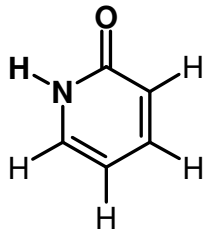
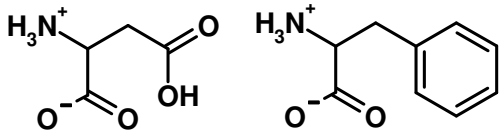
This exam consists of 100 points in 14 questions on 6 pages. Use the space provided.

1. (5 pts) Identify potential hydrogen bond donors ***and*** acceptors on the molecule shown to the right. Label them with "d" or "a", respectively (2 pts). *Briefly* explain why a group is a hydrogen bond donor (3 pts).



2. (2 pts) Two amino acids are shown on the right.
   i) Name both amino acids (full name or 3 letter) (1 pt).
   ii) *Circle* the amino acid that you would you most likely find in the core of a folded protein (1 pt).



3. (14 pts) Draw a tripeptide using the first of the above amino acids (question 2) once, and the second twice. The geometry of the peptide bonds should be drawn in the most prevalent form, i.e. *trans* (8 pts).
   i) Name your peptide, using the names you used in question 2. (1 pt).
   ii) Indicate the amino and carboxy terminus (2 pts).
   iii) Label the peptide bond and the *phi* and *psi* bonds for the second residue (2 pts).
   iv) Indicate the pKa values of ***all*** ionizable groups (1 pt).

4. (4 pts) *Briefly* explain why the peptide bond is planer ***OR*** explain why it is trans.

5. (3 pts) A solution of the peptide from question 3 has a UV absorbance of 1.0 at λ=280 nm. Assuming a path length, *l*, of 1 cm, what is its concentration?

$$A = c\,\varepsilon\,l$$

$$\varepsilon_{280}^{\text{Tryptophan}} = 5{,}000$$

$$\varepsilon_{280}^{\text{Tyrosine}} = 1{,}000$$

$$\varepsilon_{280}^{\text{Phenyalanine}} = 100$$

6. (9 pts) Please do **ONE** of the following two questions. Clearly indicate your choice.

   Choice A: Explain why solutions of weak acids act as buffers in the range of pH = pK_a +/- 1.

   Choice B: The pKa of a side chain amino group on a lysine residue in a protein is 7.0. What is the usual pKa for a group of this type? Provide a possible reason for this shift in pKa.

7. (12 pts) Please do **ONE** of the following four questions. Indicate your choice and show your work.

$$pH = pK_a + \log\frac{[A^-]}{[HA]}$$
$$f_{HA} = \frac{1}{1+R}$$
$$R = 10^{pH-pKa}$$
$$\log 10 = 1, \log 0.1 = -1$$

Choice A (pH effects on activity): A group in a protein must be *deprotonated* to be active. The pKa of this group is 5.0. What is the % activity of this protein at a pH of 6.0?

Choice B (Buffer problem): The pKa of a weak acid is 5.0. Describe how you would make 1 L of a 1.0 M buffer at pH=6.0 using this acid.

Choice C (Charge determination): Determine the isoelectric pH (pI) of the peptide from Q3.

Choice D (pH adjustment): How many *equivalents* of base do you have to add to a solution of a weak acid (pKa = 5) to change the pH from 5.0 to 6.0?

8. (10 pts)

i) *Briefly* describe the hydrophobic effect.

ii) Does it result in a change of entropy or enthalpy (circle the correct choice)?

iii) What is the role of the hydrophobic effect in defining the native structure of globular proteins?

9. (5 pts) Please do **ONE** of the following three choices. Clearly indicate your choice.

Choice A: In calculating the conformational entropy of a protein, the conformational entropy of the unfolded state is given as $S = Rln9^n$, where n is the number of residues. Briefly explain the origin of 9^n in this expression and why this formula should not be applied to proteins with a large number of glycine residues.

Choice B: A classmate has recently determined the structure of a typical protein and shows you the Ramachandran plot for their protein. The points for each amino acid are found all over the plot. What should you tell your classmate about the likelihood that they have a correct structure?

