

**Chapter 7 Answers**  
**Portrait of an Allosteric Protein**

- 1) Hemoglobin reversibly binds:
  - a) CO<sub>2</sub> \*\*\*\*\*
  - b) Phosphoenol pyruvate
  - c) CO
  - d) H<sub>2</sub>O
  - e) all of the above
  
- 2) The affinity of hemoglobin for oxygen decreases with
  - a) an increase in pH
  - b) a decrease in the concentration of BPG
  - c) a decrease in pO<sub>2</sub>
  - d) the iron in the +2 oxidation state
  - e) all of the above
  
- 3) An enzyme whose substrate binding was found to have a hill coefficient of 1.0 indicates:
  - a) That carbon monoxide is activating the enzyme
  - b) the substrate binding curve will be hyperbolic
  - c) a sigmoidal binding curve will be found
  - d) that this enzyme is allosterically regulated
  - e) none of the above
  
- 4) Deletion in genes for the hemoglobin alpha chain results in:
  - a) HbS
  - b) HbM
  - c) Hb Saskatoon
  - d) thalassimia \*\*\*\*\*
  
- 5) The affinity of hemoglobin for oxygen increases with:
  - a) A decrease in pH
  - c) A decrease in pO<sub>2</sub>
  - b) an increase in pO<sub>2</sub> \*\*\*\*\*
  - d) an increase in the concentration of hydrogen ions
  
- 6) T/F For hemoglobin, the hill coefficient is greater than one *True*
  
- 7) The primary force holding the heme in place in hemoglobin is:
  - a) hydrogen bonding
  - b) salt bridges
  - c) disulfide bonds
  - d) hydrophobic interactions \*\*\*\*\*
  
- 8) Draw the O<sub>2</sub> dissociation curve for both the normal forms of hemoglobin and a hemoglobin that has a mutation for sickle cell.  
*There should be no difference in the oxygen binding. However once dissociated, and the concentration of sickle cell Deoxy hemoglobin is high enough they will polymerize. But up to that point there is no difference for the mutant form of HbA*

9) Describe the solubility of sickle cell hemoglobin and normal hemoglobin in high pO<sub>2</sub> vs. low pO<sub>2</sub>.

*The sickling describe above will result from a mutation to the hydrophilic Glu to the hydrophobic Val. Once in the deoxy form the Val is exposed as the tertiary structure moves the mutant Val to the exterior of the protein. Prior to this point the Val was on the inside of the protein, was not involved in oxygen binding and therefore has little effect on the nature of the Hb. Now that the Val is exposed to an aqueous environment, it will "mate up" to another hydrophobic patch on another deoxy HbS. This will form long polymers of the hemoglobin and become insoluble. This is different from the wild type in that the glutamate is water soluble and will not interact with the hydrophobic patch on another hemoglobin and therefore stay soluble.*

10) Why does the coordination of oxygen to the heme Fe<sup>+2</sup> effect structure of hemoglobin. How is this different in myoglobin?

*As the O<sub>2</sub> binds it pulls the iron out of the plane. this in turn displaces the proximal histadine and results in a movement of the alpha helix to which it is part of. In myoglobin this is about the extent of the structural changes. But in hemoglobin, where there are four subunits there is a contact of several amino acids between the alpha and beta subunits. The movement in the alpha helix is felt and several new amino acids interact at the interfaces of the alpha and beta chains. An example might be how in the deoxy or T form an aspartate interacts with the hydroxyl group of a tyrosine. After the O<sub>2</sub> binding, the relaxed conformation forms an aspartate-glutamate interaction. This new interactions and several others just like it help stabilize the new conformation.*

11) To bind oxygen, the iron in hemoglobin must have a

- a) +2 oxidation state \*\*\*\*
- b) +3 oxidation state
- c) +1 oxidation state
- d) the oxidation state does not matter, just the coordination of the histadine
- e) any oxidation state

12) As the pH decreases, the ability of hemoglobin to bind to oxygen

- a) increases
- b) decreases \*\*\*\*\*
- c) stays the same
- d) drops to zero

13) Explain why the pH alters the affinity of hemoglobin for oxygen.

14) How does the reaction of carbon dioxide with water help explain the Bohr effect? Include the equation for the formation of bicarbonate ion from CO<sub>2</sub> and water, and explain the effects of H<sup>+</sup> and CO<sub>2</sub> on hemoglobin oxygenation

*The reaction of carbon dioxide with water explains why there is an concomitant lowering of pH when the concentration of CO<sub>2</sub> increases. Carbon dioxide produced by rapidly metabolizing tissue reacts with water to produce bicarbonate ions and H<sup>+</sup>*



*The hydrogen ion generated in this reaction decreases the pH of the blood and thus stabilizes the deoxy form (T conformation) of hemoglobin. The net effect is an increase in the P<sub>50</sub>, that is, a lower affinity of hemoglobin for oxygen, so that more oxygen is released to the tissue. Carbon dioxide also lowers the affinity of hemoglobin for oxygen by forming carbamate adducts*

*with the N - terminus of the four chains. this modification contributes to the stability of the deoxy (T form) conformation, thereby further increasing the P50 and promoting the release of oxygen to the tissue.*

15) Carbon dioxide binds to which site of the hemoglobin molecule?

- a) the N terminus
- b) the C-terminus
- c) the heme iron
- d) an important histadine
- e) it doesn't bind to hemoglobin

16) The contact points between hemoglobin subunits

- a) tightly associates the two subunits together
- b) occurs by interactions of different amino acids in the T and R forms
- c) occurs only my hydrophobic interactions
- d) uses the same amino acids regardless of the conformation of hemoglobin

Don't forget to be able to discuss the specific changes that occur to alter the hemoglobin affinity for oxygen. pH, CO<sub>2</sub> binding, CO binding BPG and the alternative forms of hemoglobin