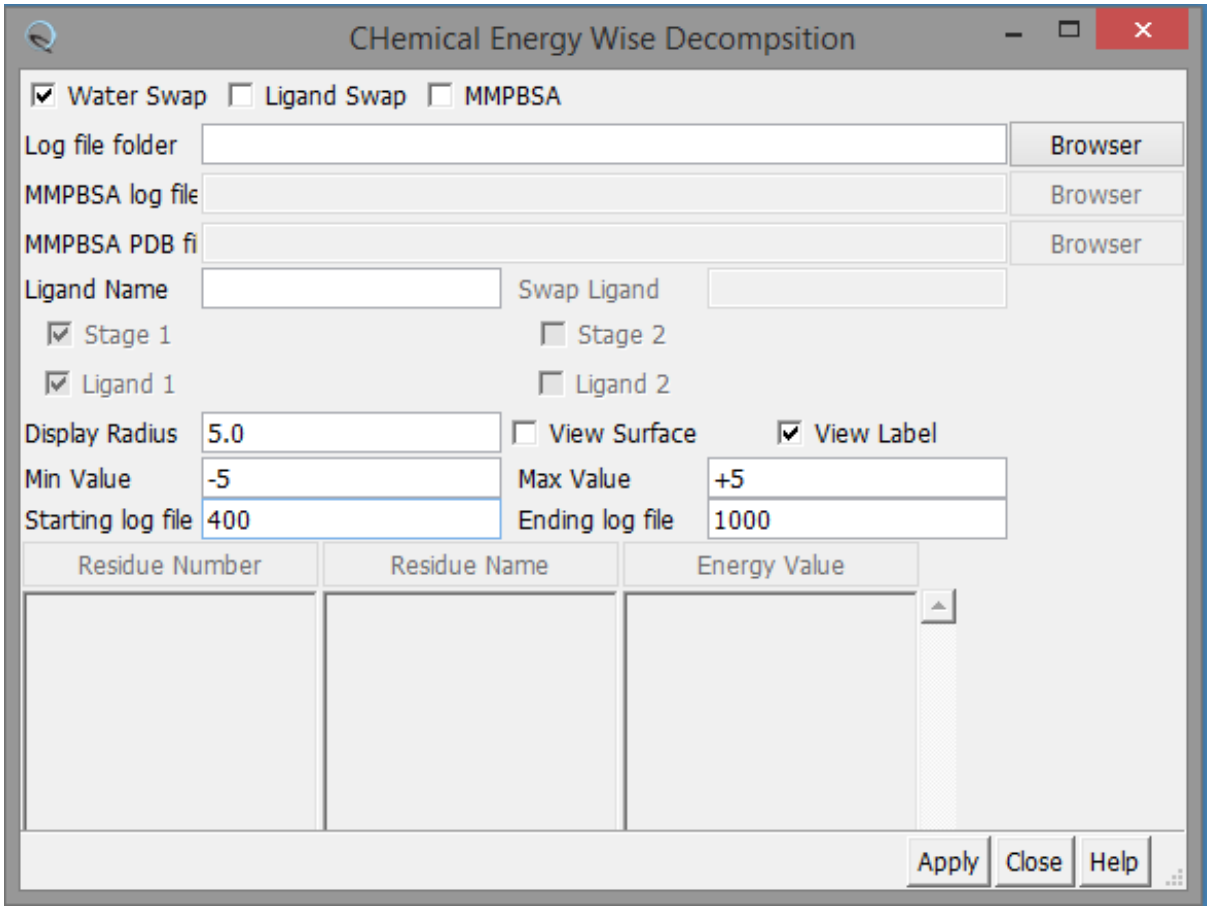
CHemical Energy Wise Decomposition (CHEWD)

The CHEWD [1] plugin is available for download from:

