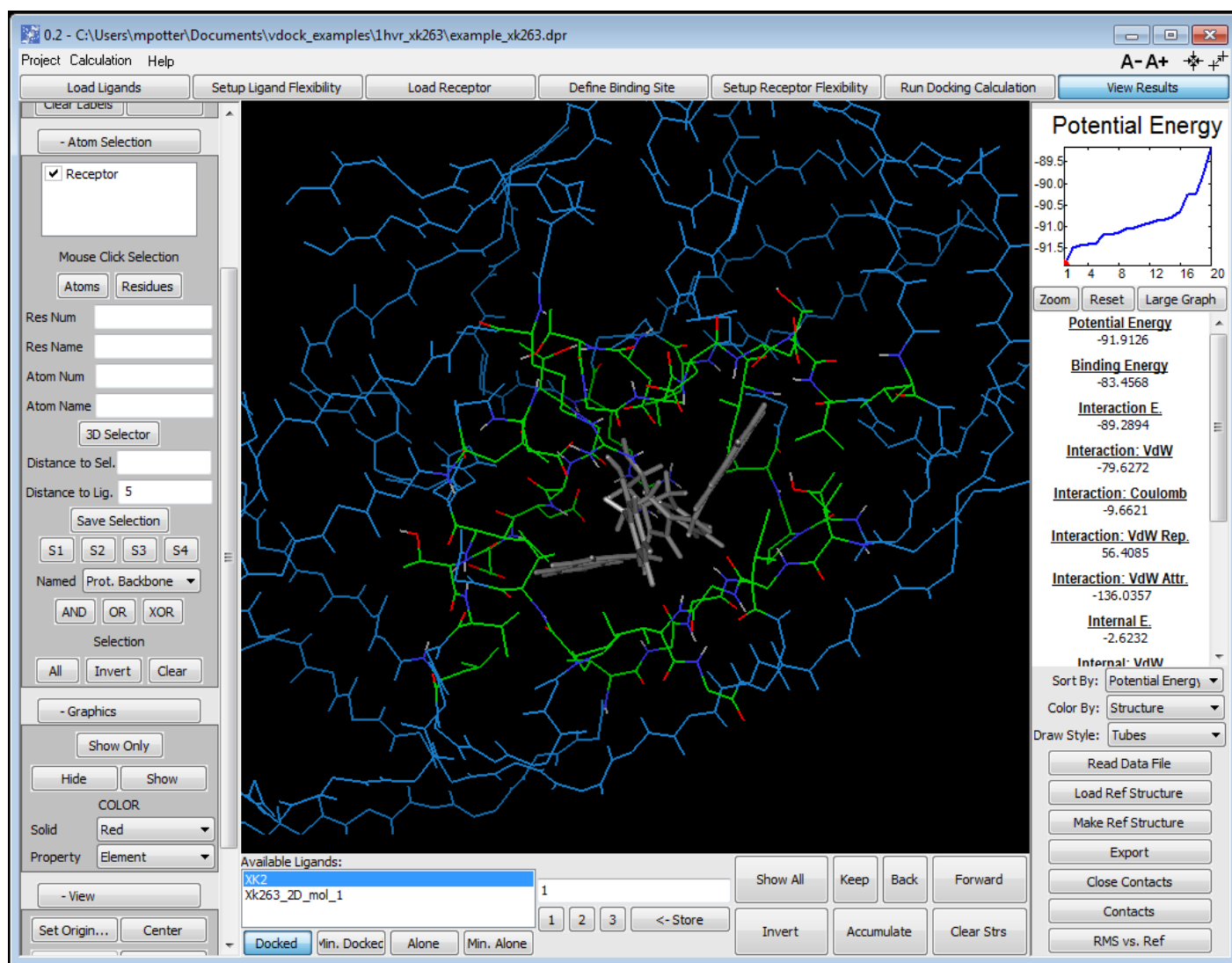


VDock Documentation



What is VDock? What does it do?

Welcome!

VDock is a software package for the generation and ranking of optimized protein-ligand binding conformations. With an sdf file of potential ligands and a pdb file defining receptor structure, you can use VDock to easily and quickly conduct a search for good bound conformations.

VDock's unique search and minimization algorithm combines ideas from a variety of techniques, including Global Underestimator Methods, Genetic Algorithms, Poling, and Tabu Search. Extremely rapid evaluation of the non-bonded interaction energy between receptor and ligand is achieved using 3D grids and interpolation. This results in a very efficient and thorough search capable of generating excellent bound conformations in less than a second on common processor types. A typical search would generate 20 candidate low energy conformations and complete in about 20 seconds (benchmark from Intel i7-9700K @ 3.6GHz, single core) This is accomplished using classical molecular mechanics force fields and does not rely on simplified scoring functions.

VDock can score and rank the conformations it finds but it is not a substitute for a package that can accurately

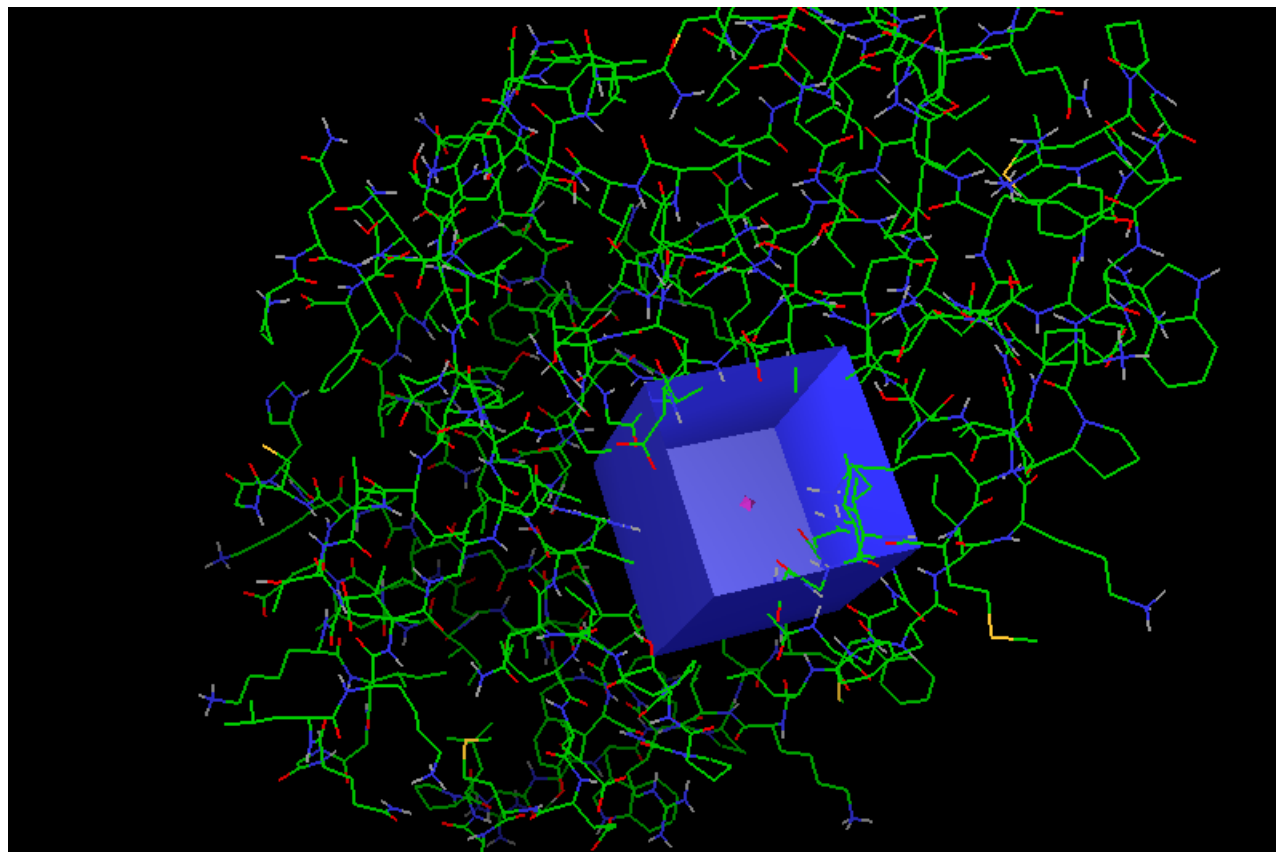
computer actual free energies of binding (as opposed to just potential energy, which is what is computed in VDock) Vdock is quite good at exploring available conformations and producing sets within which you are likely to find a structure quite similar to the actual, lowest free energy conformation. As such it can be a great tool to use in conjunction with other, more computationally expensive methods. You can use Vdock to generate a number of starting conformations for further searching and free energy evaluation. VeraChem's **VM2** software package works very well in combination with VDock and is capable of producing accurate binding free energy predictions for both host-guest and protein-ligand systems.

