

Übung I: Chimera, A Molecular Graphics Program

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1. Introduction

This is an introductory exercise to *Chimera* (<http://www.cgl.ucsf.edu/chimera/>), which is one of the more powerful programs for drawing protein structures, comparing them and performing some kinds of analyses. In future Übungen and in other courses, we will assume that you know how to play with this program and some of the things it can do.

2. Running Chimera

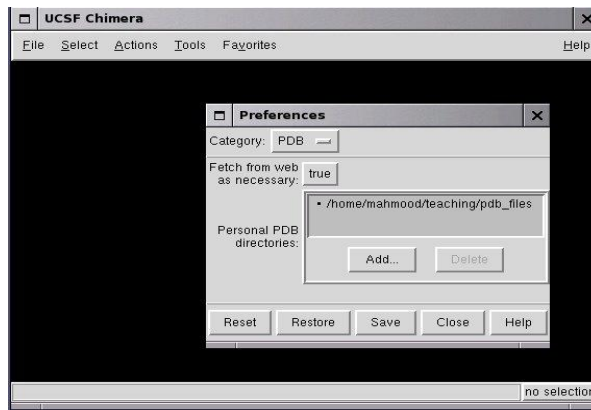
Start the program with `/usr/local/zbh/chimera/bin/chimera &`

3. The Chimera Tutorials

This is a brief version of the *chimera* tutorial. The full version is available in *chimera*'s homepage (<http://www.cgl.ucsf.edu/chimera/1.1872/docs/UsersGuide/indextut.html>).

The Getting Started Tutorial

This is a basic tutorial in two parts command line and menu interface on the same set of operations. It covers the procedure for selecting atoms, bonds, and residues in a PDB file, and how to display



molecular structure in different ways.

Downloading PDB Files:

Chimera can retrieve PDB files from the Protein Data Bank via the net or from local directories.

The directory containing all the PDB files used in the exercise is:

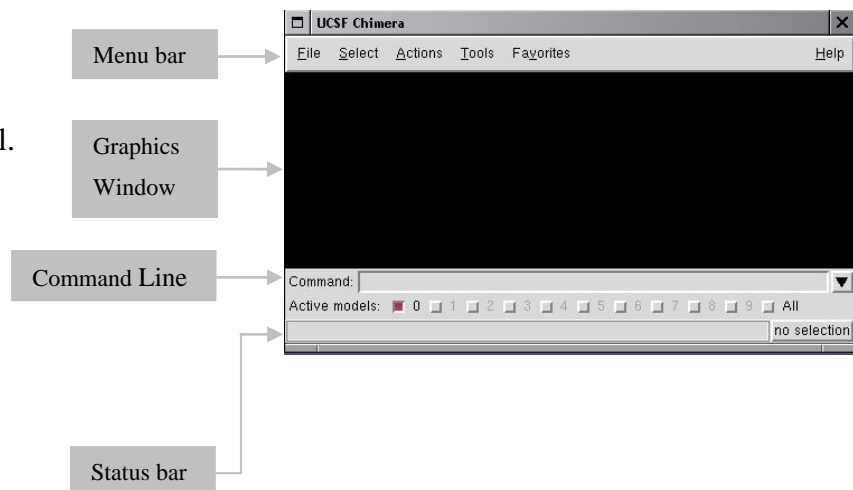
/home/mahmood/teaching/uebung1.

a) Command Line Manipulation, Selection, and Chains - Part 1

Favorites»Command Line

Activates the *command line* panel.

The *chimera* window includes a
Menu bar across the top,
A graphics window,
A command line, and
A status line.



Syntax

Command: type in the command line text field for *command line* interface.

Open a structure: *Command: open 1zik.pdb*

The structure is a leucine zipper formed by two peptides.

Command Line History:

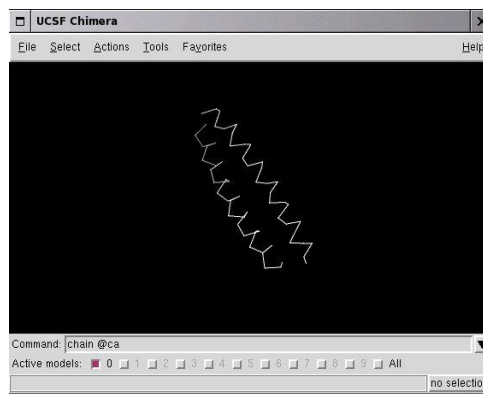
The ▼ button next to the *command line* can be used to retrieve your previous commands.

