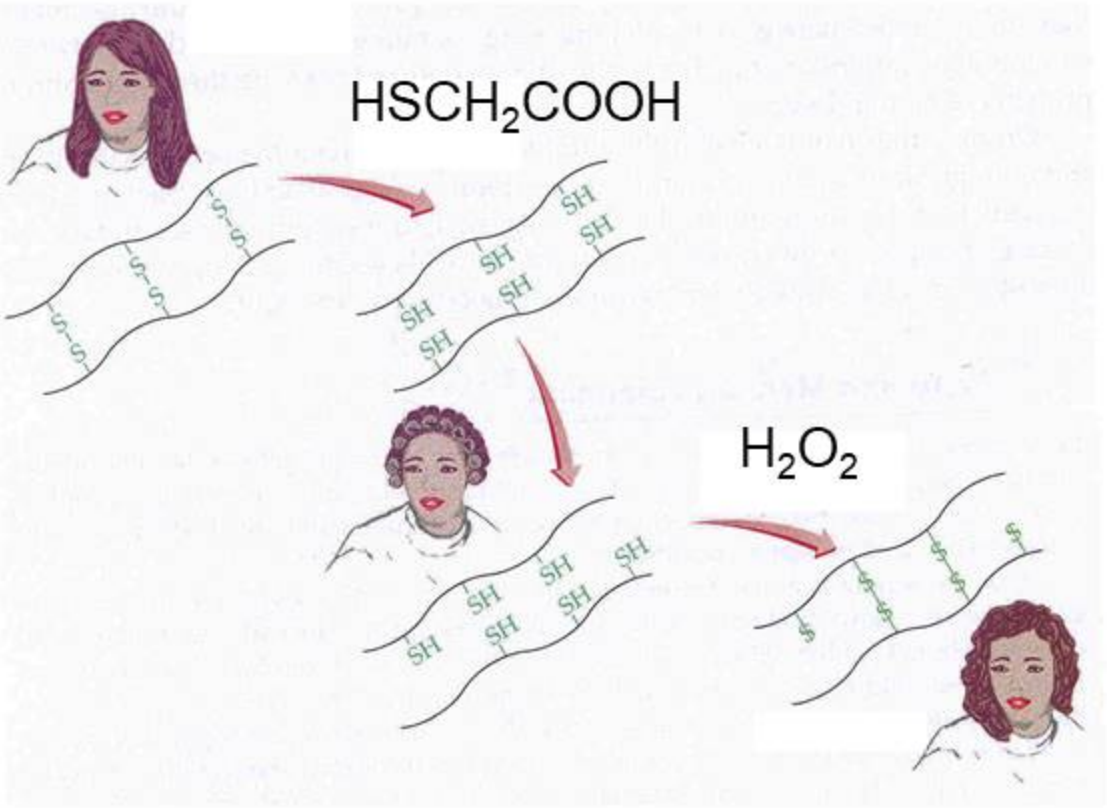
Keratin (fibrous protein) has the S containing amino acid cystine (14~18%) . S-S bonds (disulphide linkages) between cystine units give hair its strength by connecting the strands and keeping them aligned.

Do you want change a bad hair day?

To a Good Hair day?



Perm(?) – have your keratin 1o structure modified



Use some Protein Chemistry on your hair!

Slightly basic solution of thioglycolic acid is used: cleaves the disulfide links and makes new SH bonds (reset hair)

Then Dilute! Peroxide used in final Oxidation step of "perm" (otherwise bleaching effect!)

Covalent S-S bonds in new positions give permanent structure (recall : position of the disulfide linkages is part of 1° structure)

Hydrogen bonds N-H···O=C Between adjacent strands of fibrous protein are much weaker than the S-S covalent bonds, but there are many more hydrogen bonds, which form a large part of hair structure

