



SCHRÖDINGER ACADEMY

PYMOL

Introduction to PyMOL

For use with PyMOL v1.6

Introduction to PyMOL

Created December 2014 with PyMOL v1.6

In this tutorial we will review commonly used, introductory techniques in PyMOL. The tutorial is divided into the following sections:

- 1. Introduction**
- 2. The PyMOL Layout**
- 3. Mouse Controls**
- 4. Features**
- 5. Advanced Feature Previews**
- 6. Next Steps**

Required File: PyMOLTutorials.zip

1. Introduction

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About This Booklet

This is a follow-along guide for the Introduction to PyMOL classroom tutorial taught by Schrödinger. It covers the basics of PyMOL for medicinal chemists and other industrial scientists, including visualization of protein-ligand interactions, creating figures, and working with session files.

This tutorial was created for PyMOL version 1.6 or greater running under Windows, Mac, or Linux.

Typographic Conventions

Words typeset in Courier font, such as `extend`, are commands that can be typed directly into a PyMOL command line. Keystroke modifier keys are typeset in upper case, where `CTRL`, `ALT`, `ESC`, `SHIFT`, are “control,” “alt,” “escape,” and “shift,” respectively. The mouse buttons are shown as upper case letters in Courier font, where `LEFT`, `MID`, `WHEEL`, `RIGHT`, are the left mouse button, middle mouse button, wheel, and right mouse button, respectively. The word `DRAG` indicates that a mouse button should be pressed and held while the mouse is moved. For example, `CTRL-MID-DRAG` indicates the user should press and hold the control key, then press and hold the middle mouse button, and drag the mouse with the control key and middle mouse button held down. Menu navigation is shown in bold Times font as **Menu>SubMenu>...** For example, **File>Save Image As...>PNG** indicates that the user should click on the File menu, choose the Save Image As submenu, and finally choose PNG, from the submenu.

Requirements

Before starting this tutorial, please ensure that you have the following:

- PyMOL version 1.6 or greater
- A 3-button wheel mouse
- Tutorial-specific data files found in the IntroductionToPyMOL sub folder of the PyMOLTutorials archive supplied by Schrödinger. This archive is typically provided as a compressed “ZIP” file, which should be extracted on to your Desktop

Also, please make sure that your keyboard Caps Lock key is turned off when using PyMOL.

Getting Ready–Starting the PyMOL Application

If you haven’t already, please launch PyMOL by double clicking on the PyMOL icon on your desktop. On Windows PCs, PyMOL brings up two windows. The MacPyMOL version will bring up one window, which contains the same two user interface components.

2. The PyMOL Layout

Try It–Loading a File and Using the Mouse

The larger, Viewer Window is where our molecules and objects will appear. Above it is the Upper Control Window (see Figures 1 and 2).

Please load the structure file `1t46.pdb` from disk. To do this, click on the Upper Control Window and choose **File>Open**. Then, from the `PyMOLTutorials/IntroductionToPyMOL` folder on your desktop, please select the file named `1t46.pdb`. Your PyMOL should now look like Figure 2, except that the initial colors may be different.

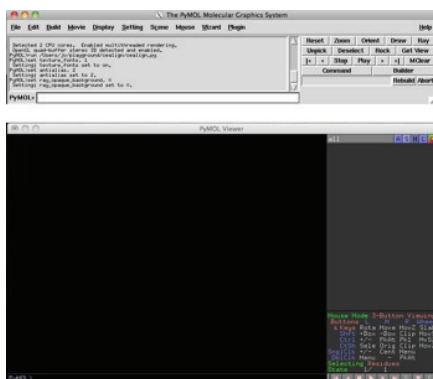


Figure 1: PyMOL immediately after being launched on a Windows PC.

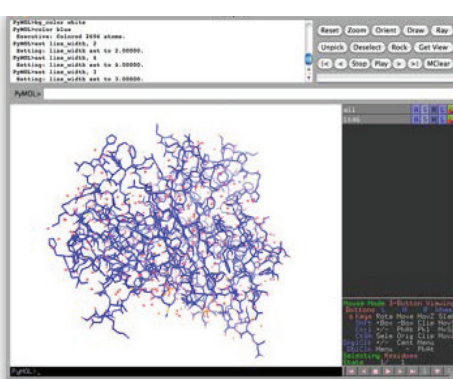


Figure 2: Kinase protein, PDB ID 1t46, loaded into PyMOL on a Mac.

At this time, please take a moment to familiarize yourself with the behavior of the mouse in PyMOL. Place your mouse cursor over the protein. Now, press and hold while moving the mouse—aka dragging—with each of the mouse buttons in turn. As Figure 3 shows, dragging with the left mouse button rotates the scene in the Display; dragging with the middle mouse button moves the molecule in the plane of the display; and dragging with the right mouse button zooms in and out.

Don't worry if you get lost. Just click the Reset button in the Upper Control Window to restore the original view.

The Viewer Window

An annotated snapshot of the Viewer Window is shown in Figure 4. The left side of the Viewer Window is called the Display Area and is where your molecules and objects will appear when loaded. Directly beneath the Display Area is a command line for entering PyMOL commands. Almost everything you can do with the mouse in PyMOL can also be done by typing commands, and this is one of two places where they can be entered. Next, the upper right hand side of the screen houses the Object Menu Panel, which is used to show/hide objects and selections as well as change many of their properties. At the bottom right of the screen are the Mouse Controls, which we discuss later.

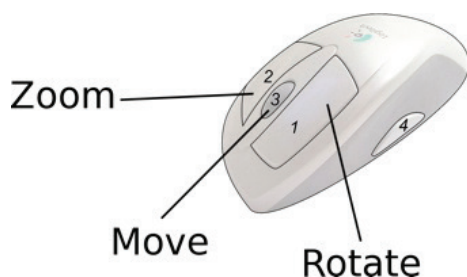


Figure 3: Basic mouse button functions in PyMOL.

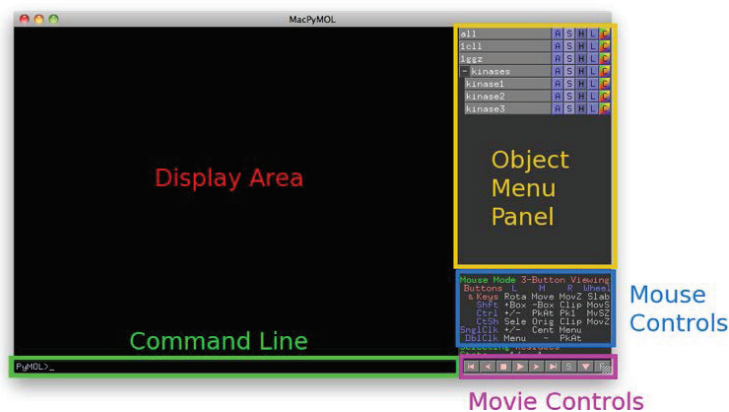


Figure 4: The Viewer Window, with annotations.

Try It—Using the Viewer Window: Entering Commands and Using the Object Menu Panel

Please click in the Display Area. Now, press the `ESC` key. Your command history and other information is shown here. Press `ESC` to return to the normal viewing mode. This feature provides a quick way of viewing PyMOL's text output. If the Viewer Window is selected as you type, what you input will appear in the lower command line.

Type `orient` and hit enter. The molecule in your scene should now be oriented, that is, displayed with the longest axis aligned with the x-axis. Now, please type `reset` and hit enter. This does the same thing as clicking on the Reset button in the Upper Control Window.

Please find the Object Menu Panel in the upper right of the Viewer Window. An example Object Menu is shown in Figure 5. Here, you'll see a list of names. The objects whose names appear with light grey backgrounds are active, and may appear in the Display Area. Click on the name to deactivate, or disable, the object, and it will be hidden from view. Your Object Menu should have entries for `all` and `1t46`, and maybe something like `(sele)`. Please click on `1t46`. This disables it. Click again to reenale it.

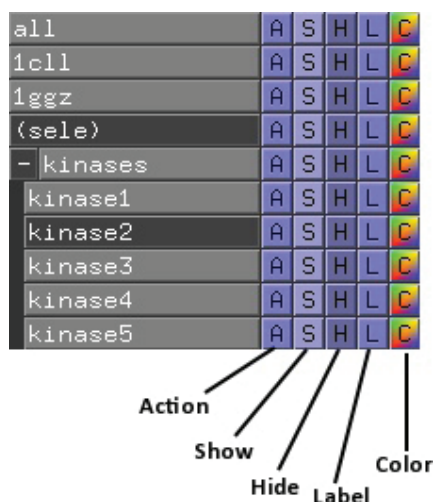



Figure 5: Example Object Menu Panel. Kinases is a group in which there are five kinase proteins; kinase2, a protein, is disabled, all other kinases are enabled. Proteins 1c1l and 1ggz are objects (sele) is a disabled selection. We will discuss groups, objects and selections later.

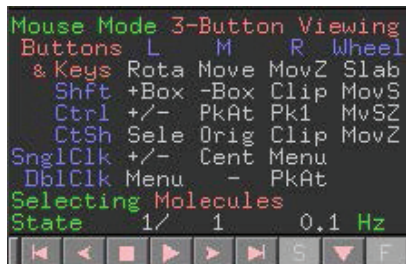
Each of the five Pop-up Menus,  is accessed by clicking on a letter. A>Actions contains lots of preset actions; S>Show allows us to control various representations; H>Hide is the opposite of Show, here you can hide various representations; L>Label is for showing and creating labels; and finally, C>Color is for coloring our objects. Click on each of the five letters to see what pops up. We'll come back to these later.

Mouse Modes

Many different tasks can be performed using the mouse inside of PyMOL, through a variety of mouse modes. Each mouse mode just reassigns the mouse buttons to perform different tasks. PyMOL's Viewing Mode is used primarily used to view, rotate, translate, and change the representations of objects. Editing Mode is used to rotate bonds, replace atoms, physically move atoms and residues, etc. The mouse mode table for each of these modes is shown, in Figures 6a and 6b.