Side View: *Favorites»Side View*

Opens the *side view* window, a miniature version of the display, which shows the relationship between the eye position, the displayed item(s), and the clipping planes. By default, the miniature is shown at full resolution, with colors and representation types the same as the main display. Setting Resolution to low simplifies the miniature to only the backbone of any peptide and nucleic acid residues shown in the main display. In the low-resolution version, surfaces and objects are indicated by bounding box outlines. Using low resolution is recommended if performance seems slow. Try moving the eye position (the small square; scales the view) and the clipping plane positions (vertical lines) with the left mouse button.

Simplify the display: *Command: chain @ca*

This command shows only the atoms named CA (alpha carbons) and connects them in the same way that the residues are connected.



Mouse:

Try manipulating the structures in the main graphics window with the mouse.

Left Mouse Button	Rotate
Middle Mouse Button	XY - Translated
Ctrl + Middle Mouse - Button	Z - Translated
Right Mouse Button	Scaled

Move and scale the structures with the mouse in the *graphics window* and the *side view* as desired throughout the tutorial.

Thicken the lines:

Command: linewidth 2

Selection:

With the Ctrl key, the mouse buttons have additional functions. By default, picking from the screen (a type of selection) is done by clicking on the atom or bond of interest with the left mouse button while holding down the Ctrl key. To add to an existing selection, also hold down the Shift key. The

selection is highlighted in green, and its contents are reported on the button near the lower right corner of the graphics window. Try picking two alpha carbons, one from each peptide (Ctrl + Shift + left mouse button).

Remember that the Shift key is needed to select both atoms; otherwise, only the most recent selection will be retained.

Labeling:

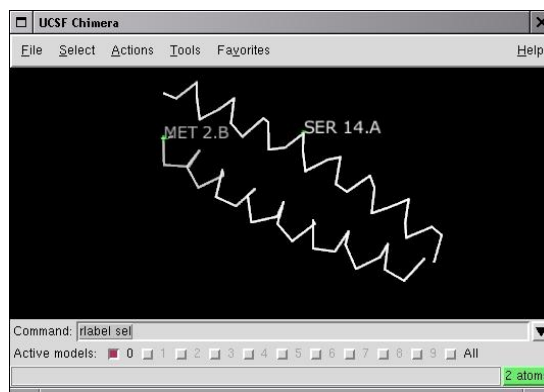
In the command line, a selection is specified by the word *selected*, *sel*, or *picked*. To label the atoms you have selected:

Command: rlabel sel

Each label is of the form:

atom_name (res_name res_number.chain)

It is now evident that one peptide is chain A, and the other is chain B.



To deselect the atoms, pick in a region of the graphics window away from any atoms or use the menu item

Select»Clear Selection.

To un-display the labels:

Command: ~rlabel

Specifying Chains:

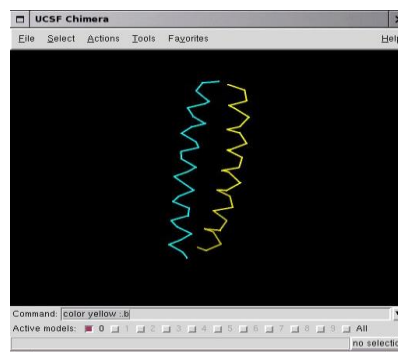
One possibility is to color the two chains with different colors:

Command: color cyan :.a

Command: color yellow :.b

Chimera labels water molecules as if they were another chain:

Command: disp :.water



It displays the water (only the oxygen are visible in the X-ray structure).

To get rid of everything except the A chain displaying all of its atoms:

Command: show :.a

To show the backbone of the A chain only (if the chain is not specified “:a” then the backbones of both chains would have been displayed):

Command: chain :a@n,ca,c

To display all the atoms:

Command: disp

To color all the atoms by the type of their elements:

Command: color byelement

The models, which are activated for motion, are shown below the command line, 0 should be in **bold** and the box next to it should be *highlighted*. Clicking the box turns off the highlighting and inactivates the model. Clicking the box again can restore it.

To close a model:

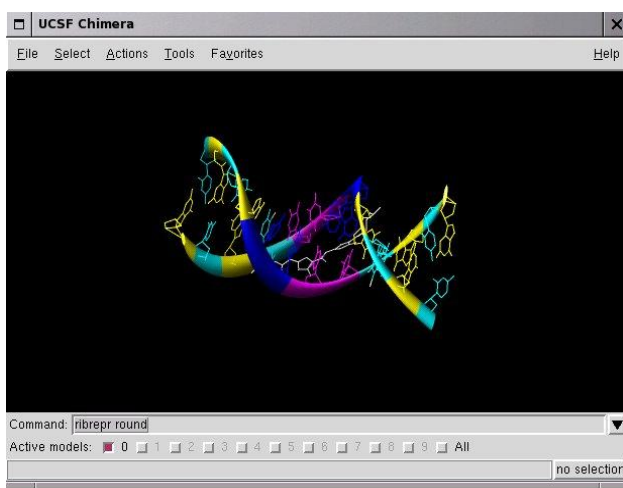
Command: close 0

b) Command Line Manipulation, Selection, and Chains - Part 2

Open another structure:

Command: open 6bna.pdb

Color the different nucleotides with different colors, and specify them by residue name:



Command: color blue :a

Command: color magenta :t

Command: *color yellow :g*

Command: *color cyan :c*

Un-display the water; *command: ~disp :.water*

Command: *ribbon*

Command: *rirepr round*

Next, try some alternate representations. Multiple representation types can be combined with each other and with surfaces (more on surfaces below).