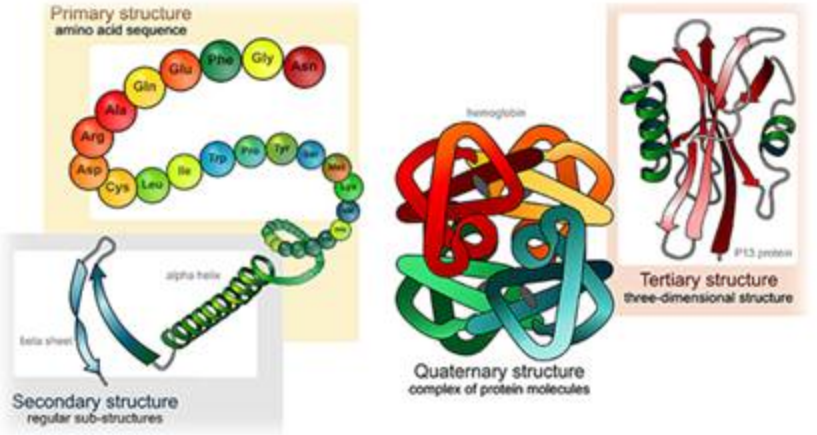
Hence excess water will break these up and permit restructuring of hair upon drying

Water not strong enough to break S-S bonds

Protein structure

- There are four levels of protein structure (primary, secondary, tertiary and quaternary)
- Protein structure depends on its amino acid sequence and local, low-energy chemical bonds between atoms in both the polypeptide backbone and in amino acid side chains.

- Protein structure plays a key role in its function; if a protein loses its shape at any structural level, it may no longer be functional.



Primary structure

- Primary structure is simply the sequence of amino acids in a polypeptide chain. At one end is an amino acid with a free amino group the (the N-terminus) and at the other is an amino acid with a free carboxyl group the (the C-terminus).
- The primary structure of a protein is its unique sequence of amino acids.
- The precise primary structure of a protein is determined by inherited genetic information.

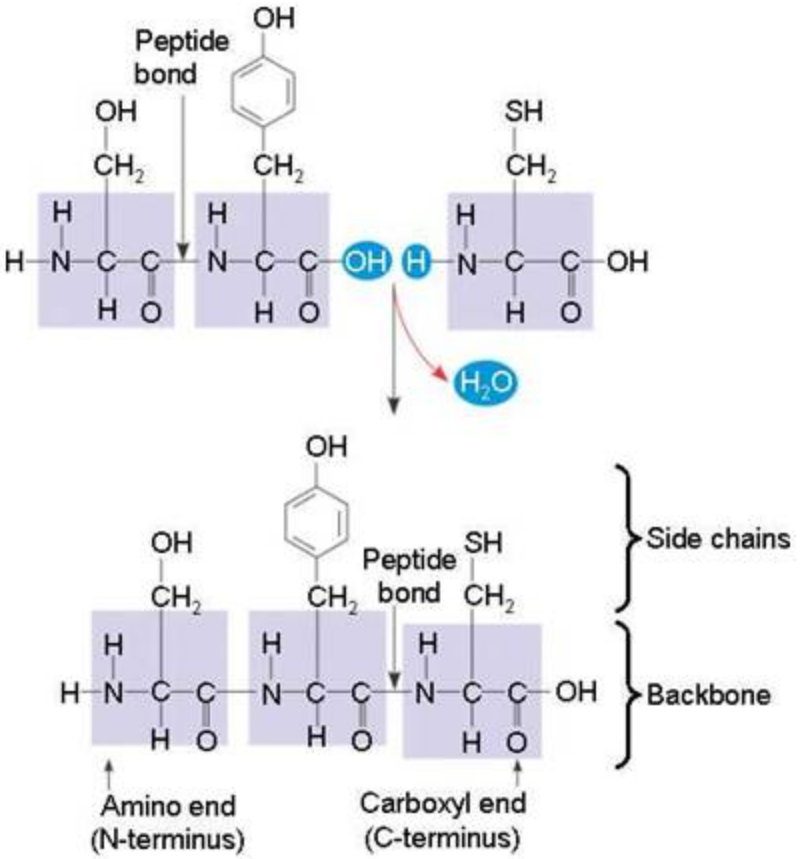


Image drawn by http://bio1151.nicerweb.com/Locked/media/ch05/peptide.html

Secondary structure

Results from hydrogen bond formation between hydrogen of –NH group of peptide bond and the carbonyl oxygen of another peptide bond. According to H-bonding there are two main forms of secondary structure:

α-helix: It is a spiral structure resulting from hydrogen bonding between one peptide bond and the fourth one.

