(iii) Tertiary structure. Tertiary structure of a protein refers to its complete three-dimensional structure. In other words, tertiary structure refers to the manner in which the entire protein molecule folds up in the three-dimensional space to produce a specific shape (or compact form). At normal pH and temperature, each protein will take up a shape (tertiary structure) that is energetically most stable. This shape is specific to a given amino acid sequence and is called the *native shape* of the protein. In other words, *primary* structure of a protein dictates its tertiary structure.

(a) Tertiary structure of fibrous proteins. Fibrous proteins have almost the same secondary ( $\alpha$ -helix or  $\beta$ -pleated) structure throughout the length of the protein. For example, the  $\alpha$ -keratins, the major proteins of hair and wool have the  $\alpha$ -helix structure. In these proteins, several  $\alpha$ -helices are coiled about each other to form molecular ropes or rods. *Thus, the tertiary structure of fibrous proteins is rope-like or rod-like*. The structure of collagen triple helix is shown in Fig. 3.10.



(b) Tertiary structures of globular proteins. Unlike fibrous proteins, globular proteins do not have the same secondary structure throughout the length of the molecule. Parts of the molecule may have the  $\alpha$ helical structure, while the other parts may have the  $\beta$ -pleated sheet structure and still other parts may be random coils. These different segments of the protein then fold up to give the entire molecule a spherical shape. This folding results through the interaction of the various side chain groups of the constituent amino acids. These interactions involve several types of forces such as van der Waals' interactions, disulphide bridges, ionic or salt bridges and hydrogen bonding as shown in Fig. 3.11.



It may, however, be noted here that folding of polypeptide chains takes place in such a manner so that maximum number of non-polar (hydrophobic) groups are pushed inwards while polar (hydrophilic) groups are pushed outwards so that they can interact with water molecules.

The tertiary structures of proteins is determined by their X-ray diffraction studies. M.F. Perutz and J.C. Kendrew of Cambridge University, England were the first to carry out complete structural analysis of **myoglobin** (in 1957) and **haemoglobin** (in 1959) by X-ray crystallography. For this work, they were awarded the 1962 Nobel Prize in Chemistry. A simplified representation of tertiary structure of myoglobin is given in Fig. 3.12. It consists of eight straight segments each one of which adops an  $\alpha$ -helical secondary structure. These helical sections are connected by bends having random coil structure. It also contains the *prosthetic group* called **heme.** Since then the complete structures of some other proteins such as lysozyme and  $\alpha$ -chymotrypsin have also been determined.



(iii) Quaternary Structure of Proteins. Although many proteins exist as a single polypeptide chain, there are certain proteins which exist as assemblies of two or more polypeptide chains called subunits or protomers. These subunits may be identical or different and are held together by non-covalent forces such as hydrogen bonds, electrostatic interactions and van der Waals' interactions. The quaternary structure refers to the determination of the number of subunits and their arrangements in an aggregate protein molecule. The best known example of a protein possessing quaternary structure is haemoglobin which transports oxygen from the lungs to the cells and carbon dioxide from the cells to the lungs through the blood stream. It is an aggregate of four polypeptide chains or subunits, two identical alpha chains (each containing 141 amino acid residues and two identical beta chains (each containing 146 amino acid residues). These four subunits lie more or less at the vertices of a regular tetrahedron Fig 3.13. Each polypeptide chain carries a heme (iron-protoporphyrin complex) group at its end.



**FIGURE 3.13.** Quaternary structure of haemoglobin. It has four subunits  $\alpha_1$ ,  $\alpha_2$ ,  $\beta_1$  and  $\beta_2$  which are arranged tetrahedrally. Each subunit has a heme group shown by a rectangle. The spheres in the rectangle represent the iron atom at which oxygen gets bound.