CHAPTER 11

Molecular Modeling

This week, you may bring a copy of this document and your lab manual with you to lab!

For this lab (Lab 5), there will be no "Pre-lab" or "Data Collection" questions.

Please read over this tutorial and have PyMol installed on your computer before coming to your lab section!

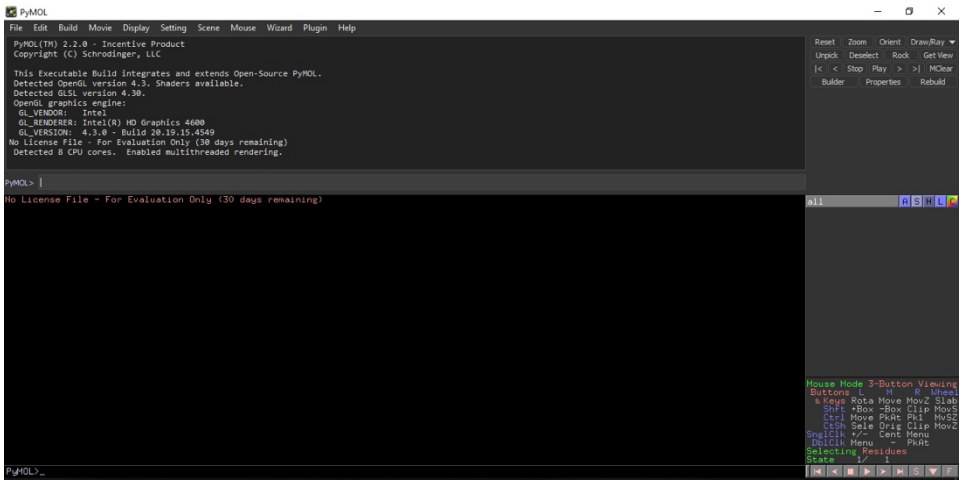
Before coming to your lab section during the week of Oct 11 through Oct 17, please install the PyMOL program on a laptop that you can bring to the lab and ensure that it is working. Also bring a **three-button mouse**, if you have one. If you do not have a laptop that you can bring to the lab, please let your TF know.

Downloading PyMOL

The Department of Chemistry has a departmental license for PyMol that allows students and TFs to use it for academic purposes. The installation instructions for PyMol are here: https://sites.bu.edu/mcneely/it-advice/pymol/. Please let me know if you have any challenges accessing PyMol. It does require you logging in with your BU username and password.

Once you download "**PyMOL 2.5**" for your operating system, you will be prompted for a License. The License document is also available on the Chemistry PyMOL website, if you would like to download it. For the PyMol download page you can also click on the "Download License File" link for existing users, and enter the details provided on the BU PyMol page. The program will operate for a trial period of several days if you want to ignore this step.

To check that the program is working, open the program. You should see the following window:



In the command line of the top half, left side of the window, type:

fetch 1IHY

And then hit enter. If a molecule appears in the display window, your PYMOL is working.

Part A. Using PyMOL for protein modeling measurements

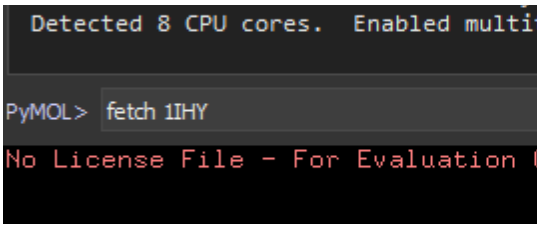
The PYMOL program can be run via command lines as well as clickable buttons. In this tutorial you will have instructions to load molecules via the command line, and then interact with your protein/ligand via a laptop touchpad/mouse.

A-1. Loading a protein of interest

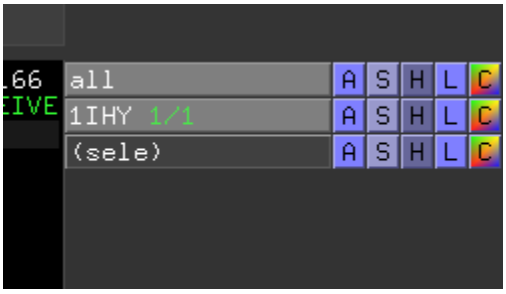
After your teaching fellow has confirmed the molecule that you will be studying for Chapter 11, you will record your four alpha-numeric Protein Data Bank code

