

Working with protein structures and sequences

Required functionality and modules: Discovery Studio Client.

Required data files: 1TPO.pdb, 1BVN.pdb.

Time: 10 minutes.

Introduction

Discovery Studio provides a range of viewers for working with molecular structures and properties. When working with proteins, the Molecule and Sequence Windows are of most value and can be used very effectively to explore different aspects of a molecule and make inferences about its functionality. For example, protein structure secondary structure predictions can be made on the sequences, and highlight the corresponding regions in the Molecule Window.

In addition to these general views, the application provides access to more specialized viewers for studying violations and anomalies in protein structures. Specifically, the Ramachandran plots and Contact Plots provide the ability to analyze high-level structural properties in detail and identify residues that may be incorrectly modeled.

In this lesson, the focus is on functionality that enables you to gain insights into a structure's function by looking at its sequence. The tutorial also covers the use of one of the more specialized views, the Ramachandran Plot.

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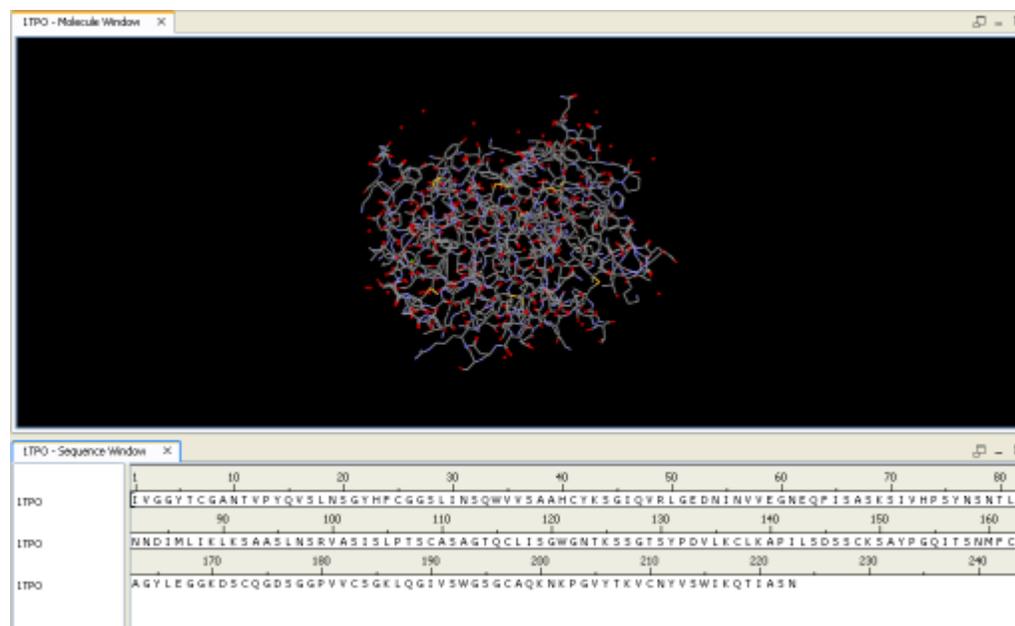
Opening and viewing a protein molecule and its sequence

In the Files Explorer, open **Samples | Tutorials | Quick Start Tutorials | 1TPO.pdb**.

From the menu bar, choose **Sequence | Show Sequence** to view the sequence for the molecule.

This opens a new Sequence Window that allows you to visualize and manipulate the amino acid sequence and the corresponding 3D structure simultaneously.

Drag the **Sequence Window** tab to the lower edge of the Molecule Window so that the Sequence and Molecule Windows are both visible.



Tip. You can easily adjust window layouts to suit the task at hand. Windows can be tabbed, set side-by-side, or