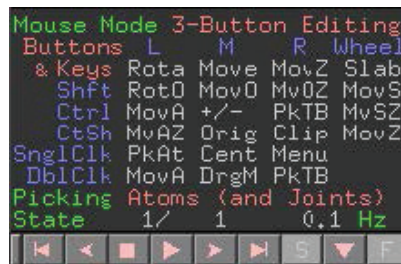
Try It–Setting and Using the Different Mouse Modes

In PyMOL, just click the table to cycle through the mouse modes. This table shows the current mouse mode (3-Button Viewing, 3-Button Editing) and what each keyboard and mouse action does.



Mouse Mode 3-Button Viewing				
Buttons	L	M	R	Wheel
& Keys	Rota	Move	MovZ	Slab
Shft	+Box	-Box	Clip	MovS
Ctrl	+/-	PkAt	Pk1	MvSZ
CtSh	Sele	Orig	Clip	MovZ
SnglClk	+/-	Cent	Menu	
Db1Clk	Menu	-	PkAt	
Selecting Molecules				
State	1/	1	0.1	Hz

Figure 6a: 3-Button Viewing Mode.



Mouse Mode 3-Button Editing				
Buttons	L	M	R	Wheel
& Keys	Rota	Move	MovZ	Slab
Shft	Rot0	Mov0	MvOZ	MovS
Ctrl	MovA	+/-	PKTB	MvSZ
CtSh	MvAZ	Orig	Clip	MovZ
SnglClk	PkAt	Cent	Menu	
Db1Clk	MovA	DrgM	PKTB	
Picking Atoms (and Joints)				
State	1/	1	0.1	Hz

Figure 6b: 3-Button Editing Mode.

Reading the Mouse Mode Table

The mouse mode table is a reference guide to PyMOL mouse functions. Column abbreviations are: L, M, and R for LEFT MID and RIGHT buttons. Actions are: Rota, rotate; PkAt, pick atom; Cent, center; PkTB, pick torsion bond; MovA, move atom. Notice that the table changes when you click on it.

Click the Mouse Mode table to enable 3-Button Viewing and locate the word **Selecting**, colored green, as shown in Figure 6a. The red word to the right of **Selecting** tells which **Selecting** mode the mouse is in. Clicking on the word **Selecting** changes the selection mode. The first mode is Residues, which means that, when we click on any atom with the mouse in the Display Area, the entire residue in which that atom resides is selected. Other selection modes are Molecules, which forces PyMOL to select the entire molecule containing the chosen atom; Chains, which will choose the chain in which the selected residue resides; Objects, which selects the entire object containing the chosen atom; C-alphas, the alpha carbon of the residue for the chosen atom; and Segments which chooses segments, which are special fields in a PDB file. Keep clicking to cycle through the options until you return to Residues. When in 3-Button Editing Mode, the word **Selecting** is replaced with **Picking** and the mouse is used to pick Atoms which represent Joints in the molecular graph.

Try It—Using Editing Mode to Move Atoms

Now, please set the mouse mode to Editing, and CTRL-Left-drag on an atom. The atom moves with the mouse in an unphysical but compliant way, tracking with the mouse. To undo the movement, type undo and hit enter in the PyMOL command line. PyMOL currently has a very limited undo system, so please do not rely on it. We introduce it here to let you know that it exists, but only for undoing changes made to atom positions. Now that we've toured the Viewer Window, let's see what is offered to us in the Upper Control Window.

The Upper Control Window

The Upper Control Window, shown in Figure 7, houses a menu bar for access to many PyMOL options and controls. The buttons allow access to many of the most commonly used functions. The second of the two command lines is here.

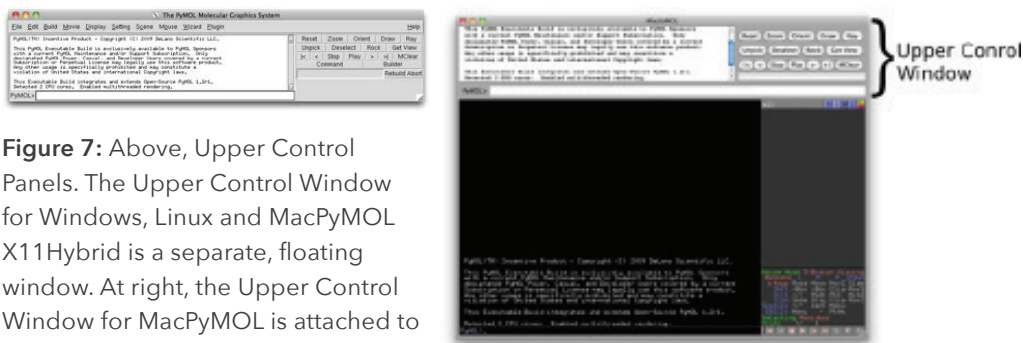


Figure 7: Above, Upper Control Panels. The Upper Control Window for Windows, Linux and MacPyMOL X11Hybrid is a separate, floating window. At right, the Upper Control Window for MacPyMOL is attached to the upper part of the single PyMOL window.

This one is different from the other in that it will accept pasted text, and you can copy from it. The history and diagnostics window is where PyMOL feedback will be shown. For example, if you wanted to calculate the distance between alpha carbons number 10 and 11 you could type `distance 10/CA, 11/CA` and the answer would show up in the window.

Please take a moment to find the following buttons: Reset, Ray, and Builder. As you know Reset restores the original orientation of the molecule. Ray is a very frequently used command for making beautiful publication quality images. We will talk about the Ray command later on. PyMOL has a built-in Builder for building small molecule fragments and peptides. Please click on the Builder button to switch to builder mode (MacPyMOL doesn't have the builder, but you can access it by launching MacPyMOL in the PyMOLX11Hybrid mode). The Builder is discussed in our Advanced Tutorials. Please click on Builder again to enable the default buttons.

2. Mouse Controls

Many different tasks are performed using the mouse in PyMOL. There is much to learn, but remember you can always rely on the Mouse Mode table if you get lost. Producing figures that look just right often takes some skilled mousing. So, let's continue with the mouse.

Getting Started

A three-button mouse is required for this tutorial, although PyMOL can support other types of mice to a lesser extent. And, please take note that when using a three-button wheel mouse,

there is a difference between clicking the wheel button and scrolling it up and down. If your mouse click turns on pink squares or small white globes, as in Figure 8, then you can always turn these off by Left-clicking on a blank part of the Display Area. Lastly, please make sure you Caps Lock key is not turned on.

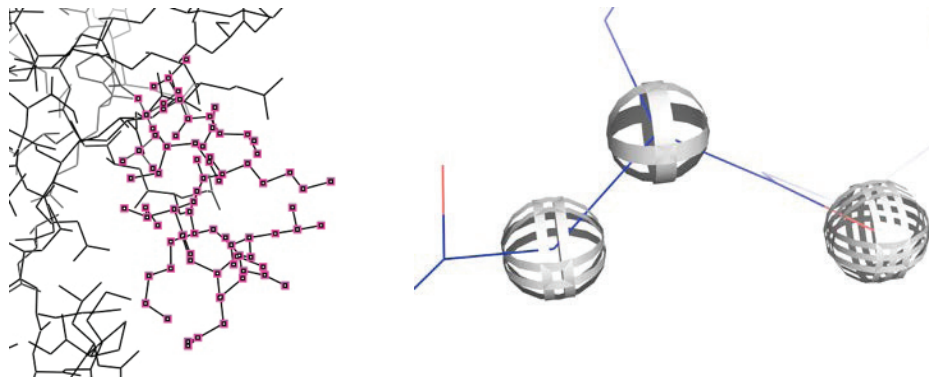


Fig. 8: If you click in the PyMOL Display Area without dragging, you may cause pink boxes (left) or white globes (right) to appear. For now, just left-click in a blank area to hide them.

Try It–Basic Mousing: Rotations, Panning and Zooming

Using the mouse mode table for reference, take a few minutes to familiarize yourself, if you haven't already, with how the mouse works. Rotate the molecule with **LEFT-drag**. Try zooming in and out (**RIGHT-drag**). Try panning with **MID-drag** to move the molecule about the screen. Don't forget, you can refer to the mouse mode table if you ever forget the mouse controls.

Trackball Mode

By default, PyMOL enables the mouse in what is called Trackball Mode. This mode allows us to make precise and sophisticated motions with the mouse. In this mode, if you click and drag through the center of the screen to rotate (left image of Figure 9), the scene rotates on an axis parallel to the plane of the screen. However, if you choose a point on one of the far edges of the Display Area and drag along the edge, the molecule rotates along an axis perpendicular to the plane of the screen (like spinning a top; right image of Figure 9).

Try It–Virtual Trackball Mode

Let's give those motions a shot. Please, select anywhere on the protein and drag through the center of the screen. Now, click near the far left-hand side of the screen and drag up. Notice the difference in rotations. By the way, in PyMOL, when you rotate objects in this way, you are actually moving the display camera around the object in space. You are not moving the object itself or changing its atomic coordinates.

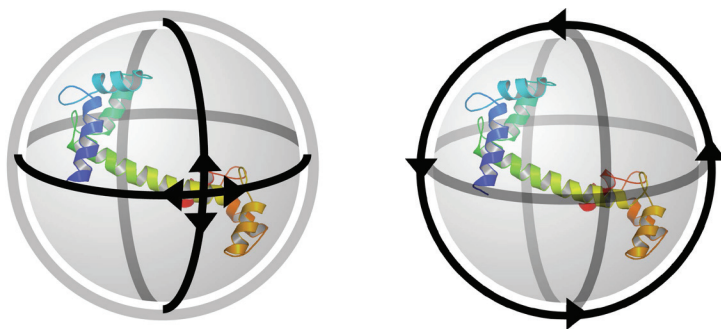


Figure 9: (Left) Trackball rotations when the mouse passes through the center of the screen; (right) trackball rotations when the mouse moves along the outer edges of the screen.

Axis Aligned Mode

If you don't like trackball mode, then you may disable it through the menus by unchecking Mouse>Virtual Trackball. When trackball mode is disabled, PyMOL uses axis-aligned mode. In this mode left-right movements rotate the molecule across the x-axis, up-down motions will rotate the molecule across the y-axis. Combining the motions of x- and y-axis rotations via a circular motion affords rotations about the z-axis.

Try It—Comparing Virtual Trackball and Axis Aligned Mode

Turn on trackball mode and rotate the molecule. Now, turn it off and notice the difference in rotations when you use the same mouse motions. Try to obtain some given orientation of the molecule in each mode. In which mode is it easier to obtain your desired orientation? Please choose whichever mode is easiest for you.

Try It—Centering

When we click—not scroll, but push down—and quickly release the middle mouse button while the cursor is over an atom, PyMOL will place that atom at the center of the screen. This represents a convenient way to roam around the protein focusing only on certain atoms. Please give this a try: `MID-click` from atom to atom in your molecule to roam around the structure.

Clipping

Before we move on, please click Reset to restore the original view of the molecule. (And, if you are using Windows or Linux, please click on the Viewer Window because we want to work in the Display Area some more.)

Now, using the scroll wheel on the mouse, scroll down, towards yourself. Parts of the molecule should disappear. Scroll up, away from yourself, and those portions should now reappear. What you are doing is controlling Clipping in PyMOL. Clipping is a way to focus in on a certain area of the protein while hiding everything else from view. PyMOL has a near clipping plane and a far clipping plane. The space between those two clipping planes is called the Clipping Slab. Objects within the clipping slab are visible. Everything outside of the clipping slab is hidden.

Try It—Adjusting the Clipping Planes

Try using the mouse wheel to clip out everything but one layer of amino acids. Once you've done that, try rotating, panning, and zooming around the scene with the left, middle and right mouse buttons, respectively. With a little practice you should be able to visualize and focus in on specific parts of a structure, such as a single alpha helix.

PyMOL allows you move the clipping slab while keeping the molecule steady with **SHIFT-Scroll**. Give it a shot: when you hold down **SHIFT** on your keyboard and scroll the wheel on your mouse, parts of the molecule should appear and disappear, depending on the position of the clipping slab. PyMOL allows you also to move the molecule and keep the clipping slab steady with **CTRL-Scroll**. Please try this mode and compare it to the other.

If scrolling to adjust the clipping planes is too coarse, then PyMOL also allows us to **SHIFT-RIGHT-drag** to more finely tune the clipping planes. **SHIFT-RIGHT-dragUp/Down** controls the near clipping plane; and, **SHIFT-RIGHT-dragLeft/Right** controls the far clipping plane. If you drag diagonally from the upper right to lower left corner of the Display Area, you move the clipping plane with respect to the objects. If, however, you drag diagonally from the upper left to lower right corner, you set the width of the clipping slab.

Well, that's it for the tour of PyMOL's Layout and basic mouse usage. Now, let's check out some basic features and common tasks that make your life easier.

4. Features

Visualization Presets

Introducing Visualization Presets

PyMOL comes with an array of preset visualizations. Through a couple clicks you can get a technical view, or a simple view, or even a view nicely set for publishing. Each preset emphasizes different aspects of your scene. You can access the preset visualizations through the **A>Actions>Preset** menu. Figure 10 shows the result of applying the **A>Actions>Preset>Ligand Sites>Trans-parent** (better). Figure 11 shows the menu of the available presets.

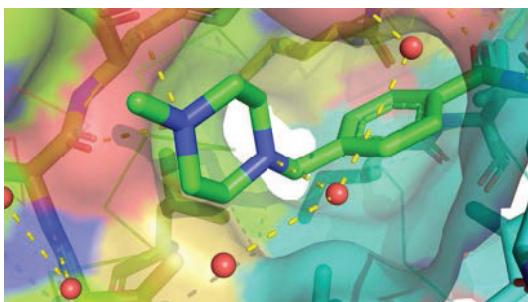


Figure 10: An example image made with one click using the Transparent Ligands site preset.

Try It—Sampling the Visualization Presets

Some visualizations may be immediately useful to you for visualizing protein-ligand complexes. Please choose the **A>Action>Preset>Simple** setting, which shows the protein as a ribbon and

the ligands as sticks. The ligands pop out of the scene while the polymer maintains a simple structure allowing us to see its topology. Do you see the ligand?

Let's now compare this to the Technical setting. Please choose the A>Action>Preset>Technical setting from the preset menu. The ligand is now obscured by lots of technical details. This is where clipping comes in handy. While the ligand is harder to see, if you zoom in on it, you will notice that PyMOL found and is displaying all the hydrogen bonds that the ligand is making with the protein. The A>Action>Preset>Ligands preset is like the Technical preset, but instead of finding all hydrogen bonds, it only finds the hydrogen bonds between the ligand and the protein. Please enable this setting to see the difference.

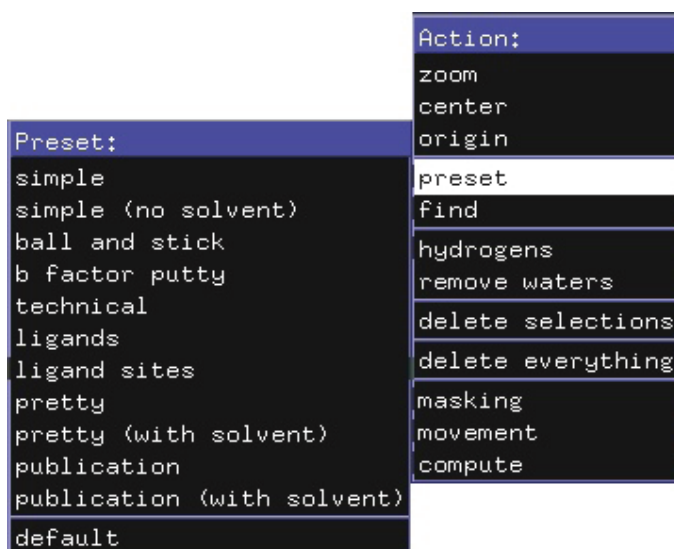


Figure 11: Menu of visualization pre-sets built into PyMOL.

The A>Action>Preset>Ligand Sites submenu opens to show more refined options, which render beautiful views of the ligand binding site as a surface. Please try the various visualization presets on this protein.

Please take a few moments to try each of the presets and consider which might be best suited for your applications. Before moving on, please choose the A>Action>Preset>Publication preset.

Saving Images

Once your display is set up, choose File>Save Image As>PNG. PNG, or Portable Network Graphic, is a popular lossless compressed image format for publishing. PNG files can be read by Microsoft PowerPoint, Microsoft Word, and many other programs. To save a ray traced image press the Ray button before selecting File>Save Image As>PNG.

Ray tracing is a technique to draw scenes with superior detail; it smooths edges, adds shadows, generates better lighting effects. Figure 12 shows the difference between a ray traced image and a non-ray traced images. The trade off for such beautiful images is time: ray tracing can take much longer, depending on the complexity of your scene. Images for publication are typically ray traced.

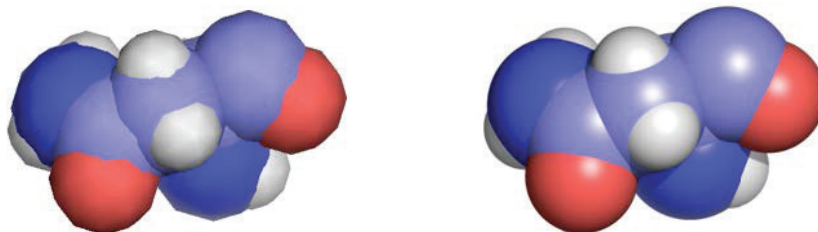


Figure 12: (Left) a non-ray traced image. (Right) the same scene, but ray traced before saving. The difference in quality is clear.

Image Resolution and Transparency

Every (raster) image has a property called resolution—usually measured in dots per inch or DPI. Images for presentation or display on a computer are best set to 72 DPI. Images for printing or for publication are typically required to be 300 or 400 DPI (or higher, ask your journal/publisher for their resolution requirements). Another property that might be useful to know about is transparency. If an image has a transparent area, then whatever is underneath the image will show through. PyMOL can save images with transparent or non-transparent (opaque) backgrounds. Figure 13 and the next paragraph illustrate the difference.

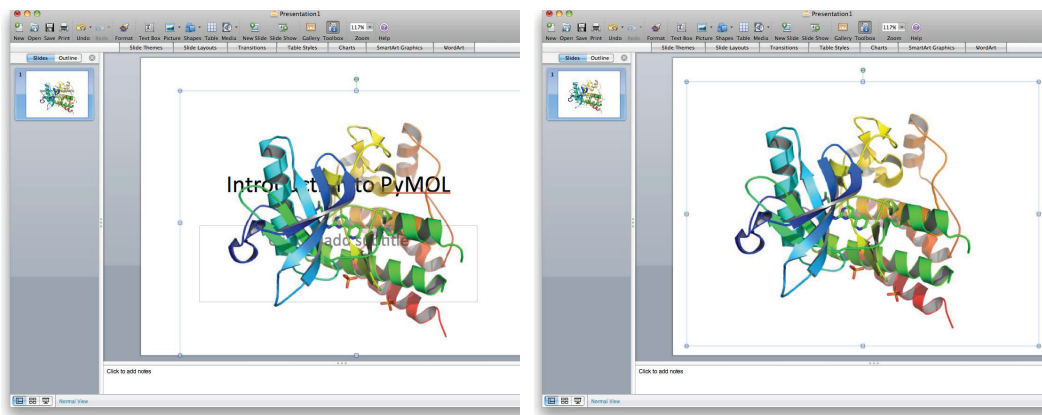


Figure 13: Images insert easily into PowerPoint, Word and other applications. The image at left was ray traced with a transparent background, and so the title and subtitle in PowerPoint show through. The image at the right was ray traced with an opaque white background, and so while the text is still there in PowerPoint it is now hidden underneath the white background.