https://github.com/saadraza128/CHEWD

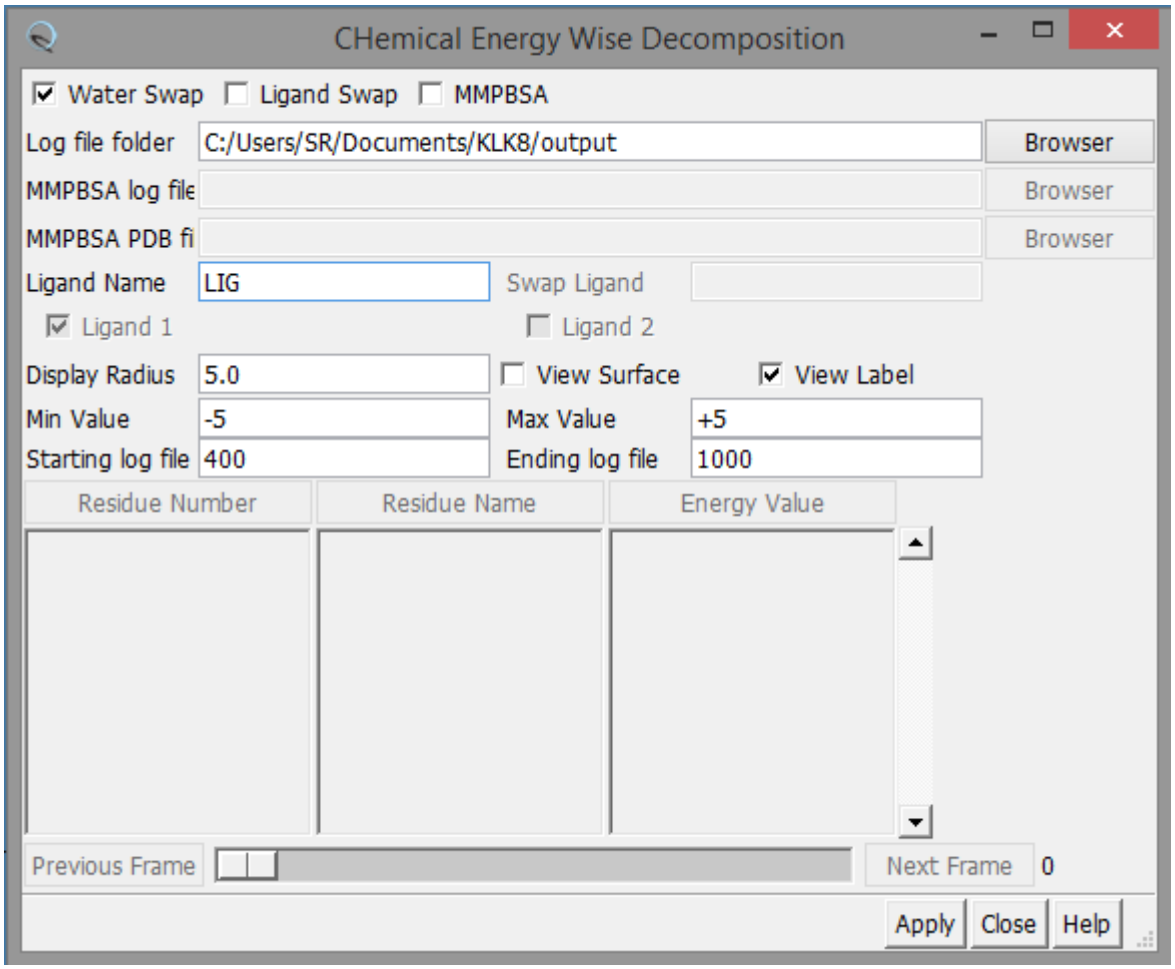
Chimera installation:

- Download the folder Chimera-CHEWD.
- Open Chimera, go to the Favorites tab > Preferences. Select Tools, Add and then browse to find Chimera-CHEWD. Select Chimera-CHEWD and then click Save.
- The plugin will be located in the menu under Tools | Utilities CHEWD. Clicking on this option will open the following GUI dialog:

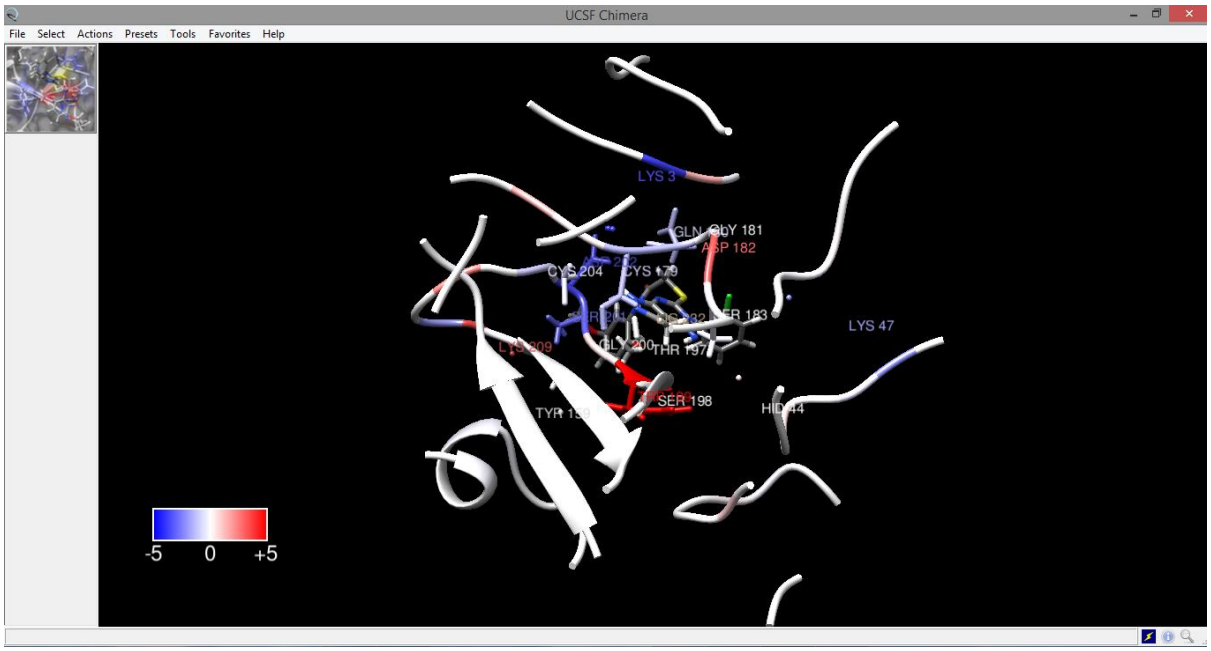


Visualisation of WaterSwap or LigandSwap results

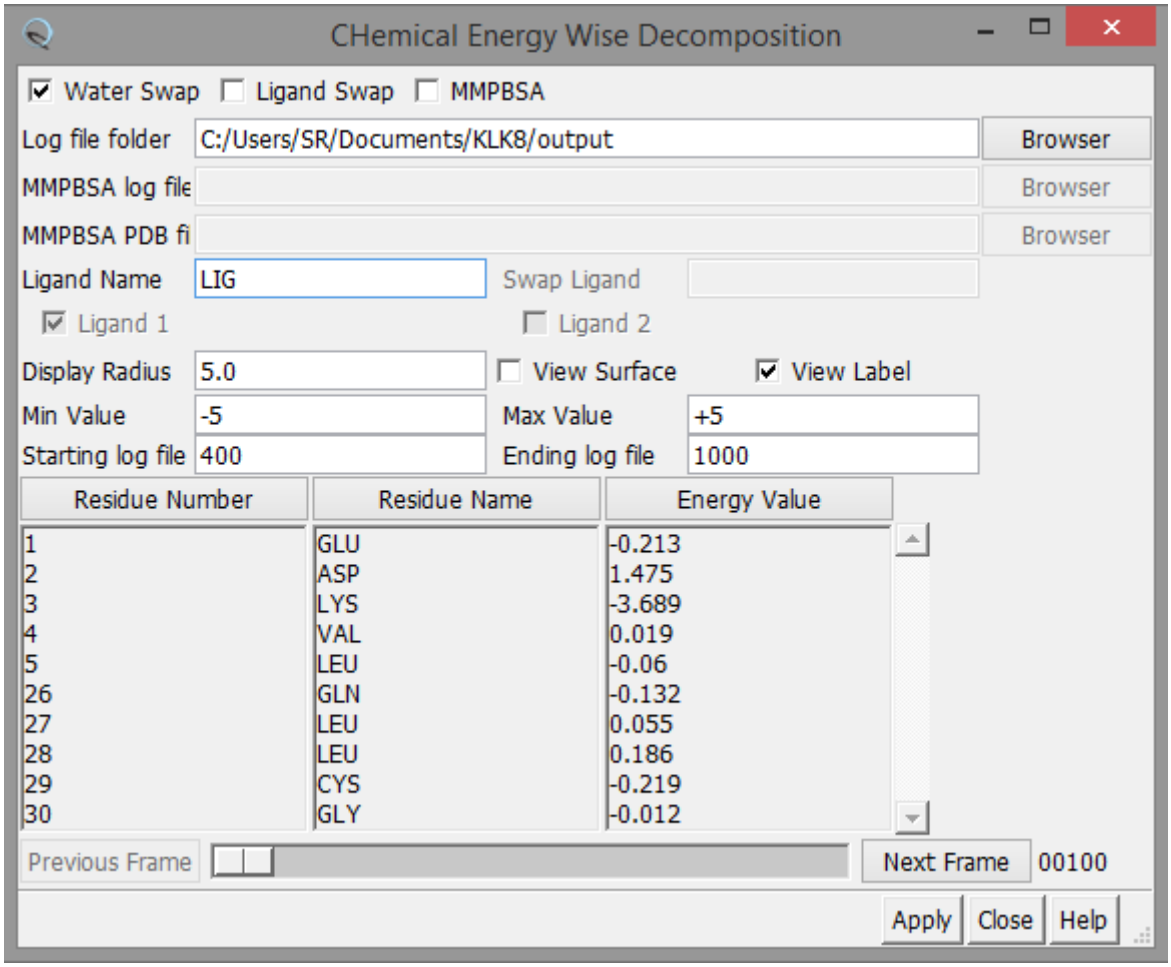
- For Waterswap [2] unzip the output folder in the example directory.
- Click Browser to open a file browser. Navigate to and select the example output directory containing all the example results.
- Next, make sure that the Water Swap box is checked at the top of the dialog. This puts the plugin into Waterswap mode. Next, set the Ligand Name according to your topology file (In this example we set it to LIG).
- Doing this, you should see that the dialog looks something like this:



- Now click Apply. It may take some time to load all the output depending on computer resources.
- Once loaded, you should see that the main chimera window looks something like this:

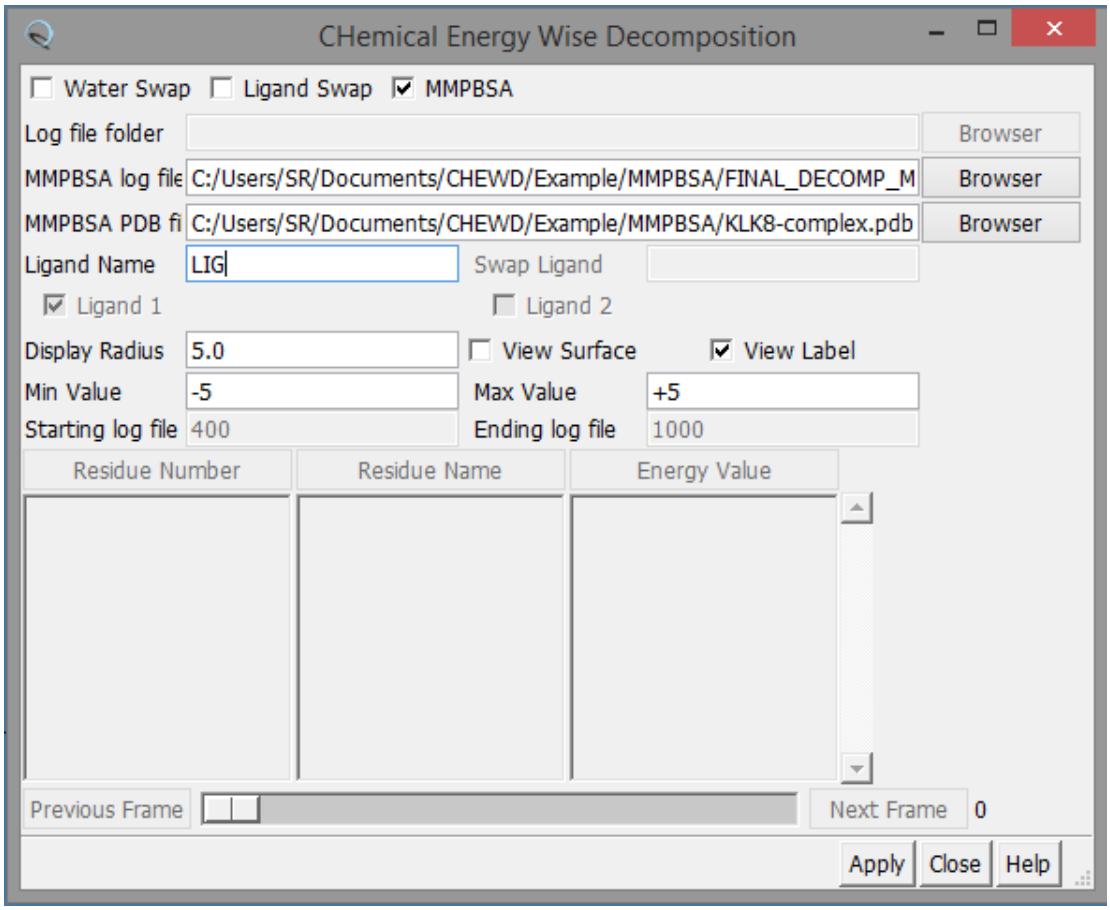


- This shows a cut-out of the full protein-ligand-water system, showing only the protein and ligand atoms that were mobile during the waterswap calculation (everything within 15 angstroms of the swapped ligand).
- The residues are colour-coded according to their preference for either ligand or water. Red shows a preference for water, whereas Blue indicates a preference for the ligand. with stronger colours indicating a stronger preference. A colour scale is used so that stronger colours imply a stronger preference.
- The minimum and maximum values of the colour scale can be adjusted to better fit the range of interactions being visualised.