The Vdock package is divided into a sophisticated, guided, workflow-based graphical interface, and an underlying, highly optimized computational engine. The graphical interface may be used to setup, run, and analyze the results, or you can use it for setup and then run the actual computation using an exported input package and the computational engine as a command line application. This allows you to take advantage of non-desktop high performance computing resources, provides for it's inclusion in scripting applications, and allows for running many docking calculations in parallel.

VDock Technical Details

It is not necessary however to learn the specifics in order to use VDock successfully. VDock's graphical user interface can guide you through the entire process of setting up, running, and analyzing the results, using reasonable default options and parameters and fully automated support whenever possible.

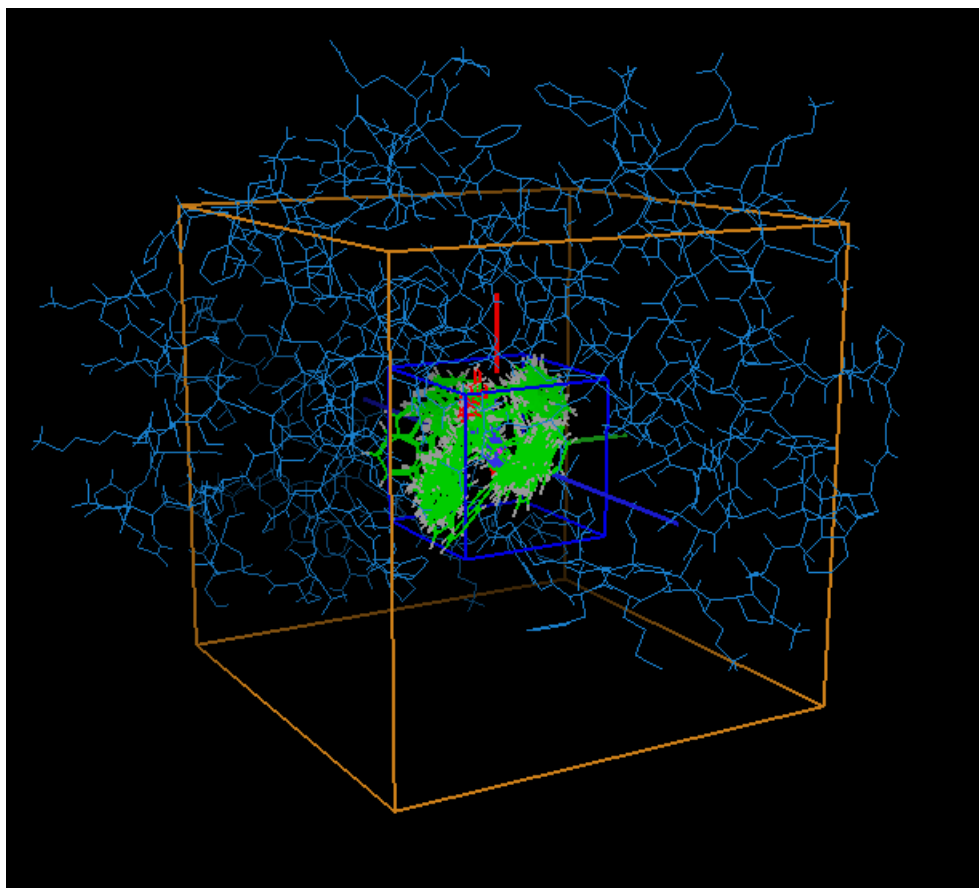
It is helpful to have a conceptual model for what VDock does. VDock randomly samples the position, orientation, and conformation of the ligand in the context of the protein / receptor binding site. It is also possible to include protein side-chains in the sampling. The volume to search is specified by the user. Ligand conformational changes during the search are limited to changes around rotatable bonds. This keeps the performance high without sacrificing much accuracy. A minimization can later be carried out for each of the low energy bound conformations located in order to relax the remaining degrees of freedom.



The search starts by randomly sampling from the entire range of positions (usually a cube centered on the expected binding site), orientations, and internal ligand conformation. As the search progresses, its center is updated to reflect the lowest energy conformations found and the range of sampling decreased. In this way low energy conformations are quickly located and refined.

VDock also keeps track of past low energy conformations it has found and occasionally "mixes" in portions of them in order to accelerate the location of especially good correlated coordinates. For example, in a large ligand there may be sequence of rotatable bonds which define a particularly low energy substructure. Remembering this allows for these rotatable bonds to be sampled in their correlated values without the need to repeatedly find them from independent random samples.

Finally, as low energy conformations are found, VDock sets up an exclusion zone around each of them. This prevents the search from sampling in the local volume about already located minima and results in increased search efficiency (preventing the same minima from being found over and over). In this way VDock constantly extends its search to new areas and conformations as it progresses and will then provide a growing set of conformations, each of which is different from the other, that fills the available low energy region of phase space.



For details of the concerning the algorithm please see the following references:

1. David, L.; Luo, R.; Gilson, M. K. Ligand Receptor Docking with the Mining Minima Optimizer. *Journal of Computer-Aided Molecular Design* 2001, 15 (2), 157–171. <https://doi.org/10.1023/A:1008128723048>.
2. Kairys, V.; Gilson, M. K. Enhanced Docking with the Mining Minima Optimizer: Acceleration and Side-Chain Flexibility. *J. Comput. Chem.* 2002, 23 (16), 1656–1670. <https://doi.org/10.1002/jcc.10168>.

VDock's implementation most closely follows that described in the second reference.

VDock Tutorial and Examples

For detailed tutorials and worked examples please see the companion document, `vdock_examples.pdf` that can be accessed via the `Help` menu of the VDock graphical interface or by navigation to the `Docs` directory of the VDock installation. This may be found at `C:\Program Files (x86)\VeraChem\Vdock` if the default location was accepted during installation.

The tutorials are the best place to start getting to know Vdock. The remainder of this document provides more general information about application of VDock as well as a detailed reference for the graphical interface.

VDock Development Status

Vdock and its graphical interface should be considered beta software. It is functional and useful but still rough around the edges. Occasional errors and problems are to be expected, especially when it comes to reading in arbitrary sdf files of ligands and pdb files for protein receptors. We've done our best with the resources available and we continue to develop Vdock as time becomes available.

If you experience problems please contact us at support@verachem.com. Please be aware that Vdock is currently provided free of charge and as such we can not promise to be able to respond to all communications. However, all reports will be viewed and added to our list of things to consider. Suggestions are also welcome!

How to Use VDock

Workflow

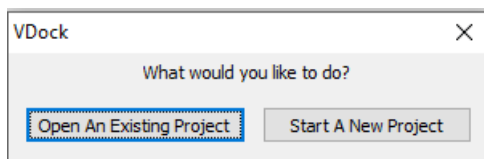
When using Vdock, it is best to follow this general order:

1. Start a new project
2. Load in sdf file that contains ligands
3. Setup the ligand flexibility using `Auto Setup All Ligands`
4. Load Receptor and read in the appropriate pdb file
5. Define the binding site by placing the box in the appropriate place
6. Run the docking calculation
7. View the results

Note: This is a simplified and quick process that can be used, but there are many other functions and features available in Vdock

Example of Simplified Workflow:

1. Upon opening Vdock, you will be asked to open an existing project or start a new one.
 - a. For this demonstration, we will be starting a new project.