β-sheets: is another form of secondary structure in which two or more polypeptides (or segments of the same peptide chain) are linked together by hydrogen bond between H- of NH- of one chain and carbonyl oxygen of adjacent chain (or segment).

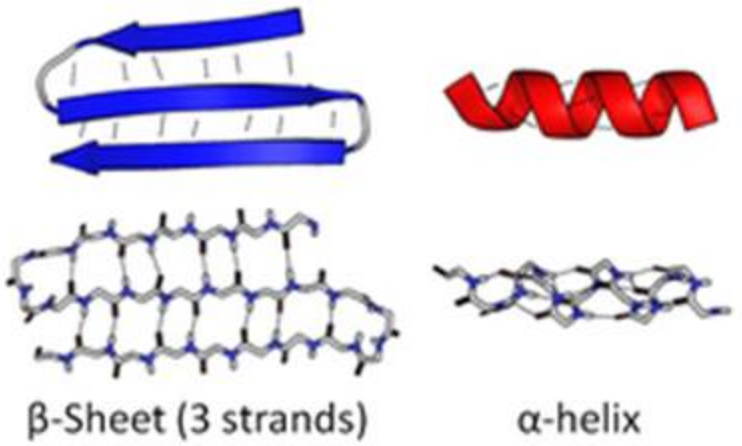


Image drawn by BYU-I student Nate Shoemaker Spring 2016

Tertiary structure

•Is determined by a variety of interactions (bond formation) among R groups and between R groups and the polypeptide backbone.

a. The weak interactions include:

•Hydrogen bonds among polar side chains.

•Ionic bonds between charged R groups (basic and acidic amino acids)

•Hydrophobic interactions among hydrophobic (non polar) R groups.

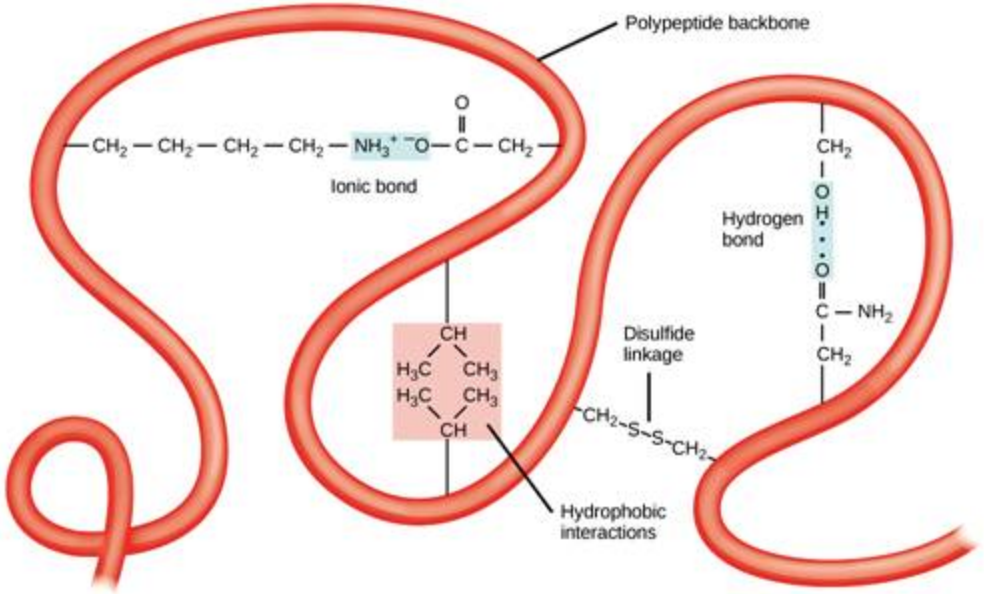


Image modified from OpenStax Biology.

Quaternary structure

- Many proteins are made up of a single polypeptide chain and have only three levels of structure (the ones we've just discussed). However, some proteins are made up of multiple polypeptide chains, also known as subunits. When these subunits come together, they give the protein its **quaternary structure**.