Try It—Images for PowerPoint, Projectors, and Computer Displays

Let's make an image and import it into PowerPoint. We will also illustrate the difference between a transparent and opaque background. Start by ray tracing your image: please press the Ray button. By default, the image has an opaque background. Save the file containing the image to your Desktop using File>Save Image As>PNG, with the filename `pymol.png`. Next, let's save an image with a transparent background. To do this, make sure Opaque is unchecked in the menu, Display>Background. Now press the Ray button. Save the file to your Desktop using File>Save Image As>PNG, with the filename `pymolT.png`, where the T stands for transparent.

Open up PowerPoint. Where it says, “Click to Add Title,” write “Introduction to PyMOL.” Now, click Insert>Picture and choose the first image, `pymol.png`. The image pastes nicely into PowerPoint. Notice that it covered up your title text. That is because the `pymol.png` file has an opaque background. Now, delete that image (click on it and then hit backspace or delete), and insert the other image, `pymolT.png`, using Insert>Picture. Now, the text should show through the background of the image. For those without PowerPoint, Figure 13 shows the results of the above procedure.

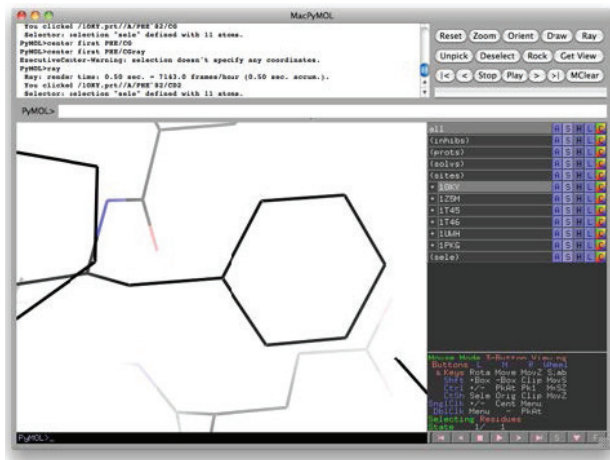


Figure 14: Zoomed in on a PHE residue.

Lastly, you can use the clipboard to copy images into PowerPoint if you have PyMOL for Windows or MacPyMOL. Simply setup the scene you want, then from the Upper Control Window menu choose Edit>Copy to copy the image to the clipboard. Now, in PowerPoint choose Edit>Copy (or type `CTRL-v`) to paste the image from computer memory.

High Resolution Images (Publication and Printing)

To save a high resolution image you need to know the size of image you want (in inches) and the resolution (in dots per inch). Then all you have to do is type one simple PyMOL command: `ray W,H` at the PyMOL command to save the high-resolution file, where H is the height in pixels, W is the width in pixels. To calculate W and H you just multiply the height or width times the DPI. For example, let’s say your publisher wants images to be 4 inches wide by 3 inches tall at 400 DPI. The height in pixels is then: 3 inches * 400 DPI = 1200 pixels; and the width in pixels is 4 inches * 400 DPI = 1600 pixels. So, the exact command to type into PyMOL would be, `ray 1600, 1200`. Lastly, just do File>Save Image As>PNG to save your high resolution image.

Taking Measurements: Distances, Angles, Dihedrals, and Neighbors

PyMOL allows you to take measurements of distances, angles, and dihedral angles, and also to find neighbors. The easiest way to do this is to click on Wizard>Measurement. PyMOL wizards operate by prompting the user to take an action (usually written as a message in the upper left side of the Display Area) and then provide controls for the user on the right side above the Mouse Mode matrix. Don’t forget, when you’re done using a Wizard, make sure you click Done—the last button in the wizard.

Try It–Taking Measurements

Please select **S>Show>As>Lines** to enable the lines visualization for 1t46. Zoom in on a residue, as shown in Figure 14. Now, please open the Measurement Wizard. Next, click on any two atoms; the distance between the two should now be annotated by a dashed line and distance measure. Let's try measuring an angle.

To change the type of measurement, click on the top button in the measurement wizard, which, in Figure 15, displays Distances. A menu will pop up, giving you the other options. If you choose Distances, you need to select two atoms. If you want to measure Angles, you need to select three atoms. Dihedrals require four atoms. Polar, Heavy and all Neighbors need just one. Please take a few moments now to make various measurements. By default, each measurement creates a new object. You can change this by merging the new object with the previous one, or by overwriting the previous object. Control of this feature is through the third menu option in the measurement wizard (see Figure 15, Delete Last Object).

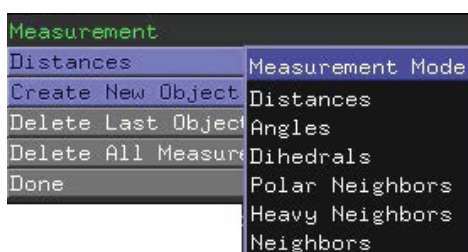


Figure 15: Measurement Modes Pop-up Menu.
Click on Distances to show this menu.

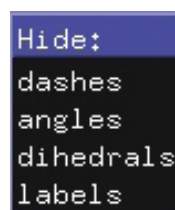


Figure 16: The hide menu.

A common use of the measurement wizard is to create a dashed line between two atoms. To do this, make your measurement and then, on the Pop-up Menu for the measurement object, hide the label with **H>Hide>Labels** (see Figure 16). Mistakes in the Measurement Wizard can be remedied by choosing Delete Last Object, or by deleting the last measurement object choosing **A>Action>Delete**, in the row of the measurement object you wish to delete.

PyMOL Sessions

PyMOL allows you to save your work as a PyMOL Session. Sessions store all of your objects, selections, views, scenes, representations, etc. This is a good way to save your work for later or share it with others. To create a PyMOL Session, just click **File>Save Session As** and then supply a file name. PyMOL sessions end in .pse. If you're in a PyMOL session and want to overwrite a saved .pse file, choose **File>Save Session**. When saving a PyMOL Session, please do not quit the program until you receive a confirmation that PyMOL has successfully written your session file. If you quit without waiting, then your work may not be saved.

To open a PyMOL session, simply double-click on the session file icon. If you are already inside PyMOL, click **File>Open** and then browse to your session file.

If you work in a pharmaceutical or biotech company, there may be computational chemists, crystallographers, or even automated systems that will prepare PyMOL sessions for you. Such prepared sessions are generally accessed via file servers, database systems, or your intranet. If such a system doesn't yet exist, consider asking your structural biologist and computational chemist colleagues about making PyMOL session files available to you.

Try It–Loading and Perusing a Prepared PyMOL Session

Please load the PyMOL session in the PyMOLTutorials/IntroductionToPyMOL folder on your desktop, called KinaseSession.pse. Figure 17 is a screen shot of MacPyMOL opened to the KinaseSession.

In the Display Area you can see the structure of Phosphoinositide–Dependent Kinase 1 (PDK1) complexed with the inhibitor Staurosporine. The structure you are viewing is Protein Data Bank (PDB) structure 1OKY. If you click on the (+) button next to 1OKY, you see that all four active objects in the Viewer Window start with the prefix 1OKY, and are contained in a group called 1OKY. Groups allow you to collect objects under one common name for better organization.

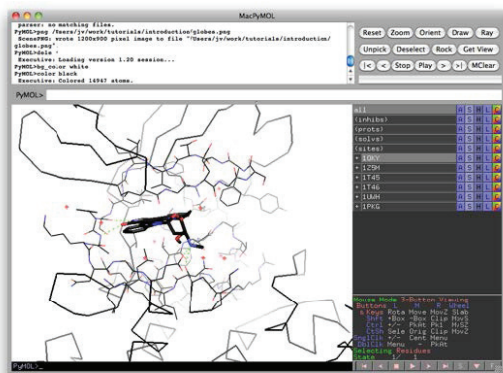


Figure 17: The example Kinase Session loaded into PyMOL.

Open groups are prefixed with minus sign (-) and closed groups are prefixed with a plus sign (+). Try turning the 1OKY objects on and off individually. The displays of the protein, the inhibitor, the solvent, and hydrogen bonds can each be enabled and disabled independently by clicking on the object names. Also note that you can click and drag downward over the object names to toggle display of multiple objects at once.

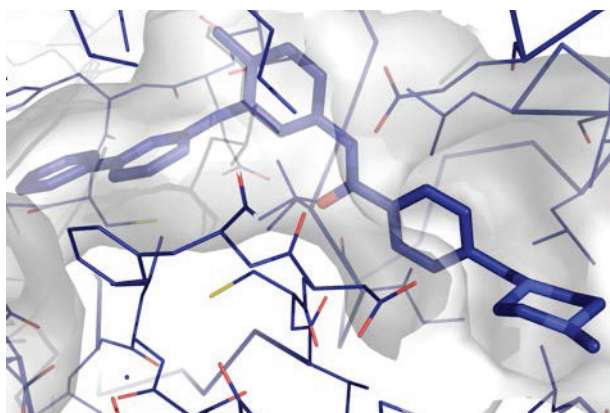


Figure 18: Gleevec in its binding pocket. The pocket is rendered as a surface, Gleevec is rendered in sticks, and the rest in lines.

Disable all of the objects except 1OKY.prt, and then enable object 1Z5M.prt, which is a crystal structure of PDK1 with a different ligand. From this view, you can observe that, while the chemical structures are the same, the two structures differ in the precise orientations of various side chains. If you enable 1OKY.inh, 1OKY.hbd, 1Z5M.inh, and 1Z5M.hbd, you can see how the two ligands interact differently with PDK1.