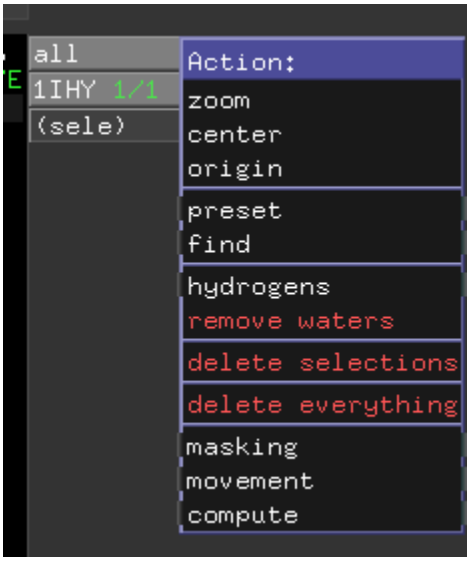
Enter this code along with the appropriate "fetch" command into the command line. For the purposes of this tutorial, we will use 1IHY for the tetramer GAPDH:

fetch 1IHY



When you have entered this code and hit enter, you will load the tetramer GADPH onto your screen. As you have noticed, the right-hand column bar has now been populated with an "all" entry, a "1IHY" entry, and a "(sele)" entry. These will be used later for customizing your enzyme (Part D). For the purposes of this exercise, we only want to work with one subunit at a time, so let's go ahead and just delete everything by going to the "all" entry, selecting "A" for "action", and selecting "delete everything"

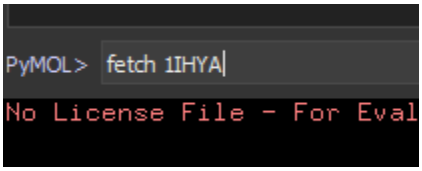




For GAPDH, there are four subunit chains with letters A, B, C, and D assigned to them, but one would not know unless they investigated this information a little more thoroughly. It's safe

to assume in most cases that the first chain will be letter A. If we only want to load the first chain we can simply affix the chain letter at the end of the PDB code:

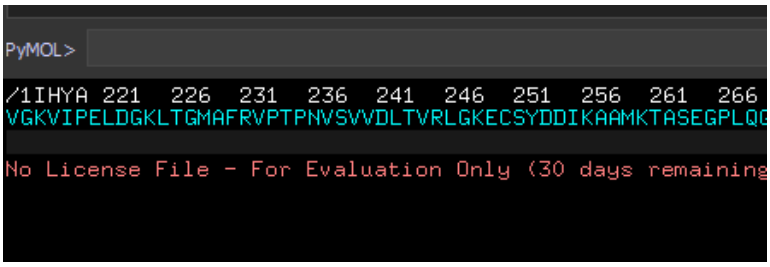
fetch 1IHYA



After pressing enter, only one subunit and its ligands will be loaded onto your PyMOL graphics user interface (GUI) window.

A-2. Moving your protein

The protein that you have successfully loaded has many amino acids and one or two ligands with it. At the bottom right of the window, there is a pink "S" button, click it, and a sequence of amino acids of your protein will show up in the GUI window.



Whenever you click on anything in the GUI, the corresponding amino acid/ligand will be highlighted in the sequence. Likewise, when you click on anything in the sequence, that amino acid/ligand will be selected in the GUI. This is a great way to pinpoint certain sequences or amino acids.

For general movement of your protein using a three-button mouse:

- Left click rotates the model
- Alt + left click moves the protein in the xy-plane
- Right click moves the protein in the z-direction
- The scroll button moves the visibility slab in the z-direction

Movements are similar for using a touch pad. If the right click feature does not work on your touchpad, pinching and stretching motions using two fingers on your touchpad will activate the zoom-in/zoom-out function.

