

Biophysical Chemistry I, Fall 2010

Homework Assignment #6, due Nov. 23

As you have learned, proteins interact with small molecules, either as substrates or co-factors (which are often involved in chemical reactions) or as structural components (such as metal ions), or just as external agents that promote crystallization. In this assignment, you will use the "Ligand Explorer" component of RCSB to learn one way to study these interactions.

1. Go to <http://www.rcsb.org>, as usual, and navigate to PDB ID 3MI4, which is for a version of trypsin. Write a short paragraph about the biological function of this protein.
2. Scroll down to "ligand chemical components", where you should see that there are four ligands (non-protein components) in this structure. One of the ligands (benzamidine) has a binding affinity listed of 31-39000 nM. Draw the conventional (two-dimensional) chemical structure of benzamidine; define what is meant by the binding affinity, and write down its relation to the binding free energy. What is the numerical value of the binding free energy? (Hint, click on the link labeled K_i ; you can use the data from Axys Pharmaceutical.)
3. Click on the ligand explorer link, start the program and choose the benzamidine ligand. List the hydrogen bonds that contribute to the binding of benzamidine to the protein. The program also has a button labeled "bridged hydrogen bonds"; what are these? how many are found for benzamidine in this crystal structure?
4. What hydrophobic contacts are found for benzamidine? One of them looks very odd to me. Can you guess which one, and why?
5. How does the calcium ion interact with the protein, that is, list the interactions that are reported. What purpose do you think the calcium ion is serving?
6. Same questions as #5, but for the sulphate ion.

Note: the Ligand Explorer program requires a system that allows the browser to start java applications via Java Web Start (or .jnlp files). This seems to work fine on Mac OS and Windows machines that I have tried, assuming that Java is installed. If Java is not installed, please visit <http://www.java.com>. It is easiest if you can get access to a Mac or Windows machine for this homework, and contact me if you have problems. For Linux, see the next paragraph.

Linux instructions: Here is what worked for me on Ubuntu 10.04: (1) Go to www.java.com, and install the latest java; (I used the 32 bit version, and installed it under /home/case/java). (2) From the RCSB web site, download the .jnlp file that you get from the "Ligand explorer" link (step 3 above). (3) Go to wherever the .jnlp file was downloaded, and type

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/home/case/java/jre1.6.0_22/bin/javaws RCSB-LigandExplorer.jnlp
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