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|---|---|---|
| rate forward = $k_{\text{forward}}[\text{reactants}]$<br>rate reverse = $k_{\text{reverse}}[\text{products}]$   | Carbonic acid $K_a = 1.6 \times 10^{-4}$<br>$K_{\text{eq}}$ for the reaction of carbon dioxide with water = $1.69 \times 10^{-3}$   | Hydrogen carbonate $K_a = 4.68 \times 10^{-11}$   |
| $K_{\text{eq}} = \frac{[\text{products}]}{[\text{reactants}]}$<br>$\Delta G = \Delta H - T\Delta S$<br>$\Delta G = \Delta G^{\circ} + RT \ln Q$<br>$Q = \frac{[\text{products}]}{[\text{reactants}]}$ | Phosphoric acid $K_a = 7.25 \times 10^{-3}$<br>Dihydrogen phosphate $K_a = 1.38 \times 10^{-7}$<br>Monohydrogen phosphate $K_a = 3.98 \times 10^{-13}$<br>Acetic acid $K_a = 1.78 \times 10^{-5}$ | $k = \frac{kT}{h} e^{-\Delta G^{\ddagger}/RT}$<br>$k = 1.381 \times 10^{-23} \text{ J/K}$<br>$h = 6.626 \times 10^{-34} \text{ J*sec}$<br>$R = 8.315 \text{ J/mol*K}$ |

**Multiple choice, 3 points each: Circle the correct answers on this test.**

- What are the conditions that are used to determine  $\Delta G^{\circ}$  ?
  - T= 298, P = 1 atm, Concentrations are 1M
  - T= 37°C, P = 1 atm, Concentrations are 1M, except  $[\text{H}_3\text{O}^+] = 1 \times 10^{-7}\text{M}$
  - T = 25°C, P = 1 atm, Concentrations are 1M, except  $[\text{H}_3\text{O}^+] = 1 \times 10^{-7}\text{M}$
  - T= 37°C, P = 1 atm, Concentrations are 1M
  - None of these, the correct conditions are \_\_\_\_\_
- In an aqueous solution, protein folding is driven to the most stable conformation. Which of the following is/are major factors that drive protein folding:
  - formation of the maximum number of hydrophilic interactions.
  - maximization of hydrogen bonds
  - placement of polar amino acid residues around the exterior of the protein.
  - maximization of entropy of bulk water molecules

A.) I and III      B.) II and IV      C.) I, II and III      D.) IV only      E.) None of these
- What effect does carbonic anhydrase have on the equilibrium concentrations of carbon dioxide, water and carbonic acid?
  - Carbon dioxide increases
  - Carbon dioxide decreases
  - Carbonic acid increases
  - Carbon dioxide does not change

A.) I and III      B.) II and IV      C.) I, II and III      D.) IV only      E.) None of these
- Which of the following binding constants is for a protein that has the highest affinity for its ligand?
 

A.)  $K_a = 1.0 \times 10^8$       B)  $K_d = 1.0 \times 10^{-10}$       C)  $K_d = 1.5 \times 10^9$       D)  $K_a = 2.0 \times 10^{-8}$   
E) None of these, they are all the same
- Which of the following statements is/are correct?
  - Almost all amino acids in proteins have trans peptide bonds
  - Almost all amino acids in proteins have cis peptide bonds
  - Proline in B turns has a cis peptide bond
  - Proline in a B turn has a trans peptide bond

A.) I and III      B.) II and IV      C.) I, II and III      D.) IV only      E.) None of these

- 6) Carbon monoxide is a deadly colorless, odorless gas. What makes it so deadly?
- a) CO binds 200 times tighter than O<sub>2</sub> binds to hemoglobin
  - b) CO binds 20,000 times tighter than O<sub>2</sub> binds hemoglobin
  - c) CO causes the heme group to dissociate from hemoglobin causing severe anemia
  - d) CO increases the affinity of hemoglobin for O<sub>2</sub>.
  - e) None of these

**Fill in the blanks:**

- 7) (10 points) What filamentous protein (elastin, collagen, keratin) fits each description? Write the name of a filamentous protein in each blank.

