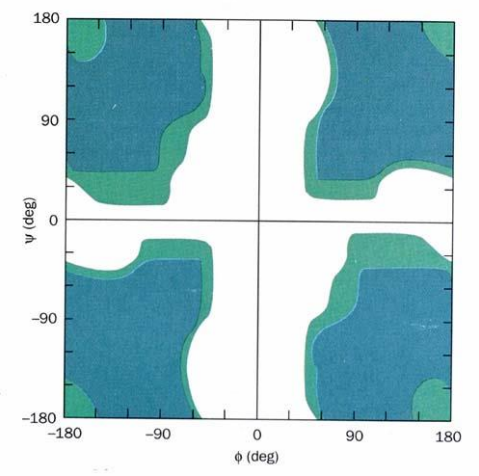
Problem Set 3 (**Due Sept 16th**)

1. Consider histidine. Draw as many resonance structures as you can. Is the ionizable proton (the proton that reacts with water) shared between the two nitrogens?

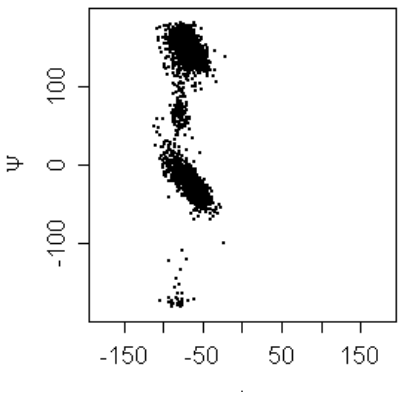
2. Consider the peptide CHECKMATE.
   a. Name this peptide.
   b. Write the peptide using three letter nomenclature.
   c. Draw the peptide.
   d. Using the standard side chain, N-terminus and C-terminus pKa values, predict the charge of the peptide at pH 6.0, 7.0 and 8.0
   e. Determine the pI of CHECKMATE.
   f. Can the side chains of this peptide be modified by any of the chemical modifications discussed in class (acetylation, phosphorylation, or disulfide formation)?
   g. Based on your chemical intuition, predict if any of the side chain pKas will be modified based on the physical proximity to other ionizable groups.
   h. Consider this peptide forming into an α-helix vs. a β sheet. Is there any preference for one over the other?

3. Please sketch a peptide bond and justify why it is planar.

4. Consider the Ramachandran Plot for polyglycine. Why is the $\Phi = 0$ and $\Psi = 0$ region not populated? Why are positive phi values allowed when they are not observed in other amino acids? A complete answer will include a couple sketches.



5. Consider the Ramachandran Plot (right). Predict what amino acid is represented here and discuss why you came to this conclusion.



6. Amphipathic proteins are peptide chains that have folded into a conformation that contains a hydrophobic region and a hydrophilic region on the **surface**. How could this be accomplished in a β-sheet structure? How about an α-helical?

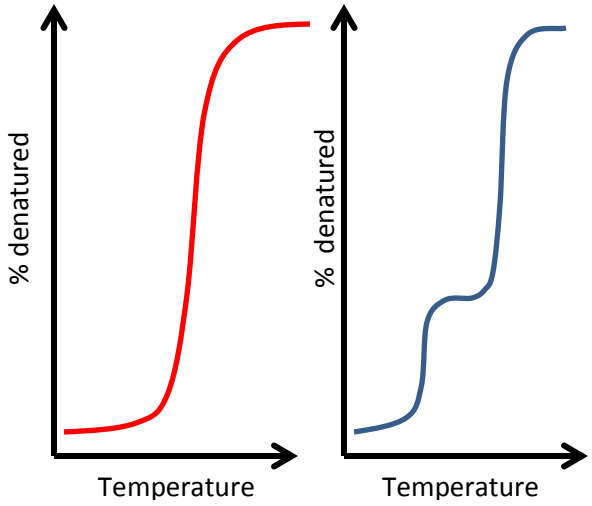
7. What are the common ϕ and ψ angles in alpha helices. What H-bonding pattern stabilizes this structure?

8. Please describe the difference between parallel and antiparallel β-sheets.

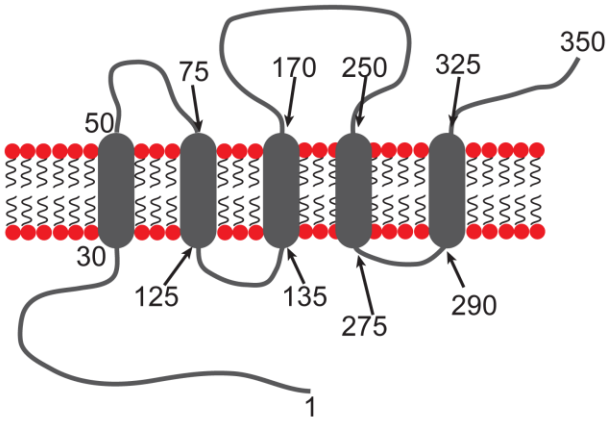
9. Consider the hydrophobic effect.
    a. What role does the hydrophobic effect play in protein folding?
    b. Is this an enthalpically or entropically driven phenomenon? Why?

10. As we discussed in class, protein unfolding can be monitored using a variety of spectrophotometric techniques.

11. Describe how you can use circular dichroism spectroscopy to determine the melting temperature of a protein.
    a. What does the red melting curve tell us about the cooperativity of protein unfolding? Do you expect folding to be the same?
    b. Think carefully about what you see in the blue curve. What does this unfolding profile suggest?
    c. Suggest a sequence of events that could lead to a polypeptide chain folding into it's native conformation.



12. Using the schematic below for a membrane spanning protein (for clarification, the solid ellipses are embedded in the biological membrane and the loops are not), predict the hydrophobicity vs. amino acid number plot.



13. Ethylene glycol (2-hydroxyethanol) is a less effective protein denaturant than ethanol. Justify this observation.

14. Using the pdbID that I sent to you on Tuesday evening, determine:
    a. The name of your protein.
    b. The chemical reaction that it catalyzes.
    c. Using the tools that you learned last week, determine if homologues exist in other organisms. List the % Identity and % Similarity (% Positives) for at least two.