Note that there are four atom selections listed at the top of the Upper Control Window: (inhibs), (prots), (sols), and (sites). Clicking on its name will activate or deactivate a selection. These selections are useful for changing the way various groups of atoms are represented across all complexes in the session. For example, the (sites) atom selection can be used to selectively display a transparent molecular surface on each protein's active site. To do this, first disable all but one of the protein objects, for example, 1T46.prt (V-Kit). Then select S>Show>Surface, next to the (sites) selection. A molecular surface will appear on the 1T46.prt object. If you enable the other 1T46 objects, you can middle click to center and scroll to move the clipping plane to visualize Gleevec inside its binding pocket (see Figure 18). To remove the surfaces, simply H>Hide>Surface for the (sites) selection.

Likewise, you can use the (inhibs) selection to change how the inhibitors are displayed. For example, try showing spheres for the (inhibs) selection in order to obtain a space-filling view of the inhibitors. Although the input PDB files used to create this session did not contain bond valence information, PyMOL will generally attempt to guess bond valences for unknown residues. To display those bond valences, select Display>Show Valences from the Upper Control Window. Figure 19 (left) shows bond valences turned on, and the binding pocket as a surface turned off (right). You can always use a session file such as this as a starting point for your own customized figures. If you get lost or make a mistake, you can start over by quitting PyMOL and reopening the original session. Please spend some more time with this session file until you feel quite comfortable with it.

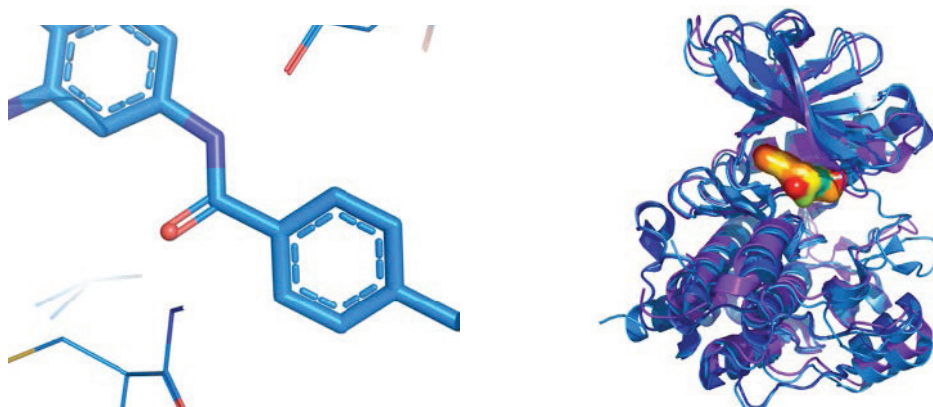


Figure 19: Bond valences are now shown on Gleevec (left). A custom representation of the kinase binding pocket, filled with ADP shown as a surface (right).

Using Sessions for Backup–Important!

Because PyMOL lacks a general undo command, you must get in the habit of saving sessions periodically (e.g. every five minutes) when using PyMOL for extended tasks. It is also generally a good idea to save multiple versions of the session as you make progress, just in case something goes wrong and you need to backtrack. An alternative approach to saving PyMOL commands, used by advanced PyMOL users, is scripting. PyMOL scripts can automate tasks and take advantage of the underlying Python interpreter for expanded functionality. PyMOL Scripting is covered in depth in an Advanced Tutorial.

Sequence Viewer

Using the Sequence Viewer

PyMOL's sequence viewer, shown in Figure 20, is turned off by default. Please find the S below the mouse mode table and click it. You can also turn on the sequence viewer by going to Display>Sequence from the Upper Control Window. You should now have the amino acid sequence of your protein in the familiar one-letter codes. The sequence viewer can be used to select residues. Using the left mouse button, please select and drag out a rectangle of residues in the sequence viewer. The residues selected will be indicated by small purple boxes in the Viewer Window. Now, try right-clicking on the selected residues in the Sequence Viewer. Notice that a context sensitive pop-up menu appears. This menu gives you access to a variety of options for this selection.

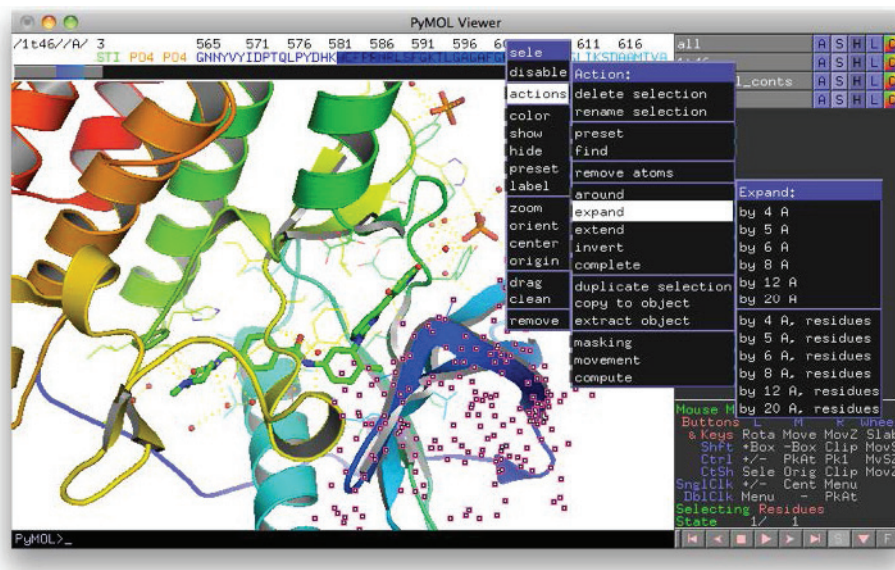


Figure 20: Example of using the sequence viewer in PyMOL. Left-click drag to select residues; right click to open up menus for those residues. The purple dots represent those residues selected from the sequence viewer. The menus appeared after a left-click on the selected residues in the sequence.

Representations and Selections

Representations in PyMOL

Representations in PyMOL are controlled through the **S H L C** pop-up menus. Again, S>Show, allows us to turn on various representations; H>Hide, the opposite of Show, turns off various representations; L>Label, creates, shows, and hides labels; and finally, C>Color, colors objects and selections. The Show menu is displayed in Figure 21.

Try It–Working with Molecular Representations

At this time, please restart PyMOL and load the 1t46 structure from disk. Please hide everything in your PyMOL window by clicking H>Hide>Everything in the all object row. Now, let's show the protein as lines. To do so for 1t46, select S>Show>Lines. Now show S>Show>Cartoon. Our

molecule will be shown as lines and cartoons because PyMOL's show command acts additively. Now show Ribbon. The ribbon traces the backbone of the protein; lines display backbone and side chains. The Hide menu works like the Show menu: when you turn off a representation, other representations are left unchanged. For example, please hide the Lines representation by choosing H>Hide>Lines. Just the ribbons and cartoons should be showing now.

Please color your molecule marine, by choosing C>Color>Blues>Marine. PyMOL allows us to use myriad colors, and even allows us to define our own. Now, try S>Show>As>Cartoon. See the difference? The Show As command turns off all other representations before drawing the one you chose.

Please note that the Surface and Mesh representations can take a long time to generate for large molecules. Try S>Show>As>Surface to see your protein as a surface.

The Show and Hide commands operate on the entire molecule. But, many times when working with molecular structures, we wish to show some portion of the structure in one representation (eg. the ligand as sticks) and then show another portion in another representation (eg. the binding pocket as a surface). Well, we can do that in PyMOL using Selections.

Understanding Selections

Selections in PyMOL are just sets of atoms that you define, and do not have any properties of their own other than a name. Selection names appear in the viewer window surrounded by parentheses, as in (sele), to distinguish them from objects. Objects are proteins, molecules, and other entities in PyMOL's memory, whereas selections are just listings of atoms in those objects. You can turn selection indicators on and off by clicking their names in the Viewer Window just as you do for objects, except that only one selection can be turned on, or enabled, at a time. Atoms in enabled selections are shown in the Display Area with purple boxes over their atom centers. To deselect atoms when in viewing mode, just left click away from any atoms in the Display Area, click the selection name, or click Deselect in the Upper Control Window.

Try It—Creating Selections

In PyMOL there are three different ways to select residues. First, you can simply click on them in the Display Area when in Viewing Mode. Please make sure your mouse is in Viewing Mode, and then try clicking on an atom. Click after click, the atoms you choose will be added to a special selection called (sele). Selected atoms are shown with little indicator boxes, the purple boxes, around them, as in Figure 22. Second, you can enable the Sequence Viewer and click on residues there. Please try that too: enable the Sequence Viewer in the Display Menu, and click on residues in the sequence. Also, try right clicking on residues in the Sequence Viewer. Last, you can use the command line, which provides a more powerful and precise way to choose atoms and residues. Because of the complexity of typed selections, we will present that material in the Advanced Selections portion of the Appendix, and our Intermediate Tutorial.

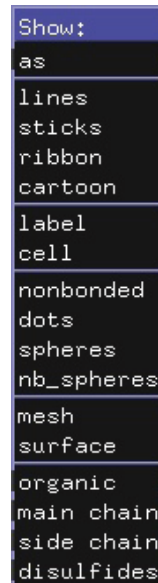


Figure 21:
The Show menu.



Figure 22: The three selected atoms are shown with purple boxes around their atoms.

Try It–Renaming Selections

PyMOL allows us to rename selections. Let's try it. First, please show 1t46 as lines. Please use your mouse to select a few residues. Make sure there are some pink boxes showing on the screen. Then, for the active selection (sele), please click on A>Action>Rename Selection. When prompted, type the name myFirstNamedSelection and return. You don't need to supply the parentheses. PyMOL will add them for you since it knows this is a selection.

Try It–Using Selections

We use selections as much as we use objects. Once you've created a selection, you can use the menus next to its name to change its representation. Please note that A>Action>Delete Selection doesn't delete the atoms, it just clears the selection name from memory. However, if you choose A>Action>Remove Atoms, for any object or selection, that indeed will remove the selected atoms from PyMOL's memory.