- a) Contains proline and hydroxyproline \_\_\_\_\_
- b) Has two alpha helices twisted in a left handed coiled coil \_\_\_\_\_
- c) Provides protection \_\_\_\_\_
- d) Has  $\beta$  sheets \_\_\_\_\_
- e) Has lysine crosslinks between coiled coils \_\_\_\_\_
- f) Provides structural support to skin and bones \_\_\_\_\_
- g) Has a high amount of glycine \_\_\_\_\_
- h) Has three alpha chains twisted in a right handed coiled coil \_\_\_\_\_
- i) Has no glycine \_\_\_\_\_
- j) Has disulfide linkages between coiled coils \_\_\_\_\_

- 8) (4 points) Write the name of a protein that does the following:

- a) Catalyzes peptide bond isomerization \_\_\_\_\_
- b) Catalyzes disulfide bond interchange \_\_\_\_\_
- c) Prevents denaturation of proteins due to increased temperature \_\_\_\_\_
- d) Hydrolyzes ATP and folds proteins via an elaborate multisubunit complex  
\_\_\_\_\_

**Short answer section (4 points each) : Give specific details in brief answers.**

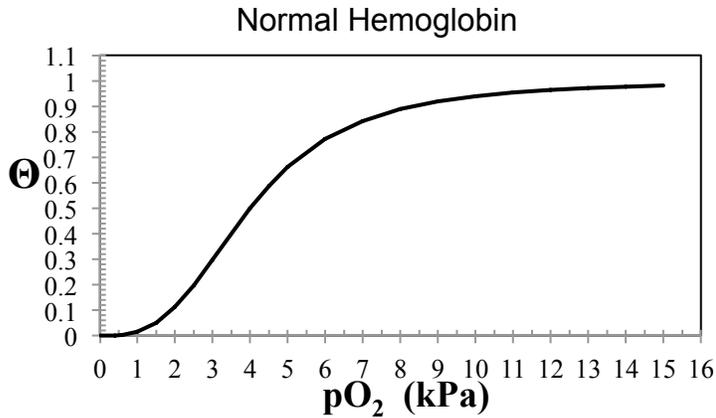
- 9) What two amino acids are commonly found in the middle of  $\beta$  turns? Why are these two amino acids present in  $\beta$  turns?

- 10) The three dimensional structure of a biochemical macromolecule is formed and maintained by noncovalent interactions. What are three types of intermolecular forces? For each type of IMF, give an example of a pair of amino acids that could have that IMF.
- 11) Where are the amino acid R (side chains) groups in an alpha helix? Draw a picture of an alpha helix and show where the side chains are located.

**This section requires longer answers, be specific and give details, show your work.**

- 12) (10 points) The rate of an uncatalyzed reaction is 0.2M/sec. With an enzyme, the new rate is  $15 \mu\text{M}/\text{sec}$ . The concentration of the reactants was 10mM for each experiment. How much did the enzyme decrease the energy of activation? (What is the difference in the two energies of activation?)

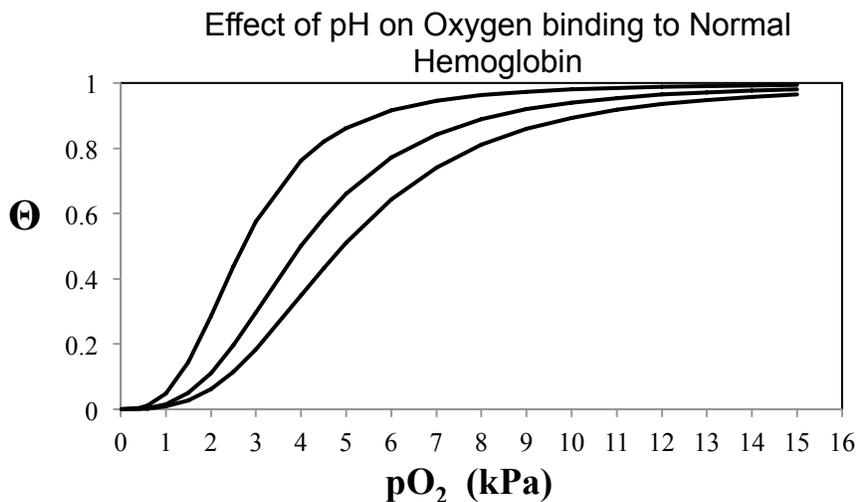
13)(6 points) Here is a graph showing the binding of oxygen to normal hemoglobin. Answer the following questions based on this graph:



