4. Structure and function of proteins and nucleic acids

4.1 The structure of proteins

Structure and function
Shortly after the discovery of X-ray diffraction by crystals the technique was used to investigate biological macromolecules, in particular proteins which could be crystallized and nucleic acids. The overriding importance of such studies is that they show the close relationship between the structure and the function of these macromolecules. Proteins have a greatest diversity of functions in an organism. These functions are performed for the most part by selective binding to molecules. The selectivity is assured by numerous weak interactions working at close range between substrate (or ligand as it is called frequently) and macromolecule, so that binding only can be sufficiently tight if there is close fitting of the ligand to the protein.

If binding links identical molecules, so that many copies of the same protein aggregate, large-scale structures are formed such as fibers or tubules. Often, however, the binding involves molecules different from the binding protein. Enzymes are the most obvious examples. But also other protein functions involve selective binding, such as binding between antigen and antibody, binding of regulating proteins to parts of DNA, binding of ligands to receptor proteins for endocytosis or recognition for the purpose distinguishing self from nonself, and so on. Virtually all the activities of proteins can be understood in terms of selective binding. Knowledge of the structure, therefore, is imperative to understand its function.

Astbury structures
Around 1930 Astbury tried to interpret the diffraction pattern obtained from crystallized protein and nucleic acid fibers. He showed that protein fibers give rise to two types of patterns which he called α and β patterns. He recognized that the α pattern was due to a more folded and dense structure (Fig. 4.1a) while the β pattern was from a more stretched structure (Fig. 4.1b). The structures in his models are held together by hydrogen bonds which are indicated in Figure 4.1 by dotted lines.

The α-helix and β-pleated sheet
Although the importance of Astbury’s models for the understanding of protein structure cannot be denied, they did not give a completely satisfactory explanation of the diffraction patterns. The helical structure proposed by...
Pauling and Corey in 1951 did fit the diffraction patterns of many fibrous proteins much better. Astbury and others have also tried helical models but they never thought of fitting a noninteger number of amino acid residues into one turn. Taking into account the known bond distances and bond angles, Pauling and Corey showed that a helical structure with 3.6 amino acid residues per turn, a diameter of about 6.8 Å, and a distance between turns of about 5.4 Å would be a definite possibility. The helical structure is stabilized by hydrogen bonds between amino acids four units apart. These hydrogen bonds are between the amino group of one peptide unit to the carboxyl group of another and do not involve the residues. The stability of the α helix, therefore, is not depending on the identity of the residues which form side chains pointing out from the helix. Thus, the same α-helical structure can accommodate almost any flexible side chain as long as they are L-amino acids and not too long to interfere sterically with the structure. Proline is an exception, however. Due to its peculiar structure (see Table 2.1), this amino acid never occurs in an α helix. It causes more or less sharp bends in the peptide chain.

This α-helical structure fits the diffraction patterns observed for synthetic polypeptides very well and there were also many aspects pointing to the α helix in the diffraction patterns of many naturally occurring fibers of the α-type. The model, which is illustrated in Fig. 4.2a, turned out to be remarkably accurate, considering the fact that it was proposed six years before an α helix was actually seen at molecular resolution for the first time in the crystal structure of myoglobin. Since then it is confirmed in many structures of biological macromolecules.

Pauling and Corey also made pleated sheet models in line with Astbury’s β structure. They did not restrict the peptide bonds to one plane (Fig. 4.2b). Both structures, the α helix and the pleated sheets, retain the idea of an α structure being folded and a β structure being stretched out.