Name _____

Chem 352 - Spring 2018 - Exam I

Some potentially useful information:

pK_a values for ionizable groups in in peptides and proteins: (*α-carboxyl*, 2.7; *α-amino*, 8.7; and the side chains of *Asp*, 4.0; *Glu*, 3.6; *His*, 6.1; *Cys*, 8.4; *Tyr*, 10.3; *Lys*, 10.5; *Arg*, 12.0)

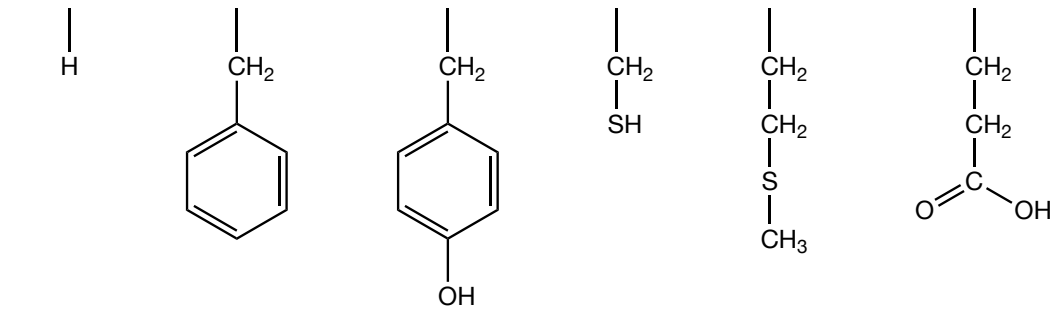
$R = 8.314$ *J/(mol•K)* = 0.08206 *(L•atm)/(mol•K)*

1. Match the following pioneers in the field of biochemistry with the contributions they each made:

a. ___Frederick Sanger	A. Was first to propose the α-helical and β-sheet secondary structures in proteins. He also received two Nobel Prizes for unrelated accomplishments.
b. ___Friedrich Wöhler	B. Characterized the components of yeast extracts that carry out the fermentation reactions as biological catalysts, and which are now called enzymes. He was also the second recipient of a Nobel Prize in Chemistry
c. ___Francis Crick	C. Was one of the first people to determine the 3-D structure of a protein, for which he shared a Nobel Prize.
d. ___Linus Pauling	D. First proposed the "central dogma" of biology concerning the flow of information in living systems. He also received a Noble Prize for another accomplishment.
e. ___John Kendrew	E. Received two Nobel Prizes in Chemistry, one for developing a method to sequence polypeptides and another for developing a method to sequence polynucleotides.
f. ___Emil Fischer	F. Demonstrated that living systems use the same chemistry as non-living systems by showing that the organic molecule urea could be synthesized from an inorganic compound, ammonium cyanate

2. Using the three-letter abbreviations, identify each of the following amino acid side chains.

A. _____ B. _____ C. _____ D._____ E._____ F._____



a. Which of these can hydrogen bond to water? (*Circle all that apply.*) A B C D E F

b. Which of these is aromatic? (*Circle all that apply.*) A B C D E F

c. Which of these is charged at *pH* 9? (*Circle all that apply.*) A B C D E F

d. Which of these is considered hydrophobic? (*Circle all that apply.*) A B C D E F

e. Which of these can form disulfide bonds? (*Circle all that apply.*) A B C D E F

3. Here is a portion the Wikipedia entry for Met-enkephalin:

> **Met-enkephalin**, also known as **metenkefalin** (INN), sometimes referred to as **opioid growth factor** (**OGF**), is a naturally occurring, endogenous opioid peptide that has opioid effects of a relatively short duration. It is one of the two forms of enkephalin, the other being **leu-enkephalin**. The enkephalins are considered to be the primary endogenous ligands of the δ-opioid receptor, due to their high potency and selectivity for the site over the other endogenous opioids.
>
> Met-enkephalin is a pentapeptide with the amino acid sequence **tyr-gly-gly-phe-met**. The tyrosine residue at position 1 is thought to be analogous to the 3-hydroxyl group on morphine.

a. Based on this description, draw the the chemical structure for the isoelectric form of met-enkephalin in water. (The pK_a's for the ionizable groups on amino acids can be found on p.1.)

