Chapter 5 Protein Function

Multiple Choice Questions

1. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 157 Difficulty: 2 Ans: D
The interactions of ligands with proteins:

A) are relatively nonspecific.
B) are relatively rare in biological systems.
C) are usually irreversible.
D) are usually transient.
E) usually result in the inactivation of the proteins.

2. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 158 Difficulty: 1 Ans: D
A prosthetic group of a protein is a non-protein structure that is:

A) a ligand of the protein.
B) a part of the secondary structure of the protein.
C) a substrate of the protein.
D) permanently associated with the protein.
E) transiently bound to the protein.

3. Reversible binding of a protein to a ligand: oxygen-binding proteins
Pages: 158–159 Difficulty: 2 Ans: B
When oxygen binds to a heme-containing protein, the two open coordination bonds of Fe^{2+} are occupied by:

A) one O atom and one amino acid atom.
B) one O_2 molecule and one amino acid atom.
C) one O_2 molecule and one heme atom.
D) two O atoms.
E) two O_2 molecules.

4. Reversible binding of a protein to a ligand: oxygen-binding proteins
Pages: 160–161 Difficulty: 2 Ans: A
In the binding of oxygen to myoglobin, the relationship between the concentration of oxygen and the fraction of binding sites occupied can best be described as:

A) hyperbolic.
B) linear with a negative slope.
C) linear with a positive slope.
D) random.
E) sigmoidal.

5. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 160 Difficulty: 2 Ans: E
Which of the following statements about protein-ligand binding is correct?

A) The K_a is equal to the concentration of ligand when all of the binding sites are occupied.
B) The K_a is independent of such conditions as salt concentration and pH.
C) The larger the K_a (association constant), the weaker the affinity.
D) The larger the K_a, the faster is the binding.
E) The larger the K_a, the smaller the K_d (dissociation constant).

6. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 163 Difficulty: 2 Ans: E
Myoglobin and the subunits of hemoglobin have:

A) no obvious structural relationship.
B) very different primary and tertiary structures.
C) very similar primary and tertiary structures.
D) very similar primary structures, but different tertiary structures.
E) very similar tertiary structures, but different primary structures.

7. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 165 Difficulty: 2 Ans: B
An allosteric interaction between a ligand and a protein is one in which:

A) binding of a molecule to a binding site affects binding of additional molecules to the same site.
B) binding of a molecule to a binding site affects binding properties of another site on the protein.
C) binding of the ligand to the protein is covalent.
D) multiple molecules of the same ligand can bind to the same binding site.
E) two different ligands can bind to the same binding site.

8. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 165 Difficulty: 1 Ans: C
In hemoglobin, the transition from T state to R state (low to high affinity) is triggered by:

A) Fe^{2+} binding.
B) heme binding.
C) oxygen binding.
D) subunit association.
E) subunit dissociation.

9. Reversible binding of a protein to a ligand: oxygen-binding proteins
Pages: 171–172 Difficulty: 2 Ans: C
Which of the following is *not* correct concerning 2,3-bisphosphoglycerate (BPG)?

A) It binds at a distance from the heme groups of hemoglobin.
B) It binds with lower affinity to fetal hemoglobin than to adult hemoglobin.
C) It increases the affinity of hemoglobin for oxygen.
D) It is an allosteric modulator.
E) It is normally found associated with the hemoglobin extracted from red blood cells.

10. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 167 Difficulty: 2 Ans: C
Which of the following is *not* correct concerning cooperative binding of a ligand to a protein?

A) It is usually a form of allosteric interaction.
B) It is usually associated with proteins with multiple subunits.
C) It rarely occurs in enzymes.
D) It results in a nonlinear Hill Plot.
E) It results in a sigmoidal binding curve.

11. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 173 Difficulty: 1 Ans: D
The amino acid substitution of Val for Glu in Hemoglobin S results in aggregation of the protein because of _____ interactions between molecules.

A) covalent
B) disulfide
C) hydrogen bonding
D) hydrophobic
E) ionic

12. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 173 Difficulty: 2 Ans: C
The fundamental cause of sickle-cell disease is a change in the structure of:

A) blood.
B) capillaries.
C) hemoglobin.
D) red cells.
E) the heart.

13. Complementary interactions between proteins and ligands: the immune system and immunoglobulins
Page: 175 Difficulty: 2 Ans: B
An individual molecular structure within an antigen to which an individual antibody binds is as a(n):

A) antigen.
B) epitope.
C) Fab region.
D) Fc region
E) MHC site.