Command: *~ribbon*

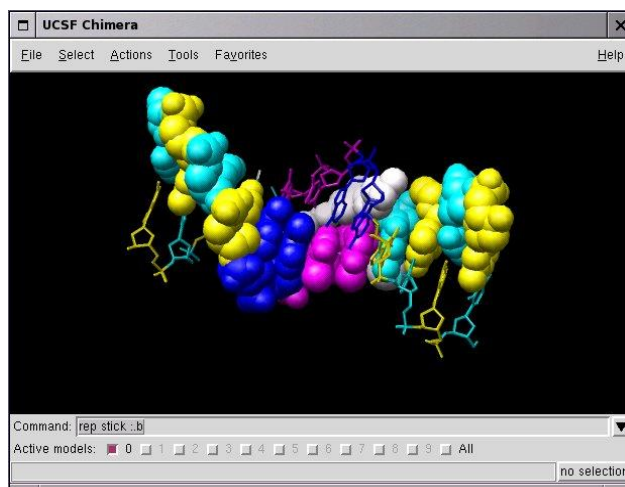
Command: *represent stick*

Command: *repr sphere*

Command: *rep stick :.b*

The latter command changes only chain B to the stick representation, with the rest remaining in the sphere representation. Note that commands (but not their keyword arguments) can be truncated to unique identifiers. For example, the command *represent* can be shortened to *repr* or *rep*.

Get ball and stick representation

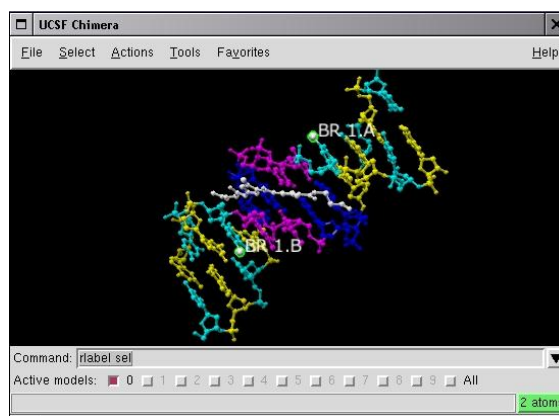


Command: *repr bs*

In the resulting ball and stick representation, pick (*Ctrl + Left click*) one of the atoms in the white molecule; it will be outlined with green, the default highlighting color.

Command: *rlabel picked*

Above command will show that the labeled residue is named **NT** and is part of chain **HET**. This chain was



assigned automatically when the structure was read in. The molecule is netropsin. Other than the white molecule, there are two additional white atoms. They are apparently attached to cytosines, which have been colored cyan (above). **Pick** and then label these two atoms:

Command: rla picked

It shows that one DNA strand is chain A, the other strand is chain B, and each strand contains a brominated cytosine.

Use *Select»Clear Selection* to deselect the atoms and then un-display the labels: *Command: ~rla*

Finally, have some fun with the *surface* command. There are *built-in categories* within structures such as *ligand* (non-solvent, non-ion single residues or bonded sequences of residues no more than ¼ the size (in terms of number of atoms) of the largest bonded sequence of residues in the model) and *main* (all remaining atoms); when nothing is specified, *surface* shows the surface of *main*. Surfaces can be rotated, translated, and scaled interactively.

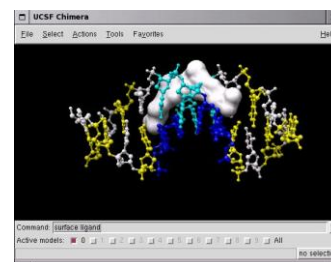
Command: surface

Command: ~surface

Command: surface ligand or

Command: surface :nt or

Command: surface :.het



By default, a surface has the same color as the corresponding atoms; however, surface color can be specified separately.