- Results from the aggregation (combination) of two or more polypeptide subunits held together by non-covalent interaction like H-bonds, ionic or hydrophobic interactions.

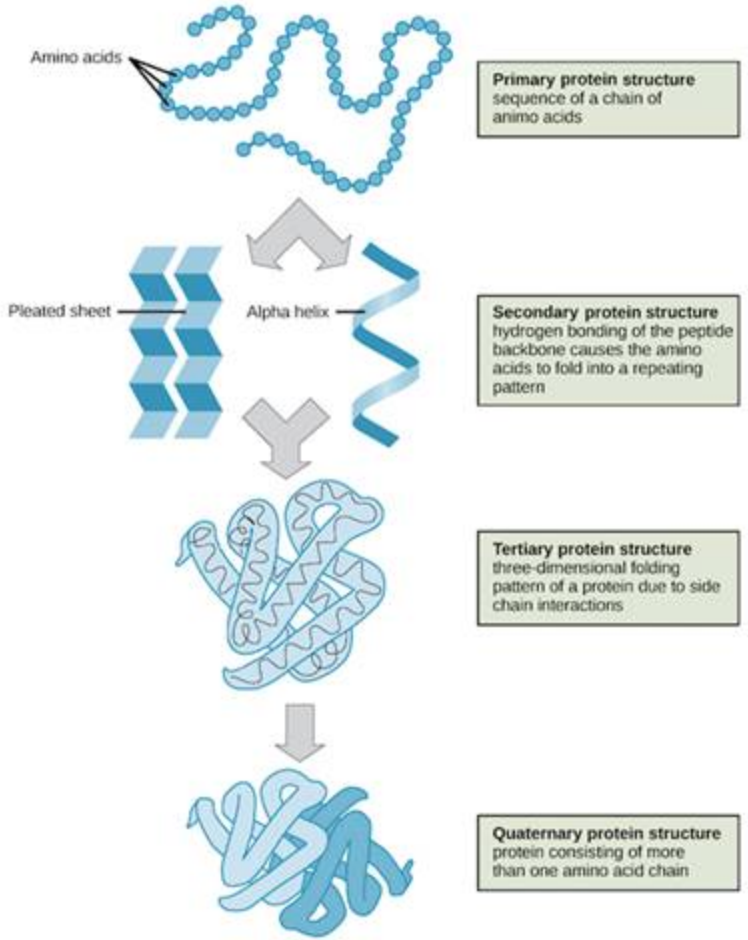


Image modified from OpenStax Biology's modification of work by the National Human Genome Research Institute.

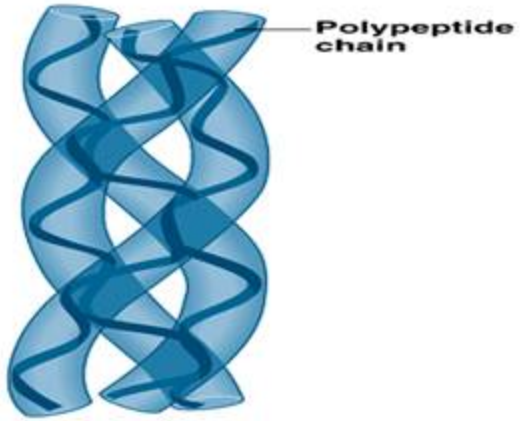
Quaternary structure

- Examples on protein having quaternary structure:
  - Collagen is a fibrous protein of three polypeptides (trimeric) that are supercoiled like a rope.

