# PS4key

Friday, February 24, 2017 10:52 AM

**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? 1st – high log P means soluble in octane
      ii. Is the most acidic? – 2nd – most acidic residues. This can be confirmed by noting that it has the most acidic pI
      iii. Is the most basic? Last one. Again, check out the pI
      iv. Is most likely to have an intrapeptide ion-ion interaction? Last – it has both negative and positive charged side groups.
      v. Is most likely to form a disulfide bond with another peptide? Last one – it's the only one that has a cysteine. Only cysteine can form a disulfide
      vi. Is most likely to have a side chain get phosphorylated? Alcohol groups are most likely to be phosphorylated. The last peptide has a serine.

   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. Low pKa values (stronger acids) scale with the stability of the basic form of an acid. If the base is in close proximity of a positive charge, this will confer an extra degree of stability through an ion-ion interaction. Consequently, an aspartic acid in close proximity to an arginine would likely have a lower pKa because the deprotonated form would be more stable.

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 Many side chains have the potential to H-bond. If two H-bonders are close together, they could help to stabilize tertiary structure. Examples are serine and threonine. However, it's also important to note that water can make H-bonds as well, so H-bonds between side chains on the surface of a protein are typically not very strong.
b. Dipole-dipole Polar amino acids in close proximity with each other will form dipole-dipole interactions. Examples include asparagine and glutamine.
c. Ion-ion anions (aspartic acid and glutamic acid) and cations (arginine and lysine) certainly attract each other. If they are brought into close proximity, they will form a stable interaction.
d. LDF The interaction of nonpolar side chains is the most important interaction in protein tertiary structure. When nonpolar side chains interact, LDF are formed.

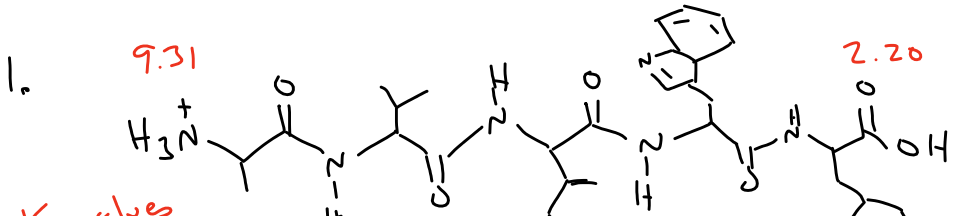
5. The formation of a hydrophobic core is the most important part of stabilizing protein structure. As we discussed with lipid bilayers, entropy is the main driving force for this process. Explain the role of entropy in protein folding. Nonpolar molecules have a large influence on the structure of water lattices. Instead of the normal H-bonding pattern that exists in liquid water, $H_2O$ that is forced to contact nonpolar molecules make a very ordered network of H-bonds that very much resemble solid water (ice). When the nonpolar molecules aggregate (protein folds), the ordered waters are shed and allowed to return to bulk solvent; this is a very large entropic contribution to 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

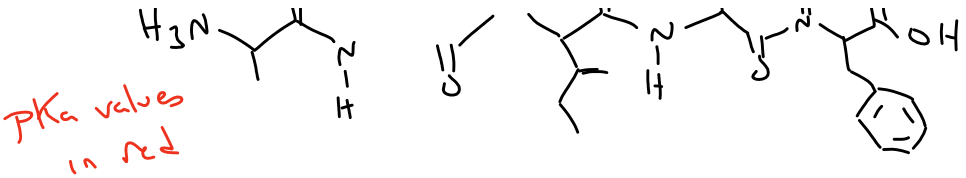
7. Using the heptad repeat approach that is applicable for alpha helices, determine if each of the peptides below could be part of a peripheral membrane protein (one that is situated at the surface of a lipid bilayer).
   a. Serine – Valine – Alanine – Threonine – Glutamine – Leucine – Arginine – Cysteine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