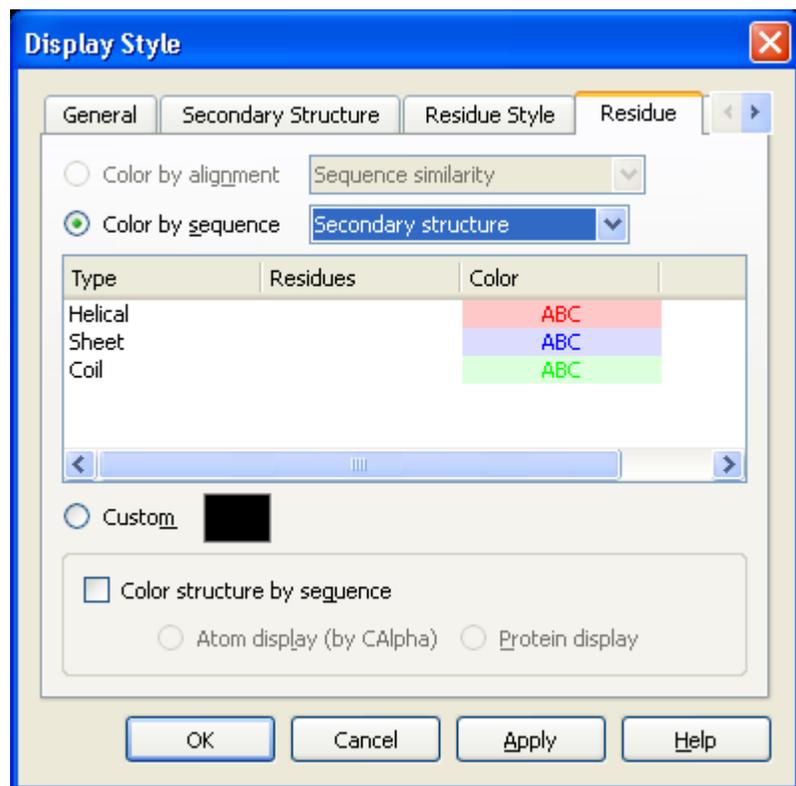
hidden from view. You configure different window layouts by dragging window tabs to desired positions. You can also adjust the interface using the actions of the *View* menu and its associated shortcut keys. For example, you can toggle the display of the Files, Tools, and Protocols Explorers using CTRL+2.

Click the **1TPO - Sequence Window** tab to make it active.

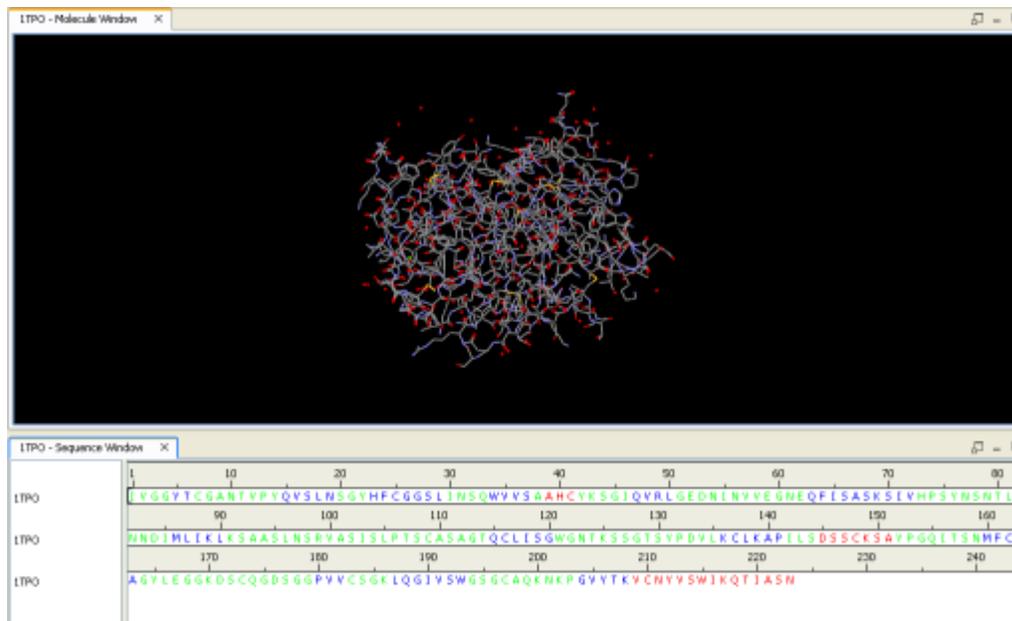
Press **CTRL+D** to display the Display Style dialog for the Sequence Window.

Click the **Residue** tab, select the **Color by sequence** option, and then choose **Secondary structure** from the list.

Click **OK**.



This changes the residue colors in the Sequence Window based on secondary structure type.



Right-click in the Sequence Window and choose **Secondary Structure Cartoon**.

This displays the PDB and Kabsch-Sander secondary structure cartoon. The coloring of the residues correspond to the secondary structure cartoon display. The blue arrows represent beta strands, and the solid red cylinders represent alpha helices.

