

NAME _____ **Key**

**MMBB 300 - FALL 2006
EXAM 2**

**You may not use a calculator for this exam.
Please read and answer each question carefully. Good Luck!**

(6,000 pts)

3) What is the minimum number of amino acids that can participate in the β -turn of a protein? (Hint: think about how the β -turns use hydrogen bonding for stabilization)

- A. Three -3 k pts
- B. Four
- C. Five -3 k pts
- D. Six
- E. Seven

(6,000 pts)

4) What is the quaternary structure of a protein? Use either titin or hemoglobin to illustrate your definition.

Quaternary structure refers to the spatial arrangement of subunits within a protein complex; i.e. spatial arrangement of the 4 subunits within the Hb protein. Alternatively, it can also be the spatial arrangement of separate domains within a single continuous polypeptide; i.e. titin is a very large protein that contains many globular domains that are linked by flexible stretches of polypeptide. The quaternary structure refers to the spatial arrangement of these domains.

(12,000 pts)

5) Creatine phosphate (phosphocreatine) can undergo the following reaction.



The enzyme that catalyzes this reaction would be best classified as a:

- A. Oxidoreductase
- B. Ligase
- C. Hydrolase (worth 6,000 pts)
- D. Lyase
- E. Transferase -3 k pts

If you had a solution where $[\text{creatine phosphate}] = [\text{creatine}] = [\text{P}_i] = 1.0 \text{ M}$ and then added this enzyme, you would expect:

- A. a net reaction of left-to-right (forward)
- B. no net reaction
- C. a net reaction of right-to-left (reverse)
- D. that the net direction of the reaction can not be determined from this information

(8,000 pts)

6) What metal is found at the center of the myoglobin prosthetic group? What is the biologically active oxidation state of the metal?

Fe²⁺

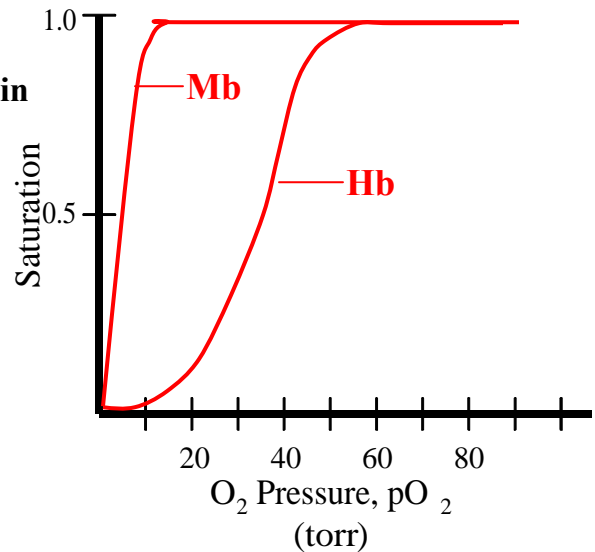
In reference to proteins, what is the general definition of a prosthetic group?

Nonpolypeptide unit or molecule that must bind the protein to confer biological activity.

(8,000 pts)

7) Using this diagram, carefully illustrate how O₂ binding differs between myoglobin and hemoglobin

Label any lines drawn.



(6,000 pts)

8) Which of the following molecules compete with O₂ for the *same* binding site in hemoglobin? Circle all that apply.

- A. CO All the others exert allosteric control over O₂ binding, not direct competition
- B. CO₂
- C. H⁺
- D. 2,3-bisphosphoglycerate (2,3 BPG)

(8,000 pts)

9) Describe the role of the proximal histidine in the biological function of hemoglobin. What role, if any, does the proximal histidine play in the cooperative binding of O₂?

Proximal His: Binds directly with the Fe²⁺ in the heme. The binding of O₂ to Fe²⁺ flattens the plane of the heme and pulls the proximal His and its helix. This results in a conformational change which increases O₂ binding in the other three subunits.

Distal His: forces bent geometry of CO & O₂ binding; this weakens CO binding but does not weaken O₂ binding

(6,000 pts)

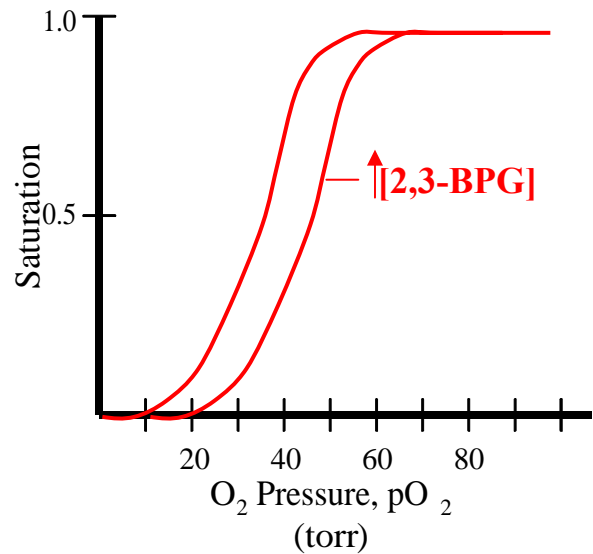
10) The alpha (α) and beta (β) subunits of adult human hemoglobin:

- A. have nearly identical primary and tertiary structures -3 k pts
- B. have nearly identical primary structures, but very different tertiary structures
- C. have very different primary structures, but very similar tertiary structures
- D. have very different primary and tertiary structures

(6,000 pts)

- 11) Using this diagram, carefully illustrate how an increase of 2,3 bisphosphoglycerate will affect the binding of O₂ to hemoglobin. Identify any lines drawn.