Let's try a few actions with selections. First, let's select all the waters and delete them. To do this, turn on the SequenceViewer and then scroll to the end of the sequence. Select all the O residues by left clicking and dragging with the mouse. Remember mouse selections are additive so, to select all the waters you can, slide the rest into the Viewer using the grey slider box under the sequence, and then select those, too. Once you've selected all of the waters, please remove them by selecting A>Action>Remove Atoms, for the selection (sele). Please also delete the selection we made earlier called myFirstSelection. (Hint: an easier way to remove waters is to select A>Action>Remove Waters.)

Let's show the ligand as spheres, select it, and then color it 'wheat.' Start by selecting S>Show>Organic>Spheres for 1t46. Now, please find the ligand in your structure. Using the mouse select it and rename the selection to "myLigand". Once that is done, please select S>Show>As>Spheres, and then C>Color>Tints>Wheat, for this selection.

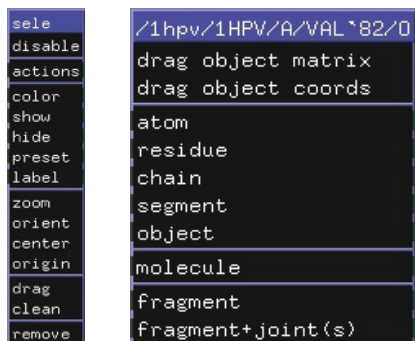


Figure 23: Comparing the menu for right clicking on an active selection (left image) or atoms that are not in a selection (right image).

Lastly, if you rapidly right-click on an active selection, PyMOL brings up a context sensitive pop-up menu. Because you've selected an active selection, PyMOL knows what to operate on, so its menu is tailored for that selection (see Figure 23, left). If you right clicked on an atom that is not in an active selection, PyMOL brings up a different menu, allowing you to operate on the atom, its residue, chain, molecule, etc (see Figure 23, right).

Here's a hint: look at the menus shown in Figure 23. Menu options that have a grey border to the right or left, such as actions, colors, and show, will open up a sub-menu. Those menu items with a solid blue border, such as zoom, orient, center, do not—clicking on them will perform the given action.

Scenes and Shows

Using Scenes, PyMOL allows you to very quickly make simple animated sequences, called Shows. A Scene in PyMOL is simply a memory-snapshot, in which PyMOL saves current colors, visualizations, representations and the position of the camera. A Show is simply an interactive 'movie' created as you advance (or reverse) through your predefined scenes. In a show, PyMOL animates smooth transitions from scene to scene, in order to provide a continuous sense of 3-dimensional context for the viewer. To see how a PyMOL Show works, please open the ExampleShow.psw file, which can be found in the PyMOLTutorials/Introduction/sessions folder on your desktop, and use the Page Down (PgDn) and Page Up (PgUp) keys to step through the presentation. Pressing the space bar also advances though scenes. Note that you can manipulate the view using the mouse anytime you want without corrupting the preset scenes. Let's take a look at making scenes and shows.

Try It—Creating and Viewing Scenes

Let's setup two scenes and make a movie that visits each one. Please start by reloading the kinase session file and expand the 1OKY group by clicking on the plus (+) next to 1OKY. Now, let's store this scene: please select Scene>Append. Next, let's create our second scene, which will be a close-up of the ligand while in the Publication preset. Please apply the Publication preset for the 1OKY group by selecting A>Action>Preset>Publication for 1OKY. Next, please orient the scene with respect to the ligand; for the object 1OKY.inh only, please select A>Action>Orient. Now, store this scene with Scene>Append.

As this demonstrates, to create a scene we start by positioning molecules, coloring them, setting their representations and getting the screen to look exactly as desired. Then, to store the scene

and assign it a name, we click Scene>Append in the Upper Control Window. PyMOL automatically assigns a name to the Scene, which we need to refer to it (eg. "001"). And, now that two or more scenes have been defined, we can switch between them with Scene>Previous/Next.

Please use Scene>Previous now to return to the first scene. If you prefer, you can also use the Page Down (PgDn) and Page Up (PgUp) keys to advance forward or retreat backward through the sequence of scenes. Also note that pressing CTRL-PgDn will insert a new scene after the current one, and CTRL-PgUp will insert a new scene before the current one.

Modifying, Annotating and Saving Scenes in a Session

The last scene displayed can be updated by selecting Scene>Update from the Upper Control Window. You can also add textual annotation to the current scene via a typed command such as scene auto, update, Some annotation information. This will display "Some annotation information" on the screen the next time the scene is recalled. When you save a PyMOL Session, all of the scenes you have defined will be saved as well. You can then share the session file with a collaborator, and he or she will be able to open up the session file into PyMOL and view the sequence of scenes you defined.

Creating Shows and Interconverting with Sessions

A Show File is simply a PyMOL Session file that contains one or more scenes and is saved with a .psw file name extension instead of the normal .pse. When a .psw file is opened, PyMOL automatically enters full-screen mode and displays the first scene in the sequence. To convert a Session to a Show, change the .pse file name extension to .psw. To convert a PyMOL Show back to a Session, change the .psw back to .pse. If you are using Microsoft Windows and cannot see the file name extension, then it may be hidden per the Windows default. To change this, click on Tools>Folder Options from the menu of the enclosing Microsoft Windows folder. Ensure that View>Hide extensions for known file types option is not checked.

Creating Movies

Introduction

Movies tell stories better than static images, but complex movies can be difficult and time-consuming to create. Here, we cover the absolute basics. Schrödinger will soon offer additional tutorials focused on intermediate and advanced movie making.

Please find the Movie menu in the Upper Control Window. Take a moment to scan through all the options and submenus.

Movie>Append will add a given number of seconds to a movie, but will not program any content for the new time. Movie>Program will program a given movie task for a new time of a given duration. PyMOL comes with some pre-programmed animations. Just select Movie>Program and then choose from Camera Loop, Scene Loop, State Loop or State Sweep. Camera loops are animations in which the camera pans around a given scene in a rocking, rolling or combined motion. This is a nice way to visualize a pocket or a simple structure. Other camera loops are xrock, x-roll, y-rock and y-roll. A roll is a complete 360 degree rotation about a given axis. A rock is a back-and-forth rocking motion. If your movie gets too long, or is not what you want, just select Movie>Reset from the Upper Control Window.

Try It—Make a Movie using Scenes and Movie Presets

Let's use the Movie>Program submenus to make a movie. We already set up our two scenes in the last section (Scenes and Shows). Now we will have PyMOL cycle through those two scenes in a Scene Loop movie. A scene loop essentially stitches together all your scenes with a predefined pause at each scene transition. Let's make our movie now by selecting, Movie>Program>Scene Loop>Nutate>2 Seconds Each. To watch the movie, press the Play button in the movie controls (lower right of the Viewer Window).

Before moving on, please clear any movies you have made by selecting Movie>Reset from the Upper Control Window. Also, please disable all objects except for the first two proteins, 1OKY.prt and 1Z5M.prt.

Working with Multiple Objects and Selections

Try It—Viewing Many Structures with Grid Mode

PyMOL has a feature called grid mode which subdivides the Display Area into as many equal sized rectangles as you have visible objects. Please enable grid mode by selecting Display>Grid>By Object in the Upper Control Window. PyMOL now displays each protein in its own grid slot. Figure 24, shows what grid mode looks like when enabled with six proteins. Rotate the scene with the left mouse button in the Viewer Window; notice how each of the molecules rotates in its own window. At this point, to illustrate the next feature, please quit PyMOL.

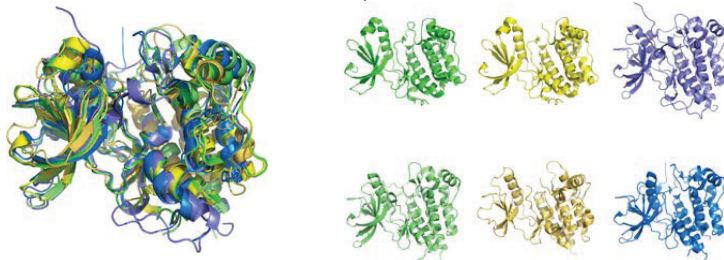


Figure 24: Grid mode turned off (left) and on (right), where each protein receives its own grid slot.

Loading Many Structures

Provided that your computer has enough memory and processing power, PyMOL can be used to simultaneously visualize dozens of structures or more. Structures can be loaded from the File menu one at a time, or if you multiple select, many at a time. Alternatively, one can use a script to load multiple files using the `load` command (or the `fetch` command, which loads structures directly from the PDB given appropriate PDB identifiers). Last, if you're launching PyMOL from the command line, you can provide file names there—and even use wild cards. For example, you may type `pymol myPDBs/*.pdb` to load all the PDB files in the directory named myPDBs.

Try It—Loading Many Files

Please load the six kinase files in the PyMOLTutorials/IntroductionToPy-MOL/kinases directory. To do this, launch PyMOL, select File:>Open, and multiple-select the files.

Sequence Based

PyMOL can perform sequence-driven structure alignment through the A>Action>Align menu, shown in Figure 25. You can align all proteins to a currently selected one (A>Action>Align>All to this), or align proteins one by one (A>Action>Align>To Molecule). Finer control over the alignment process can be exercised by creating selections that represent the two regions to be aligned. In this case, one selection (e.g. sel01) should be created in the target molecule and a second independent selection (e.g. sel02) should be created in the molecule to be aligned. Then for selection sel02, you click on the A>Action>Align>To Selection>sel01 to perform a superposition based on only those two regions. Alignments performed using the A>Action menu are based on a protein sequence alignment followed by an interactive structure superposition, and only the CA atom positions are considered.

