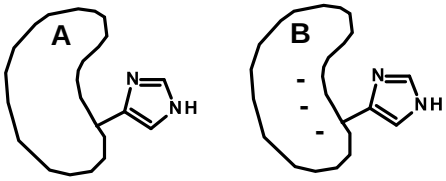
This exam consists of 6 pages and 11 questions with 1 bonus question. **Total points are 100. Allot 1 min/2 points**. On questions with choices, all of your answers will be graded and the best scoring answer will be used. Please use the space provided, or the back of the preceding page.

1. (6 pts) Please do both parts:

i) Draw two "hydrogen bonded" water molecules. Indicate on your diagram a donor and an acceptor.

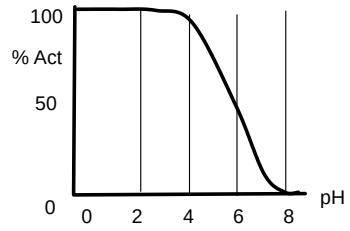
ii) What is the key property of the atoms that result in the formation of a hydrogen bond?

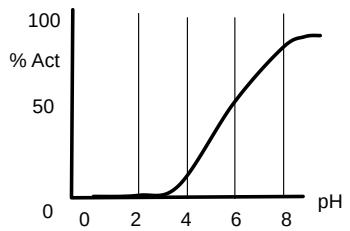
2. (7 pts) Two different proteins (A and B) both contain an imidazole group as part of one of their amino acids (histidine). The structure of these two proteins is shown on the right. The imidazole group is shown in the deprotonated state in both proteins. The "-" symbols on protein B refer to negative charges that are close to the histidine residue. Please do parts i and ii.

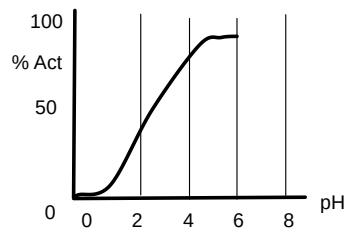


i) (3 pts) Assume that the pKa of the imidazole group in protein A is 6. Will the pK_a of this imidazole group in protein B be higher or lower? Briefly justify your answer.

ii) (4 pts) Circle the curve on the right that correspond to the % activity of protein A as a function of pH, assuming the ***deprotonated*** form of the imidazole is the active form. ***Briefly justify your answer***.







3. (10 pts) You wish to make 1L of a 0.1 M (=[A_T]) buffer solution at pH = 6. Your choices of weak acids for the buffer are the following. Please do all parts of the question.

a) Acetic acid (pK_a=5.0),
b) Hepes (pK_a = 6.0)
c) Tris (pK_a =8.0)

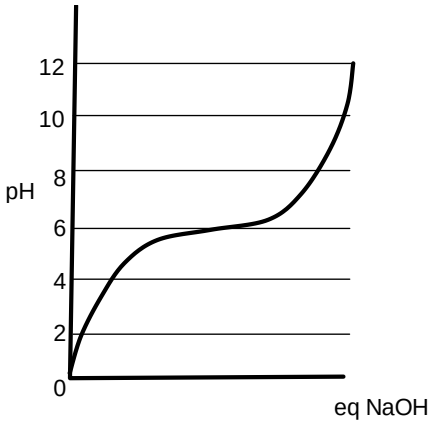
i) (2 pts) Which buffer would you choose and why?

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

$$f_{HA} = \frac{1}{1+R}$$

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

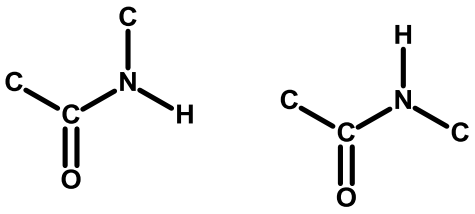
ii) (2 pt) Complete the x-axis of the titration curve shown on the right by providing a scale. Which compound, a), b) or c), corresponds to this titration curve. Justify your answer.



iii) (6 pts) Assuming that you are beginning with the fully protonated form of the buffer (HA), calculate how many **moles** of NaOH would you need to add to the solution of protonated weak acid.

4. (6 pts) The peptide bond is described as "planer and trans". Please do all of the following.

i) Briefly describe why the peptide bond has these characteristics (2 pts).
ii) Circle the trans form of the peptide bond shown on the right (2 pt).
iii) Why is the trans form generally more stable than the cis form (2 pts)?



