Protein structure

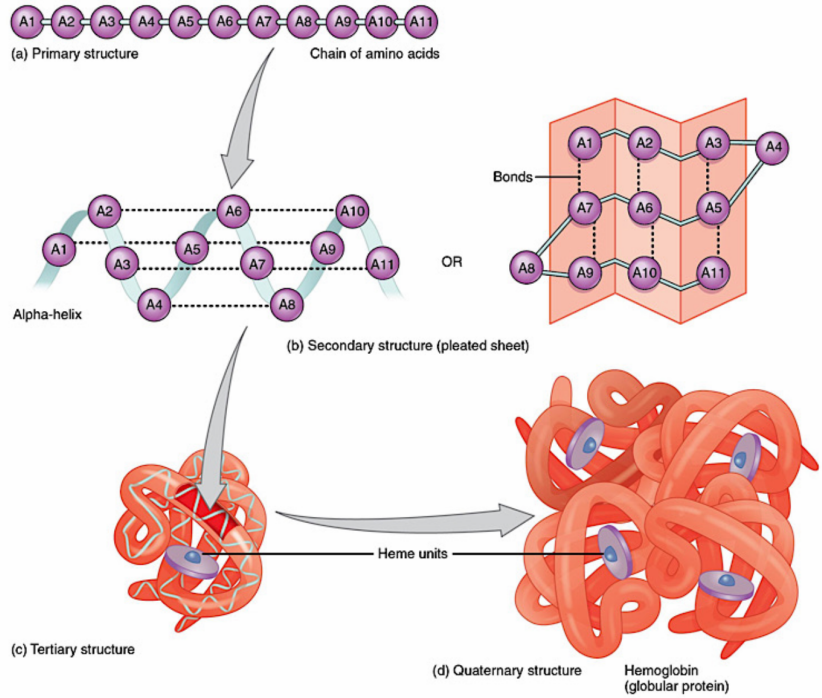
Proteins are large,complex molecules, usually made up of hundreds of amino acid subunits.The way these subunits together is highly specifc to each type of protein, and is vital to its function.

The first stage of protein production is the assembly of a sequence of amino acid molecules that are linked by peptide bonds formed by condensation reactions.This sequence forms the **primary structure of a protein** .There are many different proteins and each one has different bonds numbers and types of amino acids arranged in a different order, coded for by a cell's DNA.

The secondary structure of a protein is formed when the polypeptide chain takes up a permanent folded or twisted shape. Some polypeptides coil to produce an **α helix,** others fold to form **β pleated sheets** . **Depending on the sequence of amino acids** .
The amino acids in a polypeptide chain have an effect on each other even if they are not directly next to each other.
A polypeptide chain, or part of it, often coils into a corkscrew shape called an α-helix. This secondary structure is due to hydrogen bonding between the oxygen of the **–CO–** group of one amino acid and the hydrogen of the **–NH–** group of the amino acid four places ahead of it. Hydrogen bonding is a result of the polar characteristics of the –CO– and –NH– groups. Sometimes hydrogen bonding can result in a much looser, straighter shape than the α-helix, which is called a β-pleated sheet. Hydrogen bonds, although strong enough to hold the α-helix and β-pleated sheet structures in shape, are easily broken by high temperatures and pH changes.

The tertiary structure of a protein forms as the molecule folds still due to interactions between the R groups of the amino acids bridge and within the polypeptide chain.
The protein takes up a three-dimensional shape, which is held together by ionic bonds polypeptide between particular **R groups** , **disulfide bridges** (covalent bonds) between sulfur atoms of some R groups, and by weaker interactions between
hydrophilic and hydrophobic side chains. **Tertiary structure is very important in enzymes** because the shape of an enzyme molecule gives it its unique properties and determines which substrates can fit into its active site.
The four types of bond which help to keep folded proteins in their precise shapes
1. Hydrogen bonds
2. Disulfide bonds form between two cysteine molecules, which contain sulfur atoms.
3. Ionic bonds form between R groups containing amine and carboxyl groups.
4. Hydrophobic interactions occur between R groups which are non-polar, or hydrophobic.

The final level of protein structure is **quaternary structure** , which links two or more polypeptide chains to form a single, large, complex protein. The structure is held together by all the bonds that are important in the previous levels of structure. Examples are collagen (which has three polypeptide chains), hemoglobin (which has four), antibodies (which also hemoglobin molecule
have four) and myosin (which has six).



Globular and fibrous proteins

A protein whose molecules curl up into a 'ball' shape, such as myoglobin or haemoglobin, is known as a globular protein. Globular proteins usually curl up so that their non-polar, hydrophobic R groups point into the centre of the molecule, away from their watery surroundings. Water molecules are excluded from the centre of the folded protein molecule.