With increased 2,3-BPG, the sigmoidal curve shifts to the right



(6,000 pts)

- 12) According to the Bohr Effect, increased partial pressure of CO₂ has what affect on hemoglobin? Circle all that apply.

- A. favors the T state of hemoglobin
- B. favors the R state of hemoglobin
- C. enhances binding of O₂ to hemoglobin
- D. enhances release of O₂ from hemoglobin
- E. none of the above

(9,000 pts)

- 13) Sickle cell anemia is considered a molecular disease.

- A. Which molecule is defective in this disease? The β subunit of adult hemoglobin
- B. How does the defective molecule differ from the normal (wild-type) molecule?
Amino acid # 6 is altered; Glu₆ becomes Val₆
- C. How does this defect give rise to sickled or abnormally shaped cells?

When the pO₂ is low enough so that the hemoglobin is completely deoxygenated, a second hydrophobic domain is revealed. The hydrophobic Val-6 interacts with the 2nd hydrophobic domain from another Hb. If the second Hb is also HbS, it too can bind another Hb. This continues until large aggregates form to the point of distorting the cell into elongated or tortured shapes.

(6,000 pts)

14) A deficiency in dietary Vitamin C results in which human disease condition?

scurvy

Which post-translational protein modification is specifically disrupted by lack of Vitamin C?

hydroxylation

(6,000 pts)

15) Examination of a human patient who died prematurely due to Cruetzfeld-Jacob Disease (CJD) reveals structural information regarding both the infectious and noninfectious forms PrP protein. These two proteins would be expected to:

- A. have nearly identical primary and tertiary structures -3 k pts
- B. have nearly identical primary structures, but very different tertiary structures**
- C. have very different primary structures, but very similar tertiary structures
- D. have very different primary and tertiary structures

(6,000 pts)

16) An enzyme, E, catalyzes the reaction: $A + B \rightleftharpoons C + D$

Identify how addition of E would affect the free energy associated with this reaction. Mark one category each for A, B & C.

	Decrease	No change	Increase
A. Gibb's Free Energy of reaction (ΔG)	_____	<u>X</u>	_____
B. standard Gibb's Free Energy of reaction (ΔG°)	_____	<u>X</u>	_____
C. Gibb's Free Energy of activation (ΔG^\ddagger)	<u>X</u>	_____	_____

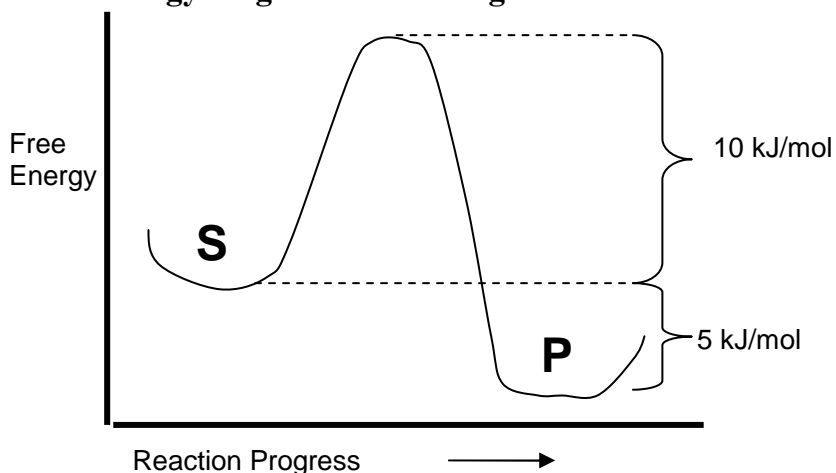
(7,000 pts)

17) Briefly describe Koshland's Induced Fit Model of enzymes.

The structure of free substrate and empty active site are not a perfect complementary match for one another. Instead, substrate binding induces a conformational change at the binding site of the enzyme; the enzyme can also cause conformational changes within the substrate.

(10,000 pts)

17) The following is a free energy diagram illustrating the chemical reaction: $S \rightleftharpoons P$.



