Problem Set 6 Partial (**Due Oct 14th**)

1. Derive an expression that allows us to determine a dissociation constant for the protein/ligand equilibrium shown below.

$$P + L \rightleftharpoons PL$$

2. If myoglobin is 50% saturated at a pO_2 of 0.7 torr, calculate the pressure of oxygen needed to reach a fractional saturation of
   a. 25%
   b. 90%

3. In Chimera, superimpose the structures of oxy (2Z6S) and apo (1MBW) myoglobin (do this through the matchmaker tool under Structural Comparison). What differences do you observe? Determine the change in the position of the proximal histidine (report in angstroms). How does this compare to the ~0.6 A for hemoglobin? Is the O_2 H-bonded to the distal histidine? What are the H-bond distances? Do the same comparison for apo and carbonmonoxy (1JW8) myoglobin. Answer all of the above questions. Additionally, comment on how CO binds to heme and how this differs from O_2 binding.

4. In problem 3, you should have noted that CO binds to myoglobin through the Carbon, not the Oxygen atom. Why?

5. Describe why cyanide ion can inhibit O_2 binding to hemoglobin and myoglobin. Make sure to include atomic orbital hybridization in your answer.

6. From our discussion in class, K_D takes on a unit of concentration. Use a simple equilibrium expression to confirm this. Why is this more useful to biochemists than association constants?

7. Please summarize the main differences between the KNF and MWC models of allostery.

8. Give the following data for O_2 binding to an O_2-binding protein isolated from *E. coli*, please approximate the K_D for O_2 binding directly from a graph. Determine the exact value of K_D using the Solver function of Excel. There is a tutorial video on the course homepage.

$[O_2]$, nM	Fractional Saturation
0.5	0.0093
1	0.0185
2	0.0364
4	0.0702
8	0.1311
16	0.2319
32	0.3765
64	0.5470
128	0.7072
256	0.8285
512	0.9062
1024	0.9508

9. Briefly summarize how O_2 binding is allosterically communicated to other subunits of hemoglobin.
10. CO_2, pH and BPG all influence the affinity of hemoglobin for oxygen.
    a. Can these be considered allosteric modifiers?
    b. Clearly discuss what role each play.