5. (12 pts) Part of the structure of a dipeptide is shown on the right. Please do all of the following.

i) Complete the diagram, as follows (3 pts):

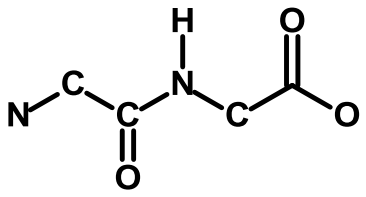
- pH=7.0
- One amino acid should be ***without*** a chiral center.
- The second amino acid can be any amino acid whose sidechain has ***both*** polar and non-polar character, but is **not** charged at pH=7.

ii) Label the amino-and carboxy-terminus of your peptide (2 pts)

iii) Give the sequence (primary structure) of the peptide (2 pts)

iv) *Estimate* the net charge on your peptide at pH=7. For partial credit (if needed), briefly justify your answer/show your work on the back of the previous page. Write your final answer in the space to the right (4 pts).

v) Indicate one hydrogen bond donor and one acceptor on your dipeptide (1 pt).



$$q_{total} = \Sigma(f_{HA} \cdot q_{HA} + f_{A-} \cdot q_{A-})$$

6. (11 pts) You are trying to sequence a **12 residue** peptide using Edman degradation. The following peptide sequences were obtained after cleavage of the initial peptide with the indicated cleavage reagents. You can assume that it was possible to sequence the first five residues of each peptide. The peptide begins with the sequence: Ala-Gly-Val. Please do both parts of this question.

CNBr fragments: CNBr1: Ala-Gly-Val-Met CNBr2: Val-Gln-Asp-Thr CNBr3: Glu-Arg-Trp-Met

Trypsin Digest: T1: Ala-Gly-Val-Met-Glu T2: Trp-Met-Val-Gln-Asp

i) (7 pts) Determine the sequence of the original peptide. Instead of writing out the sequence, you can just give the correct order of the CNBr fragments, e.g. 1-2-3. **For full credit, you must briefly justify your approach on the back of the previous page for full credit.**

ii) (4 pts) What is the absorbance at 280 nm for a 1 uM (10^{-6} M) solution of this peptide? Assume a path length (l) of 1 cm.

Amino acid	**ε**
Trp	5,500 $M^{-1}cm^{-1}$
Tyr	1,490 $M^{-1}cm^{-1}$

$$A = \log\frac{I_O}{I} = \varepsilon[X]l$$

7. (10 pts) Briefly describe the overall structure of folded globular proteins, in particular where you would find polar, non-polar, and charged side chains.

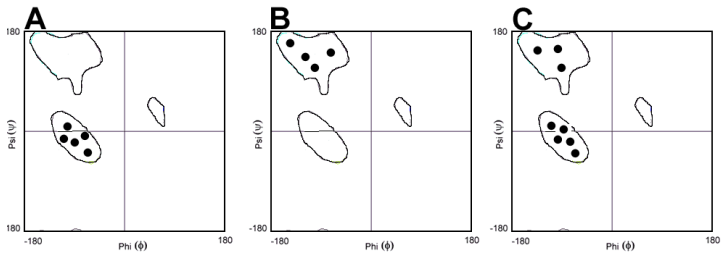
8. (12 pts) Please do ***<u>two</u>*** of the following choices:

Choice A: Briefly describe the molecular basis of the hydrophobic effect and indicate its role in the stability of folded proteins.

Choice B: Briefly describe conformational entropy and indicate its role in the structure of folded proteins.

Choice C: Briefly describe van der Waals effects and indicate their role in the structure of folded proteins.

9. (14 pts) Three Ramachandran plots are shown on the right, labeled A, B, C.). Please do all parts of this question.



i) (2 pts) Indicate which plot corresponds to which secondary/super-secondary structure (circle correct answer)

A	B	C	helical peptide
A	B	C	β-sheet
A	B	C	βαβ
A	B	C	β-barrel

ii) (2 pts) What do the regions enclosed by the contour lines represent? Why are most of the points found inside these lines?

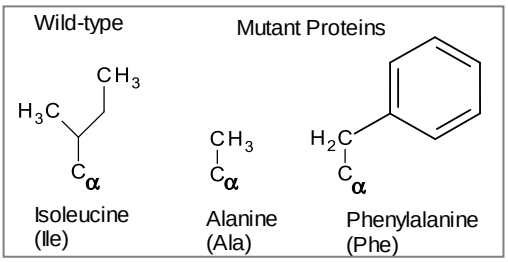
iii) (6 pts) Pick any **one** of the above four secondary/super-secondary structures and briefly describe its structure (a sketch is an acceptable answer). Your sketch should indicate the location of hydrogen bonds and sidechain atoms and some information on its geometric properties (e.g. length of one residue).

iv) (4 pts) For the same structure that you picked in iii), describe the **main (i.e. discuss only one)** energetic feature that is important for its stability.

Bonus (2 pts). Where could you find glycine residues on the Ramachandran plot? Why?

10. (6 pts) An isoleucine residue is buried in the core of a globular protein. Two different mutant proteins are studied, where the isoleucine has been replaced by Ala or Phe.

Discuss the relative stability of ***one*** these two mutant proteins with respect to the stability of the wild-type. Do you expect the mutant that you have selected to more, or less stable? Your answer should discuss ***either*** enthalpic **or** entropic terms that affect stability.



11. (6 pts) Please do **one** of the following choices. Do all parts within a choice.

Choice A: Using immunoglobulins (antibodies) as an example, briefly describe:

i) quaternary structure

ii) protein domains/motifs.

Choice B: Draw a "cartoon" diagram of an antibody and indicate on your diagram the following:

i) The location of the hypervariable loops.

ii) Where the antigen binds.

iii) Label the chains, and domains within each chain.

Choice C: What is a disulfide bond and why does it stabilize proteins which contain them?