Choice C: Briefly compare and contrast tertiary structure and quaternary structure. Give an example of a protein with a quaternary structure and discuss why the quaternary structure is essential for function (a drawing with some text is a suitable answer).

10. (10 pts) Sketch ***either*** an α-helix ***or*** a two stranded parallel β-sheet. Indicate the locations & direction of the hydrogen bonds and the sidechains.

11. (1 pt) Name *one* super-secondary structure.

12. (10 pts) A 14 residue peptide of unknown sequence was divided into two samples. The first sample was treated with Trypsin and the second with chymotrypsin. The resultant peptides in each sample were separated and sequenced and their *complete* sequences are given below. What is the sequence of the original peptide?

You need not list each residue in your answer, the order of the chymotrypsin fragments will suffice, i.e., C1-C2 or C2-C1. **Justification** of your answer is required for full credit. *Write the justification on the back of the preceding page.*

Amino Acid Names:

Alanine: Ala	Lysine: Lys
Arginine: Arg	Leucine: Leu
Asparagine: Asn	Methionine: Met
Aspartic Acid: Asp	Phenylalanine: Phe
Cystine: Cys	Proline: Pro
Glycine: Gly	Serine: Ser
Glutamine: Gln	Threonine: Thr
Glutamic Acid: Glu	Tryptophan: Trp
Histidine: His	Tyrosine: Tyr
Isoleucine: Ile	Valine: Val

Sequence of the four fragments from Trypsin:

T1: Phe-Arg

T2: Ala-Asp-Arg

T3: Gly-Met-Ser-Lys

T4: Leu-Ser-Ala-Ala-Gly

Sequence of the two fragments from Chymotrypsin cleavage:

C1: Arg-Leu-Ser-Ala-Ala-Gly C2: Ala-Asp-Arg-Gly-Met-Ser-Lys-Phe

13. (12 pts) Please do **ONE** of the following two questions (Choice B is on the following page).

Choice A: A protein has a ΔH^o of +200 kJ/mol and a ΔS^o of +600 J/mol-K.

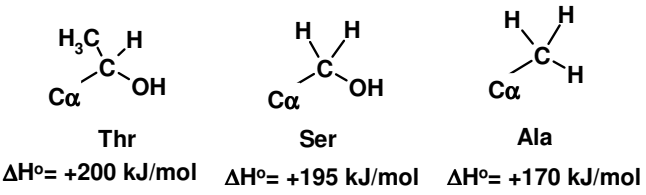
i) *Sketch* the denaturation curve of the protein, clearly marking T_M (6 pts).

ii) Briefly describe how the enthalpy would be obtained from your curve sketched in part *i* (3 pts).

iii) Determine how much of this protein is *unfolded* at 310K (3 pts).

$$\Delta G = \Delta H - T\Delta S$$
$$\Delta G^o = -RT \ln K_{EQ}$$
$$f_{Native} = \frac{1}{1 + K_{EQ}}$$
$$(N \rightarrow U)$$
$$R = 8.31 j/mol - K$$

Q13- Choice B: A Threonine (Thr) residue ***buried*** in the core of a protein is replaced by Serine (Ser) or Alanine (Ala). The ΔH^o values for unfolding of each protein are +200 kJ/mole, +195 kJ/mol, and +170 kJ/mol, respectively. The sidechains of all three amino acids are shown to the right.



i) Explain the change in enthalpy for the Threonine to Serine replacement (9 pts).

ii) Explain the change in enthalpy for the Serine to Alanine replacement (3 pts).

14. (3 pts) Define K_D in terms of kinetic on- and off-rates for a protein-ligand interaction, and then *briefly* explain why ligands that bind tightly have small K_D values.

1.	_____/ 5
2.	_____/ 2
3.	_____/14
4.	_____/ 4
5.	_____/ 3
6.	_____/ 9
7.	_____/12
8.	_____/10
9.	_____/ 5
10.	_____/10
11.	_____/ 1
12.	_____/10
13.	_____/12
14.	_____/ 3
TOT	_____/100