Problem Set 9: Due Monday, April 13th.

Estimated time: ~ 90 minutes

1. (8 pts, 15 min) View the Jmol page that displays the membrane protein bacteriorhodopsin by following the link to jmol_br. The following is the polypeptide sequence of part of one of the \( \alpha \)-helices in this protein:

\[ \text{Trp}79\text{Ala}80\text{Arg}81\text{Tyr}82\text{Ala}83\text{Asp}84\text{Trp}85\text{Leu}86\text{Phe}87\text{Thr}88\text{Thr}89\text{Pro}90\text{Leu}91 \]

i) Beginning with Ala\(_{80}\) as the second residue, write the name of the amino acid on the ‘helical wheel’ that is shown on the right (Trp\(_{79}\) has been done for you). The helical wheel represents a “top view” and shows the projection of amino acid sidechains from the helix.

ii) The angle between successive spokes or positions on this wheel is 100°. Why? (Hint: Consider the geometric properties of an alpha helix.)

iii) View the Jmol page and circle the residues names on the wheel that point outward from the protein towards the lipid and indicate whether they are predominately polar (p) or non-polar (np).

iv) In what way does the pattern of polar and non-polar residues on the helical wheel relate to the orientation of the helix with respect to the lipid acyl chains? Why is this arrangement energetically favorable?

2. (8 pts, 15 min) A peptide that is 20 residues in length is mixed with pure lipid bilayers in aqueous solution. The concentration of the peptide in the membrane and in solution is measured. From this measurement it is possible to calculate an equilibrium constant for the transfer of peptide from the solvent to the membrane (this type of equilibrium constant is often called a partition coefficient): \( K_{\text{eq}} = [P]_{\text{membrane}}/[P]_{\text{solution}} \). Note that the peptide is either completely in solution or completely buried in the membrane, as indicated in the diagram on the right that shows the equilibrium for Phe\(_6\) (part ii assumes a different composition, i.e. Ala+Phe).

i) What secondary structure will this peptide most likely assume in the membrane? Why? (2 pts).

ii) Assume that the 20 residue peptide contains \( n \) alanine residues and \((20-n)\) Phe residues. Calculate the number of Ala and Phe residues in this peptide such that an approximately equal amount of the peptide will be found in solution and in the membrane (i.e. \( K_{\text{eq}} = 1 \)). You should find the value of \( n \) that is closest to giving a \( K_{\text{eq}} \) of 1. You should use the values of free energy of transfer for Ala and Phe residues that are given in lecture 26 (6 pts).

3. (10 pts, 10 min) View the Jmol page on the potassium channel by selecting the link jmol_k_channel on the Jmol links page. Please answer the following questions.

i) Potassium ions can be seen at three sites, site A, site B, and site C. Site B is within the selectively filter of the channel while A and C are at the entry and exit to the filter. Briefly describe how the ligands (groups and/or molecules) that interact with the potassium ion differ in these three environments, i.e. what happens to the K\(^+\) as it goes through the channel?

ii) A series of buttons allow you to change the ion in the central channel, at site B. Based on the interactions between the metal ion and the groups in the central channel briefly explain, in terms of molecular interactions, why the channel is selective for potassium ions, while larger or smaller ions cannot go through the channel.

4. (8 pt, 10 min) The rate of transfer of potassium ions as a function of \([K']\) is shown on the right for a solution of 1 nmol of channels (in membranes of course).

i) Why is it appropriate to call the potassium channel an enzyme? (2 pts).

ii) Calculate \( K_{\text{CAT}} \) for this “enzyme” (3 pts).

iii) How would this plot differ if sodium ions were also present in solution? Would \( K_M \) or \( V_{\text{MAX}} \) change? (3 pts).
5. (5 pts, 10 min) Closed membrane vesicles are prepared that contain glucose channels; you can consider the movement of glucose across the membrane to be much faster than water because of the glucose channels. The interior of the membrane vesicle contains 100 mM glucose and the vesicles are placed in a solution of 500 mM glucose. Describe the flow of glucose and water in/out of the vesicle until equilibrium is reached.

6. (10 pts, 20 min) The metabolic pathway for the synthesis of threonine is shown on the right. Note that not all reactants/products are shown for each reaction.
   i) Provide a name for the enzyme (E1) that catalyzes the first step of this reaction, assuming that it uses ATP as the phosphate donor. (2 pts)
   ii) The first step in this pathway is phosphorylation of a carboxylic acid. The phosphorylation of a carboxylic acid by inorganic phosphate is unfavorable, with a $\Delta G^o$ of approximately +30 kJ/mol yet the reaction proceeds spontaneously in the forward direction while this pathway is operating. How can the Gibbs energy, $\Delta G$, become negative for this step in the pathway (Hint: see part a) (2 pts).
   iii) How would you describe the chemical changes that occur between aspartyl phosphate and aspartate semialdehyde (catalyzed by enzyme E2)? What cofactor/co-substrate is likely involved in this step? Sample incorrect answer: This step is catalyzed by a phosphatase because a phosphate is released from the substrate. [Hint: a similar reaction occurs in glycolysis, but in reverse. You can consider the reaction to be a change between a protonated carboxylic acid and an aldehyde – i.e. pretend the phosphate is not there.] (2 pts)
   iv) Show, by balancing the reaction (or counting electrons on the relevant atoms in the reactant and product), that the step catalyzed by E3 is a redox reaction. Is it an oxidation or a reduction? (2 pts)
   v) What general conclusion can you draw about synthetic pathways? Do they produce or consume energy? Do they contain oxidative or reductive steps? Briefly justify your answer with reference to the pathway for threonine biosynthesis (2 pts)

7. (5 pts, 10 min) Draw the steps in the conversion of an alkane (e.g. ethane) to a carboxylic acid (e.g. acetic acid) using a series of two electron oxidations, plus any additional reactions that might be required. Give the generic name (e.g. type of reaction catalyzed) by each enzyme in each step. A skeleton outline is given below: