**This exam consists of 95 points on 6 pages. Allot 1 min/2 pts.**

1A. (4 pts) True & false (circle the correct answer).

T or F: All 20 amino acids contain at least one chiral center.

T or F: The peptide bond is planar and usually *cis*.

T or F: Non-polar residues are found in the core of globular proteins due to van der Waals forces.

T or F: Disulfide bonds are usually found on *intra*-cellular proteins.

T or F: If the ligand concentration is less than $K_D$ then the fractional saturation is greater than 0.5.

T or F: Hydrogen bonds are seldom observed in protein-ligand interactions.

T or F: Ligands that differ in their $K_D$ values are more likely to have different kinetic on-rates.

T or F: At equilibrium, the concentration of the protein-ligand complex is constantly changing, or fluctuating.

1B. Fill in the blanks (2 pts).

a. The antigen binding _____loops are found on the _____ domains of the _____ and _____ chains in antibodies.

b. An antibody can be cleaved to produce _____ (a number) $F_{AB}$ fragments (1/2 pt).

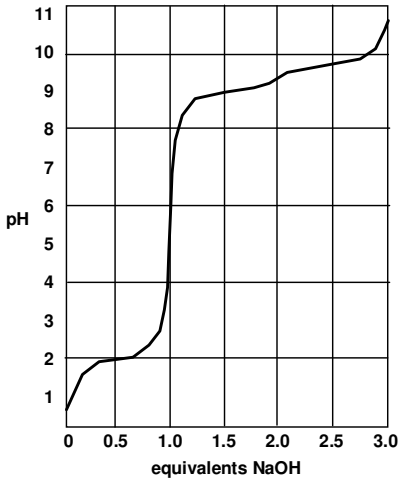
2. (10 pts) Hydrogen Bonds:

i) Define/describe the general structure of a hydrogen bond. You answer should include a description of donor and acceptor groups (4 pts).

ii) What chemical groups in a protein form main-chain hydrogen bonds? Illustrate your answer with a sketch. (2 pts).

iii) Briefly describe the importance of hydrogen bonds in stabilizing secondary structures of proteins (4 pts).

3. (5 pts) A titration curve for an amino acid is shown on the right.




i) What are the $pK_a$ values for each ionization (1 pt)?

ii) Briefly explain why weak acids act as buffers near their $pK_a$ values (4 pts).

4. (10 pts) Please do **one** of the following two choices. Both choices utilize **0.1 M** acetate ($pK_a$=5.0) as the buffer. Be sure to indicate the question that you are answering. *Use the back of the previous page for calculations.*

**Choice A:** Buffer construction, pH =4, starting with NaAcetate.

i) How many moles of NaAcetate would be needed to make 0.5 L of buffer? Please show your work (4 pts).

ii) If the desired pH of the buffer solution was 4.0, how many moles of HCl would have to be added to the solution of NaAcetate described in part i. Please show all of your work (6 pts).

**Choice B:** pH Adjustment, initial pH = 4, final pH = 6, restore to pH = 4.

i) What is the total number of moles of acetic acid and/or acetate in 0.5 L of this buffer (at any pH value)? Please show your work (4 pts).

ii) The initial pH of your acetate buffered reaction was 4.0. The pH rises to 6.0 during the course of the reaction. How many moles of HCl do you have to add to restore the pH to 4.0? (6 pts).

5. (10 pts) Draw the following dipeptide: Gly-Val, with the peptide bond in the *trans* conformation and in the correct ionization state for a pH of 6.0. If you do not know the structure of the sidechains for these amino acids, draw those that you do know, label them, and give the sequence of your modified peptide. Please do not use Glu, Phe, or Ile, as these are given elsewhere on the exam.

Label the following on your diagram:

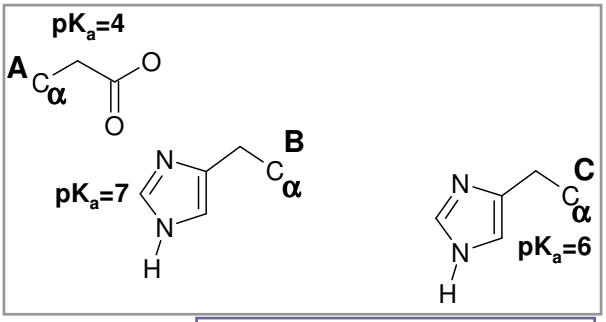
i) the amino terminus

ii) the carboxy terminus

iii) the peptide bond

iv) the single bonds corresponding to the phi and psi torsional angles (only one residue is necessary).