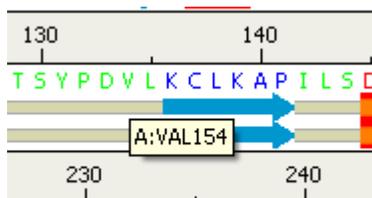
Note. Additional secondary structure cartoons are available from the **Secondary Structure** tab of the Sequence Window Display Style dialog.

Selecting residues

Discovery Studio Client offers numerous methods for selecting specific residues or other objects. Windows displaying the same data are interactive. If you make a selection in a Sequence Window, the same selection is made in the corresponding Molecule Window. Different views of the data in the Molecule Window can also be used to make selections.

Hover the cursor over any **residue** in the Sequence Window.

The residue ID is reported in a tooltip.



Find and select the three residues of the Catalytic Triad - **HIS57**, **ASP102**, and **SER195**.

HIS57, ASP102 and SER195 are at positions 40, 84, and 177 in the Sequence Window. If you make a mistake in selecting a residue - you can undo that selection action by choosing *Edit / Undo* from the menu bar, or by pressing CTRL+Z.

Tip. You can also use the Hierarchy View or Data Table View to select the residues.

Note. The numbers on the ruler in the Sequence Window run sequentially starting from 1. They do not reflect the residue numbering in the protein. However, you can hover over a residue in the Sequence Window to display a tooltip that reflects the numbering inherited from the experimental structure available from the Protein Data Bank (PDB). For 1TPO, the first residue is ILE16.

At this point it is useful to be able to save the current selection in the structure and restore it later. Discovery Studio Client supports the creation of *Groups* to provide this functionality. Groups can be created from any combination of objects that are selected in the Molecule Window. Once created, they are displayed in the Hierarchy View. Any groups

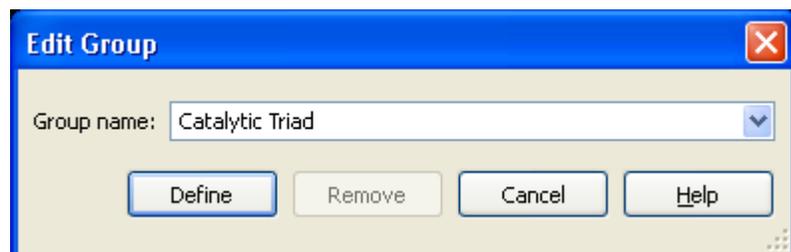
that you have created are saved in the `.dsv` format.

Click the **1TPO - Molecule Window** tab to make it active.

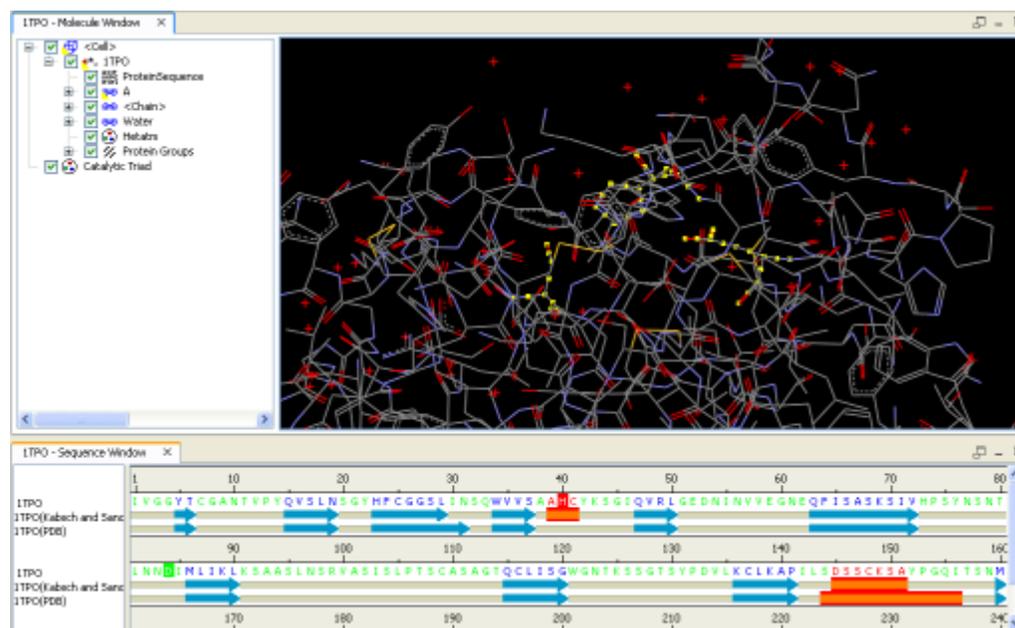
With the Catalytic Triad residues selected, from the menu bar, choose **Edit | Group...** to open the Edit Group dialog.