14. Complementary interactions between proteins and ligands: the immune system and immunoglobulins
Page: 176 Difficulty: 2 Ans: A
The proteins of the Major Histocompatibility Complex (MHC) bind and display:

A) antigen fragments.
B) B cell fragments.
C) immunoglobin fragments.
D) macrophage fragments.
E) T cell fragments.

15. Complementary interactions between proteins and ligands: the immune system and immunoglobulins
Page: 178 Difficulty: 3 Ans: B
Which of the following parts of the IgG molecule are *not* involved in binding to an antigen?

A) Fab
B) Fc
C) Heavy chain
D) Light chain
E) Variable domain

16. Complementary interactions between proteins and ligands: the immune system and immunoglobulins
Page: 180 Difficulty: 3 Ans: C
A monoclonal antibody differs from a polyclonal antibody in that monoclonal antibodies:

A) are labeled with chemicals that can be visualized.
B) are produced by cells from the same organism that produced the antigen.
C) are synthesized by a population of identical, or "cloned," cells.
D) are synthesized only in living organisms.
E) have only a single polypeptide chain that can recognize an antigen.

17. Protein interactions modulated by chemical energy: actin, myosin, and molecular motors
Page: 182 Difficulty: 2 Ans: A
Which of the following generalizations concerning motor proteins is correct?

A) They convert chemical energy into kinetic energy.
B) They convert chemical energy into potential energy.
C) They convert kinetic energy into chemical energy.
D) They convert kinetic energy into rotational energy.
E) They convert potential energy into chemical energy.

18. Protein interactions modulated by chemical energy: actin, myosin, and molecular motors
Pages: 182–183 Difficulty: 2 Ans: B
The predominant structural feature in myosin molecules is:

A) a β structure.
B) an α helix.
C) the Fab domain.
D) the light chain.
E) the meromyosin domain.

19. Protein interactions modulated by chemical energy: actin, myosin, and molecular motors
Page: 185 Difficulty: 1 Ans: A
The energy that is released by the hydrolysis of ATP by actin is used for:

A) actin filament assembly.
B) actin filament disassembly.
C) actin-myosin assembly.
D) actin-myosin disassembly.
E) muscle contraction.

20. Protein interactions modulated by chemical energy: actin, myosin, and molecular motors
Page: 185 Difficulty: 1 Ans: B
During muscle contraction, hydrolysis of ATP results in a change in the:

A) conformation of actin.
B) conformation of myosin.
C) structure of the myofibrils.
D) structure of the sarcoplasmic reticulum.
E) structure of the Z disk.

Short Answer Questions

21. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 158 Difficulty: 1
Describe the concept of "induced fit" in ligand-protein binding.

Ans: Induced fit refers to the structural adaptations that occur when a ligand binds to a protein. This often involves a conformational change in the protein that alters the binding site to make it more complementary to the ligand.

22. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 158 Difficulty: 2
Explain why most multicellular organisms use an iron-containing protein for oxygen binding rather than free Fe^{2+}. Your answer should include an explanation of (a) the role of heme and (b) the role of the protein itself.

Ans: (a) Binding of free Fe^{2+} to oxygen would result in the formation of reactive oxygen species that can damage biological structures. Heme-bound iron is less reactive in this regard. (b) Binding of oxygen to free heme can result in irreversible oxidation of the Fe^{2+} to Fe^{3+} that does not bind oxygen. The environment of the heme group in proteins helps to prevent this from occurring.

23. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 168 Difficulty: 1
Why is carbon monoxide (CO) toxic to aerobic organisms?

Ans: It binds to heme with a higher affinity than oxygen, and thus prevents oxygen from binding to hemoglobin.

24. Reversible binding of a protein to a ligand: oxygen-binding proteins
Pages: 160–161 Difficulty: 2
Describe how you would determine the K_a (association constant) for a ligand and a protein.

Ans: An experiment would be carried out in which a fixed amount of the protein is incubated with varying amounts of ligand (long enough to reach equilibrium). The fraction of protein molecules that have a molecule of ligand bound is then determined. A plot of this fraction (θ) vs. ligand concentration [L] should yield a hyperbola. The value of [L] when $\theta = 0.5$ is equal to $1/K_a$.

25. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 160 Difficulty: 2
For the binding of a ligand to a protein, what is the relationship between the K_a (association constant), the K_d (dissociation constant), and the affinity of the protein for the ligand?