Command: surfrepr mesh

Command: color red,s :nt

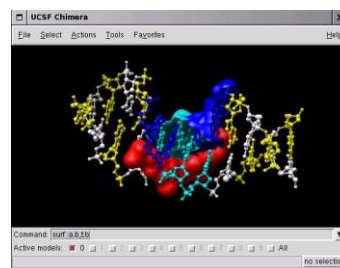
Command: surfrepr solid

Command: surf :a,b,t,b

Command: surf :a,t

Command: repr sphere :nt

Command: color green,s :t



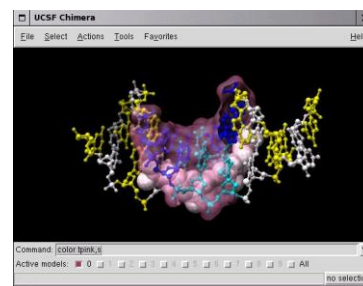
Sometimes it is helpful to make a solid surface transparent. One way to do this is to define a transparent color and then use the new color in a command:

Command: *colordef tpink 1 .5 .7 .4*

Command: *color tpink,s*

The numbers in the *colordef* command refer to red, green, blue, and opacity components, respectively.

To close the model: *Command: close 0*



c) Menu Molecular Manipulation, Selection, and Chains

In the following section, you will apply the same operations to the molecules, except that you will use the menu instead of the command line interface.

Open a structure:

File»Open

In the dialog, find and select *Izik.pdb* in */home/mahmood/teaching/uebung1/* and then *Open* to dismiss the dialog.

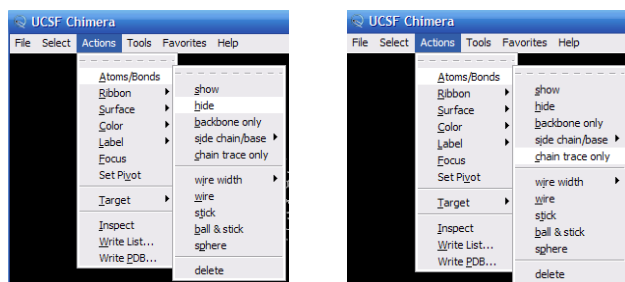
Simplify the display:

Actions»Atoms/Bonds»Hide

Actions»Atoms/Bonds»backbone

only»chain trace

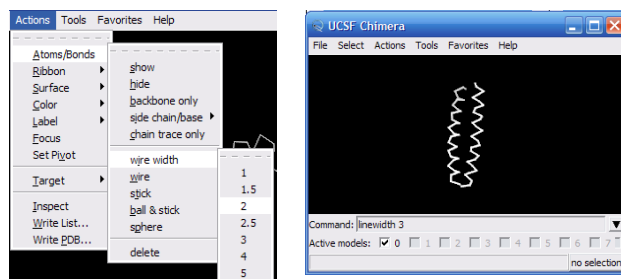
This will show only the CA atoms.



To thicken the lines:

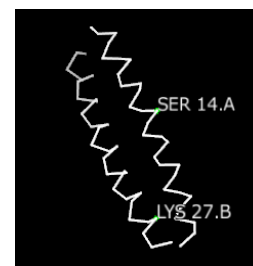
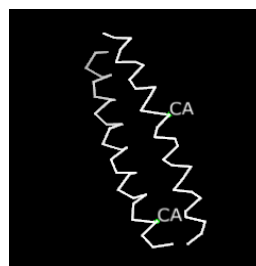
Actions»Atoms/Bonds»wire width» 2

The Actions menu applies to whatever is selected. When nothing is selected, the Actions menu applies to everything



Labeling:

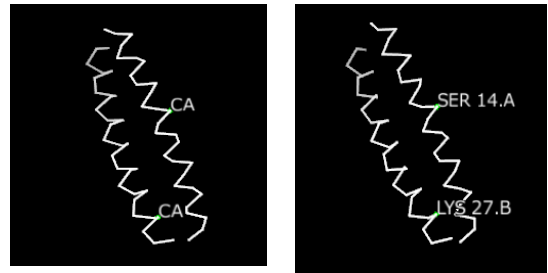
Pick two alpha carbons from each peptide. Label the atoms you have selected, first by atom name, and then by residue name and number:



Actions»Label»name

Actions»Label»off

Actions»Label»residue»name + specifier



Same as the last part, it is now evident that one peptide is chain A, and the other is chain B. To deselect the atoms, pick in the region of the graphics window away from any atoms or use the menu item *Select»Clear Selection*.

