Semester II

BSc. Microbiology(Core)

Paper- MBIO CC203

UNIT - 4

QUATERNARY STRUCTURE OF PROTEIN

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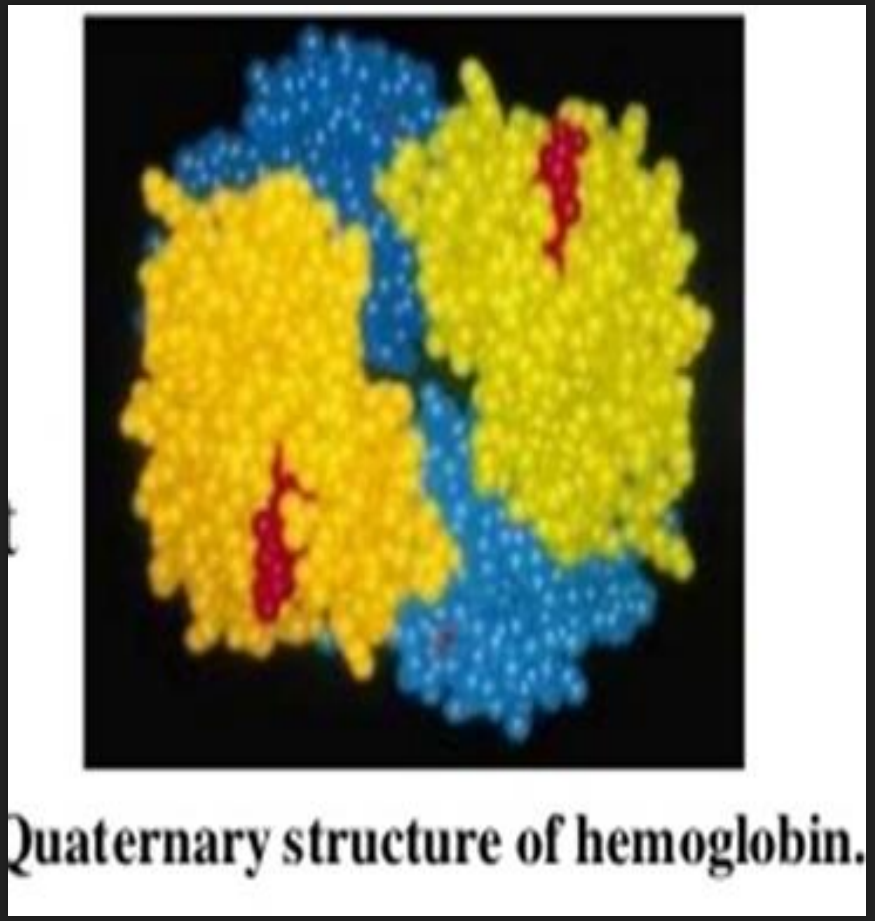
QUATERNARY STRUCTURE

- The biological function of some molecules is determined by multiple polypeptide chains- multimeric protein
- Arrangement of polypeptide subunit is called quaternary structure.
- Subunits are held together by non covalent interaction.
- Eg- hemoglobin has the subunit composition A_2B_2.



Quaternary structure of hemoglobin.

QUATERNARY STRUCTURE

- Some proteins contain two or more separate polypeptide chains, or subunits, which may be identical or different. As in case of hemoglobin it is two identical subunit of two different polypeptide.
- The **Spatial arrangement** of these protein subunits in three-dimensional complexes and **nature of interactions** between them constitutes **quaternary structure.**
- These interactions may be covalent links (e.g. disulfide bonds) or noncovalent interactions (electrostatic forces, hydrogen bonding, hydrophobic interactions).

FORCES HOLDING THE POLYPEPTIDE

- Electrostatic
- Hydrogen Bond
- Hydrophobic Forces
- Disulphide Bonds

ELECTROSTATIC FORCES

- **Electrostatic forces**: these include the interactions between two ionic groups of opposite charge, for example the ammonium group of Lys and the carboxyl group of Asp, often referred to as an **ion pair** or **salt bridge**.

- In addition, the noncovalent associations between electrically neutral molecules, collectively referred to as **van der Waals forces**, arise from electrostatic interactions between permanent and/or induced dipoles, such as the carbonyl group in peptide bonds.

