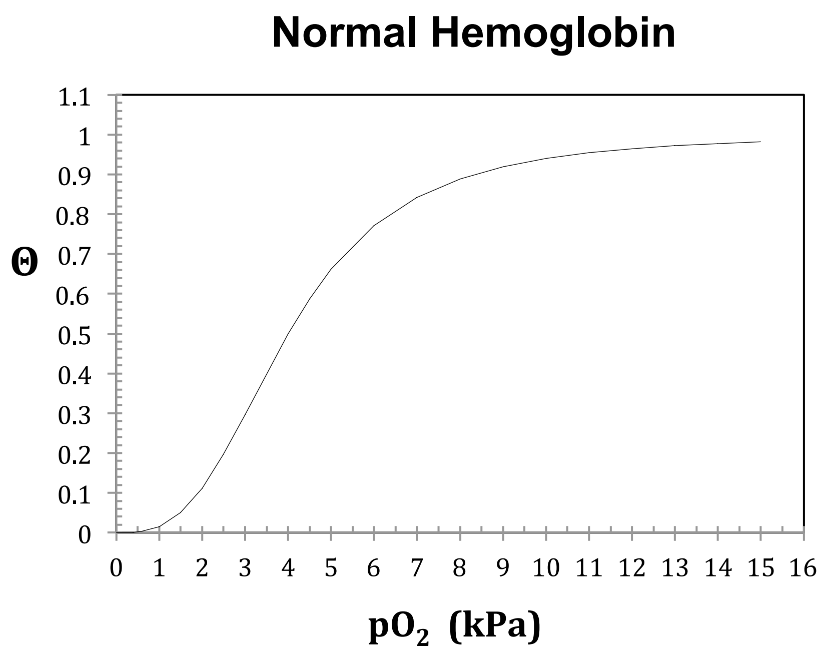
CHEM 4400 Name____________________

You may work in groups, everyone must turn in their own worksheet. This worksheet will also be posted on the web page. You may use your book and/or the internet. These are practice exam questions.

1. Here is a graph showing the binding of oxygen to normal hemoglobin. Answer the following questions based on this graph:



a. What does **Θ** (theta) represent?

b. What type of curve is this?
   i. Parabola
   ii. Hyperbola
   iii. Exponential
   iv. Sigmoidal

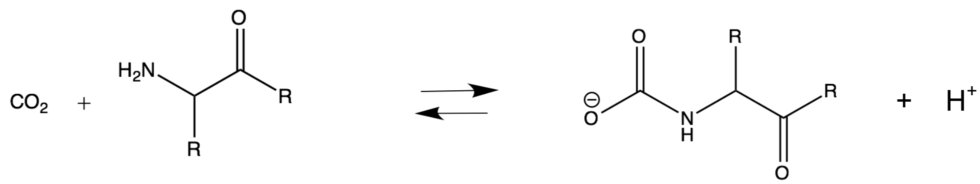
a. I and III b. II and IV c. I, II and III d. IV only e. none of these

c. What percent of hemoglobin molecules are bound to oxygen at pO_2 = 12 kPa

d. What percent of hemoglobin molecules are bound to oxygen at pO_2 = 4 kPa

e. If the lung pO_2 is 12 kPa and the tissues are at 4 kPa, what percent of pO_2 was delivered to the tissues?

2. The Bohr effect: hemoglobin also picks up hydrogen ions and carbon dioxide in the tissues. (This is like molecular carpooling.) About 20% of the carbon dioxide that is produced in the tissues (from burning fuel) is transported on the hemoglobin molecule. The carbon dioxide reacts with the free carboxylate group at the carboxy terminus of each hemoglobin subunit. This reaction produces a carbaminino group on each peptide and releases a proton that also needs a ride. This reaction is reversible:



   a. How many carbon dioxide molecules can bind to each hemoglobin?

   b. How does the other 80% of carbon dioxide move from the tissues to the lungs?

   c. Which side of the above equilibrium reaction predominates in the tissues? Why?

   d. Which side of the above equilbrium reaction predominates in the lungs? Why?

   e. These carbamino groups form salt bridges that stabilize the T form. What effect does that have on the affinity of hemoglobin for oxygen in the tissues?