6. (12 pts) A protein contains three charged residues (A, B, C), the remaining residues are either polar or non-polar. The relative location of these three residues is shown in the diagram on the right, along with their $pK_a$ values.




i) Write the names of residues A and C next to their structure (1 pt).

ii) *Estimate* the fraction protonated for each group, assuming a pH of 6.0. Use the back of the preceding page for calculations or sketching graphs. (3 pts).

**A:**

**B:**

**C:**

$$pH = pK_a + \log\frac{[A^-]}{[HA]}$$

$$R = 10^{(pH - pKa)}$$

$$f_{HA} = \frac{1}{1+R} \qquad f_{A-} = \frac{R}{1+R}$$

iii) *Estimate* the net charge on this protein at pH=6.0, don't forget to include contributions from the amino terminus and the carboxy terminus. *Use the back of the previous page if you need additional space.* (4 pts)

iv)**Explain why the two chemically identical side chains have different $pK_a$ values, assume the group with the $pK_a$=6.0 has the same $pK_a$ as the free amino acid (2 pts). *Use the back of the previous page to answer this question.*

v) Where would you typically find residues of this type: on the surface, or in the core (*circle choice*)? (2 pts).

7. (8 pts) Please do **one** of the following **two** choices, *the second choice is found on the following page*.

**Choice A:** A peptide was digested with Chymotrypsin. The peptides from this digest were separated and the sequence of the first five residues of each peptide were determined using Edman degradation, giving the following result:

*Ala-Arg-Asp-Phe* *Ser-Gly-Met-Lys-Val*

A new sample of the peptide was cleaved with cyanogen bromide, and the first five residues of each peptide were:

*Ala-Arg-Asp-Phe-Ser* *Lys-Val-Leu-Ser*

A new sample of the same peptide was cleaved with trypsin, and the first five residues of each peptide were:

*Ala-Arg-Asp-Phe-Ser* *Val-Leu-Ser*

What is the complete amino acid sequence of the peptide (you should check your answer to verify that it would account for the above data)?

**Choice B:** A protein does not contain tyrosine or phenylalanine. A 1 μM ($10^{-6}$ M) solution of this protein has a UV absorbance of 0.02. How many tryptophan residues are present in this protein?

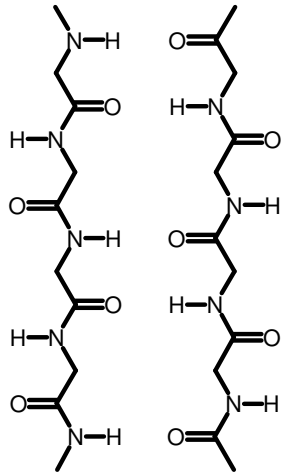
$A=\varepsilon[X]l$, $l = 1cm$
$\varepsilon_{TRP} = 5{,}000\ M^{-1}cm^{-1}$

8. (6 pts) Please do one of the following choices:

**Choice A:** Sketch an α-helix, indicate the location of a few hydrogen bonds and sidechains in your sketch. Also indicate the number of residues/turn.

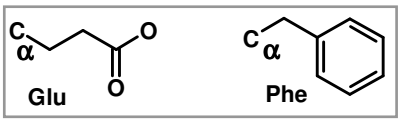
**Choice B:** Is the β-sheet shown on the right parallel or anti-parallel? Briefly justify your answer. Describe, or draw, the orientation of the sidechains in this sheet.

**Choice C:** Pick any super-secondary structure. Describe, or sketch, its structure and briefly discuss the intra-molecular forces that stabilize it.



9. (12 pts) There are two *entropy* terms that are important in protein folding/unfolding. *Briefly* describe **both** of these two terms and indicate how they stabilize (or destabilize) the native, or folded from of a protein.

