Problem Set 2: Due Monday Jan. 25th

1. (4 pts, 10 min) A Venn diagram that organizes the amino acids by the properties of their sidechains is shown on the right. Glycine is omitted since its sidechain is just a hydrogen atom. As the diagram suggests, a sidechain can be non-polar, charged (pH between 0 and 10), or polar. Some amino acids belong to more than one set, e.g. all charged residues are also polar.
   a) Explain, with reference to its sidechain atoms, where you would place Tyrosine (Tyr) on this chart (2 pts).
   b) One amino acid is very clearly in the wrong set. Which one is it and where should it be placed? Briefly justify your answer (2 pts).

2. (10 pts, 15 min) An enzyme contains a single Histidine (His) residue that must be deprotonated for the enzyme to be active. NMR was used to measure the fraction of this histidine that is protonated as a function of pH. The dry-lab associated with this problem set will allow you to measure the fraction protonated versus pH.
   a) Determine the pKa of this histidine (2 pts).
   b) The pKa for this His residue is different than free His. Based on the shift in pKa, what type of environment surrounds this His residue in the protein? (3 pts)
   c) Sketch the curve of activity versus pH (5 pts).

3. (5 pts, 10 min) The chemical structure of the naproxen, a common pain reliever, is shown on the right. When this drug was first synthesized it was shown to cause pain relief and liver damage. The current formulation of this drug does not cause liver damage (of course). What do you think is the difference between the initial batches of the drug and what you currently buy in the drug store? [Hint: Both the early and current formulations give the same chemical analysis, e.g. carbon composition, IR spectra, etc.], however the first formulation does not rotate linearly polarized light.

4. (8 points, 25 min) You are required to make a 250 ml solution of 0.05 M phosphate to use as a buffer to perform a biochemical experiment at pH 6.8. You only have the fully deprotonated form of this acid (e.g. Na₂PO₄) in the lab, plus 1M solutions of HCl and NaOH. Assume that the pKₐ values for phosphate at 2.8, 7.2, and 12.8. [Hint, it will be useful to sketch a titration curve for phosphoric acid prior to doing this problem.]
   a) How many moles of sodium phosphate would you need for your buffer solution? Why does this not depend on the pH of the solution? (2 pts)
   b) Would you use HCl or NaOH to adjust the pH of the phosphate solution? Why? [Yes, this is simple](1 pt)
   c) Calculate the number of equivalents of HCl or NaOH that you would need to adjust the pH of the sodium phosphate solution. How many moles of HCl or NaOH will be required to make this buffer (5 pts).

5. (20 points, 25 min) View the Jmol structure associated with your recitation section and answer the following questions. Please indicate your recitation section on your homework. For groups, pick the one that corresponds to the person in your group whose last name is closest to A. I suggest that all members of groups actually do this problem to get practice drawing peptides and identifying important features.
   a) Write the correct sequence of your peptide. You will need to look at the sidechain groups to determine the identity of each residue; the labels provided by Jmol are erroneous (2 pt).
   b) Sketch the titration curve for your peptide, using the pKₐ values provided in the lecture notes. Use equivalents for the x-axis. Indicate the buffer regions on your plot (5 pts).
   c) Draw the chemical structure of this peptide, assuming pH = 8.0. You do not need to draw any hydrogens attached to carbons, but you should clearly indicate the correct charge on all ionizable groups (5 pts).
   d) Draw a dotted line that completely encloses all of the mainchain atoms of this peptide (2 pt).
   e) Which pair of labeled atoms (A-F) on the Jmol structure represent the peptide bond, indicate this bond on your sketch (2 pts).
   f) Which labeled atom can act as a hydrogen bond acceptor? Indicate this atom on your sketch and draw a water molecule forming a hydrogen bond with this atom (2 pts).
   g) Which labeled atom (or pairs of atoms) on the Jmol structure can act as a hydrogen bond donor? Indicate this atom on your sketch and draw a water molecule forming a hydrogen bond with this atom (2 pts).