HYDROGEN BONDS

- **Hydrogen bonds**: these are predominantly electrostatic interactions between a weakly acidic donor group and an acceptor atom that bears a lone pair of electrons, which thus has a partial negative charge that attracts the hydrogen atom. In biological systems the donor group is an oxygen or nitrogen atom that has a covalently attached hydrogen atom, and the acceptor is either oxygen or nitrogen (*Fig.* 9).
- Hydrogen bonds are normally in the range 0.27–0.31 nm and are highly directional, i.e. the donor, hydrogen and acceptor atoms are colinear. Hydrogen bonds are stronger than van der Waals forces but much weaker than covalent bonds.
- Hydrogen bonds not only play an important role in protein structure, but also in the structure of other biological macromolecules such as the DNA double helix and lipid bilayers
- In addition, hydrogen bonds are critical to both the properties of water and to its role as a biochemical solvent.

HYDROPHOBIC FORCES

- **Hydrophobic forces**: The **hydrophobic effect** is the name given to those forces that cause nonpolar molecules to minimize their contact with water.

- This is clearly seen with amphipathic molecules such as lipids and detergents which form micelles in aqueous solution. Proteins, too, find a conformation in which their nonpolar side chains are largely out of contact with the aqueous solvent.

- hydrophobic forces are an important determinant of protein structure, folding and stability. In proteins, the effects of hydrophobic forces are often termed **hydrophobic bonding**, to indicate the specific nature of protein folding under the influence of the hydrophobic effect.

DISULPHIDE BONDS

- **Disulfide bonds**: These covalent bonds form between Cys residues that are close together in the final conformation of the protein (see *Fig. 4*) and function to stabilize its three-dimensional structure. Disulfide bonds are really only formed in the oxidizing environment of the endoplasmic reticulum, and thus are found primarily in extracellular and secreted proteins.

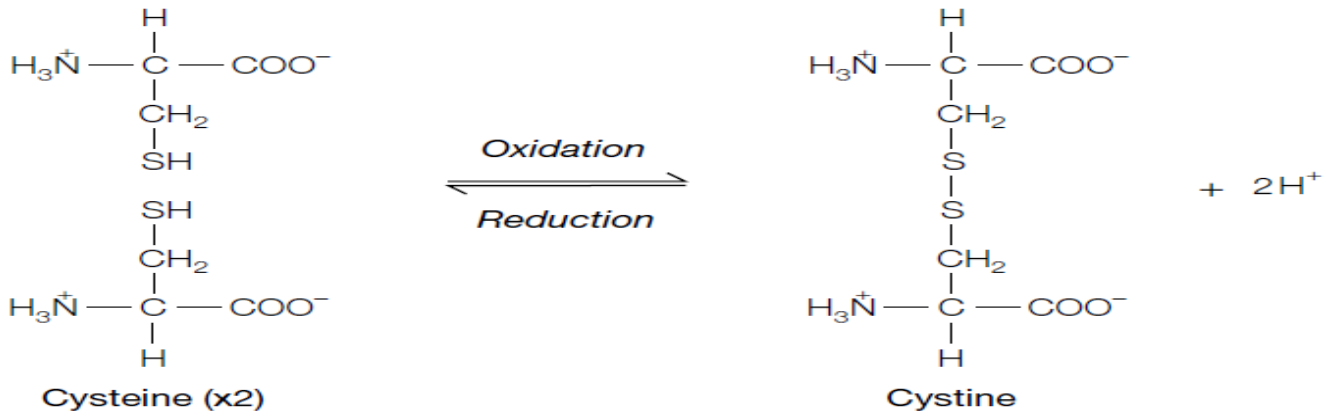
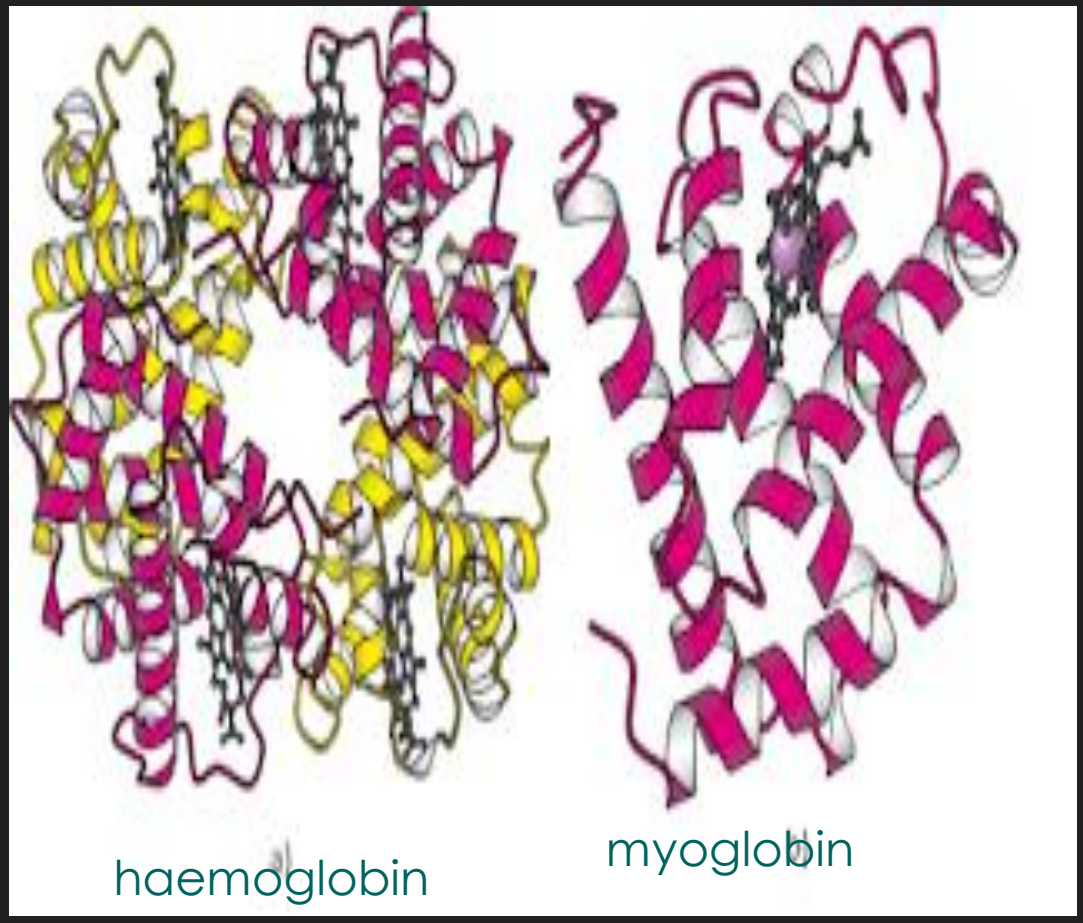