Enter **Catalytic Triad** as the **Group Name** and click **Define**.

Select **View | Transform | Fit To Screen**, or click **Fit To Screen**  on the **View** toolbar to center and zoom over the Triad.



Note. The Catalytic Triad group is added to the Hierarchy View (at the bottom) and Data Table View (Group tab).



Customizing the appearance of the protein structure

Click an empty area of the window to cancel the selection.

Select **View | Display Style...** from the menu bar.

On the **Atom** tab of the Graphics View Display Style dialog, set the **Display style** to **None**.

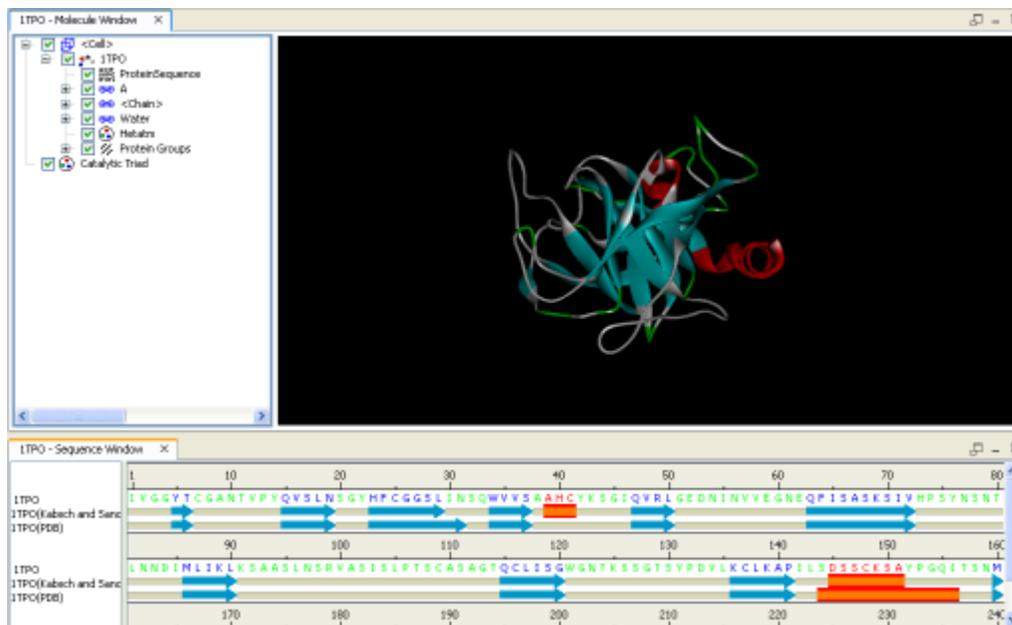
Click the **Protein** tab and set the **Display style** to **Solid Ribbon**.

Click the **Color by:** radio button in the **Coloring** group and set the value to **Secondary Type**.

Click **OK**.

Choose **View | Transform | Fit To Screen** from the menu bar, or click **Fit To Screen**  on the **View** toolbar to display the entire molecule.

This will remove all the atom-based rendering and only display the solid ribbon rendering.