- a. What does  $\Theta$  (theta) represent?
- b. What type of curve is this?
- c. If oxygen is bound in the lungs at  $pO_2 = 12$  kPa, and delivered to the tissues at  $pO_2 = 4$  kPa, what fraction of the bound  $O_2$  was delivered?

14) (10 points) The following graph shows the effect of pH on the binding of oxygen to hemoglobin. Each line shows the data for a different pH.

- a) Label the lines for pH 7.2, 7.4, 7.6.



- b) What is the pH of the lungs?
- c) What is the pH of the tissues?
- d) Explain why there are different curves depending on the pH. What affect does pH have on the affinity of hemoglobin for oxygen? How does pH change Oxygen binding. Give specific details about the structure that is related to the function.

15) (10 points) About 20% of the carbon dioxide that is produced in the tissues (from burning fuel) is transported on the hemoglobin molecule.

(a) How is carbon dioxide transported on hemoglobin? (Give specific molecular details.)

(b) How many carbon dioxide molecules can bind to each hemoglobin molecule?

(c) How does the other 80% of carbon dioxide move from the tissues to the lungs?

(d) How does carbon dioxide affect the affinity of hemoglobin for oxygen?

(e) If carbon dioxide does not leave the lungs (there is plenty of Oxygen, but no ventilation to remove excess carbon dioxide), what effect will this have on the function of hemoglobin? Will the hemoglobin deliver more or less oxygen to the tissues? Explain your answer.

16) (10 points) There is one histidine: His<sup>146</sup>, which is located on helix H, 3 residues from the carboxy terminus, (HC3) on the beta subunits. In the tissues, its pKa = 8.1. In the lungs, this histidine has its regular pKa (the value that was memorized.)

a. Draw the complete structure of histidine showing the equilibrium between the protonated and deprotonated forms.

b. Draw the energy diagram for the equilibrium of histidine in the lungs and then add the energy diagram for histidine in the tissues.

