Problem Set 4 (**Due: February 27th 5:00 PM)**

1. For this section, think exclusively about the primary structure of these three peptides (ignore secondary structure and think just about the peptides).

   Alanine – Valine – Isoleucine – Tryptophan – Phenylalanine

   Glutamic Acid – Glycine – Alanine – Leucine - Aspartic Acid

   Lysine – Cysteine – Aspartic Acid – Serine - Glutamine

   a. Sketch each peptide in their fully protonated form. Pay close attention to ensuring that the backbone is drawn correctly and that the side chains have the protonated form shown (if applicable). Also, make sure to include the correct protonation state of the N – and C – termini.

   b. How many ionizable protons exist on each peptide?

   c. What form (e.g. H_2X, H_3X, etc.) of the peptide has a net neutral charge?

   d. What is the pI of each peptide?

   e. Which peptide:
      i. Has the largest log P?
      ii. Is the most acidic?
      iii. Is the most basic?
      iv. Is most likely to have an intrapeptide ion-ion interaction?
      v. Is most likely to form a disulfide bond with another peptide?
      vi. Is most likely to have a side chain get phosphorylated?

   f. Sketch a titration curve for the addition of NaOH to each of the peptides below. Make sure to include the pH at each ½ equivalence point and each equivalence point (except the last one).

2. Clearly explain why the side chain pKa of glutamic acid can be lowered when it is in close proximity to an arginine side chain.

3. Secondary structure forms because of the H-bonding pattern within the backbone of the polypeptide chain. Explain the pattern for each of the following – a sketch would be useful:
   a. Parallel beta sheets
   b. Anti-parallel beta sheets
   c. Alpha helix

4. The tertiary structure of proteins is almost completely due to interactions between side chains. Explain how each of the following intermolecular forces could play a role in stabilizing tertiary structure:
   a. H-bonding
   b. Dipole-dipole
   c. Ion-ion
   d. LDF

5. The formation of a hydrophobic core is the most important part of stabilizing protein structure. As we discussed with lipid bilayers, entropy is the main driving force for this process. Explain the role of entropy in protein folding.

6. Using the alternating side chain approach that is applicable for beta sheets, determine if each of the peptides below could be part of a peripheral membrane protein (one that is situated at the surface of a lipid bilayer).
    a. Valine – Leucine – Alanine - Asparagine – Isoleucine – Tryptophan – Phenylalanine – Proline
    b. Alanine – Glycine – Tryptophan – Aspartic Acid – Leucine – Serine – Valine – Arginine
    c. Serine – Lysine – Threonine – Aspartic Acid – Proline – Alanine – Methionine – Isoleucine

7. Using the heptad repeat approach that is applicable for alpha helices, determine if each of the peptides below could be part of a peripheral membrane protein (one that is situated at the surface of a lipid bilayer).
    a. Serine – Valine – Alanine – Threonine – Glutamine – Leucine – Arginine – Cysteine
    b. Threonine – Serine – Aspartic Acid – Tryptophan – Phenylalanine – Asparagine – Leucine
    c. Valine – Alanine – Threonine – Lysine – Leucine – Methionine – Aspartic Acid - Isoleucine

8. Predict the amino acid composition of an enzyme active site that makes a high affinity interaction with dopamine.