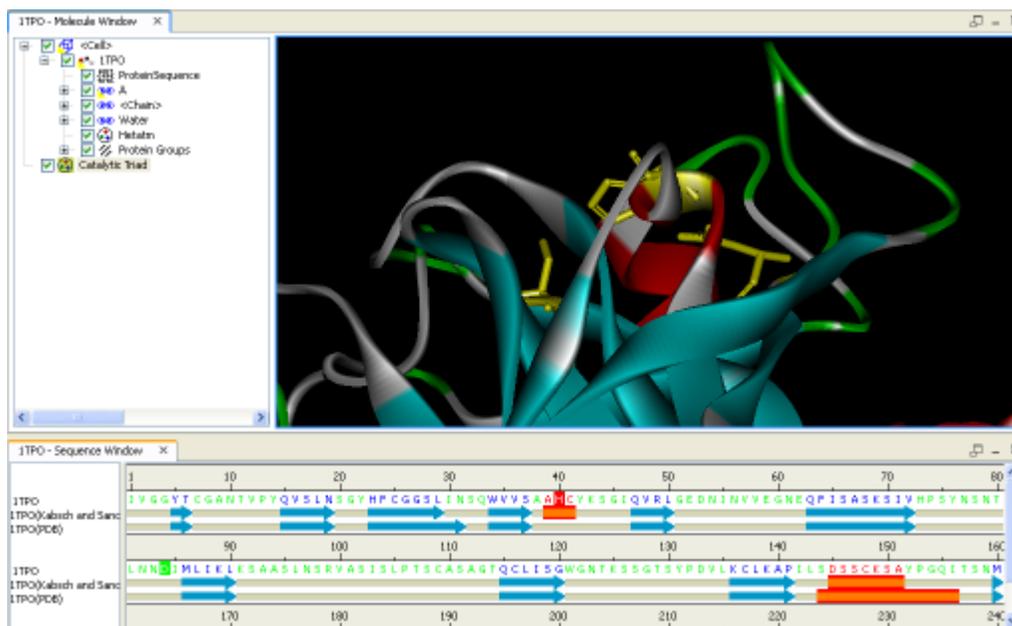
From the Hierarchy View, select the **Catalytic Triad** group.

Open the Display Style dialog and select **Stick** on the **Atom** tab.

Click **OK**.

Select **View | Transform | Fit To Screen** from the menu bar, or click **Fit To Screen**  on the **View** toolbar to show the entire molecule.

In the Graphics View, notice that only residues HIS57, ASP102, and SER195 are displayed as stick models, and the remainder of the protein is rendered as a ribbon. By only allowing a subset of residues to be visible on the Graphics View, you have a more focused view of the residues of interest, a simplified view of the Catalytic Triad in this case.



Tip. Saving files in [.dsv](#) format will retain the active view, the rendering, the labels, or any other annotations that you have made. [.dsv](#) files provide an efficient medium for sharing information with colleagues. For details, see [Sharing output with non-licensed users](#).

From the menu bar, choose **Window | Close All** to prepare for the next section of the tutorial. There is no need to save any files, so select **No** in the dialog that appears.

Exploring interactivity between the Molecule Window and the Sequence Window

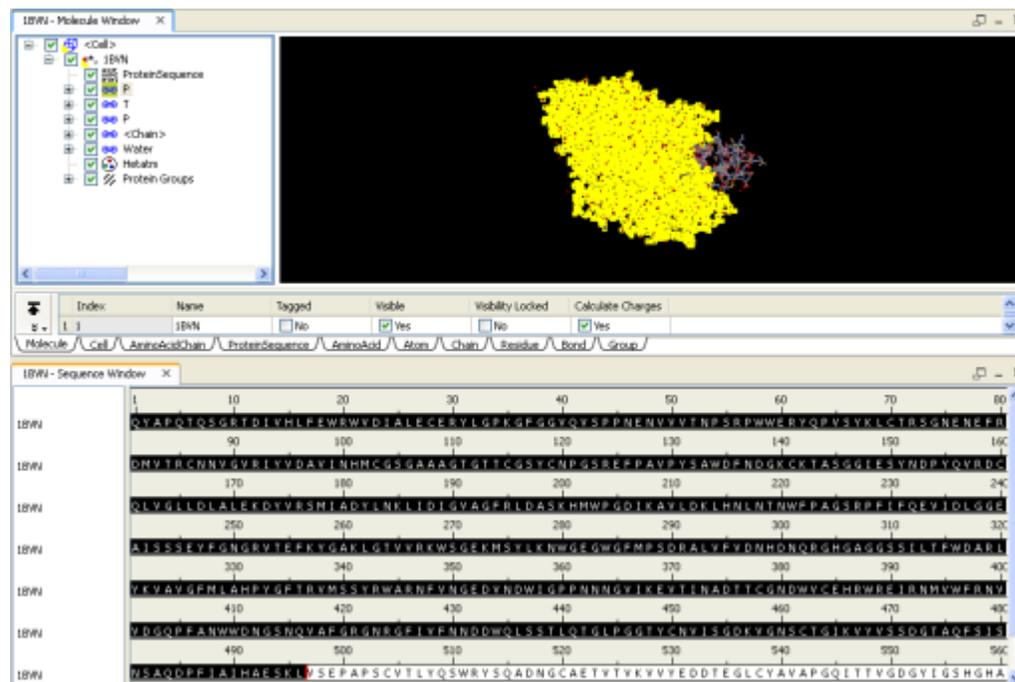
The previous section illustrated interactivity between windows by describing residue selection in the Sequence Window and display style changes in the Molecule Window. In this section, you will continue to explore examples of window interactivity and see additional examples that illustrate the value of window-to-window interactivity.