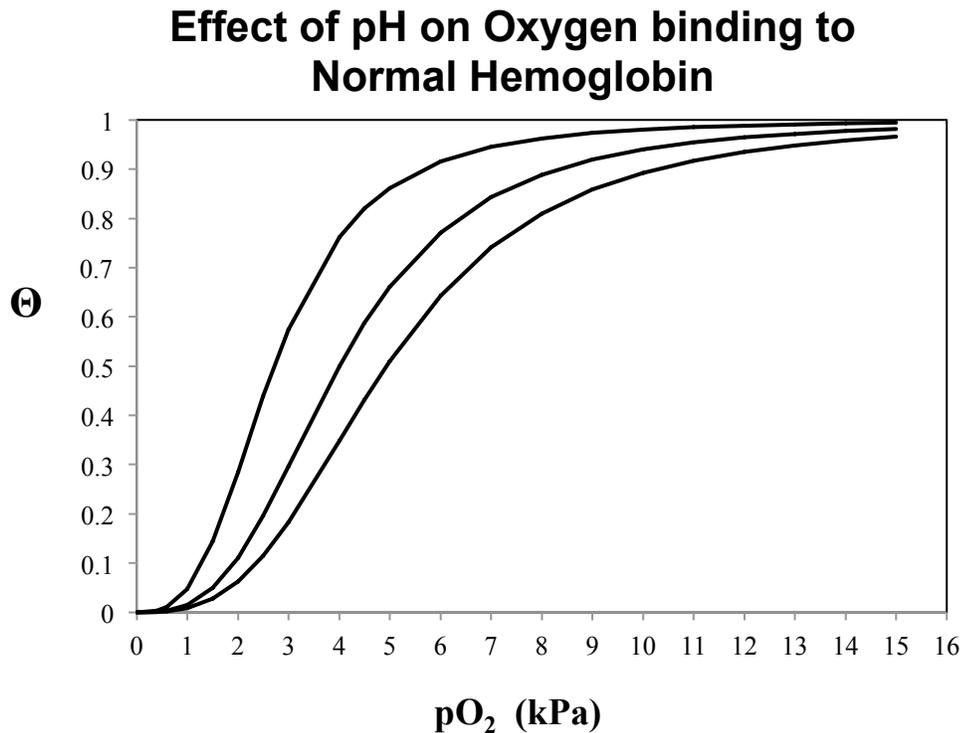
Free energy



Reaction →

c. Explain why this histidine has two different pKa values

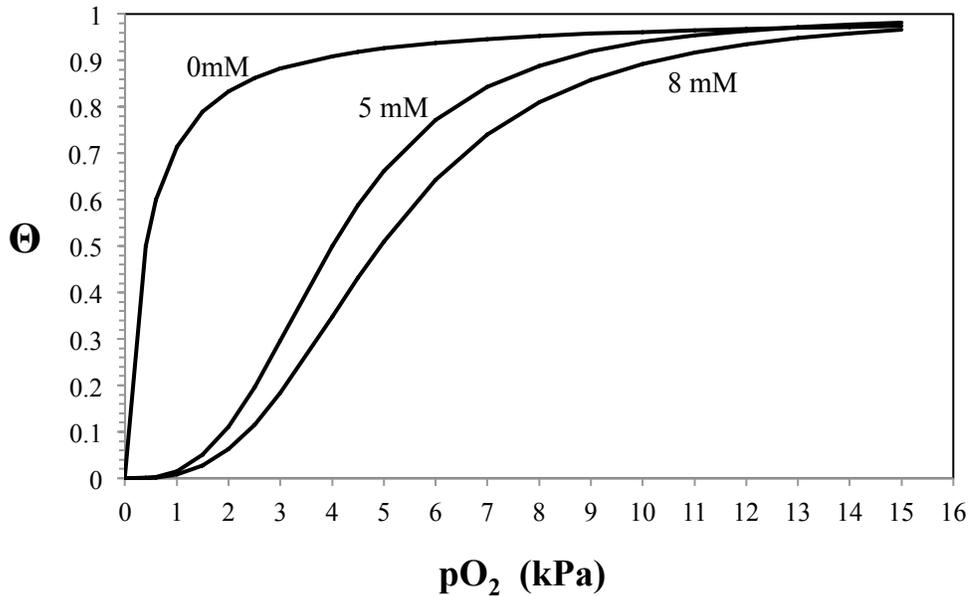
- 17) (10 points) The following graph shows the effect of pH on the binding of oxygen to hemoglobin. Each line shows the data for a different pH. Label the lines for pH 7.2, 7.4, 7.6.



- What is the pH of the lungs?
- What is the pH of the tissues?
- Explain why there are different curves depending on the pH. What affect does pH have on the affinity of hemoglobin for oxygen?

- 18) (10 points) 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 2,3-BPG (by diverting glucose in the glycolysis pathway.) The following graph shows the binding curves for three concentrations of 2,3 BPG.

## Effect of 2,3-BPG binding on Hemoglobin



- What does BPG do to hemoglobin? (How does it interact, what is stabilized?)
  - 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.
    - 5 mM 2,3-BPG
    - 8 mM 2,3-BPG
  - Compare the amount of oxygen delivered to the tissues at each concentration of BPG at 11,300 ft (the summit at Vail, CO), the partial pressure of oxygen gas in the lungs is 6.5 kPa.
    - 5 mM 2,3-BPG
    - 8 mM 2,3-BPG
2. 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?