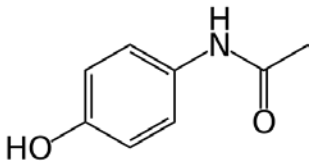
This exam consists of 5 pages and 15 questions. Total points are 100. Allot 1 min/2 points. On questions with choices, all of your answers will be graded and the best scoring answer will be used. Use the space provided, or the back of the previous page. The full name and three letter abbreviation of the amino acids is on the last page.

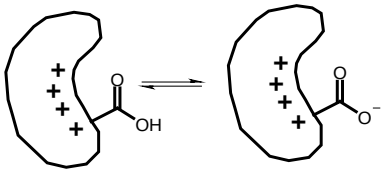
1. (4 pts) The following compound is a common drug (acetaminophen). Draw one water molecule ***accepting*** a hydrogen bond from this molecule. State the general rules for identifying donors and acceptors on any molecule.



2. (6 pts) Entropy plays an important part in affecting the solubility of ions and non-polar compounds. Select one of these (ions **or** non-polar compounds) and briefly discuss the role of entropy in solubility.

3. (8 pts) Sketch a titration curve of a **monoprotic** acid on the right, assuming the pKa=8. What is the "buffer region" of a titration curve and explain why weak acids act as buffers.

4. (8 pts) Please do **one** of the following choices:



Choice A: A carboxylic acid residue is located in a positively charged pocket in a protein. The normal pKa for this group, free in solution, is 4.0. Will the pKa be higher or lower for the residue in the protein? Briefly justify your answer.

Choice B: A carboxylic acid group in a protein must be **de**protonated for biological activity. Sketch the graph of activity versus pH for this protein, assuming the pKa of the group is 4.0. Briefly justify you answer.

5. (12 pts) Please do one of the following two choices:

Choice A:

i) Assuming that you have a monoprotoic weak acid with a pKa of 8, calculate the number of *equivalents* of NaOH required to make a buffer solution at pH 9, assuming that you are beginning with the fully protonated form of the acid.

ii)How would your answer to i) change if this were a diprotic acid, with the first pKa =2 and the second pKa = 8?

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

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

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

Choice B:

You have a solution of a monoprotic weak acid at pH=9. How many *equivalents* of HCl do you need to add to bring the pH to 8.0? The pKa of the acid is 8. Briefly justify your answer.

6. (15 pts)

i) Draw the dipeptide Alanine(Ala)-Lysine(Lys) at pH=7.0, with the peptide bond in the trans conformation. The sidechain of Alanine is a methyl group (4 pts).

ii) Place the following labels on your drawing (3 pts):
   a) amino terminus
   b) carboxy terminus
   c) peptide bond

iii) What is the charge on this dipeptide, at pH=7. Briefly justify your answer with reference to individual pKa values (4 pts).

iv) Could you use the absorption of UV light (280 nm) to measure the concentration of this peptide? Why or why not? (3 pts).

7. (6 pts) The four atoms associated with the peptide bond are planar and usually found in the trans configuration.
   i) Briefly explain why it is planer and trans (5 pts).
   ii) The peptide bond assumes one conformation in the folded and unfolded state. If the peptide bond could assume more than one conformation in the unfolded state, but still one conformation in the folded state, how would it affect the stability of proteins (1 pt)?

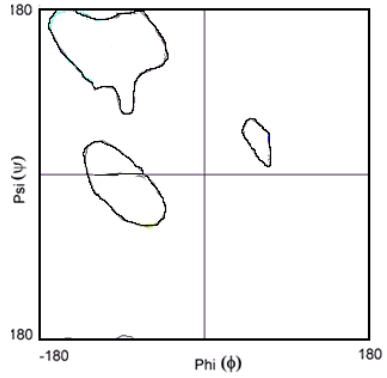
8. (8 pts) A 10 residue peptide was sequenced with Edman degradation. You should assume that only the first 5 residues can be obtained from any peptide, even though the peptide might be longer.

Cyanogen Bromide Cleavage (CNBr):	Ala-Gly-Met	&	Ser-Thr-Lys-Trp-Ser
Trypsin cleavage:	Ala-Gly-Met-Ser-Thr	&	Trp-Ser-Leu-Leu
Chymotrypsin cleavage:	Ala-Gly-Met-Ser-Thr	&	Ser-Leu-Leu

Please write the correct sequence of the peptide below. Justification of your approach (on the back of the previous page) will be rewarded with partial credit if your answer is wrong. Otherwise there is no need to justify your answer.

_____	_____	_____	_____	_____	_____	_____	_____	_____	_____
1	2	3	4	5	6	7	8	9	10

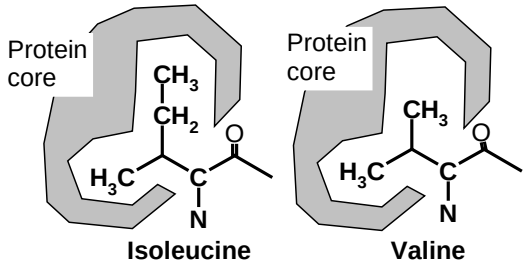
9. (10 pts) There are only three stable secondary structures.
   i) What are their names?
   ii) Describe, or sketch, **<u>one</u>** of them, indicating the location of H-bonds and sidechains.
   iii) Assuming that your secondary structure faced the core of the protein, what distribution of polar and non-polar amino acids along the polypeptide chain would you expect to observe?
   iv) What is the role of van der Waals forces in stabilizing these structures, and what is the relationship between van der Waals and Ramachandran plots (a Ramachandran plot is shown if you would like to use it to illustrate your answer)?



10. (5 pts) Please do **one** of the following two choices:
Choice A: Describe, or sketch, any super-secondary structure and briefly describe the forces that stabilize it.
Choice B: What are disulfide bonds, and how do they stabilize the folded form of proteins?

11. (1 pt) Typical globular proteins contain _____ % of their polar and charged residues on their _____ (location).

12. (5 pts) The core of a protein contains an isoleucine residue in the wild-type enzyme. This is replaced by valine in a mutant. The thermodynamic parameter associated with unfolding of each of these proteins is provided below the diagram. The direction of the reaction is considered to be from the native state to the unfolded state (N→U).



ΔH^o	+200 kJ/mol	+190 kJ/mol
ΔS^o	+600 J/mol-deg	+610 J/mol-K

Explain the difference in enthalpy (ΔH^o) between the two proteins.

Bonus 2 pts: Explain the difference in entropy (ΔS^o) between the two proteins.

13. (6 pts) Draw the structure of an antibody and:
  i) Name the protein chain(s) and indicate the location of the hypervariable loops
  ii) Indicate the location(s) of the bound antigen.
  iii) Indicate **either** a Fab **or** an Fv fragment

14. (2 pts) Briefly discuss **one** of the uses of antibodies.

15. (4 pts) In the case of ligand binding, the formation of the ligand-protein complex depends on the kinetic on-rate (k_{ON}) and the rate that the complex dissociates to free protein and ligand (kinetic off-rate, k_{OFF}). Which of these two parameters is most likely to differ when comparing different ligands binding to a protein? Why?

$$M + L \underset{k_{off}}{\overset{k_{on}}{\rightleftharpoons}} ML$$

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