1. 9.31 2.20



b) 2 Ionizable
c) HX

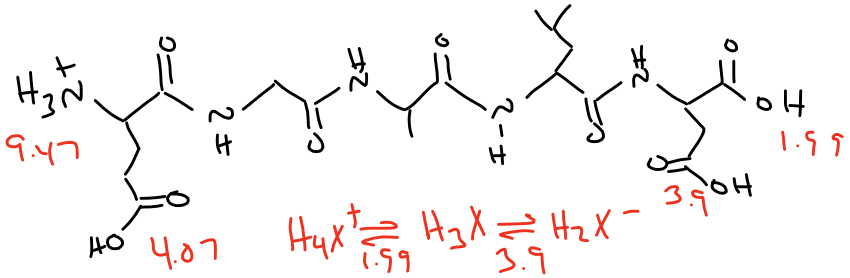


pKa values in red

b) 2 Ionizable

c) HX

d) $\frac{2.20 + 9.31}{2} = 5.76$



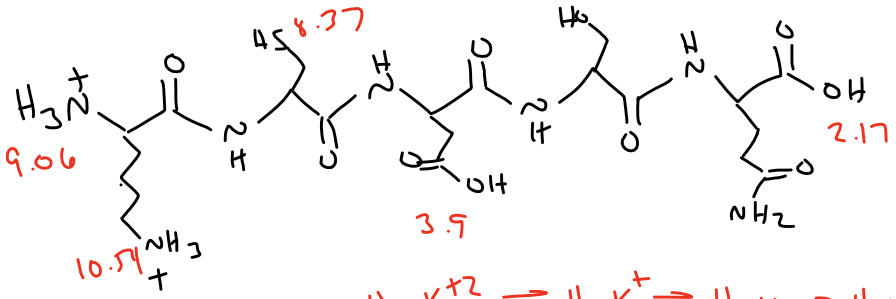
9.47 4.07 1.99 3.9

$H_4X^+ \underset{1.99}{\rightleftharpoons} H_3X \underset{3.9}{\rightleftharpoons} H_2X^-$

b) 4

c) $H_3X$

d) 2.945



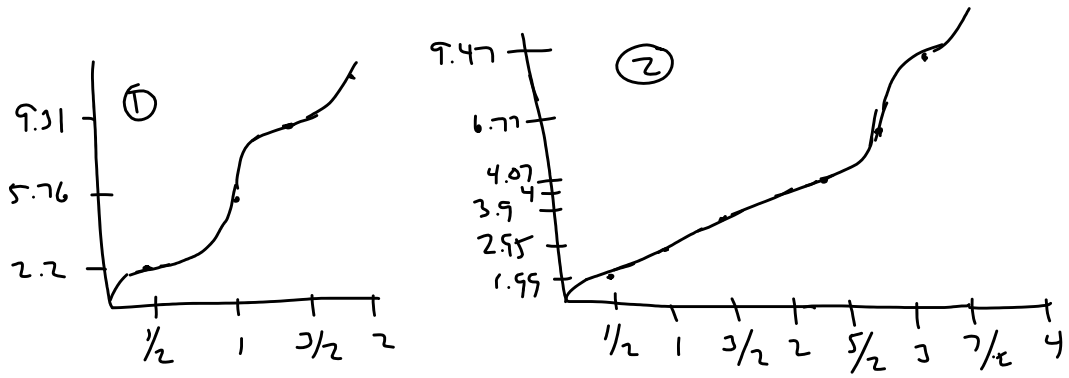
9.06 10.54 3.9 8.37 2.17

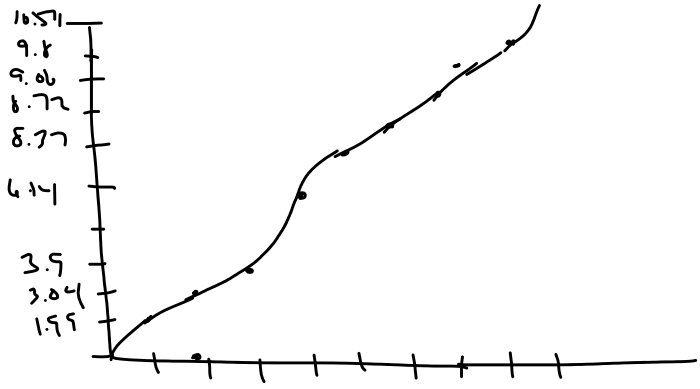
$H_5X^{+2} \underset{2.17}{\rightleftharpoons} H_4X^+ \underset{3.9}{\rightleftharpoons} H_3X \underset{8.37}{\rightleftharpoons} H_2X^{-1}$

