Name _____

Chem 352 - Spring 2011 - Exam II

Potentially useful information:

pK_a values for ionizable groups in proteins: (*α-carboxyl*, 3.1; *α-amino*, 8.0; *Asp* & *Glu* side chains, 4.1; *His* side chain, 6.0; *Cys* side chain, 8.3; *Tyr* side chain, 10.9; *Lys* side chain, 10.8; *Arg* side chain, 12.5)

$R = 8.314\ J/(mol \bullet K) = 0.08206\ (L \bullet atm)/(mol \bullet K$

1. In class, we discussed four levels of hierarchy in the structures or proteins.
   a. Describe the role that protein secondary structure plays in conjunction with the other levels in this hierarchy.

   b. The myoglobin molecule is homologous with the four subunits of the hemoglobin molecule. In comparing the functions of these two proteins, discuss how the presence of quaternary structure in hemoglobin makes it better suited to its function in comparison to myoglobin.

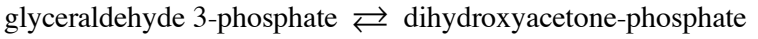
2. Which of the following non-covalent interactions that stabilize protein tertiary structure, *vander Waals*, *hydrogen bonding* and *ionic*, can the side chains of each of the following amino acids contribute to at *pH*7?
   a. Ile:

   b. Arg:

   c. Tyr:

   d. Ser:

3. Triose phosphate isomerase catalyzes the conversion of glyceraldehyde-3-phosphate to dihydroxyacetone phosphate



The K_M of this enzyme for the substrate glyceraldehyde 3-phosphate is 1.8 x 10^{-5} M. When the concentration of glyceraldehyde-3-phosphate is 30 μM, the rate of the reaction, v_o, is observed to be 82.5 μmol/mL•s

a. Use structural formulas to write the chemical equation for this reaction.

b. What class of enzymes does triose phosphate isomerase belong to?_____

c. Assuming this enzyme exhibits Michaelis Menton kinetics, what is the V_{max} for this enzyme catalyzed reaction? _____

d. Assuming that the total enzyme concentration used in this experiment was 3 nM, how many reactions per second does this enzyme catalyze when operating at its maximum velocity?

e. Is the catalytic efficiency of this enzyme limited by the rate at which substrate diffuses into the active site?

4. Myoglobin contains eight α-helices, one of which has the following sequence:

...-Gln-Gly-Ala-Met-Asn-Lys-Ala-Leu-Glu-His-Phe-Arg-Lys-Asp-Ile-Ala-Ala-...

a. Circle the residues with side chains that are more likely to be on the side of the helix that faces the interior of the protein.

b. Underline the residues with side chains that are more likely to face the aqueous exterior of the protein.

c. Account for the spacing of the residues facing the interior:

5. In class, we examined in detail the step-by-step mechanism for the reaction that is catalyzed by the serine protease *chymotrypsin.* We saw that it provides a number of examples of the different strategies used by enzymes to increase the rates for enzyme-catalyzed reactions.

   a. For the players listed below from chymotrypsin, use one or two complete sentences to describe the contribution that each makes to implementing one of these strategies:

      - Serine-195

      - Aspartate-102

      - Histidine-57:

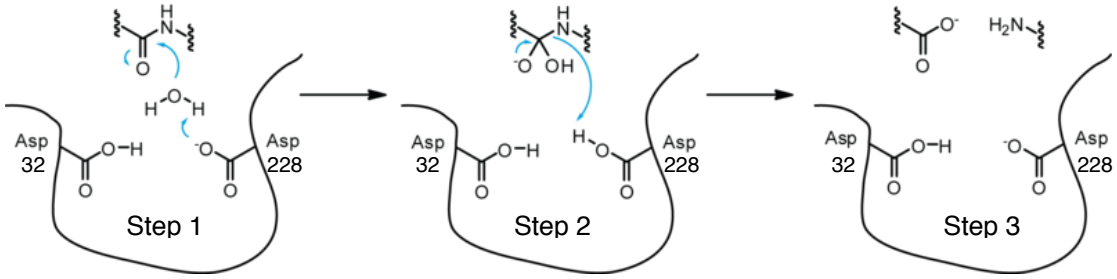
      - The oxyanion "hole"

   b. Of the strategies we discussed in class, which typically makes the greatest contribution to the increased rate relative to the uncatalyzed reaction?

6. Draw a representative structure for a portion of glycogen that is large enough to illustrate the two possible types of glycosidic bonds found in glycogen. Also circle the monosacharide in your structure that is closest to the reducing end of the glycogen molecule.

7. There are a number of serine residues in α-chymotrypsin, but only serine-195 reaate repidly when the enzyme is treated with the irreversible inhibitor disopropyl fluroophosphate (DFP). Provide a possible explanation for this observation.

8. β-Secretase is an aspartic-acid protease that is involved in the pathogenesis of Alzheimer's disease. The figure below illustrates the three steps in the pathway that cleaves a peptide bond, and which leads to the formation of the amyloid β-peptide.



a. What class of enzyme is β-secretase? _____

b. In terms of the modes of enzymatic catalysis that we discussed in class, describe the role that Asp-228 plays in Step1.

c. Which of these three steps represents the transition state, and what characteristics of this state might the enzyme take advantage of in order to stabilize the transition state and thereby enhance the overall reaction rate?

d. Sketch the expected *pH* activity profile (activity *vs pH*) for β-secretase, if the pK_a for Asp-228 is 2.1, while that for Asp-32 is 4.5. (Be sure to label the axes of your plot.)

e. At what *pH* value do you expect the activity to be maximum? _____

Extra Credit:

1. Ask the one question that you wanted me to ask, but I did not ask. (Up to 2 points will be awarded for an insightful, probing and well-worded question, which could be used on the Final Exam.)

2. Answer the question you posed in part 1. (Up to 1 point will be awarded for answering your question correctly.)