In the Files Explorer, open **Samples | Tutorials | Quick Start Tutorials | 1BVN.pdb**.

Tip. Use CTRL+H and CTRL+D to control the display of the Hierarchy View and Data Table View.

From the menu bar, choose **Sequence | Show Sequence** to open the Sequence Window.

Notice three chains in the Hierarchy View named P, T, and P. Click the first **P** chain to select it.



A selection will be made in the Graphics View and also in the Sequence Window. If you select residues in the Sequence Window, they are also selected in the Graphics View, the Hierarchy View, and the Data Table.

On the **Sequence Window**, slowly click and drag from left to right starting from residue 1 in the ruler.

In the Sequence Window, the selection will have a black background. The selection in the Hierarchy View and the Graphics View is highlighted in small yellow squares. A selection is also made in the Data Table.

Use the **Select** tool to select a region of the structure in the Graphics View.

Notice that residues in the Sequence Window are highlighted as well.

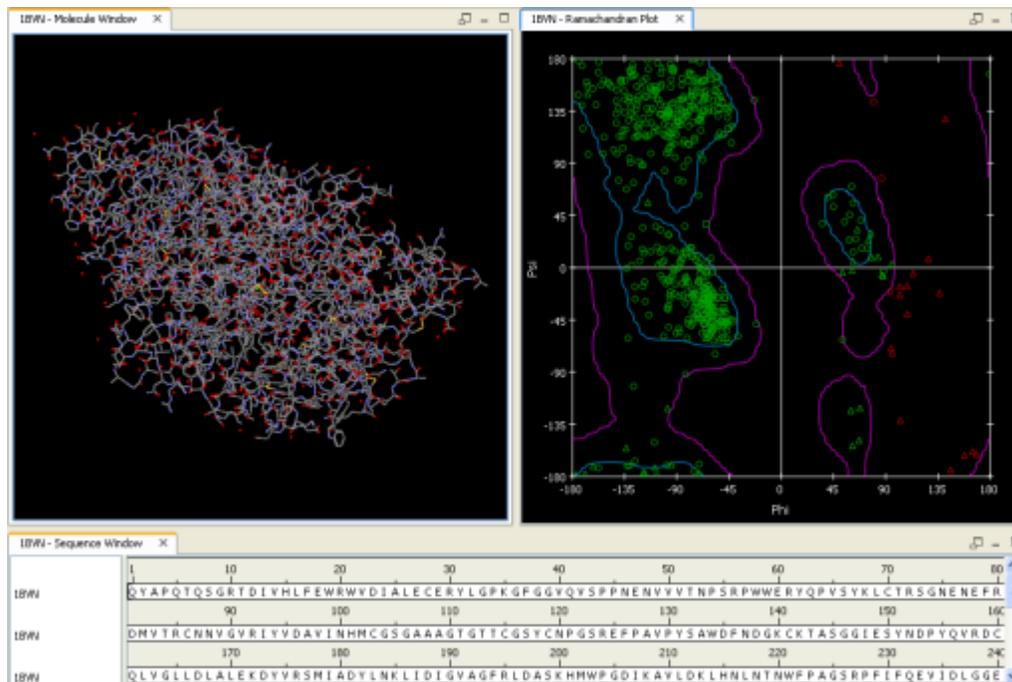
Exploring interactivity between the Molecule Window and a Ramachandran Plot

Deselect the residues in the Molecule Window by clicking in an empty region of the Molecule Window.

Press **Ctrl+H** and **Ctrl+T** to turn off the Hierarchy and Data Table Views.

Click the **1BVN - Molecule Window** tab to make it active.

From the menu bar, choose **Chart | Ramachandran Plot**.



A new Ramachandran Plot opens.

On the **View** toolbar, make sure the *Select* tool is enabled.

In the Ramachandran plot, select residues in the region of the plot at approximately **(-60, -60) degrees** for Phi and Psi respectively.

Highlighting points on the Ramachandran Plot also highlights the associated data in the other views. This allows you to identify residues in the structure which adopt defined Phi and Psi angles. Residues outside typical Phi, Psi regions can be quickly located and selected on the Ramachandran Plot, and then examined in the Graphics View.