

## CHECKLIST OF KEY CONCEPTS

### Amino acids and polypeptides

1. Proteins are polypeptides, up to about 5000 amino acids in length.
2. All amino acids except proline are  $\alpha$ -amino acids, existing in solution as zwitterions.
3. All amino acids except glycine can exist in L and D forms.
4. Formation of a peptide bond requires the elimination of water.

### Introduction to protein structure

5. The order of amino acids in a polypeptide is called the primary structure.
6. Proteins take up a folded configuration that is stabilised by noncovalent bonds. These bonds are easily destroyed by heat.
7. Proteins fold with the hydrophilic groups outwards and the hydrophobic ones inwards.

### Amino acids and their properties

8. 20 amino acids are used for protein synthesis.
9. There are 8 amino acids with hydrophobic side chains and 9 with hydrophilic side chains. Glycine, with an H side chain is not particularly either.
10. Cysteine has an SH side chain that allows it to form cross linking –S-S- bonds and proline is not an  $\alpha$ -amino acid but an imino acid.
11. When amino acids are present within a polypeptide only the side chains can ionize.
12. Aspartate and glutamate have acidic side chains and lysine, arginine and histidine have basic side chains.

### Secondary structure

13. Secondary structure describes the local folding of the polypeptide chain.
14. In  $\alpha$  helices the chain turns right handed, with 3.6 amino acids per turn. Some amino acids, such as leucine and methionine, favour  $\alpha$  helix formation and others, particularly proline, prevent  $\alpha$  helix formation.
15.  $\beta$  pleated sheets are an additional stable secondary structure.

### Tertiary and quaternary structure

16. Tertiary structure describes the overall arrangement of amino acids in 3 dimensions, including the organization of different secondary structure elements.
17. Some proteins, such as myoglobin, only have  $\alpha$  helices and connecting loops. Others, such as staphylococcal nuclease, have both forms of secondary structure.
18. Disulphide bridges between cysteine residues lock chains together.
19. Many proteins contain more than one polypeptide chain, with the chains being held together by weak bonds. This type of organisation forms quaternary structure.

### Evolution of proteins

20. Often proteins have evolved from a single ancestor. They are described as homologous.
21. Protein domains are regions within a larger protein that are themselves relatively stable and self-contained.
22. Domains often catalyze partial enzymic reactions.
23. Proteins can evolve by the recombination of domains from more than one source. Often exons code for a single domain.

### Types of proteins

24. Proteins often have metal ions or other structures such as carbohydrates covalently attached to the polypeptide chain.
25. Extracellular matrix proteins include collagen, elastin and fibronectin.
26. Collagen is assembled from tropocollagen and contains the modified amino acids hydroxyproline and hydroxylysine. It is a triple helix.
27. Elastin contains  $\alpha$  helices with cross linking between lysine residues.
28. The proteoglycans of the matrix contain amino sugar disaccharides and exist in multiple forms. Some of these have covalently attached sulphate groups.
29. Fibronectin stabilises the matrix structure by binding proteoglycans, collagen and cell surfaces together.
30. Integrins are transmembrane signaling proteins. They bind components of the connective tissue outside the cell and signal transduction molecules within the cell.

### Myoglobin and hemoglobin

31. Myoglobin is a monomeric protein made up of  $\alpha$  helices and connecting loops, with a molecule of heme bound to it. It has a higher affinity for oxygen than hemoglobin and this allows it to remove oxygen from the blood.
32. Hemoglobin is a tetramer of polypeptide chains, two  $\alpha$  subunits and two  $\beta$  subunits.
33. The oxygen binding characteristics of hemoglobin mean that it is loaded with oxygen in the lungs, where oxygen levels are high, and then unloads almost completely in the tissues.
34. Interaction between the subunits of heme results in homotropic cooperativity and a plot of binding against oxygen level is sigmoid in shape.
35. The two models for cooperativity are called the concerted model and the sequential model.
36. It has been possible to characterize the changes in shape that occur during oxygen binding using X-ray diffraction on crystals.

### Modifiers of oxygen binding to hemoglobin

37. 2:3-bisphosphoglycerate moves the oxygen binding curve to the right i.e. it decreases the affinity of hemoglobin for oxygen. This is because it binds to the deoxygenated form but not the oxygenated form.

38. When oxygen binds to hemoglobin it causes the release of protons because the oxygenated form has a lower affinity for protons than the deoxygenated form.
39. In the tissues carbon dioxide enters the red blood cells, is converted to  $\text{H}_2\text{CO}_3$  and release protons. These protons stimulate oxygen unloading.
40. In the lungs the process is reversed.

### **Genetic diseases**

41. A variety of genetic diseases exist that are caused by the loss of certain types of collagen.
42. Similarly single amino acid changes in hemoglobin can have substantial effects on its oxygen binding properties.