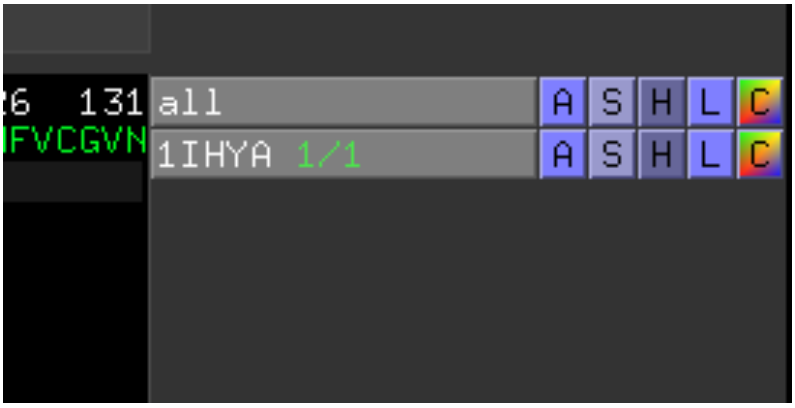
A-3. Navigating through the different features of your protein/ligand

Check the sequence line in the GUI window. At the end of the amino acid chain for the monomer of GAPDH, you will find two sulfate molecules that were also crystalized with the

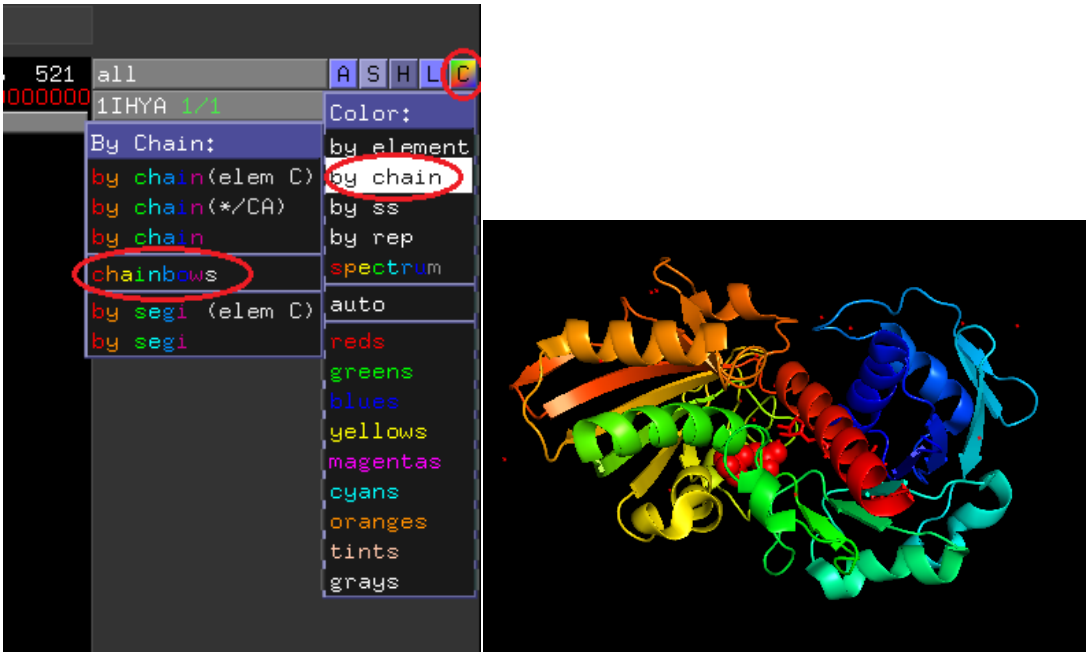
protein, as well as the ligand APR. If the ligand isn't already visible, you can select the APR abbreviation in the sequence line. In the selection "(sele)" feature to the right, you can click on the "S" button to show it. You can have it shown in different forms, such as sticks or cartoons.

A-4. Customizing your protein

Aside from "showing" and "hiding" different parts of your PDB model using the "S" and "H" buttons for different features:



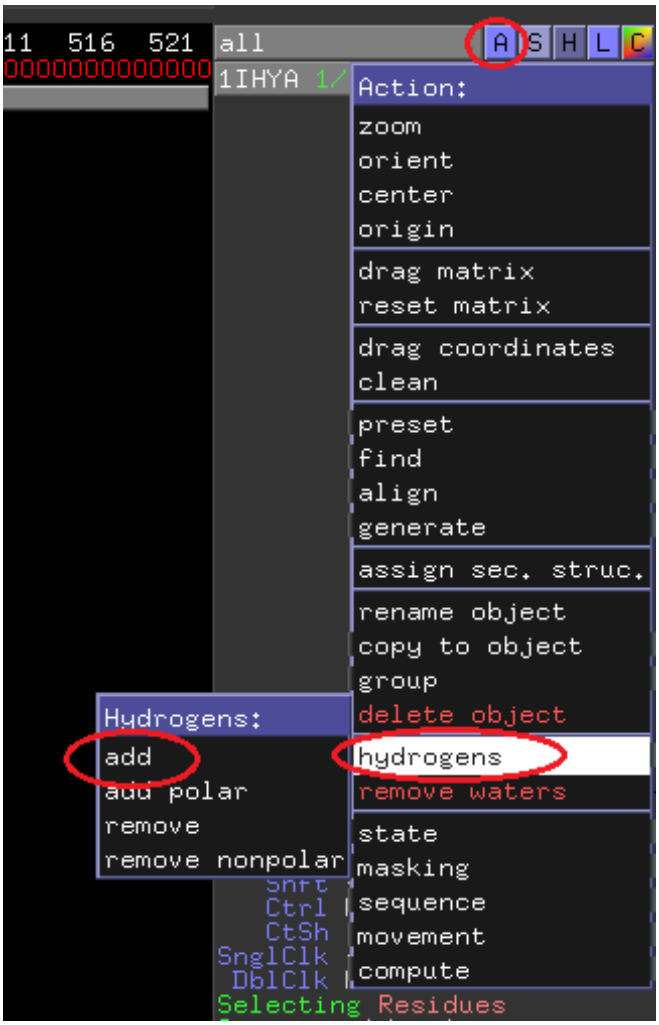
You can also decorate your protein to make different parts standout. Try using the "chainbow" command to decorate different segments of your protein by different colors. Click on the "C", then "by chain", then "chainbows".



Additionally, you can select different parts of the protein to select certain "invisible" amino acid residues, or select them individually on the top scroll bar if there is a specific amino acid at a certain position you are looking for. If you have an amino acid(s) selected, you can make them appear by using the Show "S" button and have them appear in "sticks". If you want to deselect items, just click on the black background canvas.

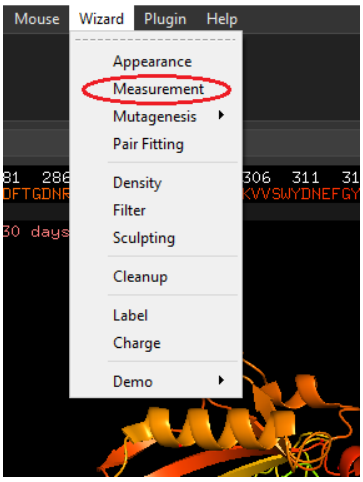
A-5. Showing hydrogen bonds

When you are going to measure hydrogen bonds, you have to measure the distance between a hydrogen bond donor and acceptor. For simplicity's sake, PDB files are loaded without hydrogen bonds visible. In order to show these for any feature, your protein, your ligand, or your cofactor, click on the "A" of any feature you are interested in showing the hydrogen bonds, then go to "hydrogens" and then "add".

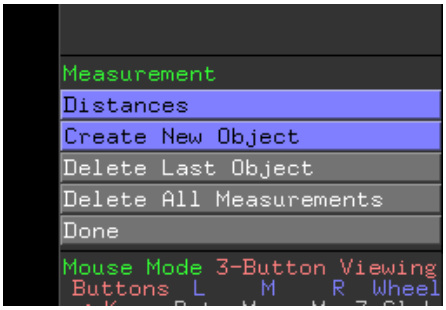


A-6. Making measurements

To make a few measurements, go to top toolbar and click on “Wizard” and then on measurement”:



The wizard will activate on the lower right side and it will ask you to click on your first atom, and then click on your second atom. Once you have completed selecting on two atoms, the program will display the measurement in angstroms. This new measurement will also be added as a feature in case you want to change any aspects about it or delete it entirely. Please note that you need to exit out of the wizard before you click on anything else, otherwise the program will continue making measurements for you. To exit out of the wizard, you can simply click on the “Done” button from the lower right panel.



Pro Tip: Whether you found a good PDB code on your own with your TFs approval, or was given a PDB code by your TF after a few unsuccessful attempts, you can always type this PDB code into the PDB site to check out the full details and specifications of your protein and ligand.

A-6. Saving Images

To save an image of your PyMol screen click on “File” in the upper bar, and select “Export Image as” a “PNG” file. With the newest version of PyMol a window will open with options about the type of file you want. Select “capture current display” or “ray trace with opaque background”. We recommend saving your image with a title that includes the protein name and the feature you are illustrating.