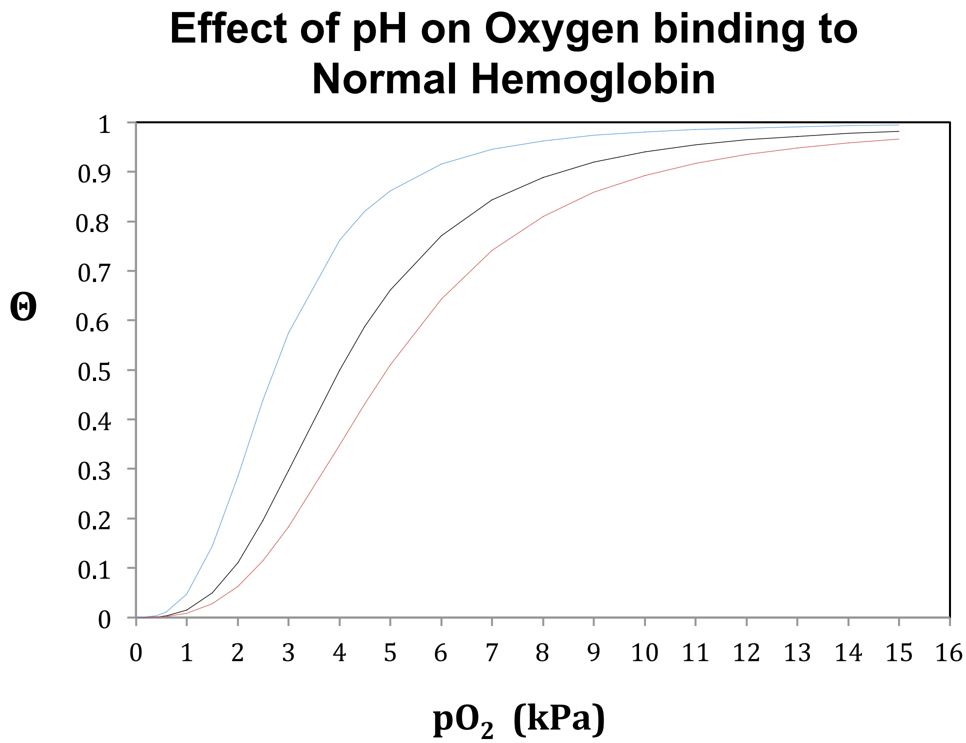
3. More Bohr: now what about those hydrogen ion passengers? Where are they riding? The hydrogen ions produced in the tissues, are picked up by histidines in hemoglobin. There is one very important histidine: His^{146}, which is located on helix H, 3 residues from the carboxy terminus, (HC3) on the beta subunits. When it is protonated, it forms a salt bridge with Asp^{94}, which is the first amino acid in the linker region between helix F and G, (FG1). The formation of this salt bridge stabilizes the protonated form of histidine and thus increases its pKa. (Remember larger $\Delta G° = -RT\ln K_{eq}$, thus an increase in $\Delta G°$ will decrease the Ka).

   a. Draw the energy diagram for the equilibrium of histidine in the lungs (no salt bridge) and then add the energy diagram for histidine in the tissues (with salt bridges.)

Free energy

Reaction (reactants → products)

b. The following graph shows the effect of pH on the binding of oxygen to hemoglobin. Remember that salt bridges stabilize the T form and the T form has less affinity for oxygen. Label the lines for pH 7.2, 7.4, 7.6.