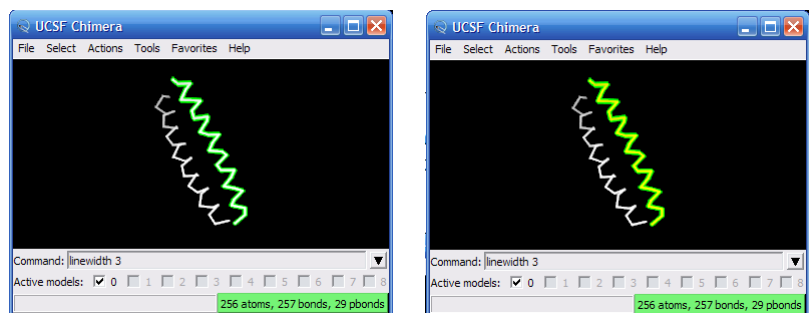
To un-display the residue labels:

Actions»Label»residue»off

Color the two chains with different colors:

Select»Chain»A

Actions»Color»yellow



Repeat the process to color chain B cyan. Another way to select an entire chain is to pick an atom or bond in the chain and then hit the up arrow key twice, once to expand the selection to the entire residue and another time to expand it to the entire chain

Now select the water molecule as the last part:

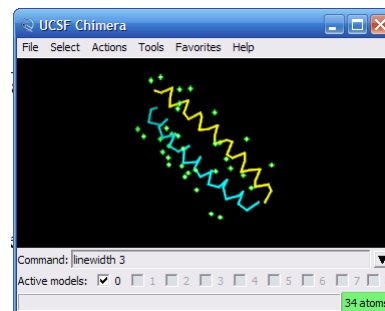
Select»Chain»water

Actions»Atoms/Bonds»show

Select»Clear Selection

Alternatively, the water could have been selected using

Select»Structure»solvent, or Select»Residue»name»HOH



To display all atoms of the A chain only:

Actions»Atoms/Bonds»hide

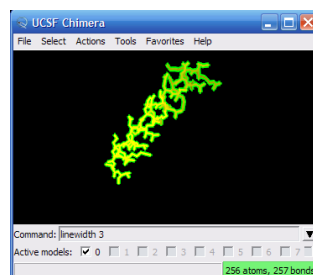
Select»Chain»A

Actions»Atoms/Bonds»show

Then to show the backbone only,

Actions»Atoms/Bonds»Backbone only»full

Only the A chain's backbone is displayed because chain A was selected.

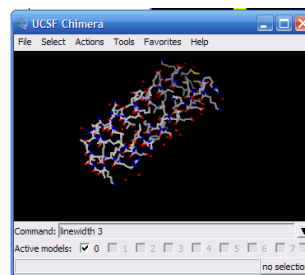


To display all the atoms and to color them according to element:

Select»Clear Selection

Actions»Atoms/Bonds»show

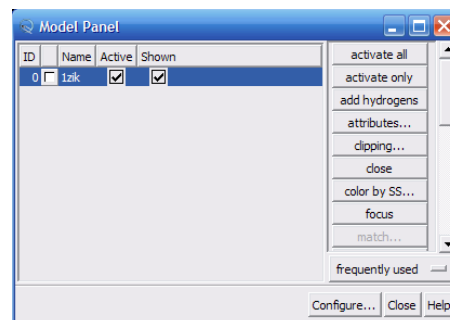
Actions»Color»by element



There is a checkbox in the Active column of the **Model Panel**

Tools»General Tools»Model Panel, or

Favorites»Model Panel



It shows that the model is activated for motion; un-checking the box inactivates the model. It can be restored by checking the box again. Close the model by highlighting **1zik.pdb** on the left side of the **Model Panel**, and then click **Close** on the right.

d) Menu Molecular Representations and Surfaces

Open another structure:

File»Open. In the resulting **dialog**, find and select *6bna.pdb*, and then *Open* to dismiss the **dialog**.

Try coloring the different nucleotides with different colors. For example, color the adenosine (A) residues blue:

Select»Residue»A

Actions»Color»blue



Analogously, color cytosine (C) residues cyan, guanine (G) residues yellow, and thymine (T) residues magenta. Undisplay the water (the white dots) as you did in the last part.

Next, try some alternate representations.

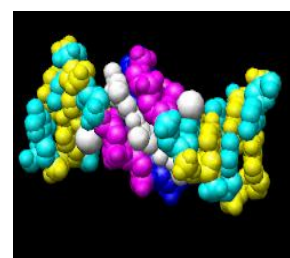
Select»Clear Selection

Actions»Ribbon»show

Actions»Ribbon»hide

Actions»Atoms/Bonds»stick

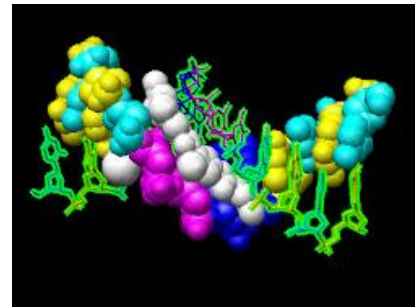
Actions»Atoms/Bonds»sphere



Change the representation of only one of the DNA strands, chain B:

Select»Chain»B

Actions»Atoms/Bonds»stick



Next, change everything to a ball-and-stick representation:

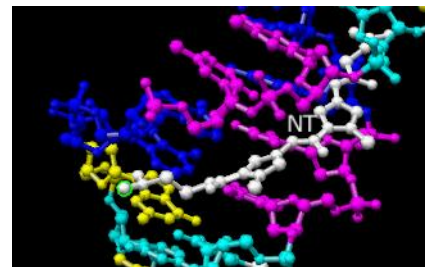
Select»Clear Selection Actions»Atoms/Bonds»ball & stick

In this representation, pick one of the atoms in the white netropsin molecule. Label the residue by residue name:

Actions»Label»residue»name

Since it is a residue label, the label may be closer to other parts of the residue than to the selected atom. Remove the label:

Actions»Label»residue»off



The first submenu under Label controls individual atom labels, while the second controls residue labels. *Actions»Label»name* would have shown the name of the atom instead of the name of the residue. Other than the white netropsin molecule, there are two additional white atoms. They are apparently attached to cytosines, which have been colored cyan. Pick and then label these two atoms:

Actions»Label»residue»name + specifier

It shows that one DNA strand is chain A, the other strand is chain B, and each strand contains a brominated cytosine. Use *Select»Clear Selection* to deselect the atoms and then un-display the labels.

Actions»Label»residue»off

Actions»Label»off

Finally, have some fun with surfaces:

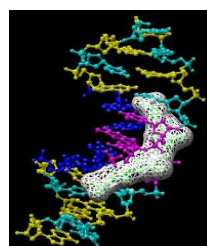
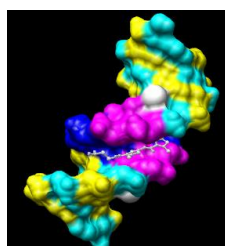
Actions»Surface»show

Actions»Surface»hide

Select»Structure»ligand

Actions»Surface»show

Actions»Surface»mesh



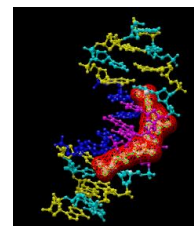
By default, a surface has the same color as the corresponding atoms; however, surface color can be specified separately.

To change the surface color of only netropsin (which is still selected)

Actions»Color»surfaces to change the coloring target

Actions»Color»red

Actions»Color»all of the above to restore the default coloring target.

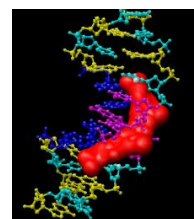


Clear the selection, change back to solid surface, and then un-display the surface:

Select»Clear Selection

Actions»Surface»solid

Actions»Surface»hide



As an example of a more complicated selection process, show the surface of the adenine and thymine in chain B only:

Select»Selection Mode»append (to change selection mode)

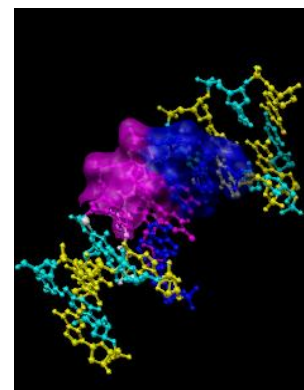
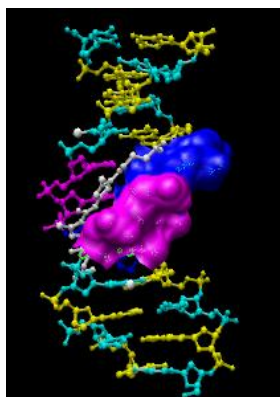
Select»Residue»name»A

Select»Residue»name»T

Select»Selection Mode»intersect (to change selection mode)

Select»Chain»B

Action»Surface»show



To prepare for any future commands, restore the selection mode and clear the selection:

Select»Selection Mode»replace

Select»Clear Selection

Sometimes, it is helpful to make a solid surface transparent:

Actions»Surface»transparency»50%

This is the end of this section. You can close the model. At this point, you can decide, which is easier to operate ? The menus or command-line ?

The Model Panel and Ensembles Tutorial

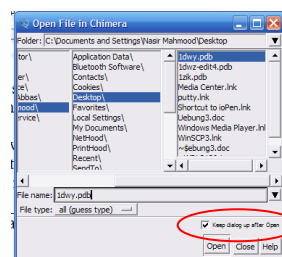
This tutorial introduces one of the most useful windows in *chimera*, and gives a little more information on how the *chimera* data-model works. The aim is to analyze a PDB file containing an ensemble of models that have been generated from NMR data.

From NMR data, one does not usually have a single structure. Instead, one often has a group (ensemble) of possible structures. This tutorial focuses on using the **Model Panel** and handling ensembles of structures (such as those determined by NMR). Note that the **Model Panel** is generally useful whether or not ensembles are being viewed.

You will work on two PDB files, which contain NMR-determined structures of a bovine prion protein fragment. `1dwz-edit4.pdb` contains the first four members of an ensemble of 20 structures (present in the original PDB entry `1dwz`), whereas `1dwy.pdb` is a single representative minimized structure.