2. After selecting **Start a New Project** you will be asked to name the new file and hit **Open**

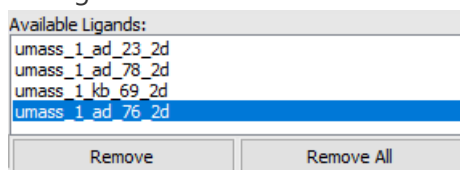
Load Ligands Tab

3. This will bring you to the first tab of Vdock's interface: Load Ligands

- a. Click the **Load Ligands** button

- b. Then, select and open the appropriate sd or sdf file

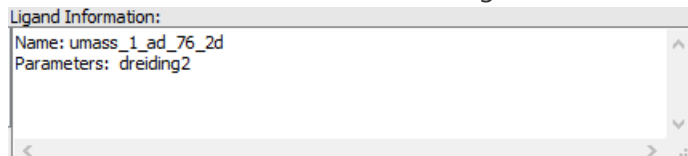
- i. The ligands that have been loaded will appear in at the bottom of the screen



- ii. More than one sdf file can be loaded in by pressing **Load Ligands** again

- iii. Ligands can be removed from the list by clicking on the ligand name in the list and pressing the **Remove** button

- iv. More information about the selected ligands can be found to the right of the list



Setup Ligand Flexibility

4. Under the second tab: Setup Ligand Flexibility

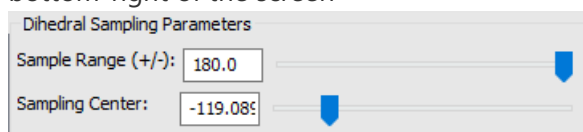
- a. Click the **Auto Setup All Ligands** button in the bottom-left of the screen.

- i. This will automatically select which dihedrals will be sampled.

1. These selected dihedrals will appear under **Dihedrals to be Sampled:**

2. The **Deselect Dihedral** **Deselect All** buttons can be used to deselect one or all the dihedrals that were automatically selected to be sampled

- ii. Sample range and sampling center can be manually adjusted using the sliding scales in the bottom-right of the screen



Load Receptor

5. Under the third tab: Load Receptor

- Click the **Load Receptor** button (in the lower-left corner)
- Select and **Open** the appropriate pdb file

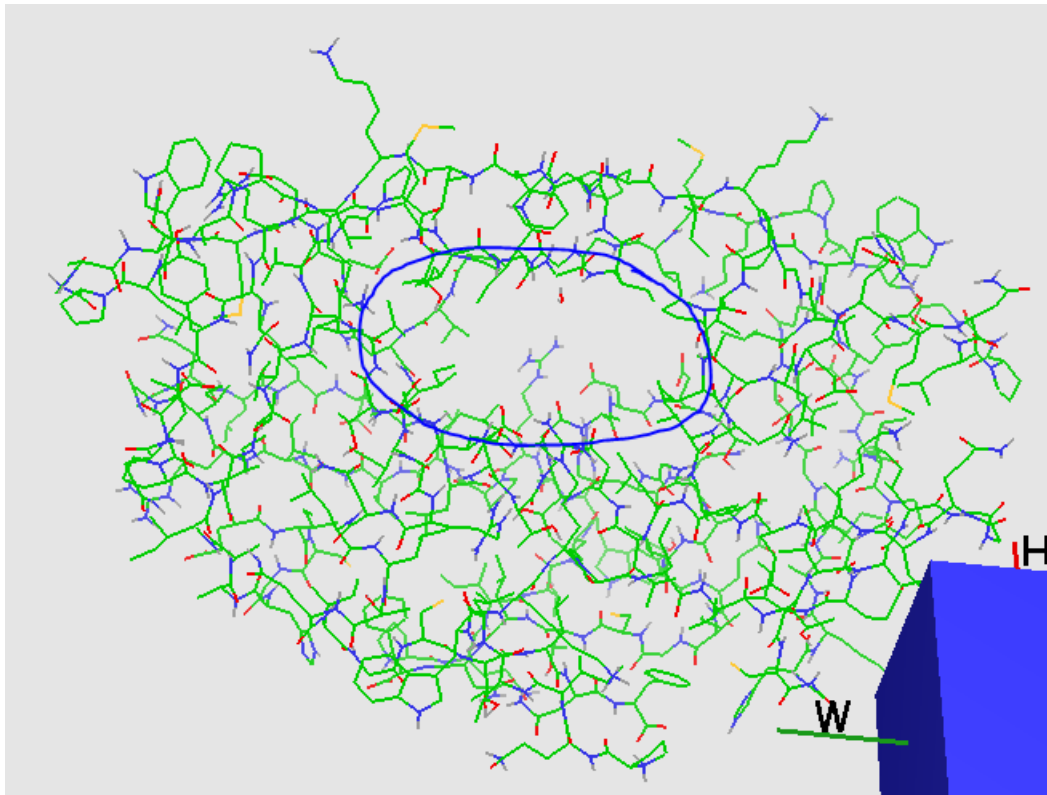
Define Binding Site

6. Under the fourth tab: Define Binding Site

- Click the **Place Box** button (in the lower-left corner)

Note: The box will appear at coordinates 0,0,0 by default, but cannot be placed until the **Place Box** button is clicked


- Use the left-mouse-button to rotate the protein until you are looking down into the active site (see example below; active site circled)

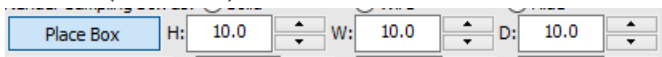


- Hold down the **Ctrl** key and click the middle-mouse-button to drop/place the box

Note: You should not be randomly clicking the middle mouse button, rather you should be clicking somewhere within the active site. Clicking on a specific atom will help center the box.

- You can then use **Ctrl** + left-mouse-button and **Ctrl** + right-mouse-button to shift the box into a better position (if needed)

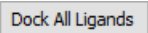
- e. You can also use the  keys next to the height (H), width (W), and depth (D) to adjust the size of the box (if needed)

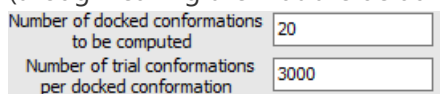


Setup Receptor Flexibility

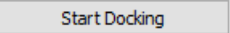
7. Under the fifth tab: Setup Receptor Flexibility
 - a. It is not necessary to do anything under this tab
 - b. If you would like to learn more about the features of this tab, please visit the "Other tools: Setup Receptor Flexibility" section

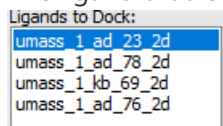
Run Docking Calculation

8. Under the sixth tab: Run Docking Calculation
 - a. Click the  button to dock all the prepared ligands that are listed
 - b. Number of docked conformations and number of trial conformations can be set as desired (though leaving them at the default numbers will usually work)

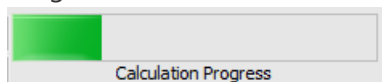


Note: These numbers are the main determinants of how long the calculations take to run. If you want a shorter calculation time, it is suggested that you decrease one or both numbers

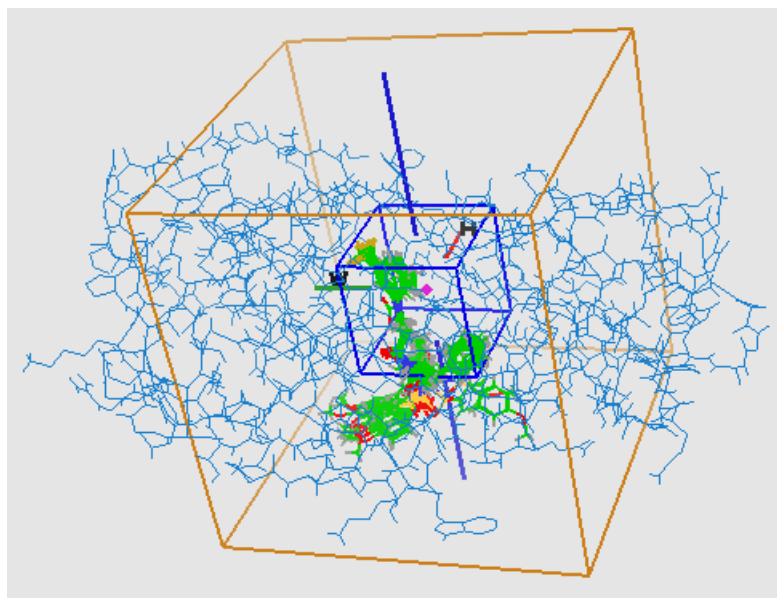
- c. Click the  button to begin the calculations
 - i. The ligand that is being processed at the time will be highlighted in the list



- ii. Progress of calculations for the selected ligand will be shown on the right



- iii. As new conformations are found, they will be displayed in the right-window

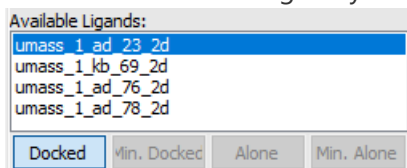


- d. Once the status bar shows that the calculation has been completed, you can move on to viewing the results