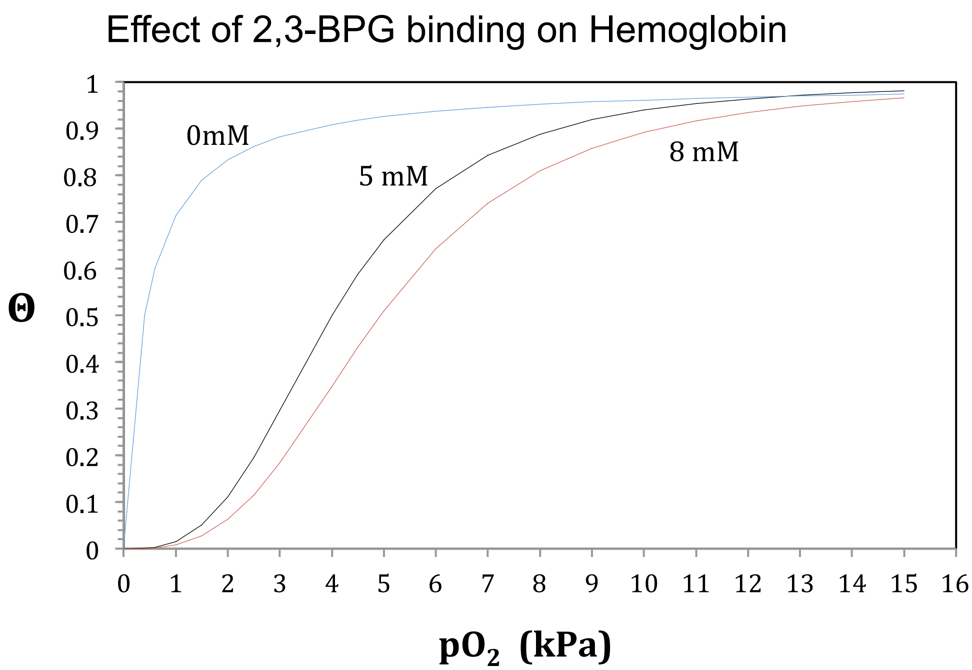


c. What is the pH of the lungs?

d. What is the pH of the tissues?

e. If carbon dioxide does not leave the lungs (there is plenty of Oxygen, but no ventilation to remove excess carbon dioxide), the carbamino product will predominate in the lungs and this will stabilize salt bridges that stabilize the T form. The pH will remain low as well (see reaction in #3), what effect will this have on the function of hemoglobin? Will the hemoglobin deliver more or less oxygen to the tissues? Explain your answer.

4. At high altitudes a person can become light headed, fatigued and nauseous. These effects are exacerbated upon exertion, and can be very dangerous. This effect is due to a lower concentration of oxygen in the air at high altitudes. The body adjusts by making additional red blood cells, so more oxygen can be delivered at the tissues (each hemoglobin delivers about 30% of the oxygen that is bound to it.) But that takes several days, and who wants to wait precious vacation days before having fun on the slopes? The more immediate response (about 8-12 hours) is for the red blood cells to increase their concentration of 2,3BPG (by diverting glucose in the glycolysis pathway.) The following graph shows the binding curves for three concentrations of 2,3 BPG.



a. What does BPG do to hemoglobin? (How does it interact, what is stabilized?)

b. Compare the amount of oxygen delivered to the tissues at each concentration of BPG at sea level, the partial pressure of oxygen gas in the lungs is 12 kPa, the partial pressure of oxygen In the tissues is 4kPa.

   i. 5 mM 2,3-BPG

   ii. 8 mM 2,3-BPG

c. Compare the amount of oxygen delivered to the tissues at each concentration of BPG at 9800 ft (the summit Kirkwood), the partial pressure of oxygen gas in the lungs is 7.3kPa.

   i. 5 mM 2,3-BPG

   ii. 8 mM 2,3-BPG

5. Fetal hemoglobin does not have beta chains, instead it has two gamma subunits and two alpha subunits. This fetal tetramer (HbF) does not bind 2,3-BPG. The "0 mm BPG" curve represents the oxygen binding to HbF. Why does the fetus require this type of binding curve? (See also problem #7 in our text.)