The polar, hydrophilic R groups remain on the outside of the molecule. **Globular proteins** , therefore, are usually soluble, because water molecules cluster around their outward- pointing hydrophilic R groups.

Many globular proteins have roles in metabolic reactions. Their precise shape is the key to their functioning. Enzymes, for example, are globular proteins.

Many other protein molecules do not curl up into a ball, but form long strands. These are known as fibrous proteins. Fibrous proteins are not usually soluble in water and most have structural roles.

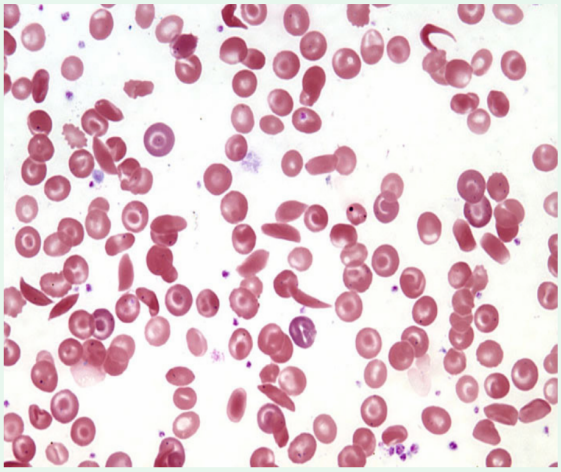
For example, keratin forms hair, nails and the outer layers of skin, making these structures waterproof. Another example of a fibrous protein is collagen.

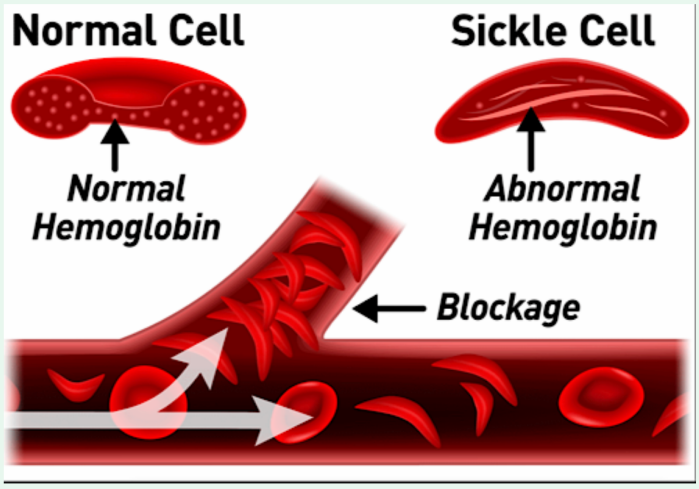
Haemoglobin – a globular protein

Haemoglobin is the oxygen-carrying pigment found in red blood cells, and is a globular protein. It is made up of four polypeptide chains, so it has a quaternary structure. Each chain is itself a protein known as globin. Globin is related to **myoglobin** and so has a very similar **tertiary structure** .There are many types of globin – two types are used to make haemoglobin, and these are known as **alpha-globin (α-globin) and beta-globin (β-globin).** Two of the haemoglobin chains, called α chains, are made from α-globin, and the other two chains, called β chains, are made from β-globin.

The four polypeptide chains pack closely together, their hydrophobic R groups pointing in towards the centre of the molecule, and their hydrophilic ones pointing outwards.The **interactions between the hydrophobic R groups** inside the molecule are important in holding it in its correct three-dimensional shape.

The outward-pointing hydrophilic R groups on the surface of the molecule are important in maintaining its solubility. In the genetic condition known as sickle cell anaemia, one amino acid which occurs in the surface of the β chain is replaced with a different amino acid. The correct amino acid is glutamic acid, which is polar. he substitute is valine, which is non- polar. Having a non-polar R group on the outside of the molecule makes the haemoglobin much less soluble, and causes the unpleasant and dangerous symptoms associated with sickle cell anaemia in anyone whose haemoglobin is all of this 'faulty' type .

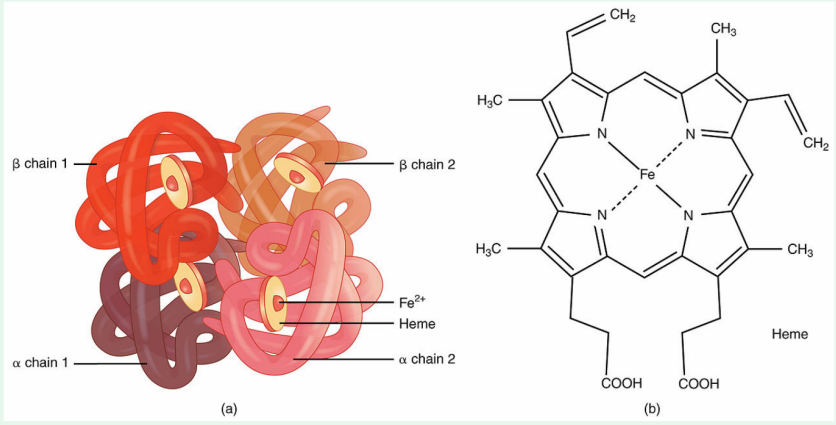




In addition, many proteins contain prosthetic groups and are called conjugated proteins. Prosthetic groups are not polypeptides but they are able to bind to different proteins or parts of them. For example, hemoglobin is a conjugated protein, with four polypeptide chains, each containing a prosthetic heme group.