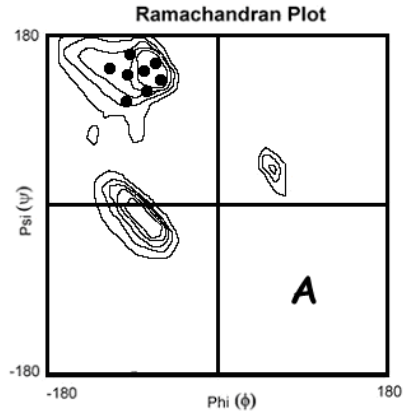
10. (12 pts) Please do one of the following two choices:




**Choice A:** A 8 residue segment of a protein is found on the *surface* of a protein. The sequence of this segment is:

*-Glu-Phe-Glu-Phe-Glu-Phe-Glu-Phe-*

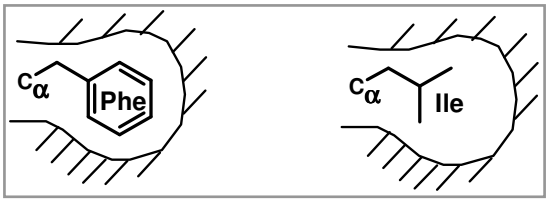
The Ramachandran plot for this segment of the protein is shown to the right. Each "dot" represents the phi and psi angles for a residue in this sequence.




i) What is the most likely secondary structure for this section of the protein? Why would it be energetically favorable for this segment to form this structure? Briefly justify your answer. (8 pts)

ii) Why is it energetically unfavorable to find residues in the region labeled "A" (4 pts)

**Choice B:** A protein normally contains a phenylalanine residue buried in its non-polar core (left structure). Would replacement of this residue by leucine (right structure) increase or decrease the following terms? *Briefly* justify your answer. Assume the reaction direction is *native* → *unfolded.*




i) The $\Delta H^o$ of unfolding.

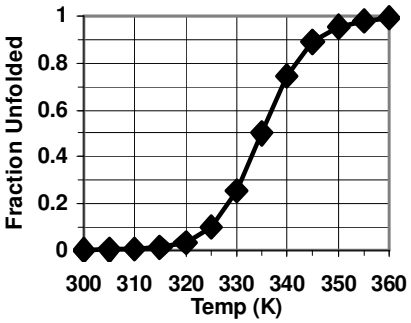
ii) The $\Delta S^o$ of unfolding.

11. (4 pts) Do **one** of the following choices. Indicate your choice.

**Choice A:** The curve to the right shows a denaturation curve for a protein.

i) What is the standard energy change, $\Delta G^o$ at T= 335 K (2 pts)?

ii) Determine the equilibrium constant at T = 335 K? (2 pts).




**Choice B:** A protein denatures with a $\Delta H^o$ of +200 kJ/mol and an entropy change, $\Delta S^o$ of +600 J/mol-K.

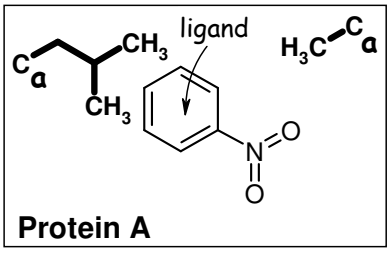
i) Calculate the equilibrium constant and fraction folded (native, N) at 300K. R=8.31 J/mol-K (4 pts)

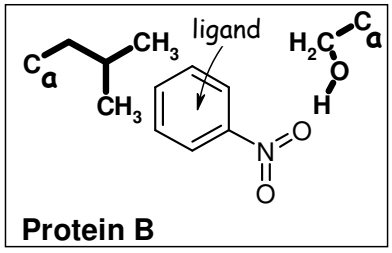
$$\Delta G^o = \Delta H^o - T\Delta S^o = -RT \ln K_{EQ}$$

$$f_N = 1/(1+K_{EQ}) \qquad f_U = K_{EQ}/(1+K_{EQ})$$

**Choice C:** Two different proteins bind the same ligand, nitrobenzene. The structure of the protein-ligand complexes are shown on the right. The two sidechains from the protein that contact the ligand are in bold.

Which protein would show a *lower* $K_D$, protein A or protein B? Why?

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