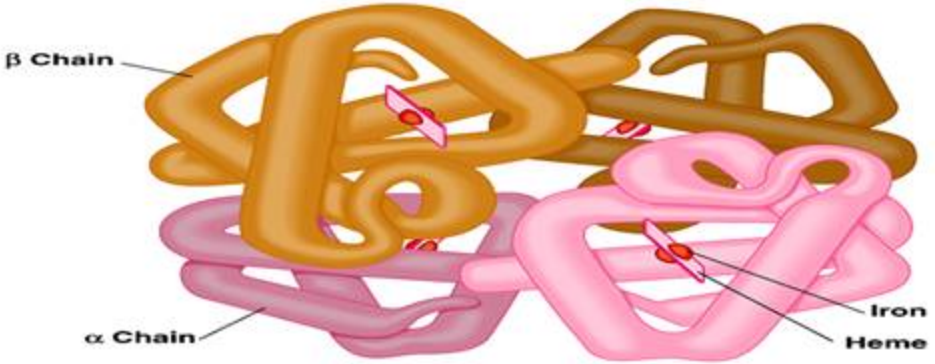
- This provides the structural strength for their role in connective tissue.

  - Hemoglobin is a globular protein with four polypeptide chains (tetrameric)

  - Insulin : two polypeptide chains (dimeric).



(a) Collagen



(b) Hemoglobin

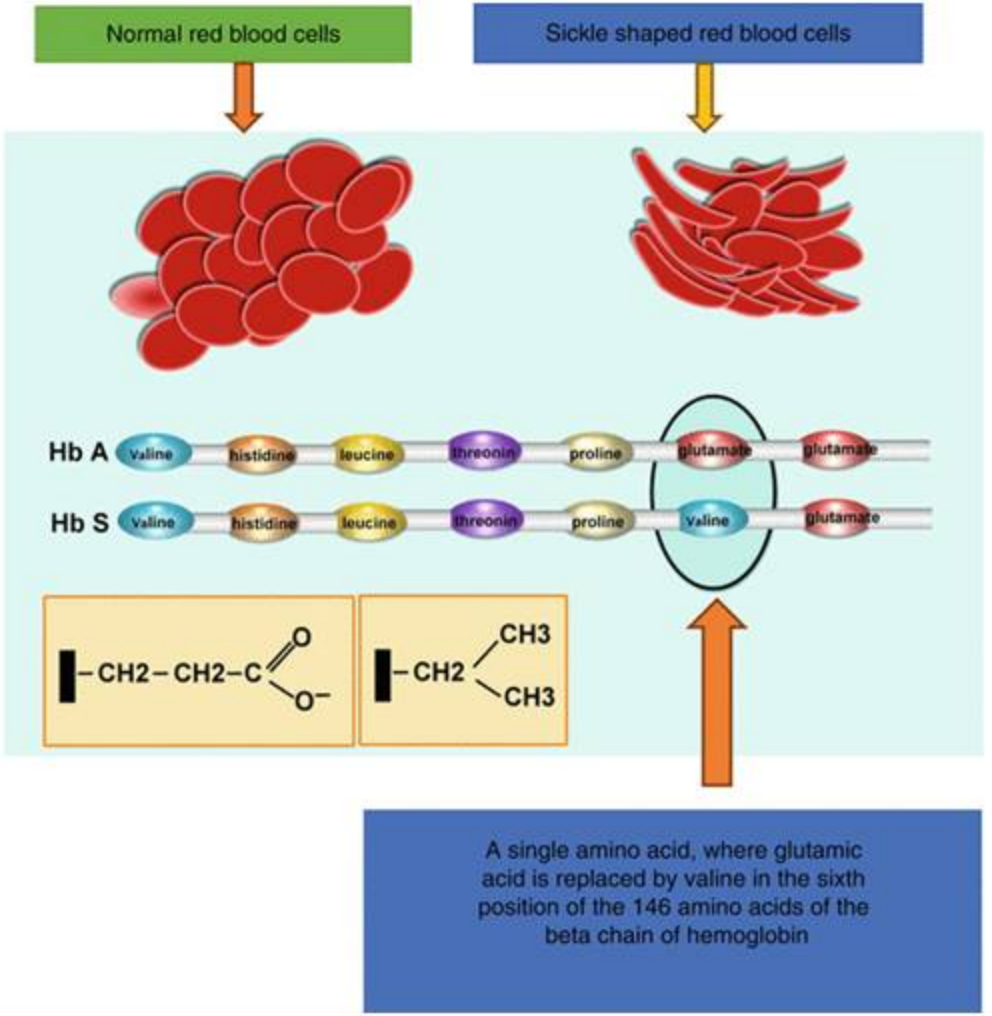
Sickle-Cell Anemia

Sickle-cell anemia is a disease caused by an abnormality in the shape of one of the subunits of the hemoglobin protein. In the B chain, the sixth amino acid, glutamic acid, which is polar, is replaced by valine, a nonpolar amino acid.