Make the window a convenient size, then choose the menu item *File»Open*.

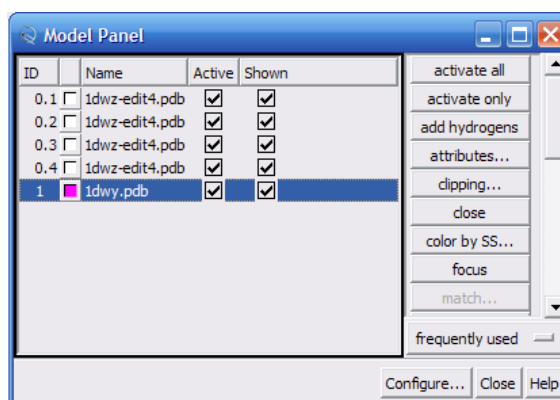
In the resulting **dialog**, find and select `1dwz-edit4.pdb` and check the box ‘*Keep dialog up after Open*’ so that the dialog does not disappear; next, open `1dwy.pdb`, click **Close** to also dismiss the **dialog**.



Thicken the lines: *Actions»Atoms/Bonds»wire width»3*. The structure includes all atoms, even the hydrogens. Simplify the display using *Actions»Atoms/Bonds»backbone only»full*. Now, only the N, CA, and C atoms are shown.

Open the Model Panel (*Favorites»Model Panel*). Each file of coordinates opened in *chimera*

becomes a model with an associated model ID number and model-level color. Some PDB files are further subdivided into multiple structures designated with MODEL and ENDMDL records; when the input file contains more than one set of such records, sub-model numbers are assigned sequentially starting with 1. In this case, the four ensemble members in *1dwzedit4.pdb* are sub-models 1-4 of model 0. Each sub-model (0.3, for example) can be treated as a separate model. Thus, "models" will be used to



indicate sub-models and/or models that are not subdivided into sub-models. By default, the **Model Panel** shows the model-level colors behind the names. Once one or more models have been chosen within the left side, any of several functions represented by buttons on the right side may be

executed. At first, most buttons are grayed out since no model has been chosen in the left side of the panel. Individual models or blocks of models may be chosen (highlighted) using the left mouse button. Ctrl-Click adds to an existing choice rather than replacing it. To highlight a block of models without having to hold down the mouse button, click on the first (or last) and then Shift-Click on the last (or first) in the desired block. Click on *1dwy.pdb* in the left side of the **Model Panel** and then try various functions on the right side:

show only hide the other models

trace chains display the chain trace, which includes only CA atoms

show all atoms display all atoms

select select the entire model for further operations

Complete the follow steps in the menu:

Actions»Color»by element

Select»Chemistry»element»H

Actions»Atoms/Bonds»hide

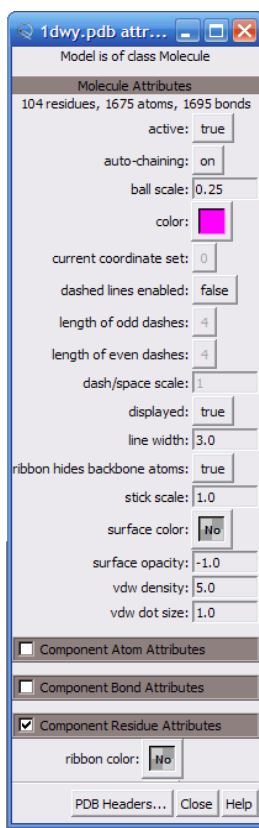
Select»Clear Selection (important, or else the invisible hydrogens will still be selected)

Back to the Model Panel:

sequence opens a **sequence panel** for the model; Click-Select one or a string of residues in the sequence and see how the corresponding residues of the structure become selected. Next, **Close** the panel and perform some action in the menu upon the new selection, such as:

Actions»Atoms/Bonds»sphere

Select»Clear Selection



Back to the Model Panel:

attributes opens a **molecule model attributes panel**; Click on the

Component Residue Attributes:

set **ribbon display** to on

set **ribbon cross section** to round

set **ribbon display** back to off

click **Close** to dismiss the panel

uncheck the **Shown** checkbox for *1dwy.pdb* *check* the **Shown**

checkbox for *1dwy.pdb*

Note that using the **Shown** checkbox is not the same as using the command **display**, which works on individual atoms and bonds; instead, it enables/disables the whole model's display. Checking **Shown** enables the display, but the display settings of individual atoms and bonds are not changed; in this example, the hydrogens are still un-displayed, as they were before the model was hidden. Toggling checkmarks in the **Shown** column is the same as using the **hide** and **show** buttons; toggling checkmarks in the **Active** column is the same as using **activate** and **deactivate** buttons. By default, these buttons are not included on the right side of the **Model Panel** because they are classified as **infrequently used**.