Each haem group contains an iron atom. One oxygen molecule, O2, can bind with each iron atom. So a complete haemoglobin molecule, with four haem groups, can carry four oxygen molecules (eight oxygen atoms) at a time.

It is the haem group which is responsible for the colour of haemoglobin. This colour changes depending on whether or not the iron atoms are combined with oxygen. If they are, the molecule is known as oxyhaemoglobin, and is bright red. If not, the colour is purplish.



Thalassemias are inherited blood disorders characterized by decreased hemoglobin production.

Thalassemias are genetic disorders inherited from a person's parents. There are two main types, alpha thalassemia and beta thalassemia .

The severity of alpha and beta thalassemia depends on how many of the four genes for alpha globin or two genes for beta globin are missing.

Both α- and β-thalassemias are often inherited in an autosomal recessive manner. For the autosomal recessive forms o f the disease, both parents must be carriers for a child to be affected.

If both parents carry a hemoglobinopathy trait, the risk is 25% for each pregnancy for an affected child.

Oxygen-hemoglobin affinities

There are several important factors that affect the affinity of hemoglobin to oxygen as therefore affect the oxygen-hemoglobin dissociation curve.

These factors include

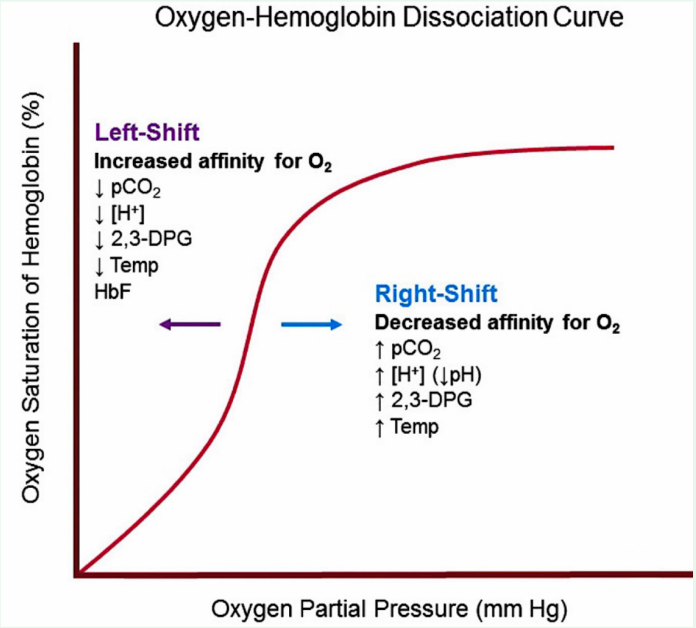
(1) pH.

(2) temperature

(3) carbon dioxide

(4) 2,3-BPG and

(5) carbon monoxide. By increasing the hydrogen ion concentration (and therefore the pH), the temperature, the carbon dioxide concentration or the amount of 2,3-BPG present in the red blood cell, we ultimately decrease the affinity of hemoglobin to oxygen and



Myoglobin is an iron and oxygen binding protein found in the muscle tissue of vertebrates in general and in almost all mammals. It is distantly related to hemoglobin which is the iron- and oxygen-binding protein in blood, specifically in the red blood cell. In humans, myoglobin is only found in the bloodstream after muscle injury. It is an abnormal finding, and can be diagnostically relevant when found in blood.
Myoglobin is the primary oxygen carrying pigment of muscle tissues.High concentrations of myoglobin in muscle cells allow organisms to hold their breath for a longer period of time. Diving mammals such as whales and seals have muscles with particularly high abundance of myoglobin.

Like hemoglobin, myoglobin is a cytoplasmic protein that binds oxygen on a heme group. It harbors only one heme group, whereas hemoglobin has four. Although its heme group is identical to those in Hb, Mb has a higher affinity for oxygen than does hemoglobin. This difference is related to its different role: whereas hemoglobin transports oxygen, myoglobin's function is to store oxygen.

Myoglobin

- Was the first protein the complete tertiary structure was determined by X-tray crystallography
- Has 8 α-helical region and **no β-pleated**
- Hydrogen binding stabilize the α-helical region
- Consist of **a single polypeptide** chain of 153 a.acid residue and includes prosthetic group- one heme group
- Store oxygen as reserve against oxygen deprivation