Name

This exam is schedule for 150 minutes and I anticipate it to take the full time allotted. You are free to leave if you finish. The exam is split into two sections. Part 1 is non-existent. Do nothing with it. Part 2 is composed of several short answer questions.

Amino Acid	α-carboxylic acid	α-amino	Side chain
Alanine	2.35	9.87	
Arginine	2.01	9.04	12.48
Asparagine	2.02	8.80	
Aspartic Acid	2.10	9.82	3.86
Cysteine	2.05	10.25	8.00
Glutamic Acid	2.10	9.47	4.07
Glutamine	2.17	9.13	
Glycine	2.35	9.78	
Histidine	1.77	9.18	6.10
Isoleucine	2.32	9.76	
Leucine	2.33	9.74	
Lysine	2.18	8.95	10.53
Methionine	2.28	9.21	
Phenylalanine	2.58	9.24	
Proline	2.00	10.60	
Serine	2.21	9.15	
Threonine	2.09	9.10	
Tryptophan	2.38	9.39	
Tyrosine	2.20	9.11	10.07
Valine	2.29	9.72	

1. DNA/RNA Structure
    a. Sketch a GC base pair as it would look in double stranded DNA. Do not abbreviate structures (i.e. show me a complete backbone with connectivity to adjacent monomer). You may draw the bases separately if you wish, just clearly indicate all hydrogen bonds. (15 pts)

    b. On the sketch above, indicate the major groove and minor groove (5 pts)

    c. Sketch an AU base pair as it would look in an RNA chain with the uracil bound to the **Hoogsteen** face of adenosine. You may draw the bases separately if you wish, just clearly indicate all hydrogen bonds. (15 pts)

    d. What base modification might promote this Hoogsteen interaction over a standard Watson-Crick base pair? Why? (5 pts)

2. Consider a peptide with the following sequence

CHARGES

a. Sketch a polymer composed of the first 4 amino acids in this peptide at **pH 8.0**. (10 pts)

b. What is the charge of CHARGES at pH 6.0? pKa values are available at the beginning of this exam (10 pts)

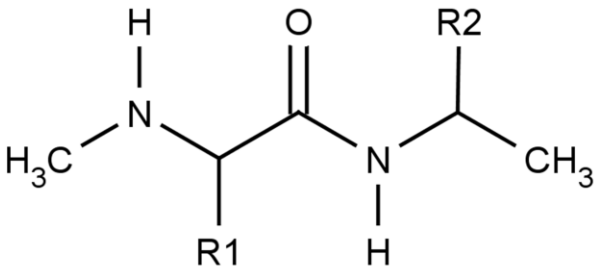
c. Calculate the pH at which CHARGES will have a net charge of 0. pKa values are available at the beginning of this exam (10 pts)

d. What residue on CHARGES is most likely to be phosphorylated? Draw the resulting structure of that amino acid. (5 pts)

3. The image below shows the common combinations of the peptide chain torsion angles θ and ψ.

   a. What is this plot called (2 pts)

   b. On the peptide below, indicate what bonds θ and ψ correspond to. (5 points)



