# Exercise in Protein Structure Exploration

CHE 255 - Biochemistry

**Assignment Overview:**

This straightforward assignment will require you to do three things: 1) learn how to use a tool for the graphic display of molecular structures called Protein Explorer, 2) use Protein Explorer to explore the structures of biomacromolecules (proteins mostly) and capture (and print) a graphical image of your molecule, 3) record your observations from your exploration of molecular structure.

**Learning Objectives:**

My hope is that exposure to this tool through these assignments will create awareness about a resource that is available to you to assist in learning biochemistry. This tool has particular value in aiding the visualization of what complex biochemicals might look like and should deepen your appreciation for the nature of interactions between biochemicals and the requirements of their specificity.

- Develop proficiency in use of Protein Explorer and in accessing PDB files
- Depict complex biochemical structures to display features and convey information
- Develop ability to discover useful information by observing molecular structures

**Getting set up:**

Protein Explorer is a so-called Chime resource, so you must use it from a browser (MS Internet Explore will not work on Mac) that is equipped with the Chime plug-in (version 2.0 or later). However, because the program is browser-based, it has the advantage of being available from a PC or a Mac computer. In addition, the browser-based nature of this tool has allowed menu command options to be developed as useful features in addition to the line command options available with other graphic display programs (i.e. RasMol). This makes Protein Explorer more accessible to first time users who have not learned all the necessary line commands. Basically, it is tons of fun!

All the computers on campus have the Chime plug-in. If you want to know if your computer has the Chime plug-in, you may figure this out by inspecting the Netscape or Explorer Plug-ins folder for Chime. If it is absent, you may obtain the Chime plug-in from IT's Windows download page. Run the installer software on your computer. You will need to indicate the proper folder for its installation, so you may wish to determine this ahead of time. Once Chime is installed, you should re-start your browser and proceed as indicated below.

Protein Explorer can be run entirely over the web. You *may* also download the software and run it locally through your browser, however, I have tried this and it takes a long time to download and requires supporting downloads to operate. It would be my recommendation to use the program from the web. You can quick-start the program and then upload your desired file or enter your PDB identification code (4 characters) and start the program with the upload of this data file. To do either, go to the following URL:

- http://molvis.sdsc.edu/protexpl/frntdoor.htm

There are some additional helps that may be of interest to you in using the Protein Explorer program. First, there is a tour at the site above available by selecting the hyperlink for "1-hour tour." In addition, if you do not have the PDB identification code for your structure, you may find it by searching at the Research Collaboratory for Structural Bioinformatics (RCSB - database of structure data) at http://www.rcsb.org/pdb/ if you follow the URL with the suffix *searchlite.html* or choose the

SearchLite hyperlink from the right column. Once you find a structure of interest, you can record the PDB code and return to the Protein Explorer site to load the data, OR you can follow the hyperlinks from the RCSB site to launch Protein Explorer directly from the RCSB site.

Once you have Protein Explorer running, you will see three windows. One will display the structure you have uploaded, one will have menu choices and be titled First View, and one will have line command options. You can proceed to explore your protein structure by choosing the *Explore More!* hyperlink from FirstView. It will then be replaced by a QuickViews window that will give you menu choices for changing the appearance and exploring your uploaded molecular structure. You are ready to go! Note that from the QuickViews window, you can upload other molecules via the *Different molecule* hyperlink. This will give you a window to load a built-in example of a DNA-protein complex (a famous one from yeast!), to enter an additional PDB code to upload a new molecule, or to browse your hard drive for PDB files you may have saved. A hyperlink to the PDB Lite search options also exists in this window.

**The first assignment:**

For the first assignment, I want you to explore the structure of the molecule you read about in your first paper summary (trying for some continuity here....). So, enter the PDB code for your molecule in the window for upload choice in the Protein Explorer FrontDoor menu. If you were unable to find this code in your paper, you will need to visit the RCSB site to search for the structure and its code as described above. Once you have this molecule uploaded, use the pull-down menus to change the appearance of the structure as you wish (you may want to turn off the water molecules). ***Explore!***

To complete the assignment, you will need to obtain and complete the form available at http://molvis.sdsc.edu/protexpl/rec-obs.htm (to be handed in) *and* print a copy of the image of your molecule. Your image should be configured as follows. Change the water molecules so that they are displayed in the *ball and stick* mode. Display the protein structure in the *cartoon* mode. If there is more than one polypeptide, color the protein using the *chains* option. Display anything in the structure that *IS NOT* either protein or water (use *ligand*) in the *ball and stick* mode and with the *Element(CPK)* color scheme. Orient the molecule so as to demonstrate that you have displayed the molecule as directed (use zoom?). To obtain a copy of this image, go to the MDL icon in the lower right of the structure window and select it with the mouse. Use the Edit option to *Copy* the image. I have found that I need to use a PowerPoint window to *Paste* (and actually obtain) the image, but you can try other graphics or editing programs if you wish. Once captured, type the PDB code and your name on the top of the page and print a copy of the image to hand in along with the observation form (due **Oct. 7**).

**The second assignment:**

For the second assignment, I want you to explore the structure of a complex between a protein and nucleic acid molecule (excluding the Gal4 protein from yeast). I would recommend two potential routes to identify a candidate PDB file. First, you may wish to search the literature using the PubMed search tool to determine if your favorite protein-nucleic acid interaction has been solved structurally (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi). If it has, you can either retrieve the paper describing this structure to find the PDB code, or you may search the RCSB using *SearchLite* to find the structure and then browse the header information for different structures to find the one with the correct reference. A second route would be to search the RCSB directly using key words to find some structure containing a protein-nucleic acid interaction. Once you have found your structure, enter its PDB code in the window for upload choice in the Protein Explorer FrontDoor menu, and use the pull-down menus to change the appearance of the structure as you wish. ***Explore!***

To complete the assignment, you will need to again complete the form available at http://molvis.sdsc.edu/protexpl/rec-obs.htm (to be handed in) *and* print a copy of the image of your molecule. Your image should be configured as follows. Change the water molecules so that they *are not* displayed. Select the protein and display its structure using the *ball and stick* mode and color by chain. Select the nucleic acid, and display this in the *surfaces* mode. Display anything in the structure that *IS NOT* either protein, nucleic acid or water (use *ligand*) in the *spacefill* mode and with the *Element(CPK)* color scheme. Orient the molecule so as to demonstrate that you have displayed the molecule as directed (zoom ?) and copy the image. Type the PDB code on the top of the page along with your name and print a copy of the image to hand in along with the completed observation form (due **Oct. 14**).

**Notes:** There is a tutorial that is more than the 1-hour tour and it can be found at the URL http://molvis.sdsc.edu/protexpl/pe_tut.htm. If you are interested in learning more about how to use the line commands, you can get a short list at http://www.umass.edu/microbio/rasmol/seleccmd.htm. If you would like a more complete exposure to these options, consider the RasMol instruction guide at http://www.umass.edu/microbio/rasmol/getras.htm#rasmanual.

In addition, there are a few macro commands that you may find useful. If you hold down the *shift* key while grabbing the structure with your mouse arrow, you can draw it toward you or move away from you in order to zoom in and out, respectively. You can also hold down the *alt* key with the mouse button selected in order to move the structure across the display in the directions up, down, left, or right.

A PDF file version of the handout to be completed for these assignments can be found at http://molvis.sdsc.edu/protexpl/rec-obs.pdf.