Ans: $K_a = 1/K_d$. The larger the K_a (and hence the smaller the K_d), the higher the affinity of the protein for the ligand.

26. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 162 Difficulty: 2
Explain briefly why the relative affinity of heme for oxygen and carbon monoxide is changed by the presence of the myoglobin protein.

Ans: The geometry of binding O_2 and CO to heme is slightly different. In myoglobin there is a histidine residue that does not interact with the heme iron, but can interact with a ligand that is bound to the heme. It does not affect O_2 binding but because of steric hindrance, it may prevent CO binding. As a result the relative affinity of protein-bound heme for CO and O_2 is only 200, compared to 20,000 for free heme.

27. Reversible binding of a protein to a ligand: oxygen-binding proteins
Pages: 161, 166 Difficulty: 3
Explain why the structure of myoglobin makes it function well as an oxygen-storage protein whereas the structure of hemoglobin makes it function well as an oxygen-transport protein.

Ans: The hyperbolic binding of oxygen to the single binding site of myoglobin results in a high affinity even at the relatively low partial pressures of O_2 that occur in tissues. In contrast, the cooperative (sigmoidal) binding of O_2 to the multiple binding sites of hemoglobin results in high affinity at high partial pressures such as occur in the lungs, but lower affinity in the tissues. This permits hemoglobin to bind O_2 in the lungs and release it in the tissues.

28. Reversible binding of a protein to a ligand: oxygen-binding proteins
Pages: 167–170 Difficulty: 2
Describe briefly the two principal models for the cooperative binding of ligands to proteins with multiple binding sites

Ans: In the concerted model, binding of a ligand to one site on one subunit results in an allosteric effect that converts all of the remaining subunits to the high-affinity conformation. As a result, all of the subunits are either in the low- or high-affinity conformation. In the sequential model, each subunit is changed individually to the high affinity conformation. As a result, there are many possible combinations of low- and high-affinity subunits.

29. Reversible binding of a protein to a ligand: oxygen-binding proteins
Pages: 171–172 Difficulty: 2
How does BPG binding to hemoglobin decrease its affinity for oxygen?

Ans: BPG binds to a cavity between the β subunits. It binds preferentially to molecules in the low-affinity T state, thereby stabilizing that conformation.

30. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 170 Difficulty: 2
a) What is the effect of pH on the binding of oxygen to hemoglobin (the Bohr Effect)? (b) Briefly describe the mechanism of this effect.
Ans: (a) The affinity decreases with decreasing pH. (b) At lower pH (i.e., higher H^+ concentration) there is increasing protonation of protein residues such as histidine, which stabilizes the low affinity conformation of the protein subunits.

31. Reversible binding of a protein to a ligand: oxygen-binding proteins
Page: 173 Difficulty: 2
Explain how the effects of sickle cell disease demonstrate that hemoblobin undergoes a conformational change upon releasing oxygen.

Ans: In Hemoglobin S, the wild-type glutamate at residue 6 of the B-chain is replaced by valine. When oxygen is bound, both Hemoglobin A and Hemoglobin S are soluble, but in the deoxy- form. Hemoglobin S (but not Hemoglobin A) becomes very insoluble, due to exposure of the hydrophobic valine residue. This exposed "patch" causes aggregation of deoxy-Hemoglobin S into long insoluble fibrous aggregates, resulting in distorted shapes of the red blood cells (and leading to the symptoms of the disease). (See p. 173 and Fig. 5-20.)

32. Complementary interactions between proteins and ligands: the immune system and immunoglobulins
Page: 175 Difficulty: 1
Why is it likely that the immune system can produce a specific antibody that can recognize and bind to any specific chemical structure?

Ans: As a result of genetic recombination mechanisms, antibody-producing B cells are capable of producing millions of different antibodies with different binding specificities.

33. Complementary interactions between proteins and ligands: the immune system and immunoglobulins
Page: 176 Difficulty: 2
What is the role of the Major Histocompatibility Complex (MHC) in the immune response?

Ans: MHC proteins are present on the surface of specialized immune system cells. Antigen fragments that are derived from external proteins are bound to the MHC proteins and elicit an immune response. A selection process eliminates those cells with MHC complexes that might bind normal cellular proteins, leaving only those that can bind foreign proteins. Thus the MHC plays a role in the ability of the immune system to discriminate between self and nonself.

34. Complementary interactions between proteins and ligands: the immune system and immunoglobulins
Page: 178 Difficulty: 2
Describe briefly the basic structure of an IgG protein molecule.