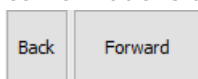
View Results

9. Under the seventh tab: View Results

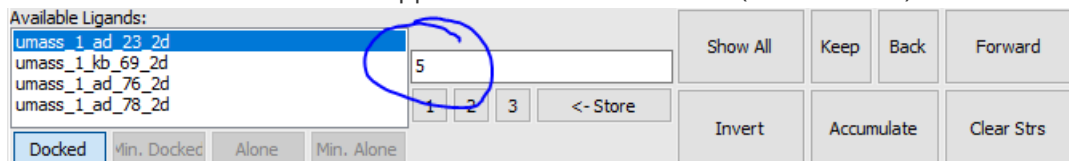
- a. You can select which ligand you would like to view under **Available Ligands:**



- b. You can then use the **Forward** and **Back** buttons (bottom-right) to step through the different conformations that have been found for that ligand



- i. The conformation number will appear in the center textbox (circled below)

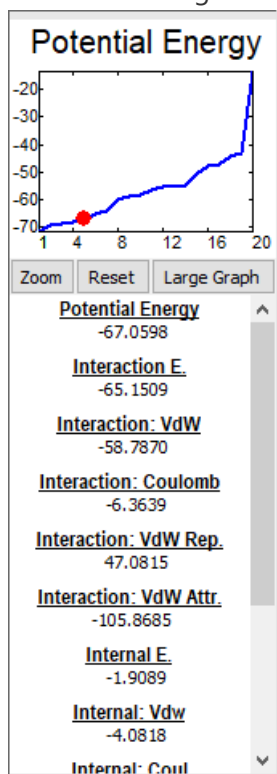


- ii. More than one conformation can be viewed at once by typing more than one number (with a space between numbers) into this textbox

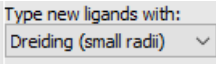
Note: Selecting **Color By: Structure** in the panel on the right may allow you to view each ligand more clearly.

- c. Different information about the selected conformation can be viewed in the right panel (see image below)

- i. The red dot on the **Potential Energy** graph indicates where this conformation lies on the scale amongst the other conformations found



Other tools: Load Ligands

- **Type new ligands with:** in the lower-left corner of the screen refers to which forcefield is being used to type the ligand
 - The forcefield being used can be changed using the drop-down menu
- 
- The **Export Ligands** button can be used to export and save the ligands that you are currently working on using Vdock

Note: As a default, they will save as ligand set (*.set) files

Labels Panel:

- See the "Tools Used in Several Tabs" section for information on this panel

View Panel:

- See the "Tools Used in Several Tabs" section for information on this panel

Other tools: Setup Ligand Flexibility

- For selected dihedrals:
 - The blue spheres indicate which end of the dihedral will rotate (the side with the larger spheres is the side that will rotate)
- The **Auto Setup** button will automatically select dihedrals to sample for the ligand that has been selected under **Available Ligands:**
 - This is similar to the **Auto Setup All Ligands** button, which automatically selects dihedrals to sample for all ligands under **Available Ligands:**
- The **Select Dihedrals...** button allows you to manually select dihedrals to sample
 - To select dihedrals: click on any of the light-grey spheres


Note: Select may be left-mouse button or **Shift** + left-mouse-button depending on your preference settings

- To deselect dihedrals: click on any of the red spheres

Note: Select may be left-mouse-button or **Shift** + left-mouse-button depending on your preference settings

- A **red** sphere indicates a dihedral that **has been selected** to sample
 - A **light-grey** sphere indicates a dihedral that **has not been selected** to sample
- The **Select Trans. Center...** button allows you to manually select an atom to be the translational sampling center
 - To select an atom, left click on the atom you want to select

Note: Select may be left-mouse-button or **Shift** + left-mouse-button depending on your preference settings

- The selected trans. center will be indicated by a pink diamond ()

- The **Preview** button allows you to see a preview of the volume sampled by the atoms moved by the selected dihedral
 - Select different dihedrals under the **Dihedrals to be Sampled:** list in order to see previews for other dihedrals
 - As discussed in the "Example of Simplified Workflow" section:
 - The sample range and sample center sliders can be used to adjust the dihedral sampling parameters that you see in the preview

- The button will set the sampling range slider and the sampling center slider back to their default positions of 180.0 and -60.779 respectively.

Labels Panel:

- See the "Tools Used in Several Tabs" section for information on this panel

View Panel:

- See the "Tools Used in Several Tabs" section for information on this panel

Other tools: Load Receptor

- More information on the receptor will appear under **Receptor Information:**
 - **Parameters: Present** indicates that the forcefield parameters are present
- The **Remove Water** checkbox allows you to decide whether the water molecules are shown/loaded
 - If **checked** = all water molecules will be removed
 - The default state of the box is checked
 - If **unchecked** = all water molecules will be shown alongside the receptor

Note: This checkbox must be clicked **BEFORE** you load in the receptor

- There are many buttons in the bottom panel that are grayed-out
 - These buttons are part of a future implementation that has not yet been completed
 - Once implemented, they will allow for various editing and selection functions

Labels Panel:

- See the "Tools Used in Several Tabs" section for information on this panel

Atom Selection Panel:

- See the "Tools Used in Several Tabs" section for information on this panel

Graphics Panel:

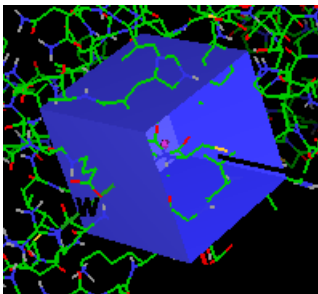
- See the "Tools Used in Several Tabs" section for information on this panel

View Panel:

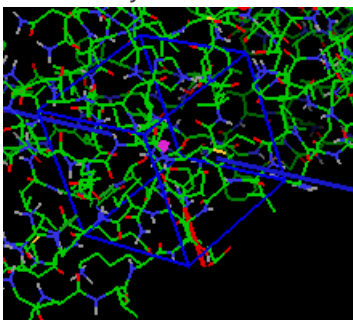
- See the "Tools Used in Several Tabs" section for information on this panel

Other tools: Define Binding Site

- The **Render Sampling box as:** buttons can be used to change the appearance of the box
 - **Solid** - makes the box solid throughout, obscuring the view of the atoms inside
 - Atoms inside the box will be visible only through one side of the box



- **Wire** - only shows the outline of the box, so atoms that are inside can be viewed



- **Hide** - hides the box from view completely
- The **Center on Ligand** button will center the box on the ligand
 - However, this will only be useful if there is information in the files you loaded that places the ligand in the active site
 - Otherwise, the ligand is placed somewhere separate from, but near the protein
- The **Center on Selection** button will center the box on the area of the selected atoms

Note: The box will be centered on the average location of your selection(s). Therefore, if more than one thing is selected, the box will be placed on a location that is the average of the coordinates of both/all selections.

- The position of the box can also be adjusted using the X, Y, Z coordinates

X: 20.67163 Y: 29.70911 Z: 19.67132

- You can adjust the range of the Euler angles (**E1:**, **E2:**, **E3:**) in order to change the rotational range that will be sampled for the ligand
 - The **E1:** range can be adjusted to any number within the limits of 0 - 180

- The **E2:** range can be adjusted to any number within the limits of 0 - 360
- The **E3:** range can be adjusted to any number within the limits of 0 - 360
- The NB grid is used to calculate the influence of the protein.
 - At the start of the calculation, Vdock calculates the distance and influence of each protein atom on each point in the NB grid.
 - The **Grid Spacing(Ang): 0.20** number refers to the distance between points in the grid
 - The interaction of the ligand with the rest of the protein is then approximated by interpolation from this pre-computed grid.
 - Therefore, it is important that the grid be **large enough** such that during sampling, no ligand atoms ever fall outside the grid
 - Anything outside the grid will have zero influence
- The software generates a default size that should work with most ligands

Note: If you moved the trans. center of the ligand (especially towards the edge of the ligand) you will likely need to increase the size of the NB grid.

- The size of the NB grid can be adjusted by changing the **NB Buffer (Ang):** number

Note: As the (Ang) indicates, the number is in Angstroms.