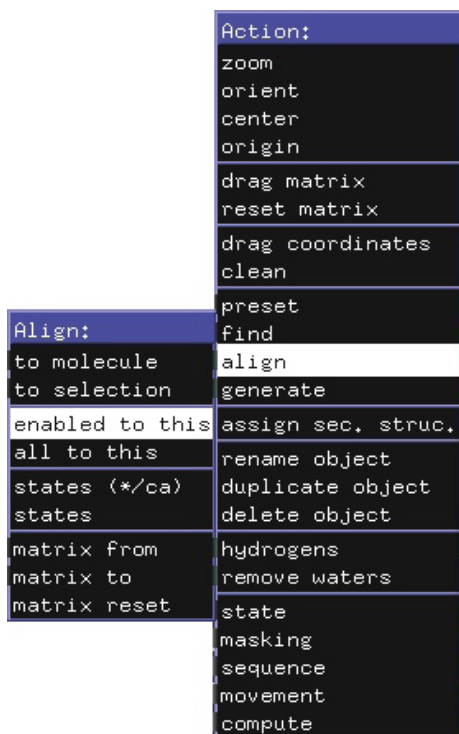


Figure 25: To perform a structure alignment, choose A>Action>Align, as shown in this screenshot.

Greatest control over alignment can be exercised by typing an `align` command in the command line. For example, the kinase structure 1uwh actually contains two copies of the enzyme, chains A and B, whereas 1t46 only contains one copy. The default alignment of 1t46 and 1uwh matches only the 1uwh B chain. To force alignment of 1t46 against the "A" chain of 1uwh, type the following command: `align 1t46////CA, 1uwh//A//CA`. This command uses selection macros, which are discussed in the Advanced Features at the end of this tutorial. PyMOL comes with a more robust alignment command called `super`. Use `super` if `align` doesn't do so well.

Try It—Quickly Align Multiple Structures to One Target

Let's align all of the kinase proteins in our session to 1Z5M. For 1Z5M, choose A>Action>Align>All to this. All enabled proteins should now be aligned to 1Z5M. To see the alignment more clearly, please select S>Show>As>Ribbon.

Specific Atom Pairs

Sometimes we don't want a global alignment of two proteins, but rather, an alignment based on specific atom pairs. If you already know which atoms in protein A should be matched with which atoms in protein B, then you can use a fitting procedure instead of an alignment procedure. The difference is that fitting is an easy problem to solve, and PyMOL can fit perfectly. In fact, there's a wizard to help us with fitting.

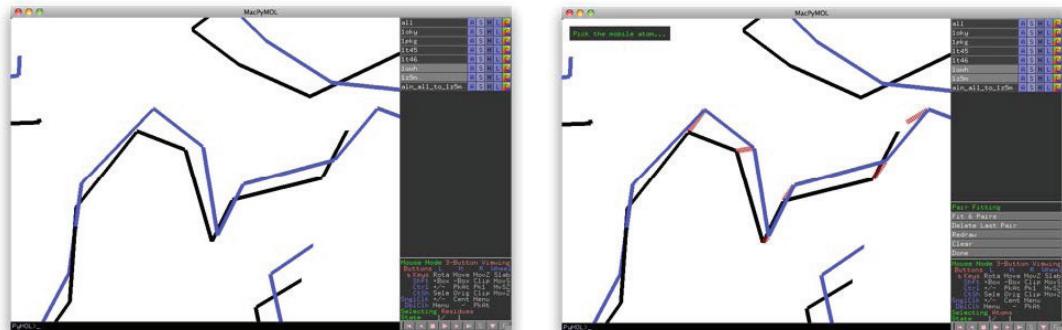


Figure 26: (Left) Thin-slab view of two proteins ready to be fitted. (Right) The red lines shown paired atoms from the two structures. The goal is to optimally pair and align those atoms to maximize structural overlap.

Try It—Pair Fitting

Please disable all proteins except 1Z5M and 1UWH. Because we just aligned all proteins to 1Z5M, corresponding atoms from 1UWH should be nearby their mates in 1Z5M. Next, zoom in and make the clipping slab thin so just a few residues are visible, as in Figure 26 (left). Now, open the Pair Fitting Wizard by selecting Wizard>Pair Fitting. At this point PyMOL will be prompting you to select a "mobile atom." Please select an atom from one structure. PyMOL now asks you to select a "target atom," so select an atom from the other structure. PyMOL should have connected the two atoms with a dashed line. Please continue pairing atoms until you have four pairs. Once you are done selecting atoms, please choose the Fit 4 Pairs. PyMOL will fit those four pairs, by moving the mobile structure. Next, click Delete Last Pair to remove the last pair. Now, refit the 3 pairs; notice that PyMOL updates the RMSD of the fit in the Display Area. Clicking Clear will remove your atom pairings. Done will dismiss the Pair Fitting Wizard. At this time, please click Done.

Pair Fitting from the Command Line—The `pair_fit` Command

Clicking atoms pairs can be tedious, so PyMOL has another way to pair fit. Now, please type `pair_fit 1uwh// A/563-582/CA, 1z5m///193-212/CA` into one of PyMOL's command lines. This command superimposes the alpha carbons in chain A of 1UWH for residues 563-582 to the alpha carbons of 1Z5M for residues 193-212.

Please note: to fit atoms you must identify exactly the same number of atoms in one object to fit to the other. Also, no spaces are allowed inside selection macros.

Editing Molecular Objects

PyMOL allows you to create and replace bonds, atoms, residues, and commonly used chemical groups. After modification, you can clean the structure using an open-source implementation of the Merck Molecular Force Field (MMFF).

Removing Unwanted Atoms

PyMOL provides a quick way of removing waters or hydrogens, by simply clicking A>Actions>Remove Waters or Remove Hydrogens, shown in Figure 27. You can also remove a specific atom, residue, chain, segment, or covalent molecule from a molecular object by right-clicking on an unselected atom in the graphics area to display the atom's default pop-up menu, following the desired level in the hierarchy, and then choosing remove atoms. Selections can also be used to remove groups of atoms. To do this, create a selection consisting of those atoms that you wish to remove, and then choose A>Actions>Remove Atoms for that selection. Finally, you can type the `remove` command to specifically eliminate a specified set of atoms. For example, to remove chains B and Y in PDB structure 1uwh, one could enter the following command: `remove /1uwh//B+Y`. Please try removing all waters from these proteins.

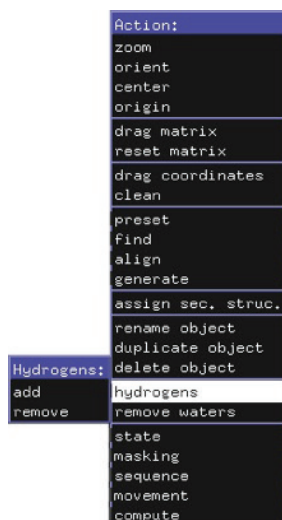


Figure 27: How to easily remove waters or hydrogens.

Changing Bond Valences

One of the problem with PDB files is that they do not contain bond valences for ligands. As a consequence, it is not possible to display correct chemistry for ligands. PyMOL may not always recognize the correct hydrogen-bonding interactions between proteins and ligands until the valences have been properly specified.

Try It—Changing Bond Valences

To edit bond valences on a Windows PC, please click on the Builder button in Upper Control Window. Next, *CTRL-Right-click* to pick the bond whose valence you wish to change. You should see a white band appear about the bond as in Figure 28. Please cycle through the available bond valences by clicking on the Cycle button in the Builder area of the Upper Control

Window, or by pressing `CTRL-W` on your keyboard. Once you have set the correct valence for that bond, you can `CTRL-right-click` to select the next bond to fix, continuing until all valences have been fixed. Note that PyMOL adds missing hydrogens to the atoms involved in the bond. If hydrogens are not desired, use `A>Actions>Remove Hydrogens` for the object, after correcting all of the bond valences.

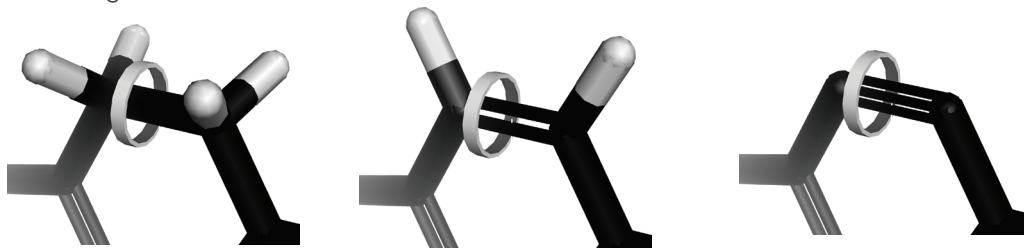


Figure 28: Cycling valences. First, select the bond with `CTRL-right-click`. Then type `cycle_valence` at the command line or click `Cycle` in the Builder. Notice the automatic addition of hydrogens. If they are not desired, you can remove them after setting the valence.

5. Advanced Feature Previews

Label Customization

Introduction

In addition to labeling atoms based on identifiers and properties, PyMOL supports custom labels with arbitrary text. Here, we will touch on a few useful ideas. To get the most out of this, you should be comfortable with typing commands in the command line and also making named selection (either with the mouse or from the command line).

Setting the Label

You can label a selection by clicking `L>Label` and then choose the appropriate label type desired. To make a custom label, however, you need to type commands into the PyMOL command line. Basic labeling is accomplished by typing in the command line `label selectionName, labelText` and return, where `selectionName` is any valid PyMOL selection or selection name, and `labelText` is the string or keyword you want to use as the label. PyMOL will also accept interpreted strings as well (see the intermediate Tutorial or PyMOLWiki for more details). An example label command is `label name CA, resn`, which labels each alpha carbon with the three letter code of the amino acid it which it resides. Other keywords of interest are: `resi`, and `b`. `Resi` is the residue number and `b` is the b-factor.

Now that we know how to make more advanced labels, let's learn how to customize them using PyMOLs options for labels. This requires using the `set` command at the command line.

Label Color

You can set `label_color` in PyMOL to any valid PyMOL color, for example by typing: `set label_color, blue`. Colors can be valid PyMOL color names, found in the color menus for each object or selection.

Label Size

You can change the size of the label with `set label_size, nSize`, where `nSize` is a number representing the size of the label. If `nSize` is positive then the label is rendered at a size of `n` points (72 points/inch). However if `nSize` is less than 0, it is converted to the absolute value and the label is rendered in that many Angstroms. For example, to render a 14 point font, `set label_size, 14`; to set labels to be 2 Angstroms (big), `set label_size, -2`.