Ans: An IgG protein contains two copies of a large polypeptide (heavy chain) and two copies of a small polypeptide (light chain). β structure contributes significantly to the tertiary structure of domains of both chains. Disulfide bonds link the heavy chains to one another and to the light chains. The chains are arranged in a Y-shaped structure where the two arms are linked to the base by a protease sensitive ("hinge") region.

35. Complementary interactions between proteins and ligands: the immune system and immunoglobulins
Page: 180 Difficulty: 2
What is the chemical basis for the specificity of binding of an immunoglobin antibody to a particular antigen?

Ans: Specific binding results from complementarity between the chemical properties (such as size, charge, and hydrophobicity) of the antigen and the antigen-binding site of the antibody.

36. Complementary interactions between proteins and ligands: the immune system and immunoglobulins
Page: 180 Difficulty: 2
What is the concept of "induced fit" as it applies to antigen-antibody binding?

Ans: The conformations of the antigen and antigen-binding site of the antibody are influenced by each other and change as binding occurs. These conformational changes increase the chemical complementarity of the sites and result in tighter binding.

37. Complementary interactions between proteins and ligands: the immune system and immunoglobulins
Pages: 180–181 Difficulty: 2
Describe how immunoaffinity chromatography is performed.

Ans: The specific antibody is covalently attached to an inert supporting material, which is then packed into a chromatography column. The protein solution is passed through the column slowly; most proteins pass directly through, but those for which the antibody has specific affinity are adsorbed. They can subsequently be eluted by a buffer of low pH, a salt solution, or some other agent that breaks the antibody-antigen association.

38. Complementary interactions between proteins and ligands: the immune system and immunoglobulins
Pages: 181–182 Difficulty: 2
What properties of antibodies make them useful biochemical reagents? Describe one biochemical application of antibodies (with more than just the name of the technique).

Ans: The important properties are the high specificity of protein recognition, and the high affinity of the antibody-antigen association. These make possible immunoaffinity chromatography, immunocytochemistry, enzyme-linked immunosorbent assay (ELISA), and immunoblotting, all of which are described on pp. 181–182.

39. Protein interactions modulated by chemical energy: actin, myosin, and molecular motors
Page: 182 Difficulty: 2
Describe briefly the structure of myosin.

Ans: Myosin contains two copies of a large polypeptide (heavy chain) and four copies of a small polypeptide (light chain). The α helix contributes significantly to the structure of the heavy chains. At their carboxyl termini, the heavy chains are wrapped around each other in a fibrous left-handed coil. At their amino termini, they each have a globular domain with which the light chains are associated.

40. Protein interactions modulated by chemical energy: actin, myosin, and molecular motors
Page: 184 Difficulty: 1
What is the relationship between G-actin and F-actin?

Ans: G-actin is a monomeric protein that can polymerize to form a long polymeric filament known as F-actin.

41. Protein interactions modulated by chemical energy: actin, myosin, and molecular motors
Page: 185 Difficulty: 2
What is the role of ATP and ATP hydrolysis in the cycle of actin-myosin association and disassociation that leads to muscle contraction?

Ans: ATP binding to myosin results in a conformational change that causes dissociation of actin from the myosin. ATP hydrolysis results in a change of orientation of the myosin relative to the actin filament, which allows movement to the next actin subunit. This is followed initially by release of the phosphate hydrolysis product and weak binding of the myosin to this actin subunit, and, subsequently, by tight binding and release of the ADP hydrolysis product.

42. Protein interactions modulated by chemical energy: actin, myosin, and molecular motors
Pages: 185–186 Difficulty: 2
Describe the cycle of actin-myosin association and disassociation that leads to muscle contraction.

Ans: First, ATP binds to myosin and a cleft in the myosin molecule opens, disrupting the actin-myosin interaction so that the bound actin is released. Second, ATP is hydrolyzed, causing a conformational change in the protein to a "high-energy" state that moves the myosin head and changes its orientation in relation to the actin thin filament. Myosin then binds weakly to an F-actin subunit closer to the Z disk than the one just released. Third, as the phosphate product of ATP hydrolysis is released from myosin, another conformational change occurs in which the myosin cleft closes, strengthening the myosin-actin binding. Fourth, this is followed quickly by a "power stroke" during which the conformation of the myosin head returns to the original resting state, its orientation relative to the bound actin changing so as to pull the tail of the myosin toward the Z disk. ADP is then released to complete the cycle. (See Fig. 5-33, p. 186.)