

# CS 663: Algorithms in Structural Molecular Biology

## Assignment #2

Please email to your TA by 1/23/2013

### Molecular Visualization with PyMOL

#### Retrieve PDB file

Go to the Protein Data Bank website at <http://www.rcsb.org>. Search and download the file 1EBZ.pdb. This is the structure of HIV-1 Protease dimer bound to an inhibitor.

#### Download PyMOL

Go to the Supplemental Materials page on the course website and follow the instructions to download and install PyMOL.

#### About HIV-1 Protease

HIV-1 Protease is an essential enzyme in the life-cycle of HIV, a retrovirus that causes AIDS. It falls under the class of aspartic proteases, which have two highly conserved aspartate residues in the active site. HIV-1 protease is a homodimer, each chain containing 99 residues. The active site is located at the interface of the two subunits and the essential residues in the active site are Asp25-Thr26-Gly27. The two Asp25 residues from both the chains are the catalytic residues.

Because of its importance in the life cycle of the virus, HIV-1 Protease is a prime target against which drugs are developed. The enzyme in the PDB file 1EBZ is bound to an inhibitor. Also HIV-1 Protease is known to develop resistance towards a lot of drugs and hence it becomes increasingly difficult to design drugs to block the function of the enzyme.

#### Visualization exercises

Open the PDB file 1EBZ.pdb in PyMOL. You will be able to see the two chains and the inhibitor molecule bound in the active site. Select the inhibitor molecule and hide it from view. Select the enzyme and display it as cartoons, with different colors for alpha helices, beta sheets and loop regions. (Look at the HELIX and SHEET entries in the PDB file to find out which residues belong to which category.) Orient the molecule to a view of your choice. Save the image as a .png. For the second image, color the two chains with a separate color and save the image as a .png.

Orient the molecule so that you are looking down the active site. Choose any of the above coloring scheme for the protein. Select the inhibitor and show it as sticks, in CPK coloring. Now display the six active site residues (three from each chain) as sticks and display them with a different coloring scheme from the inhibitor. Save the image.

Zoom in on the two active site residues. What atoms of the inhibitor are closest to the two aspartate residues (use the distance measuring wizard for this)? Draw lines connecting the closest atoms on the inhibitor and the two aspartate residues. Save the image.

Turn off the active site residues. Display the enzyme as well as the inhibitor as surfaces. You can make the surfaces partially transparent so that the cartoons and the stick figures are visible. Choose a good overall view of the enzyme and the inhibitor and save the image.

One of the coolest things about PyMOL is that it helps you generate a series of PNG images which can later be combined to make a movie. Turn off the surface display for the enzyme and the inhibitor, keeping the cartoon and the stick figures. Use PyMOL to generate a series of PNG images to make a movie which shows the protease and the inhibitor rotating 360 degrees.

Now repeat the above exercises with a protein or protein-ligand complex of your choice.

## **Submission**

Zip/Tar the saved images and the movies, along with a small description of what each image and movie shows, and email it to your TA. Please see the website for the due date.