- The **Default** button can be used to return the size of the NB grid to the default setting
- The **Show NB Grid** button will display a "wire" version of the NB grid in the viewer
 - Click the **Show NB Grid** button again to hide the grid
- The **Show Ligand** button can be used to display the selected ligand in the viewer
 - Click the **Show Ligand** button again to hide the ligand
 - Different ligands can be selected under the **Available Ligands:** list
- The **Load Ref** button can be used to load in a reference structure to be viewed alongside the current ligand
 - The loaded file should contain a single conformation of a ligand/structure
- The **Remove Ref** button can be used to remove the reference structure from the screen

Labels Panel:

- See the "Tools Used in Several Tabs" section for information on this panel

Atom Selection Panel:

- See the "Tools Used in Several Tabs" section for information on this panel

Graphics Panel:

- See the "Tools Used in Several Tabs" section for information on this panel

View Panel:

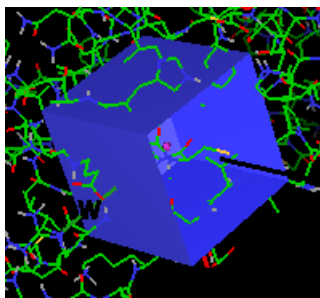
- See the "Tools Used in Several Tabs" section for information on this panel

Other tools: Setup Receptor Flexibility

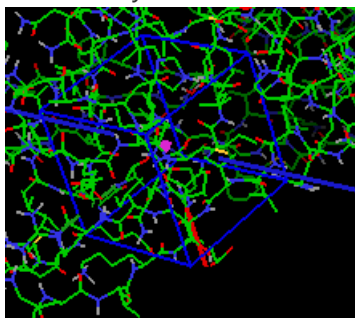
- The **Select Dihedrals...** button allows you to manually select dihedrals to sample
 - To select a dihedral, simply select the two central atoms

Note: Select may be left-mouse-button or **Shift** + left-mouse-button depending on your preference settings

- The **Samp.box:** buttons can be used to change the appearance of the box
 - **Solid** - makes the box solid throughout, obscuring the view on atoms inside *Atoms inside the box will be visible only through one side of the box



- **Wire** - only shows the outline of the box, so atoms that are inside can be viewed



- **Hide** - hides the box from view completely

- Any dihedrals that are selected will appear in the **Mobile Dihedrals** list
 - The **Remove** button can be used to remove the selected dihedral from the list
 - The **Rem. All** button can be used to remove all dihedrals from the list
 - Typing a new value into the **Range(+/-)** textbox allows you to change the rotational range of the selected dihedral
 - Typing a new value into the **Center** textbox allows you to change the set center of the selected dihedral
 - The **Default** button returns the **Range(+/-)** and **Center** values to their default settings
 - The **Reverse** button can be used to reverse which end of the dihedral will rotate
 - The blue spheres indicate which end of the dihedral will rotate (the side with the larger spheres is the side that will rotate)
- The NB grid is used to calculate the influence of the protein.
 - At the start of the calculation, Vdock calculates the distance and influence of each protein atom on each point in the NB grid.
 - The **Grid Spacing(Ang): 0.20** number refers to the distance between points in the grid
 - The interaction of the ligand with the rest of the protein is then approximated by interpolation from this pre-computed grid.
 - Therefore, it is important that the grid be **large enough** such that during sampling, no ligand atoms ever fall outside the grid
 - Anything outside the grid will have zero influence
- The software generates a default size that should work with most ligands

Note: If you moved the trans. center of the ligand (especially towards the edge of the ligand) you will likely need to increase the size of the NB grid.

- The size of the NB grid can be adjusted by changing the **NB Buffer (Ang):** number

Note: As the (Ang) indicates, the number is in Angstroms.

- The **Default** button can be used to return the size of the NB grid to the default setting
- The **Show Grid** button will display a "wire" version of the NB grid in the viewer
 - Click the **Show Grid** button again to hide the grid
- The grayed-out buttons will be available in future versions of Vdock

Labels Panel:

- See the "Tools Used in Several Tabs" section for information on this panel

Atom Selection Panel:

- See the "Tools Used in Several Tabs" section for information on this panel



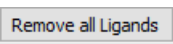
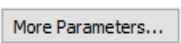
Graphics Panel:

- See the "Tools Used in Several Tabs" section for information on this panel

View Panel:

- See the "Tools Used in Several Tabs" section for information on this panel

Other tools: Run Docking Calculation

- The  button can be used to add ligands to the **Ligands to Dock:** list
- The  button can be used to remove ligands from the **Ligands to Dock:** list
- The  button can be used to view an expanded list of calculation parameters
- The  button can be used to view an expanded list of calculation parameters

Calculation Parameters

Additional Docking Parameters

Random seeds (integers) 9061 5846 2485 2456

Distance Dependent Dielectric(1/coef*r) Coefficient 4.0

Fixed Dielectric Dielectric Constant 20.0

Coulombic 1-4 scaling factor 0.5

Size of Exclusion Zones

Translational (Angstroms) 0.5 Rotational (Degrees) 7.5 Dihedral (Degrees) 15.0

Non-bonded grid spacing (0.07 - 1.0 Ang) 0.2

Non-bonded grid energy cutoff (kcal/mole) 2.0

Non-bonded grid distance cutoff (Ang) 10.0

Energy cutoff between nonbonded pairs(kcal/mole) 1.0

Number of fine tune shots 3000 Number of hunts per docking (Nsearch) 4 Search range narrowing rate 3.0

GA strength 0.1 Number of poses per ligand conformation 20

Number of isolated ligand conformations to generate 20 Number of isolated ligand trial conformations 3000 Number of isolated ligand fine tune shots 3000

Gradient tolerance for minimization 1e-07 Maximum minimization steps 400 CG or QN minimizer 1 for CG 2 for QN 2 Distance Dependent Dielectric (1/coef*r) in minimizations 4.0

OK Cancel

- The **Write Vdock Input** button allows you to write out a set of files that will contain the input for Vdock, meaning you can run the calculations on a different computer

Tip: You could use this to write a template file that could be used for many ligands


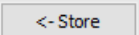
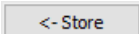



- The **Calculate Grid** button allows you to calculate the grid before starting the docking calculations
- The **Optimize Ligand Alone** button will conformationally search the ligand by itself
 - This will give you a better estimate of the energy of the ligand by itself
- The **Minimize Ligand Alone** button carries out a full minimization in all degrees of freedom on the ligand by itself
 - Normally, Vdock only optimizes conformation with respect to rotatable bonds, it does not optimize bond angles or bond lengths
 - **Minimize Ligand Alone** will optimize rotatable bonds, bond angles, and bond lengths

- The **Minimize Docked** button carries out a full minimization in all degrees of freedom on the docked ligand that is currently selected in the **Ligands to Dock:** list
 - Normally, Vdock only optimizes conformation with respect to rotatable bonds, it does not optimize bond angles or lengths
 - **Minimize Docked** will optimize rotatable bonds, bond angles, bond lengths, and will allow the protein to move
- The **Minimize All Docked** button carries out a full minimization in all degrees of freedom on all docked ligands in the **Ligands to Dock:** list
 - Normally, Vdock only optimizes conformation with respect to rotatable bonds, it does not optimize bond angles or bond lengths
 - **Minimize All Docked** will optimize rotatable bonds, bond angles, bond lengths, and will allow the protein to move
- The **Run Complete Calculations** button runs all calculations that it can given the complete setup (e.g. grid, docking, optimized ligand alone, minimized ligand alone, etc.)
 - As compared to the **Start Docking** button, which only runs docking calculations
- The **Run PLP** button will provide the piece-wise linear score for each docked conformation of each ligand in the **Ligands to Dock:** list
 - This is a simple empirical energy function that takes into account Hydrogen bonding and steric compatibility
 - For more details see: [this paper](#) (Gehlhaar et al., 1995)
 - This can be complimentary to the energy in determining which things bind best
- The **Write Result Summary** button writes out a text-file providing the results of the calculations
 - In a format that should be able to load in excel or other spreadsheet programs
- The **Terminate Calculation Now** button allows you to stop the calculation at its current point




Other tools: View Results

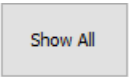
- The **Docked** button will show the first docked conformation of the selected ligand
 - As mentioned in the "How to Use Vdock" section, the **Forward** and **Back** buttons can be used to step through the different docked conformations
- The **Min. Docked** button will show the fully minimized version of the first docked conformation of the selected ligand
- The **Alone** button will show the first conformation of the selected ligand, without the protein (the ligand




will be shown alone)

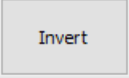

- The  button will show the fully minimized version of the first conformation of the selected ligand without the protein (the minimized ligand will be shown alone)
- The  button can be used to store specific ligand selections
 - To store a ligand selection: Click the  button and then select one of the numbered buttons (, , )
 - To return to the stored selection, click on the numbered button it was stored under

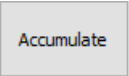
Note: If you try to store a conformation in a numbered button that already contains something, the new conformation will be added alongside the saved one.

