Modeling and Molecular Simulations
Laboratory Exercises
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Lab No. 1: Introduction to VMD

I. OBJECTIVE

VMD is a program for displaying molecular structures and analyzing them. It can also display animations of molecular motion, a feature which we may use in a future lab. VMD is a widely used graphics program therefore a good introduction to its use is necessary. VMD is a free program that runs on many platforms (SGI, linux, Windows) so you can install it on your own computer and use it at home. In this first lab you will become acquainted with VMD and learn its basic controls. You will learn how to move and rotate the molecule, to select colors, choose atoms to display, and to modify the molecule. Today's lab is largely based on the VMD Introductory tutorial. For more info on the program, visit the WEB site http://www.ks.uiuc.edu/Research/vmd.

II. PROCEDURE

We will be using the Linux operating system. You all have your own account and personal password on the machines.

Log in to the computer. Start a console so you can type in Linux (Unix) commands. In this window, you will be in your home directory.

- Type **pwd** to verify it.

– Make a directory called lab1 and change to that directory (**cd** lab1).
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Starting the VMD session

To start vmd type /home/user1/bin/***vmd*** on the command line of your shell (Unix). VMD should start up in a window titled *vmd console*, a display window entitled *OpenGL Display*, and a button bar entitled main. Text commands are typed in the console window, graphics are displayed and manipulated in the display window, and most commands are available from the menu interface, accessible through the button bar. (The menus are built on the Forms or FLTK library so all future references in the documentation will refer to them as forms and not menus.) All the forms except the main form can be turned off by pressing the button in the center top. There are two ways to perform almost all functions in VMD, either use the forms or the text console. Some of the more sophisticated commands, such as Tcl scripting, are only available in the text interface. Structures can be read into VMD in different format. Today, we will focus on reading PDB (Protein Data Bank) formatted files. The PDB file contains data about the atom, residue, and segment names, the occupancy and beta factor, and one coordinate set. When VMD loads a file it requires information about atom names and coordinates and tries to fill in the rest. Since the PDB file contains all this information, it does not need to be loaded with any other data files. However, the PDB file doesn't contain the atom types, masses, and charges, so these are guessed.

B. VMD 1.8.3 A new version of VMD has become available, vmd1.8.3. We have tried to update the lab manuals as much as possible to give you info relevant to version this version. However, there might still be some remnants of the other commands that escaped our vigilance. If the lab manual refers to a command that you do no find as indicated, try to use your best judgement to find a substitute.

We'll begin by doing the first part of the vmd tutorial, which deals with the small protein UBIQUITIN. The vmd tutorial, source code, executables and lab manuals can be found at www.ks.uiuc.edu.

Download 1UBQ.pdb from the protein databank. Please follow the VMD tutorial that has been provided to you.

C. **Viewing myoglobin** We will load a PDB (Protein Data Bank) file containing the coordinates of the atoms in myoglobin. Click on ***File – New Molecule*** form in the main ***VMD*** menu and load the pdb structure ***1dwr.pdb***, using a procedure similar as described for ubiquitin after having downloaded the structure from the Protein DataBank. After you have loaded a myoglobin structure, you can type « **rotate stop** » in the vmd console to stop the molecule rotation if rotating. You can also change the view in perspective by going into the **Display** form and change the **projection** to **orthographic**. You can use the mouse to manipulate the structure in the display window. There are *three* basic mouse modes: *rotation, translation, scaling*. The mode can be changed from the Mouse form, or by pressing ***r***, ***t***, or ***s*** on the keyboard. Experiment with these modes, and note how the cursor changes to indicate the current mode. In rotation mode, the left mouse button controls rotation about axes parallel to the screen, and the middle button controls rotation about the axis perpendicular to the screen. In translation mode, the left mouse button controls translation parallel to the screen, while the middle button controls translation in and out of the screen. Finally, in scaling mode, both the left and middle buttons control global scaling when the mouse is moved left or right, but the middle button causes larger changes. These mouse/keyboard combinations might change depending on your computer (desktop machine with a three button mouse or a portable computer with a trackpad). Once you have your molecule in VMD, you want to examine it, calculate distances, angles, etc.