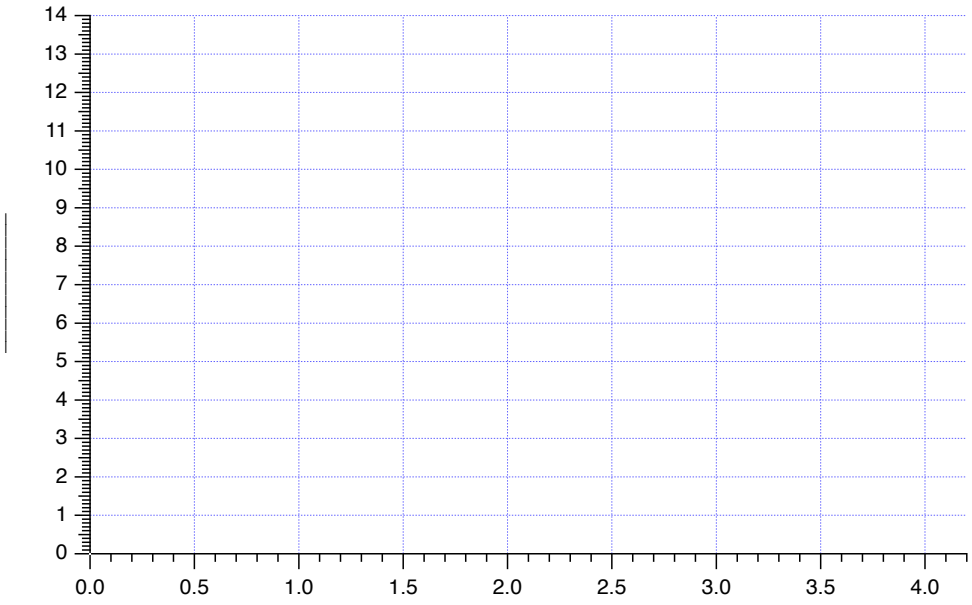
b. Circle all of the chiral carbons in your structure.

c. Label one example each of a φ, a ψ, and an ω bond in your structure.

d. What is the isoelectric *pH* (*pI*) for met-enkephalin? _____

e. Propose a primary structure for leu-enkephalin. _____

f. Using the pK_a's provided, calculate the *pH* of a 120 mM solution of the fully protonated form of met-enkephalin. (Show your calculation below.) *pH* = _____

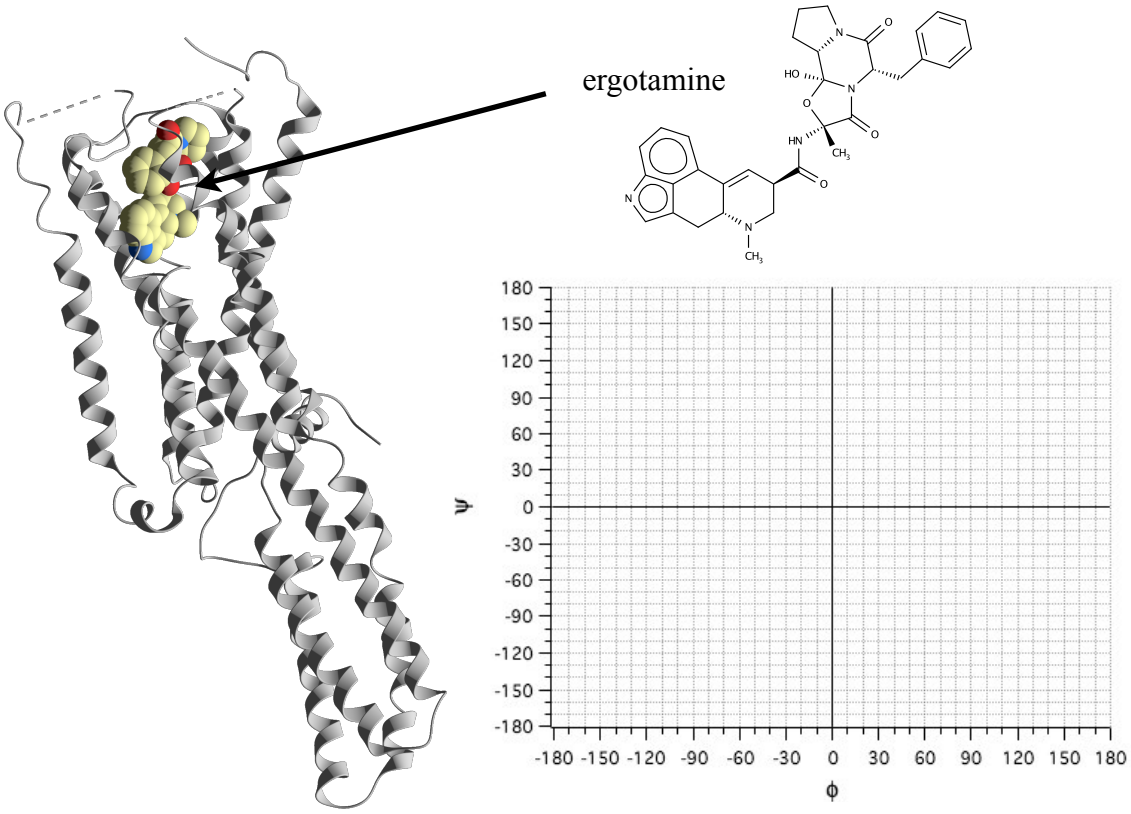


g. Using the graph provided on previous page, draw the titration curve for a 120 mM solution of met-enkephalin. Label each of the endpoints with the net charge of the predominant species at that *pH*. Also, be sure to label the axes.