- For example, if conformation 9 is saved under  and you attempt to store conformation 3 under , then  will contain both conformations 9 and 3
- To clear the numbered button, right-click on it

- The  button will show all available conformations of the selected ligand

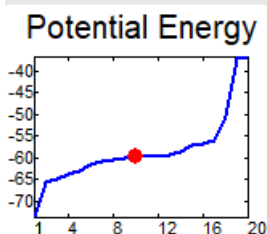
- The  button will allow you to continue viewing the current conformations while you view other conformations of the same ligand (when you switch ligands,  will be cleared)
 - **Example:** If you are viewing conformation 9 and you click , and then you select conformation 11, conformation 9 will be shown along with conformation 11

- The  button will display all conformations except for the conformation that is currently being viewed (it inverts which conformations you are viewing)
 - **Example:** If you are currently viewing conformations 3 and 5, then you click , all conformations except conformations 3 and 5 will be shown

- The  button will allow you to turn the "accumulate" setting on and off
 - The "accumulate" setting refers to whether the structures you are viewing will accumulate as you continue viewing different structures
 - If the accumulate setting is turned on: the next structure you view will be shown along with your current structure(s)
 - If the "accumulate" setting is turned off: only the next structure you view will be shown, replacing the current structure(s)

Clear Strs

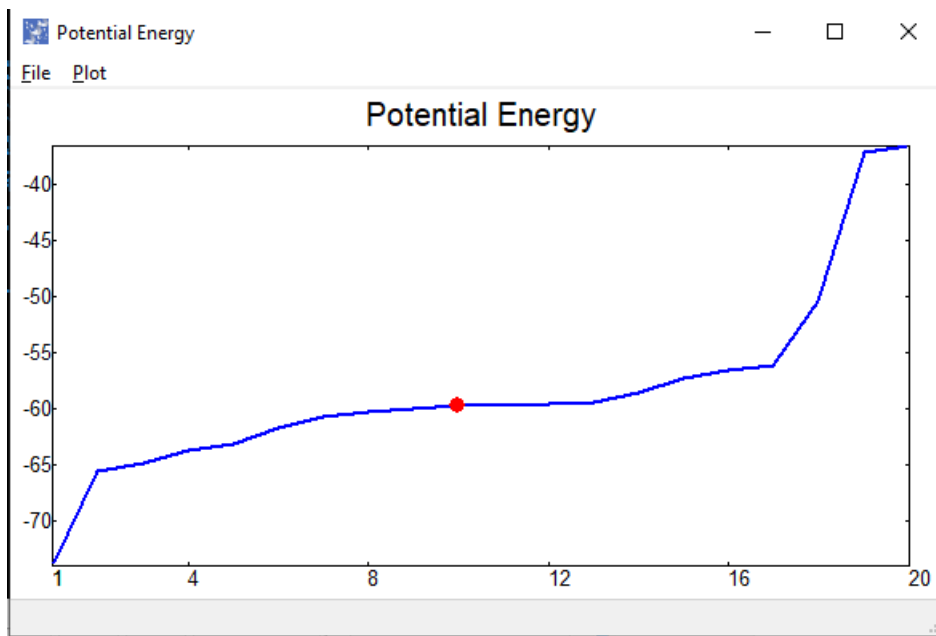
- The **Clear Strs** button will clear all the structures except the last structure to be displayed
 - **Example:** If you are viewing conformation 4, and then 4 and 5, then 4, 5, and 6, and then you click **Clear Strs**, Vdock will clear all structures except for conformation 6
- The **Potential Energy** graph displays the different conformations that have been found and their respective potential energies (kcal/mol)
 - **x-axis** = conformation number
 - **y-axis** = potential energy in kcal/mol



- The red sphere indicates the conformation that is currently being viewed

Note: If multiple conformations are being viewed, the red sphere will indicate the conformation that is last (farthest right) in the list

- You can click on the different points on the graph in order to select different conformations to view
- The **Zoom** button will allow you to zoom in on a specific area of the graph
 - To do this, click the **Zoom** button and then use the left-mouse-button to drag-select the area of the graph that you would like to zoom in on
- The **Reset** button will reset the graph to the default (zoomed out) view
- The **Large Graph** button will open a new window with a larger version of the graph



- This new window also offers more functions such as:
 - Save current plot (under **File**)
 - Print current plot (under **File**)
 - Enable Grid (under **Plot**)
 - Enable Legend (under **Plot**)
- The scrollable window has more information about the currently selected conformation

Note: If more than one conformation is selected, the information will refer to the last conformation (farthest right) in the list

Potential Energy -59.7346	Interaction: VdW Rep. 34.7153
Binding Energy -47.6215	Interaction: VdW Attr. -91.8585
Interaction E. -55.2084	Internal E. -4.4230
Interaction: VdW -54.3081	Internal: Vdw -2.7477
Interaction: Coulomb -0.9003	Internal: Coul -4.1462
Interaction: VdW Rep. 32.3734	Internal: Dihedral 2.4708
Interaction: VdW Attr. -86.6814	Probability 0.0000
Internal E. -4.5262	
Internal: Vdw	

- The **Sort By:** drop-down menu allows you to choose how the conformations are sorted
 - A few possible options that will appear here (depending on which type of ligands are selected)
 - Potential Energy

- Binding Energy
- PLP Binding Energy
- Interaction E.
- Interaction:VdW
- Interaction Coulomb
- Interaction: VdW Rep.
- Interaction: VdW Attr.
- Dihedral
- Bond
- Internal E.
- Internal: VdW
- Internal: Coulomb
- Internal: Dihedral

Note: This may change how they are displayed on the graph (upper-right), because the order in which they are sorted may be different.

- The **Color By:** drop-down menu allows you to choose how the ligand(s) is colored, such as:
 - By: Structure
 - By: Element
- The **Draw Style:** drop-down menu allows you to choose which style you want the ligand(s) to be drawn in, such as:
 - Lines
 - Tubes
- The **Read Data File** button allows you to read in a file with a new property
 - This property will appear under the **Sort By:** drop-down menu and the scrollable window
 - Example of a new property you could load in: **Surface Area**

Note: The file must contain information for each of the conformations. Information for conformations should be in the original order (seen under **Sort By:**)

- Format of file you load in:
 - The first row of the file should contain the new properties, with a space separating each property (should be no spaces in the name of the property)

- **Example:** Property_1 Property_2 Property_3

- All following rows should contain values for each property for all conformations (with spaces in between each value; each column = one property)

- **Example:** If you had four properties and four conformations

```
Prop1 Prop2 Prop3 AnotherProp
2.3 10.4 6.7 8.9
1 12. 7.2 8
16 4.5 6.0 8.75
2.3 4.5 4.76 8.2
```

- Conformations should be listed in the "Original order" which can be seen by selecting "Original order" in the **Sort By:** drop-down menu
- You can use the **Export** button to export the conformations in the "Original order" and run calculations on them for new properties

Note: It always exports in the original order, regardless of what is chosen in the **Sort By:** drop-down menu

- The **Load Ref Structure** button allows you to load in a file with single conformation of a ligand, allowing you to view it alongside other ligands/conformations
 - The loaded structure will appear in and stay in the viewer until explicitly cleared
 - Reference structure file types that are currently supported include:
 - crd, pdb, trj, mol, mol2, sd, sdf, mdl

Note: Other file types may be available in future implementations

- The **Make Ref Structure** button allows you to write out the currently viewed structure as a reference file
- The **Export** button allows you to write the results out to a file so that you can use them in other software

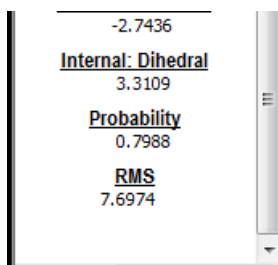
Note: It always exports in the original order, regardless of what is chosen in the **Sort By:** drop-down menu.