As protein structures can be very large, it is important to display the protein in the clearest way. This can be done by using different colors, or by only looking at parts of the structure. We are now going to learn manipulating atom display and colors. By default the myoglobin bonds are represented as lines and non-bonded atoms as points, with the color in both cases representing the atom type (expl C, 0, N..). This representation is easy for the computer to draw but is not always informative, especially when there are a large number of atoms.

VMD allows you to display many of the common molecular representations. To access these, open the ***Graphics –Representation*** form using the button bar. Now try to view the myoglobin structure with its protein backbone represented as a tube, the heme represented as licorice, the ion and molecule represented as van der Waals spheres, and histidines 64 and 93 represented as CPK models.

First, type backbone in the atom selection text ('***Selected Atoms***') entry area and press '*enter*' to select the myoglobin backbone. All of the protein except for the backbone will disappear. Choose drawing method `***Tube***' from the ***Drawing method*** chooser to render the backbone as a tube, and chose ***Coloring method*** `***Backbone***' from the coloring method chooser to color the tube with the 7 predefined backbone color. Click on the ***Create Rep*** button. This causes a new line to appear on the browser identical to the first line. The new line can be changed without affecting the first one, so clear the atom selection text area ('***Selected Atoms***') and then enter ***resname HEM*** to select the heme. At this point the heme isn't visible because it cannot be drawn as a tube, so choose the `***Licorice***' ***drawing method*** to make it appear.

Click on ***Create Rep*** again to make a new view, and enter ***resname SO4 CMO*** to select the ion and the molecule, and choose the drawing method `***VDW***' to render them as Van der Waal spheres. Try the different coloring methods possible. Once again, press the ***Create Rep*** button and enter ***resid 93 64*** to select the two histidines, and render them as ***CPK***'. Many more ways to represent atoms are possible.

Experiment with the options available in the ***Graphics*** form. (For example to entirely delete the view of one representation you can click on the ***delete*** button).

D. Atom Selection possibilities VMD has a rather powerful atom selection language available. It is based around the assumption that every atom has a set of associated parameters with it values which can be accessed through keywords. These values could be boolean (is this a protein atom?), numeric (as in the atom index or atomic mass), or string (the atom name). You start from your myoglobin created in the first section (protein backbone in tube, heme in licorice, SO4 and CMO in VDW spheres and histidines 93 & 64 in CPK model, see above). Atoms may be selected on the basis of a *property*, i.e. protein or not protein, water, or nucleic backbone. They may also be selected by atom name, such as atom C, by residue name, such as ***resname HEM***, or by many other identifiers. Multiple atoms may be specified with one keyword. For example, the selection ***name C CA N O*** will select the backbone atoms. (A similar effect may be obtained with the command ***protein backbone***.) VMD can handle regular expressions, so that ***name "C.*"*** will select all atoms with names starting with C.

VMD also understands the boolean operators and, or, and not, so the selection ***resname HEM and not name "N.*"*** selects all non-nitrogen atoms in the heme group of myoglobin. *Some examples to try:* There are two types of selection modes. The first is a keyword followed by a list of either values or a range of values. For example, ***name CA*** selects all atoms with the name CA (which could be a C or a calcium); 8 ***resname ALA PHE ASP*** selects all atoms in either alanine, phenylalanine, or asparagine; ***index 5*** selects the 6th atom (in the internal VMD numbering scheme).

VMD can also do range selections: ***mass 5 to 11.5*** selects atoms with mass between 5 and 11.5 inclusive, ***resname ALA to CYS TYR*** selects atoms in alanine, arginine, asparagine, aspartic acid, cystine, and also tyrosine. The keyword selection works by checking each term on the list following the keyword. The term is either a single word (eg, name CA) or a range (eg resid 35 to 90). Selections can be combined

with the boolean operators and and or, collected inside of parenthesis, and modified by not, as in ***(name CA or name CB) and mass 12 to 17*** which selects all atoms name CA or CB and have masses between 12 and 17 amu (this could be used to distinguish a C-alpha from a calcium). VMD has operator precedence similar to C so leaving the parenthesis out of the previous expression, as in: ***name CA or name CB and mass 12 to 17*** actually selects all atoms named CA or those that are named CB and have the appropriate mass ie it is the same as *name CA or (name CB and mass 12 to 17).*