The change in free energy of activation of S being converted to P would be:

- A. -15 kJ/mol
- B. -10 kJ/mol -2.5 k pts
- C. -5 kJ/mol
- D. 0 kJ/mol
- E. +5 kJ/mol
- F. +10 kJ/mol**
- G. +15 kJ/mol -2.5 k pts

The change in free energy of activation of P being converted to S would be:

- A. -15 kJ/mol -2.5 k pts
- B. -10 kJ/mol
- C. -5 kJ/mol
- D. 0 kJ/mol
- E. +5 kJ/mol
- F. +10 kJ/mol -2.5 k pts
- G. +15 kJ/mol**

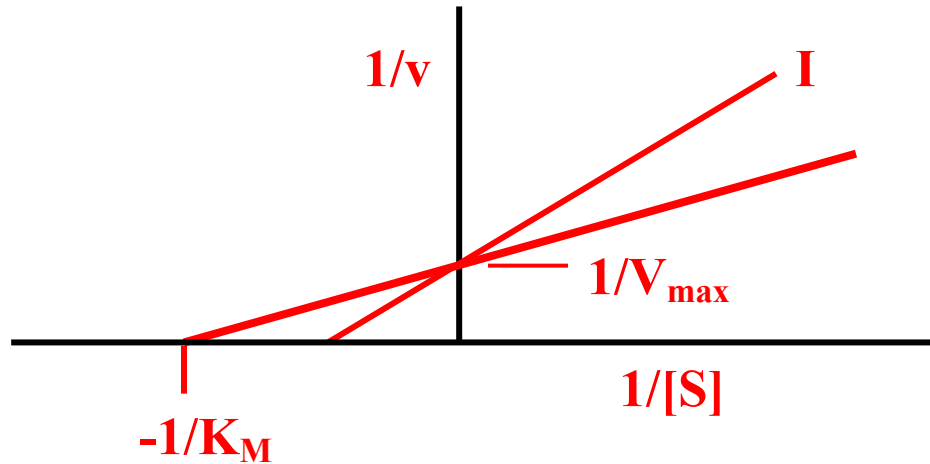
(6,000 pts)

18) *Briefly* describe how a MALDI mass spectrometer (MS) ionizes and transfers peptides to a gas phase.

MALDI = Matrix-assisted LASER desorption ionization. MALDI uses a LASER to simultaneously ionize and vaporize the peptides.

(12,000 pts)

- 19) Use the following axes to diagram a double reciprocal (Lineweaver-Burk) plot for an enzyme catalyzed reaction, $S \rightleftharpoons P$. Label both axes and show how this diagram can be used to determine V_{\max} and K_M . Show how a competitive inhibitor would affect this plot.



(6,000 pts)

- 20) You identify a non-competitive inhibitor for an enzyme that follows Michaelis-Menten kinetics. You would expect this inhibitor to alter K_M and/or V_{\max} as follows. Circle all that apply.

- A. increase K_M
- B. decrease K_M
- C. increase V_{\max} -4 k pts
- D. decrease V_{\max}

(6,000 pts)

- 21) The fastest known enzyme can turn over how many reactions per second?

- A. 40,000
- C. 400,000
- D. 4,000,000 -3 k pts
- E. 40,000,000

(6,000 pts)

22) ~~Under standard conditions, the change in Gibb's free energy of reaction for hydrolysis of the gamma phosphate of ATP (producing ADP) is:~~

~~-30.5 kJ/mol~~

Thrown out because this was not covered in class; 380 covered it in the extra hour.

(6,000 pts)

23) The ratio of k_{cat}/K_M for an enzyme is considered to be:

- A. a direct measure of affinity between substrate and enzyme
- B. the catalytic efficiency when substrate is much less than K_M**
- C. inversely proportional to V_{max}
- D. the fraction of sites filled with substrate

(6,000 pts)

24) A suicide inhibitor like penicillin is best characterized as a/an:

- A. competitive inhibitor **-3 k pts**
- B. noncompetitive inhibitor
- C. uncompetitive inhibitor
- D. irreversible inhibition**

(10,000 pts)

25) Provide the Michaelis-Menten equation describing enzyme kinetics.

$$v = V_{max} \frac{[S]}{K_M + [S]}$$

Which of the terms, if any, in this equation vary as the concentration of enzyme varies?

v & V_{max}

(6,000 pts)

26) What is the k_{cat} of an enzyme? Provide a single name and a definition.

Turnover

Defintion:

The maximum # of reactions that a single enzyme can catalyze in a single sec.

Bonus Question (8,000 pts)

A common type of osteogenesis imperfecta (brittle bone disease) results from a specific mutation of one collagen gene that results in a single amino acid substitution that weakens the collagen fibers found in bone. Identify which of the 20 common amino acids is most likely altered in the mutated state and explain the rationale behind your decision.

Based on lecture, one could make an argument for glycine, proline or lysine. Glycine is, in fact, the culprit because the triple helix requires every third amino acid be Gly because the side chain sticks directly into the middle of the triple helix. Since there isn't any room inside the triple helix, even a substitution of Ala for Gly disrupts the structure and can significantly weaken the collagen fibers.

Page #	Points Possible	Points
2	20,000	
3	32,000	
4	28,000	
5	21,000	
6	25,000	
7	16,000	
8	24,000	
9	34,000	
Bonus	8,000	
Total	200,000	