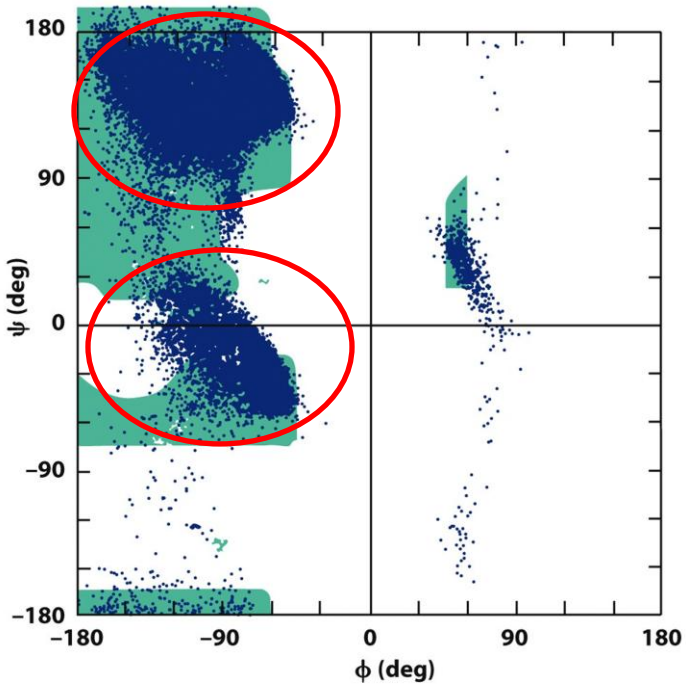


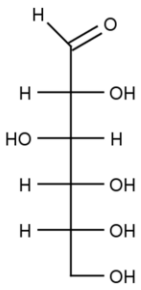
Figure 8-8
Courtesy of Scott Hollingsworth and Andrew Karplus, Oregon State University, Corvallis, Oregon

   c. Explain why peptide bonds are planar. (3 pts)

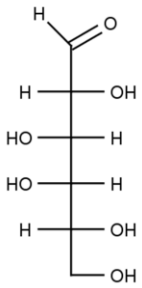
   d. Why are the two circled regions so densely populated? For full credit, your discussion should include more than just naming 2˚ structure. (10 pts)

   e. Describe differences in the **backbone** hydrogen bonding patterns between α-helices and β-sheets? (15 pts)

4. The Lac Repressor (LacI) is a transcriptional **repressor** that senses the intracellular concentration of lactose (β-D-galactose (1→4) D-glucose).
    a. Given the Fisher Projections below, please draw lactose in its cyclical form. (15 pts)



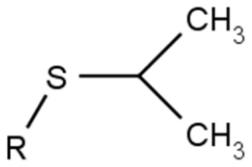
D-Glucose



D-Galactose

    b. Circle the reducing end if there is one. (2 pts)

    c. LacI is commonly used by biochemists to generate proteins in *E. coli*. In this case, isopropyl-β-D-1-thiogalactose (IPTG) is used to trick the LacI into disassociating from the RNA polymerase promoter. IPTG looks similar to lactose, however it replaces glucose with a S-isopropyl as seen in the image below (where 'R' is galactose). What does this tell you about the interaction between lactose and LacI? (3 pts)



    d. Lac I regulates the expression of β-galactosidase (LacZ) in *E. coli* in a process similar to repression by AraC. Describe how this process (transcriptional repression) works. Make a sketch if you like. Include any necessary information about RNA Polymerase binding to the promoter. (15 pts)

e. LacI uses an allosteric mechanism to function. Please discuss how allostery can play a role in lactose sensing. Feel free to make as many parallels to the hemoglobin model or your answer to part d as you like and/or include an image. (20 pts)

f. β-galactosidase is a **hydrolase** responsible for breaking lactose into glucose and galactose. Propose a mechanism for this process? Make sure to include an intermediate structure (transition state) and regenerate the active site if necessary. (10 pts)

g. Consider the transition state you proposed above. Speculate on how the enzyme active site might stabilize this intermediate. (5 pts)

5. Topoisomerase
    a. Describe the role(s) topoisomerase plays in DNA replication. Include why this is necessary for full credit. (5 pts)

    b. Part of the catalytic mechanism for this enzyme is an endolytic cleavage of the phosphodiester backbone of one strand of DNA. Why is this necessary? (5 pts)

    c. Propose a mechanism for this endolytic cleavage. Recall that the topoisomerase we discussed contains a critical tyrosine residue. (10 pts)

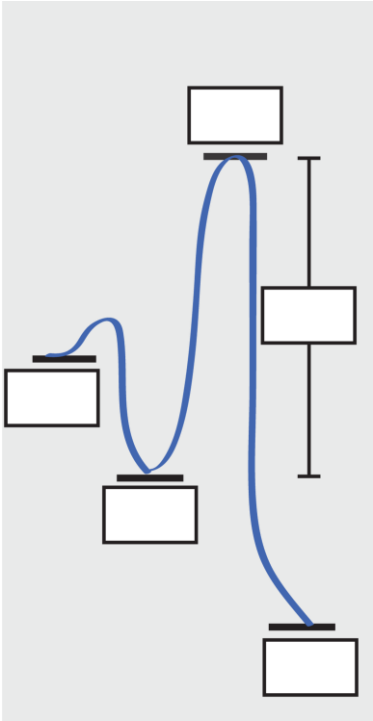
    d. You are a biochemist trying to verify that this specific tyrosine residue is important. You decide to mutate the tyrosine to another amino acid to investigate the changes in catalytic efficiency. What amino acid would you choose **and why**? There are a number of acceptable answers, but one more correct than others. (5 pts)