b) 5

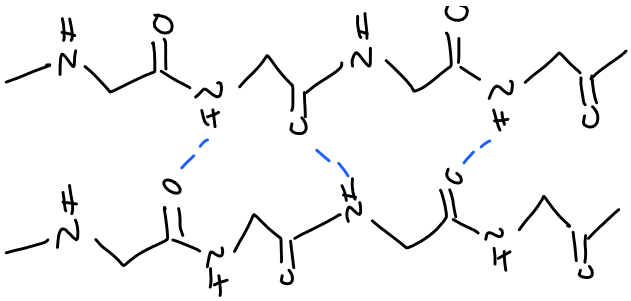
c) $H_3X$

d) $\frac{3.9 + 8.37}{2} = 6.14$



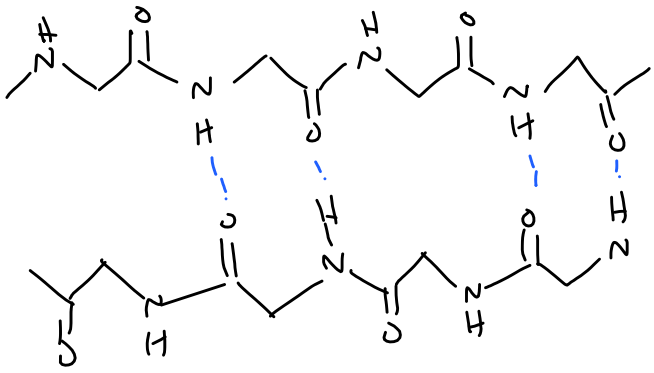



③ Parallel



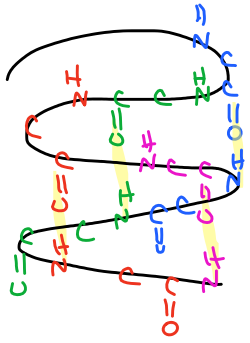
H bonds @ angle
- not ideal
- weaker than antiparallel

antiparallel



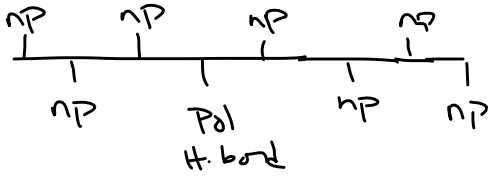
- ideal H-bond
- stronger than parallel

alpha helix

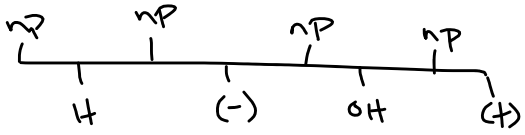


H-bonds between C=O & N–H of amino acids separated by 4 residues

6. a.




b.




this one

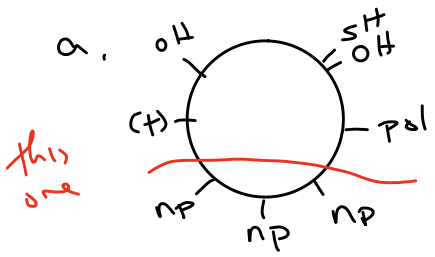
c.


7. a


b

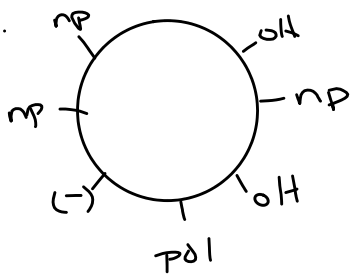
7.

a.

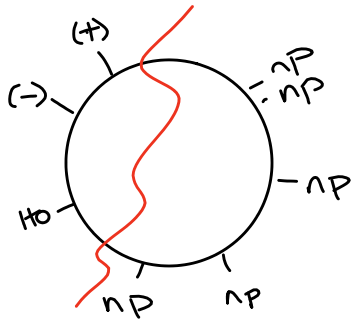



this one

b.




c.




this one

8.