h. Generally, the solubility of peptides in water will increase with the *net charge* on a peptide. At what *pH* do you expect met-enkephalin to be *least soluble*? _____

i. The met-enkephalin represents one out of how many possible pentapeptides sequences that can be made from the standard set of 20 amino acids. (Show your calculation.) *n* = _____

4. Back in August, 2013, the serotonin receptor protein was the Protein Data Bank's *Molecule of the Month.* It was introduced there in this way, "Are you feeling happy today? Are you feeling hungry? Do you get migraines? All of these behaviors, and many more, are controlled in part by the neurotransmitter serotonin." Serotonin exerts these effect by binding to the serotonin receptor protein. *Ergotamine* is an alkaloid isolated from the ergot fungus that also binds to the serotonin receptor protein and is used medicinally to treat migraines.



a. In the 3-D model or the serotonin receptor protein shown above, the ergotamine is shown bound to the receptor protein as a spacefilling model, where the spheres have radii equal to each atom's vander Waals radius. Describe how the vander Waal radius is related to intermolecular interactions.

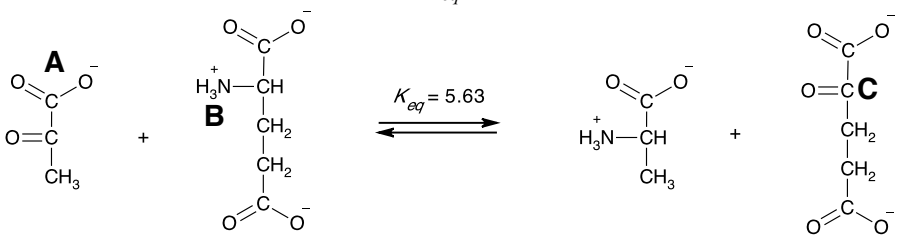
b. On the φ/ψ plot provided, shade the region where you expect the *majority* of the φ/ψ angle pairs to be found for the serotonin receptor protein.

c. What is the name used to describe this type of plot?_____

d. What role does secondary structure play in the folding of the serotonin receptor protein

e. Like serotonin and other molecules that bind to neurotransmitter receptor proteins, ergotamine is derived from amino acids, four different amino acids to be precise. On the 2-D structure for ergotamine molecule shown above, circle one example of a portion that could likely be derived from an amino acid and label it with the name of the amino acid you believe it is derived from.

5. Later this semester, we will study some of the reactions that lead to the biosynthesis of amino acids. We will see that a number of pathways are involved. For example, the pathway leading to the synthesis of the amino acid *alanine* involves the transamination of *pyruvate*, which is the end-product of glycolysis. Another amino acid, *glutamate*, is used as the source of the amino group. This produces the amino acid *alanine* along with *α-ketoglutarate,* which is a citric acid cycle intermediate. The chemical equation for this reaction is shown below. Under standard state conditions and 37°C, the equilibrium constant for this reaction is K_{eq} = 5.63.



pyruvate *glutamate* *alanine* *α-ketoglutarate*

a. Determine the standard free energy change for this reaction under standard state conditions at 37°C. $\Delta G°' =$ _____

b. Is this reaction favorable (spontaneous) under standard state conditions? (Y/N?) _____
Explain:

c. If the cellular concentrations of *pyruvate*, *glutamate*, *alanine*, and *α-ketoglutarate*, are 10mM, 5mM, 25mM and 30mM is respectively, is the reaction favorable under cellular conditions (Y/N) _____
Explain:

d. In the reaction equation shown above, three *functional groups* have been labeled with the letters A, B & C. Identify these by name:

A _____

B _____

C _____

6. In the lab you have isolated a sample of the serotonin receptor protein, which is known to be unstable if not maintained at a pH of 7.0. You therefore wish to make up a buffer solution to suspend your protein in that will be good at maintaining the *pH* at 7.0. You also want that buffer solution to have a concentration of 150 mM. You look around the lab and find, that in addition to distilled water, you have the following solutions available to you,

- 150 mM acetic acid ($pK_a = 4.75$)
- 150 mM sodium acetate
- 200 mM sodium dihydrogen phosphate ($pK_a = 7.21$)
- 200 mM disodium monohydrogen phosphate ($pK_a = 12.1$)
- 1.0 M sodium hydroxide

Describe the steps that you would use to make 500 mL of a 150 mM buffer solution having a *pH* of 7.0