Fig. 4. Formation of a disulfide bond between two cysteine residues, generating a cystine residue.

HUMAN HAEMOGLOBIN STRUCTURE

- The three-dimensional structure of hemoglobin was solved using **X-ray crystallography** in 1959 by Max Perutz. This revealed that hemoglobin is made up of four polypeptide chains, each of which has a very similar three dimensional structure to the single polypeptide chain in myoglobin.

- Haemoglobin and myoglobin amino acid sequences differ at 83% of the residues.



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- very different primary sequences can specify very similar three-dimensional structures. The major type of hemoglobin found in adults (HbA) is made up of two different polypeptide chains: the **-chain** that consists of 141 amino acid residues, and the **-chain** of 146 residues ($\alpha_2\beta_2$).
- Each chain, like that in myoglobin, consists of eight -helices and each contains a heme prosthetic group. Therefore, hemoglobin can bind four molecules of O2. The four polypeptide chains, two and two , are packed tightly together in a tetrahedral array to form an overall spherically shaped molecule that is held together by multiple noncovalent interactions.

HAEMOGLOBIN

- Their main function is to carry hemoglobin, which is dissolved in the cytosol at a very high concentration (~34% by weight).
- In arterial blood passing from the lungs through the heart to the peripheral tissues, hemoglobin is about 96% saturated with oxygen. In the venous blood returning to the heart, hemoglobin is only about 64% saturated.
- Hemoglobin, with its multiple subunits and O2-binding sites, is better suited to oxygen transport.
- Interactions among the subunits in hemoglobin cause conformational changes that alter the affinity of the protein for oxygen. The modulation of oxygen binding allows the O2-transport protein to respond to changes in oxygen demand by tissues.

HAEMOGLOBIN

- Hemoglobin (*M*r 64,500; abbreviated Hb) is roughly spherical, with a diameter of nearly 5.5 nm. It is a tetrameric protein containing four heme prosthetic haemoglobin groups, one associated with each polypeptide chain.
- Adult hemoglobin contains two types of globin, two chains (141 residues each) and two chains (146 residues each).
- Their structures are very similar to that of myoglobin. Amino acid sequence of alpha, beta and myglobin are only similar at 27 positions but they belong to same family.
- The helix-naming convention described for myoglobin is also applied to the hemoglobin polypeptides, except that the subunit lacks the short D helix. The heme-binding pocket is made up largely of the E and F helices.
- Along with oxygen transport hemoglobin also transports hydrogen and carbondioxide.
- Mutation in the amino acid sequence leads to disease called sickle cell anemia.

SICKLE CELL ANAEMIA

- Sickle-cell anemia is a genetic disease caused by a single amino acid substitution (Glu6 to Val6) in each chain of hemoglobin. The change produces a hydrophobic patch on the surface of the hemoglobin that causes the molecules to aggregate into bundles of fibers This homozygous condition results in serious medical complications.


Thank you