- The **Close Contacts** button shows you places where the ligand is in very close contact to the protein
 - The areas indicated are places in which a reduction in contact could result in a decrease in binding energy
- The **Contacts** button shows you places where the ligand is in contact with the protein

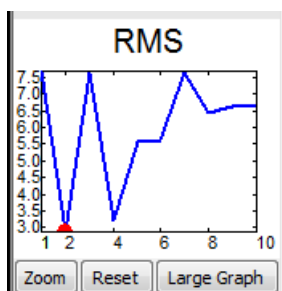
- The areas that are empty are places in which new things could be added to the ligand without disrupting the binding
- The **RMS vs. Ref** button calculates the root-mean-squares deviation between whether structure/conformation you are viewing and a reference structure
 - In other words, it will give you a number that tells you how different the currently selected structure is from the reference structure

Note: This button will only work if you have loaded in a reference structure.

- The calculated RMS value will appear in the scrollable window (under the graph)



- If you click on the "RMS" label, the graph will display ligands based on RMS



Labels Panel:

- See the "Tools Used in Several Tabs" section for information on this panel

Atom Selection Panel:

- See the "Tools Used in Several Tabs" section for information on this panel


Graphics Panel:

- See the "Tools Used in Several Tabs" section for information on this panel


View Panel:

- See the "Tools Used in Several Tabs" section for information on this panel

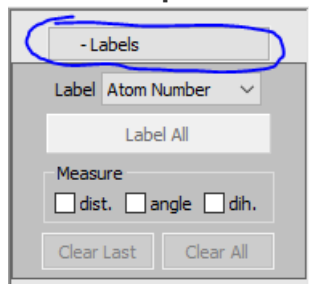
Tools Used in Several Tabs

- The **A-** button allows you to decrease the font size of all atom labels
- The **A+** button allows you to increase the font size of all atom labels
- The  button allows you to center the molecule in the viewing screen

Note: This will center the molecule using the default origin (not the set origin)

- The  button allows you to set the view and rotational centers on a new origin/atom

Note about panels: Panels can be collapsed/expanded by clicking on the title button above the panel



Labels Panel:

- This panel allows you to label the ligand
 - You can label the ligand based on several different things, such as:
 - Atom number
 - Element
 - Atom name
 - Dreiding atom type
 - Formal charge
 - Partial charge
 - MOL atom parity
 - To label the ligand based on one of these criteria, simply select the desired criterion from the drop-down menu and hit the **Label All** button
 - The **Clear Last** button will allow you to clear the last label that was applied
 - Any measurements displayed also count as labels and will therefore also be cleared by **Clear Last**
 - The **Clear All** button will allow you to clear all labels that have been applied
 - Any measurements displayed also count as labels and will therefore also be cleared by **Clear All**
- This panel also allows you to measure different things on the ligand

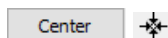
- Including:
 - Distance
 - Angle
 - Dihedral Angle
- To measure distance - click on the **dist.** checkbox and use **Shift** + left-mouse-button to select two atoms
- To measure angles - click on the **angle** checkbox and use **Shift** + left-mouse-button to select three atoms
- To measure dihedral angles - click on the **dih.** checkbox and use **Shift** + left-mouse-button to select four atoms

View Panel

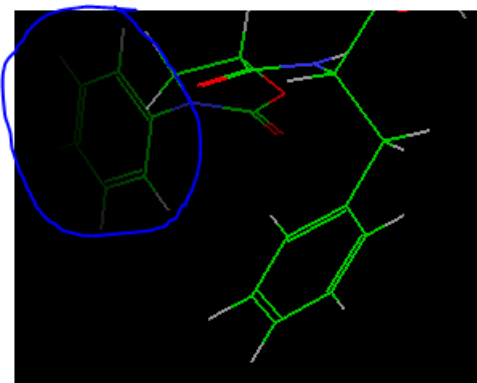
- The **Set Origin...** button allows you to set the view and rotational centers on a new atom
 - To do this, select a new atom

i Note: Select may be left-mouse-button or **Shift** + left-mouse-button depending on your preference settings

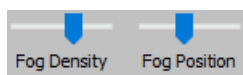
- Under the **View Results** tab, the origin can only be set on an atom within the receptor
- In order to restore the default origin, use one of the center buttons (see below)



- The **Auto Spin** button slowly spins the ligand around the point of origin
 - The **+** button allows you to reverse the direction of the spin
- The **Show Fog** checkbox allows you to toggle the "fog effect" on and off
 - The "fog effect" refers to the slight "fog" that clouds any parts of the molecule that are farther away from the viewers perspective
 - **Example:** Notice the farther (circled) part of the molecule is partially obscured by "fog"; whereas the closer part of the molecule is not



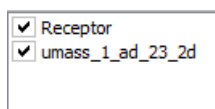
- Fog density and position can be adjusted using the sliders



- Fog density - slider left --> right = less dense --> more dense
- Fog position - slider left --> right = further back --> further forward
- The **Background** drop-down menu allows you to change the color of the background to
 - Black
 - Light grey
 - White

Atom Selection Panel:

- If you have multiple molecules:
 - The checkboxes (see image below) allow you to select which molecule you will be interacting with when using the functions in the **Atoms Selection** panel



- The **Atoms** button allows you to select individual atoms in the molecule

i Note: Select may be left-mouse-button or **Shift** + left-mouse-button depending on your preference settings

- The **Residues** button allows you to select residues by selecting one atom in the residue

i Note: Select may be left-mouse-button or **Shift** + left-mouse-button depending on your preference settings

- You can select a specific residue using:

Res Num	<input type="text"/>
Res Name	<input type="text"/>

- Res Num (residue number) - type in a residue number and hit enter to select it

i Note: You can also type in ranges using a dash (4-10)

i Note: You can also select more than one at once using spaces and/or commas

(4,5 or 4, 5 or 4 5)

- Res Name (residue name) - type in a residue name and hit enter to select it

- You can select a specific atom using:

Atom Num	<input type="text"/>
Atom Name	<input type="text"/>

- Atom Num (atom number) - type in an atom number and hit enter to select it

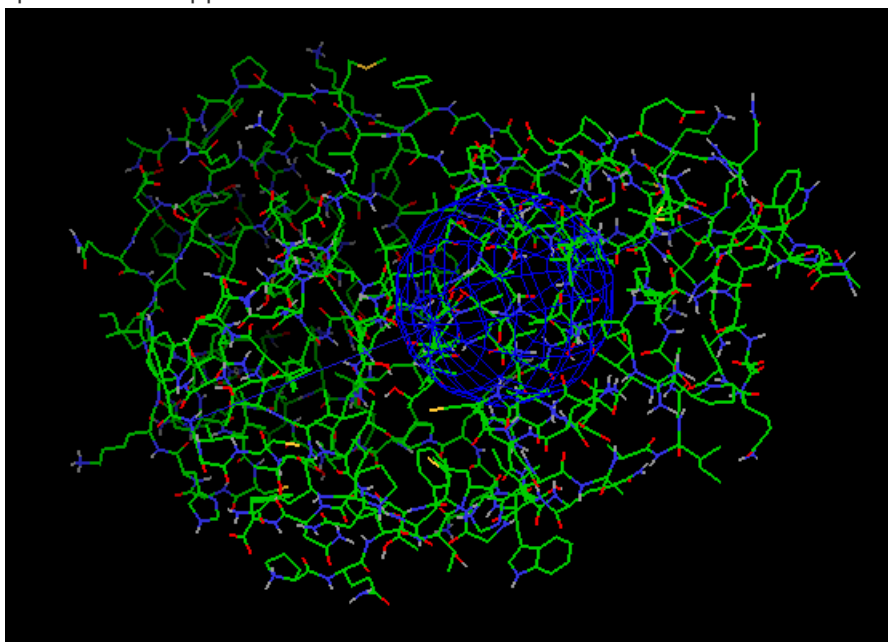
i Note: You can also type in ranges using a dash (4-10)