6. Enzyme Kinetics
    a. Write a complete chemical scheme, including the generation of any necessary intermediate(s), which describes enzyme kinetics (5 pts)

    b. Simplify your scheme to accommodate the standard assumptions of Michaelis-Menten kinetics. (10 pts)

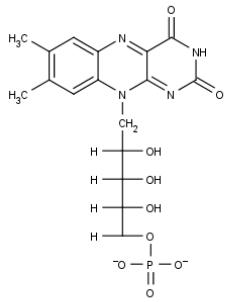
    c. In the scheme in part B, **circle** the part that is governs the turnover number (k_{cat}) and put a **box** around the part that dictates the catalytic efficiency. **Write out** the equilibrium (A ⇌ B) that the Michaelis Constant (K_M) describes. (10 pts)

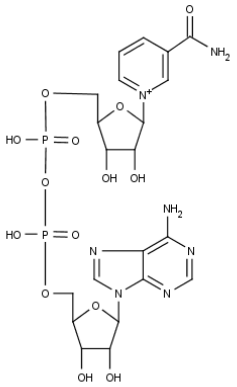
    d. Label the figure to the right with the appropriate component of the reaction (e.g. E+P). (10 pts)



7. Using the diagram above as a guide, discuss how each scenario influences enzyme kinetics. Make sure to label all important information and/or redraw the diagram as you see fit. Recall that $k = Ae^{-E_a/RT}$. (20 pts)
    a. Increased affinity of the enzyme for the substrate.
    b. Enzyme stabilizes the transition state more effectively.
    c. Both of the above.

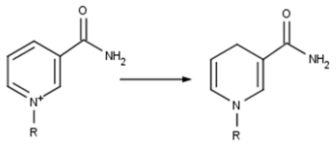
8. Shown are the oxidized forms of two cofactors we discussed. Name them and draw the reduced form. Feel free to use 'R' for any region not involved in redox. (10 pts)



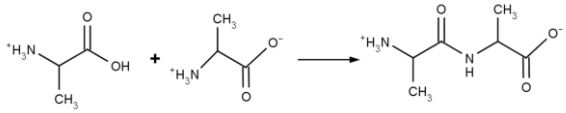


9. For each of the following reactions, indicate what **class of enzyme** is required to catalyze the reaction. Note that the reactions are not necessarily balanced (5 pts each)

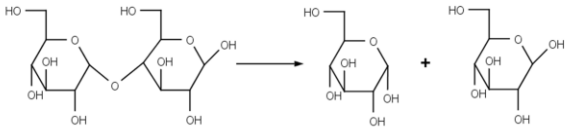
a.



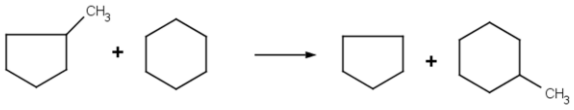
b.



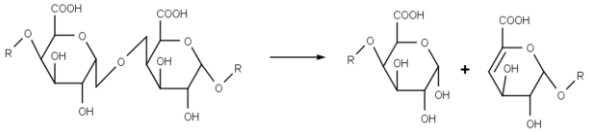
c.



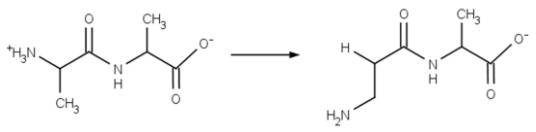
d.



e.



f.



Bonus (up to 15 points)

Select one process and describe it in as much detail as possible. The more **correct** and **relevant** information you include, but more bonus credit you will receive.

Transcription Translation Replication