uncheck the **Active** checkbox for *1dwy.pdb* deactivate the model for motion (so it cannot be moved with the mouse) *check* the **Shown** checkbox for all of the models. Move the four sub-models of 0 so that they do not overlap with model 1 (which is deactivated and will not move). Scaling the view down with the mouse or **Side View** may be helpful.

check the **Active** checkbox for *1dwy.pdb*

Choose sub-model #0.1 in the **Model Panel**, select it, and use the **Actions** menu to color it. Repeat the process with the three other sub-models (choosing different colors), then clear the selection (*Select»Clear Selection*) and **Close** the **Model Panel**.

We will use the extension **EnsembleMatch** to compare the four NMR structures in *1dwzedit4.pdb* with the minimized structure in *1dwy.pdb*. **EnsembleMatch** is useful for comparing the members of two different ensembles, where each member of each ensemble contains the same molecule(s) with the same atom names. One ensemble serves as the *reference* to which the members of the other ensemble (the *alternative*) are compared. In general, comparison of ensembles may be helpful in examining different segments of a simulation trajectory, or in comparing sets of configurations generated by a variety of possible methods (distance geometry, Monte Carlo, *etc.*) with different input parameters. Generally, an ensemble will be input as a multiple-model PDB file in which each model record designates an individual ensemble member. Each of the two ensemble files should be opened in **chimera** before **EnsembleMatch** is invoked. If an ensemble file is opened as model 0 (for example), individual ensemble members are designated as sub-models #0.1, #0.2, *etc.* Each ensemble must have at least one member.

Start **EnsembleMatch** (*Tools»MD/Ensemble Analysis»EnsembleMatch*) and choose the minimized structure in model 1 as the reference and the NMR structures in model 0 as the alternative. **Parts to Match** are the atoms to be used for superimposing the structures. Each model contains residues

124-227 of chain A; it would be possible to use all atoms, but often it is more meaningful to compare only the backbone atoms or alpha-carbons. To use the backbone atoms N, CA, and C, enter the **Parts to Match** (atom specification)

@n@ca@c

which in this case is equivalent to

:124-227.a@n@ca@c

The **atom specification** describes the atoms to be used in *each* structure. Thus, if residue numbers are given, the residues in one structure must have the same numbers as the matching residues in the other structures. If atom names are given, they should specify equal numbers of atoms occurring in the same order in the different structures (if **@ca** is entered, the first CA in a structure is matched with the first CA in other structures, the second CA with the second in other structures, *etc.*).

Clicking **Okay** brings up the **EnsembleMatch** window. In this case, it is a 1 x 4 table with entries for all pairwise comparisons between the 1 reference and 4 alternative structures. The A and D buttons for each model control whether the model is activated for motion and displayed (actually shown or hidden, as explained above). The numbers in the table are the **RMSDs** between pairs of structures using the atoms specified as **Parts to Match** in the first dialog. The structures are not superimposed yet. Clicking a button next to an **RMSD** value in the table performs the corresponding superimposition, and the number of atom pairs used to calculate the **RMSD** is reported in the *status line*. Superimpose all four structures in model 0 onto the minimized structure in model 1 using these buttons.

Finally, for fun, start **EnsembleTile** (*Tools»Ensemble»EnsembleTile*). **EnsembleTile** "tiles" the structures within an ensemble: it separates individual ensemble members and spaces them evenly in the viewing plane. This type of display can be useful for showing the conformations and configurations generated by NMR structure determinations and molecular simulations. Pick model 0 as the **Ensemble to Tile**, and click **Okay**. *Tilings* are sometimes used in figures to compare different molecules or different conformations of the same molecule. Choose **File»Quit** from the menu to terminate the *chimera* session.

- *How do different models of the same NMR structure appear in a PDB file? (Try looking at some other NMR structures in the PDB, too)*

4. Summary

The first two introductory tutorials for *chimera* introduce you to:

- Menu and mouse driven selection and the *command line* equivalents for specifying the rendering style of an atom or molecule.
- Another way of rendering molecules, by *molecular surfaces*.
- The concept of **atom specification**.
- The different states that a particular model or set of models may have (active, inactive, hidden, displayed).
- Handling of ensembles of structures (such as those determined by NMR).ensembles of structures (such as those determined by NMR).

5. Assignment

Please answer the following questions in a brief written report (1page), and email it to *gst_uebung[at]zbh.uni-hamburg.de* not later than *November 21, 2008* with your *full name* printed on it.

- What is the most *observable* feature in the rendering of DNA and netropsin when the surface styles are applied?
- What is difference between *label* and *rlabel* commands?
- What does #0:1-50.a@C mean?