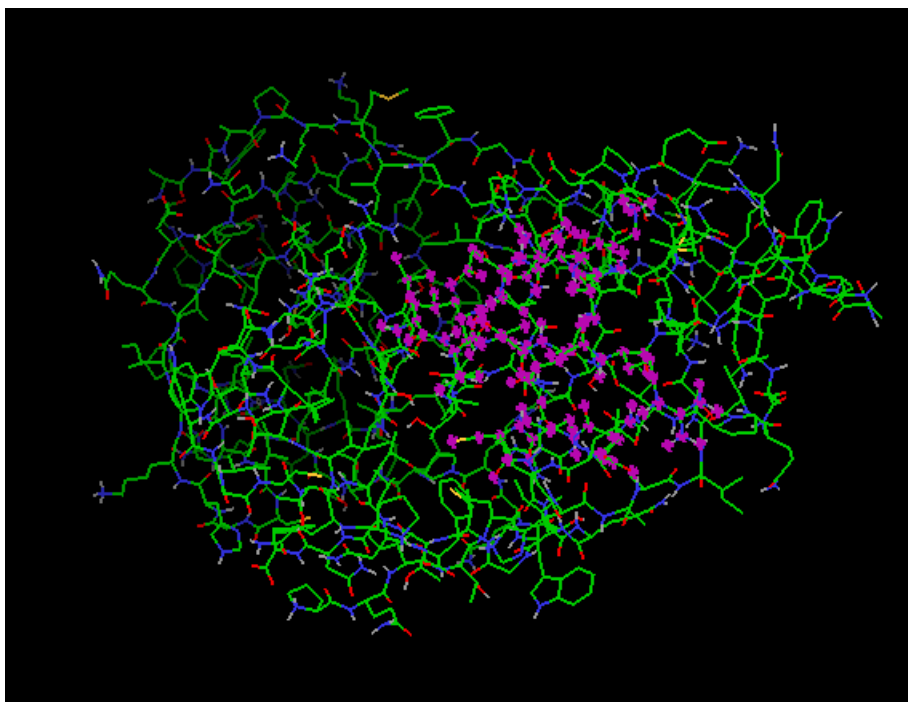
i Note: You can also select more than one at once using spaces and/or commas (4,5 or 4, 5 or 4 5)

- Atom Name - type in an atom name and hit enter to select it

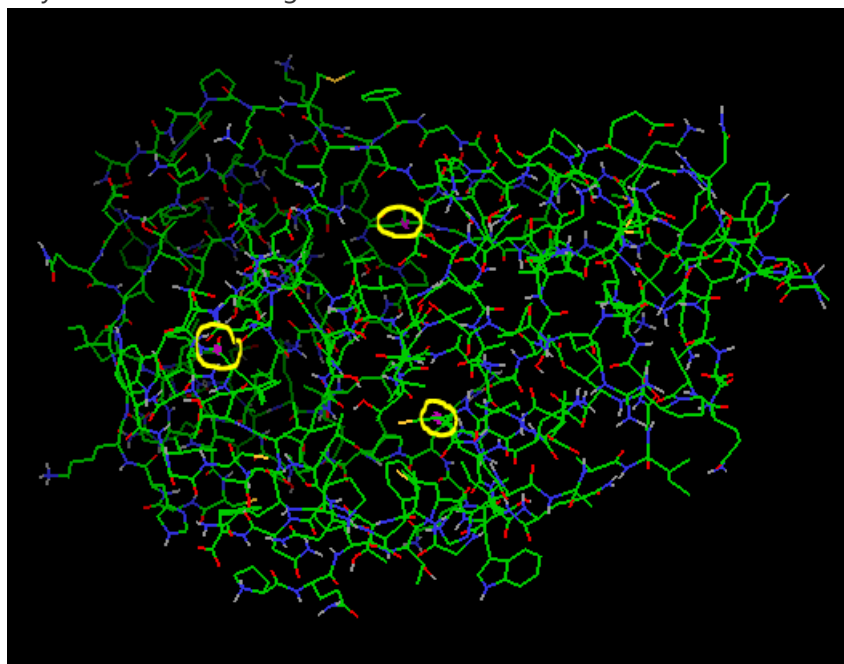
- The button opens a tool that allows you to select a 3D region of the molecule

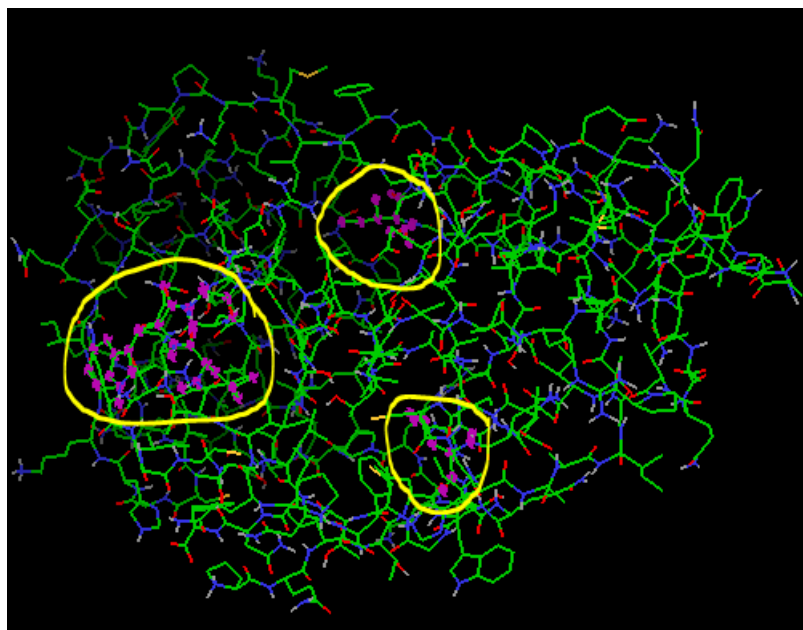
- Use **Ctrl** + middle-mouse-button to place the 3D selector sphere
- When you click the button, a blue sphere will appear in the viewer
- When you click the button again, anything within the blue sphere will be selected and the blue sphere will disappear





- You can use **Ctrl** + left-mouse-button to adjust the size of the sphere
- You can use **Ctrl** + right-mouse-button to move the sphere along the center line
- The **Distance** textbox allows you to select all atoms within a chosen distance (in Angstroms) of any atom currently selected
 - **Example:** If you type "3" into the textboc while three atoms are selected, Vdock will select
 - Any atoms within 3 Angstroms of the first atom
 - Any atoms within 3 Angstroms of the second atom
 - Any atoms within 3 Angstroms of the third atoms





- The button allows you to save different selections that you have made
 - To save a selection:
 - Click on the button
 - Click on one of the S# buttons ()
 - Then, you can return to that selection by clicking on the S# button that the selection was saved under

Note: Buttons that you have saved something under will change color

- To overwrite a saved selection, simply hit the button again and click on the S# button that you wish to overwrite

Note: If you want to view the molecule without any selections, you can hit the button. It will not change the saved selection.

- The drop-down menu allows you to select different named selections, including:
 - Last Sel. (last selection) - the selection previous to your current selection
 - This will still work even if you currently have nothing selected
 - Prot. Backbone (protein backbone) - will select all atoms in the protein backbone
 - Hydrogens - will select all hydrogens in the molecule
- The buttons allow you to compare/contrast different selections

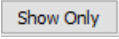
- You can compare:
 - Two saved selections
 - An unsaved selection and a saved selection
- You cannot compare:
 - Two unsaved selections
- To compare two saved selections:
 - Click the first S# button () that you want to compare
 - Click one of the comparison buttons ()
 - Click the other S# button of the saved selection that you want to compare
- To compare an unsaved and a saved selection:
 - Select the set of atoms/residues you'd like to compare (unsaved selection)

i Note: When comparing unsaved selections with a saved selection, you must select the unsaved selection **first**

- Click one of the comparison buttons ()
- Click the S# button of the saved selection that you want to compare
- The button will select any atoms that are in both selections
- The button will select any atoms that are in either one or both selections
- The button refers to exclusive or, meaning it will select any atoms that exist in one selection, but **not** in both selections
- The button selects all atoms in the viewer
- The button inverts the selected and deselected atoms
 - Meaning it selects all atoms that are currently deselected **and** deselects all atoms that are currently selected
- The button clears all current selections

Graphics Panel:

- The button will show only selected atoms and hide all deselected atoms
- The button will hide all selected atoms
- The button will show all selected atoms

- This is similar to the  button, but it will not hide any atoms
- The **COLOR** sections allows you to color the molecule based on different criteria
 - The **Solid** drop-down menu allows you to color every selected atom a chosen color, such as
 - Red
 - Green
 - Blue
 - Orange
 - Light Blue
 - Light Green
 - Yellow
 - Cyan
 - Violet
 - The **Property** drop-down menu allows you to color selected atoms based on
 - Element
 - Res. Type (residue type)
 - Res. Charge (residue charge)