Label Font and Extended Unicode Characters

PyMOL supports Unicode fonts to display characters such as α , β and Å. To use Unicode characters you need to know the correct character code for your symbol; please visit <http://unicode.org/charts/symbols.html> for the list of codes. Once you know the proper code, for this example it is `\316\261`, you can issue the label command: `label 5/CA, "\316\261-Helix"` will print "α-Helix" on the 5th atom's alpha carbon. PyMOL allows us to change the font that our labels are rendered in. For that, use `set label_font_id, nLabel`, where `nLabel` is an integer in the range 5-15. To use Unicode fonts, first set the PyMOL option `label_font_id` to 15 or 16.

Label Position

In Editing Mode, you can **CTRL-Left-drag** labels around your scene. Use **CTRL-Right-drag** to move the label toward or away from the camera. This is a useful feature as many times a surface or structural feature will hide a label.

Saving Coordinates

PyMOL has a limited ability to write out coordinates for input into other programs. The interchange file formats supported are: PDB (Protein Data Bank), MOL (MDL MOL-file), and MMD (Macromodel). PyMOL can also save molecules in an internal PKL (Pickle) file format, which is able to preserve all of the molecular information, including bond valences and atomic properties, something none of the other file formats do well. To save a molecule, first make sure that the atoms you wish to save are contained in either a distinct object or are pointed to by a named selection. Then choose **File>Save Molecule...**, pick the name of the object or selection in the next window, and enter the filename. Add the correct file name extension is appended to the file name (e.g. ".pdb"), and then click **Save**.

Probing Electrostatics

Quantitative electrostatics calculations are typically difficult and time-consuming to perform. They require the specialist skills of a computational chemist to carefully consider missing protein segments and side chain atoms, histidine ionization, and the presence of specific counter-ions from bulk solvent. Furthermore, calculations involving ligands usually require high-level quantum calculations to obtain reasonable atomic partial charges for novel scaffolds. Assuming that such issues have been addressed, PyMOL can call upon the Adaptive Poisson-Boltzmann Solver (APBS) under a Unix environment to perform quantitative electrostatic calculations. The program can also read pre-calculated potentials from the Grasp, Delphi, or Zap electrostatics solvers.

In lieu of rigorous calculations, a simple, local (but technically incomplete), quasi-Coulombic calculation can often help answer the qualitative question, "Is this region of the protein surface likely to be positive, negative, or neutral relative to the rest of the protein?" PyMOL provides such answers for proteins by performing an automated calculation that amounts to smoothing

out the local charge density from nearby atoms (within 10 Å ngstroms), without taking into account solvent screening effects. To perform this calculation, select Actions>generate>vacuum electrostatics> protein contact potential. After a minute or two, PyMOL will create a new object with the protein shown as an electrostatic surface colored blue in the positive regions and red the negative regions. You can then CTRL-click-and-drag along the slider to change the color levels.

Atom Selection Syntax

PyMOL has a powerful atom selection language that is covered in-depth in the PyMOL Users Manual. Here we provide some simple example selections that you can hopefully adapt for your needs:

1. To select a numbered residue in a specific object (e.g. 1t46):

```
select my_resid, 1t46///640/
```

2. To select all residues with a given identifier in any object:

```
select my_resids, 606/
```

3. To select specific residues and ranges of residues by identifier:

```
select my_range, 601-610/
```

```
select my_resids, 1t46///602+606+621-631/
```

4. To select specific residues by residue type:

```
select my_negative, 1t46///GLU+ASP/
```

5. To select specific atoms by name:

```
select my_main_chain_atoms, 1t46///N+CA+C
```

6. To select one or more chains:

```
select my_chain, A+B//
```

```
select my_chains, 1uwh//A+B//
```

7. To select atoms in multiple objects

```
select my_object, 1uwh///CA or 1t46///CA
```

Automating Tasks with Scripts

Scripts are text files that contain a sequence of PyMOL commands, and they can be used to perform repetitive tasks automatically. For example, if you wish to prepare a series of standardized figures, but would like to use a different crystal structure for each figure, then it would make sense to use a script to perform some or all of the figure preparation tasks automatically.

To run a script, select File>Run, or type “@” followed by the file name path into a command line. The following example PyMOL command script contains six commands that color and represent the target and ligand in a standard way. To use a different input structure with this script, you would just update the first command in the file with a new PDB filename.

Code 1: Example script to automate figure generation.

```
# load a PDB file
load kinases/1t46.pdb
# show the ligands as space-filling spheres
# and show the protein as a cartoon
hide everything
show spheres, organic
show cartoon, polymer
# color the protein carbons cyan
# and the ligand carbons yellow
color cyan, polymer and elem c
```

In addition to command scripts, PyMOL can also be controlled using the Python programming language, which also makes it possible to create custom applications that integrate PyMOL for molecular visualization.

Advanced Molecular Editing

Rotating Bond Torsions

Bond torsions can be rotated by CTRL-Right-Drag near the mobile end of the bond. Once a bond has been picked with the mouse using CTRL-Right-click you can also rotate the atoms on either end of the bond by CTRL-Left-Drag. If you make a mistake, CTRL-Z will undo recent conformational changes.

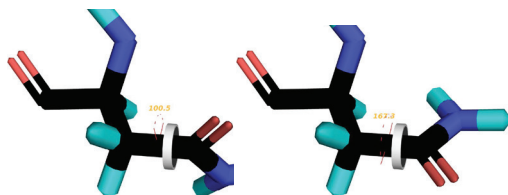


Figure 29: Rotating torsion bonds. Right side of the bond is selected (left image); and molecule is modified by rotating the torsion bond with CTRL-RightDrag (right image). Notice that the white cuff is on the right half of the bond. This indicates that the right side of the bond will be rotated. The left side is unchanged. Compare this to Figure 30.

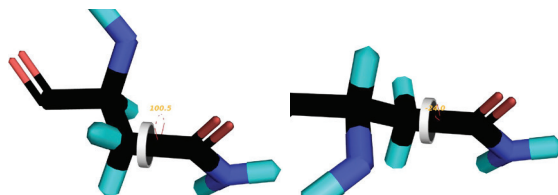


Figure 30: Similar to Figure 29, but left side of the bond is selected (left image), and the white cuff indicates this fact, as it is located on the left half of the bond. (Right image) Molecule shown after slight rotation. The right side of the molecule is unchanged.

Creating or Removing Bonds

Bonds can be formed by picking two atoms sequentially and then Build>Create Bond in the Upper Control Window or by pressing CTRL-T. Once a bond has been created, the valence can be changed as described in Figure 28. To delete a bond, pick it by CTRL-right-clicking on it. The picked bond can then be deleted by pressing CTRL-D or by hitting the Delete key.

Creating One Object Out of Another

Atoms in a selection can be copied into a new object by choosing the A>Action>Create Object for the selection. A new object name will appear in the names list, and you can then rename this object using A>Actions>Rename Object. Certain properties of atoms in a newly created object can be manipulated independently from those in the source object(s), while those properties of a selection cannot. For example, independent objects can have different transparencies, while a selection must have the transparency of its parent object.

Mutating Protein Residues

PyMOL can suggest alternate rotamers (conformations) for existing side chains and even mutate individual side chains of proteins. Such actions are performed using the Mutagenesis Wizard. To launch the Mutagenesis Wizard, select Wizard>Mutagenesis in the Upper Control Window. Then click on the side chain you wish to alter. Initially, PyMOL will load the set of common rotamers for the existing side chain, in the order of most frequent occurrence. You can use the left and right arrow keys or the movie controls, below the mouse mode table, to step through the side chain rotamer conformations. To choose a different residue type for mutation, click on the first pop-up menu (initially set to No Mutation, as shown in Figure 31). Once you have chosen the mutation and set the desired rotamer, click the Apply button in the Viewer Window. When you are finished making mutations, click Done.

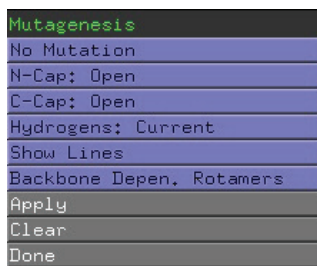


Figure 31: Mutagenesis Wizard menu. Click on No Mutation to display the residue list of possible mutant residues.

6. Next Steps

Other Courses

Congratulations on finishing the Introduction to PyMOL tutorial. We hope you enjoyed the lesson and are motivated to use PyMOL for your molecular visualization, movie-making, scripting, and editing tasks. This isn't the end, though: Schrödinger will soon have other courses available covering Intermediate Topics, Scripting/Programming, Moviemaking, and Molecular Editing and Cleanup. Please contact us for more information on those courses via support@delsci.com.

Joining the PyMOL–Users Mailing List

As of Summer 2009, well over 1,000 PyMOL users subscribe to the pymol–users mailing list, which is where the community exchanges tips on how to use the software effectively and how to solve any problems that come up. To join the mailing list, please click on the Mailing List link that appears at the top of the PyMOL Home Page, (<http://www.pymol.org>). Or, to quickly search the mailing list archives for posts on a specific topic, click the Mailing List Archive link.

Visiting the PyMOLWiki Community Web Site

The community also runs a “Wiki” dynamic content site that aggregates information from the mailing list and provides other kinds of PyMOL–related documentation (<http://www.pymolwiki.org>). PyMOLWiki users can create their own pymol–related pages, on this site or elaborate upon useful information that is already posted. The site boasts over 1,000 users, over 3,000,000 page views, is typically accessed between 3,000–4,000 times a day, and has many useful scripts, plugins and tutorials free for download .

Accessing the Official Documentation Site

PyMOL subscribers access Schrödinger’s Official Documentation site (<http://pymol.org/dsc>) using the subscription credentials shown from their most recent PyMOL receipt. This site contains the latest chapters from an updated PyMOL Manual, an assortment of narrated ScreenCasts, and plenty of reference information to help users on their way becoming PyMOL experts.