E. Comparing Two Structures Let's start from scratch by deleting everything: open the ***Molecule*** form, select every line in the browser (there should be only one), and press the ***Delete*** button. Start by loading the ***1dwr*** structure with the ***Files*** form. Turn on just the heme, CO, and histidines by using the selection commands ***resname HEM CMO or resid 64 93***. The dot (probably green) in the middle is the iron and you can verify that by picking it with the mouse. Open the ***Mouse*** form and select the ***Label - Atoms*** for the pick mode. The label *HEM154:FE* should appear both on the display and in the text console. The ***label*** form allows you to manange the labels (delete them etc…) Change the ***Label*** in the ***Mouse*** form to ``***Bonds***". To get the distance between the iron and the oxygen of the CO, click with the left mouse button first on the iron and then on the oxygen. The first click turned the FE label on and the second turned the O label on and drew a line between the two atoms with the distance 9 drawn in the middle and a bit to the right. What is the distance of these two atoms? (Answer: The distance between the two atoms is _____ Å) Now measure the distance between the FE and the C of the CO (Answer: distance = _____ Å). In order to experiment with more complex picking modes, consider the angle made by the O of the CO with the FE of the heme and the NE2 of residue 93 (you can click on the atoms to find which ones are which). Using the Mouse form, change the ***Label*** mode to ***Angles***. Click on each of the three atoms using the left mouse button. After the third pick, a shallow angle will appear. What angle do these three atoms form? (____ °).

Now load another structure of myoglobin ***1dws.pdb*** file which can be downloaded from the Protein DataBank. Again use the ***Molecules*** form to do this. Both of the molecules will be loaded side by side. Go to the ***Graphics*** form and change the selection so it the same as the first, i.e. ***resname HEM CMO or resid 64 93***. The two molecules are almost atop each other, making it hard to distinguish the two, so change the colors to simplify things. First, in the Graphics form, change the Coloring method to `***Molecule***'. Use the Selected Molecule chooser to change the ***1dwr.pdb Coloring method*** to `***Molecule***' as well. Open the ***Graphics-Color*** form and scroll the Category browser down until the line `***Molecule***' is visible. Click on it then, click on the line that corresponds to ***1dwr.pdb***. Go to ***Colors*** in the Graphics menu, and figure out how to display ***1dwr.pdb*** in silver. Display the molecule ***1dws.pdb***. in a color scheme that suits you and allow to see clearly the difference between the myoglobin with the bound CO and a dissociated, intermediate state. At this point it is easy to measure the change in position between the two different states by using the middle mouse button to pick the same atom in the two conformations. Once that is done, it is easy to point out one interesting aspect of the way VMD handles the graphics. Go to the ***Molecule*** form, select one of the two molecules, and press ***Toggle Fixed***. Enter translation mode and move the other molecule around. Notice that the number which lists the distance between the two atoms never changes. That's because the mouse only affects the way the coordinates are translated to the screen image. It does not affect the real coordinates at all. It is possible to change the coordinates in a molecule using the text command interface, or by using the atom move pick modes). By the way, unfix the molecules and do a `***Reset View***'. You can now compare: a) the distances between iron and oxygen of the CO; b) the distances between iron and the carbon of CO; c) angle between the O of the CO with the FE of the heme and the NE2 of residue 93. Read in a third structure of myoglobin, ***1dwt.pdb***, which you can obtain from the Protein Data Bank. What is different in this third structure of myoglobin with respect to the other two? Hint: Look at the Heme site as you did with the first two structures.

E. Saving your work After creating a set of interesting/informative representations of your molecule, you may want to save your work so that you can regenerate the scene later. Save your configuration as explained in the ubiquitin tutorial.

To end your VMD session, click on the main ***VMD*** window's ***QUIT*** button (or VMD). Check take your configuration has been saved as you wanted by restarting vmd.

To learn more about these three structure of myoglobin, look up the article
Chu K, Vojtchovsky J, McMahon BH, Sweet RM, Berendzen J, Schlichting I.
Structure of a ligand-binding intermediate in wild-type carbonmonoxy myoglobin.
Nature. 2000 Feb 24;403(6772):921-3.