Because valine has a hydrophobic side chain, it draws the hydrophobic pocket that binds to oxygen to the surface of the hemoglobin. The affected red blood cells change from a rounded shape to a crescent shape, like a sickle, which interferes with their ability to transport adequate quantities of oxygen. Hydrophobic attractions cause several sickle-cell hemoglobin molecules to stick together, which forms long fibers of sickle-cell hemoglobin. The clumps of insoluble fibers clog capillaries, where they cause inflammation, pain, and organ damage. Critically low oxygen levels may occur in the affected tissues.

Sickle-Cell Anemia

In sickle-cell anemia, both genes for the altered hemoglobin must be inherited. However, a few sickled cells are found in per- sons who carry one gene for sickle-cell hemoglobin, a condition that is also known to provide protection from malaria.



Denaturation

Each protein has its own unique shape. If the temperature or pH of a protein's environment is changed, or if it is exposed to chemicals, these interactions may be disrupted, causing the protein to lose its three-dimensional structure and turn back into an unstructured string of amino acids. When a protein loses its higher-order structure, but not its primary sequence, it is said to be **denatured**.

Disruption of secondary, tertiary and quaternary protein structure by

Heat/organics :	Break apart H bonds and disrupt hydrophobic attractions
Acids/ bases :	Break H bonds between polar R groups and ionic bonds
Heavy metal ions :	React with S-S bonds to form solids
Agitation :	Stretches chains until bonds break

Detergents

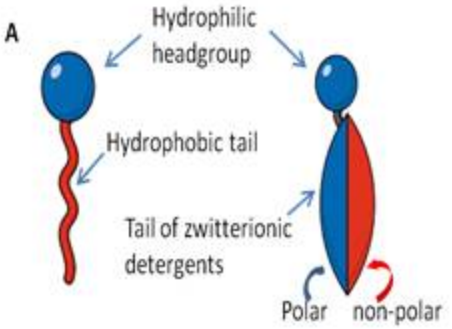
Disrupt hydrophobic interactions in protein molecules.

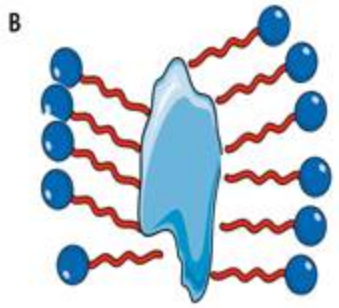
Detergents are amphiphilic molecules which contain both hydrophobic and hydrophilic parts.

Hydrophobic parts of the detergent associates with the hydrophobic parts of the protein.

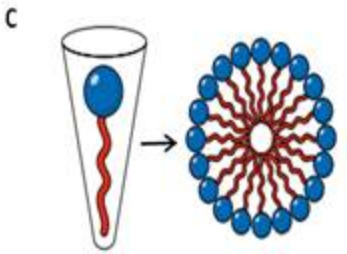
Hydrophilic parts of the detergent interact with water molecules

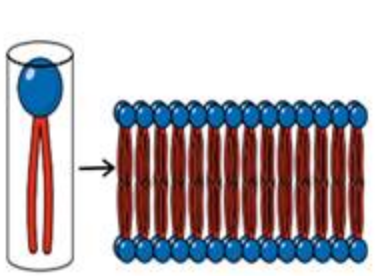
Thus, hydrophobic parts of the protein do not need to interact with each other.





Protein-detergent complex





Diseases caused by protein denaturation

Protein misfolding is believed to be the primary cause of Alzheimer's disease, Parkinson's disease, Huntington's disease, Creutzfeldt-Jakob disease, cystic fibrosis, Gaucher's disease and many other degenerative and neurodegenerative disorders.

The End

Thank You All

Reference: General, organic,& biological chemistry structures of life.
Timberlake. Pearson Education. 2002