- The exact values of these free energy component preferences are shown in the CHEWD dialog, which looks something like this:


CHemical Energy Wise Decomposition
Water Swap
Ligand Swap
MMPBSA
Log file folder
C:/Users/SR/Documents/KLK8/output
Browser
MMPBSA log file
Browser
MMPBSA PDB fi
Browser
Ligand Name
LIG
Swap Ligand
Ligand 1
Ligand 2
Display Radius
5.0
View Surface
View Label
Min Value
-5
Max Value
+5
Starting log file
400
Ending log file
1000
Residue Number
Residue Name
Energy Value
1 GLU -0.213
2 ASP 1.475
3 LYS -3.689
4 VAL 0.019
5 LEU -0.06
26 GLN -0.132
27 LEU 0.055
28 LEU 0.186
29 CYS -0.219
30 GLY -0.012
Previous Frame
Next Frame
00100
Apply
Close
Help

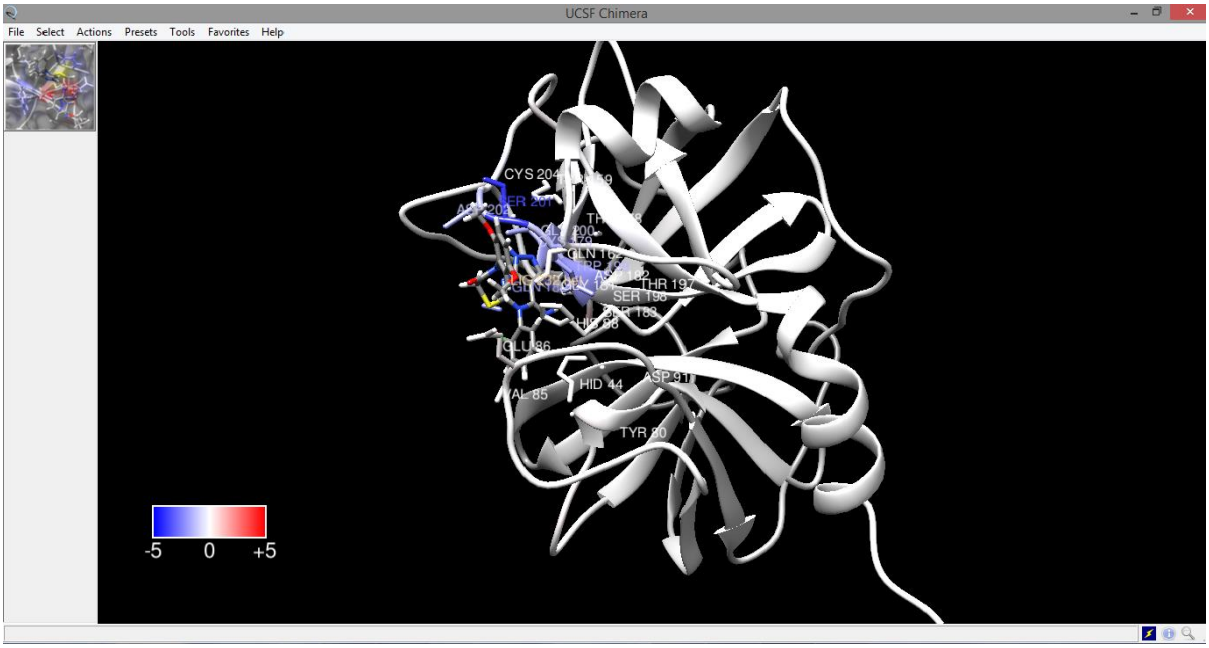
Visualisation of MM/PBSA results

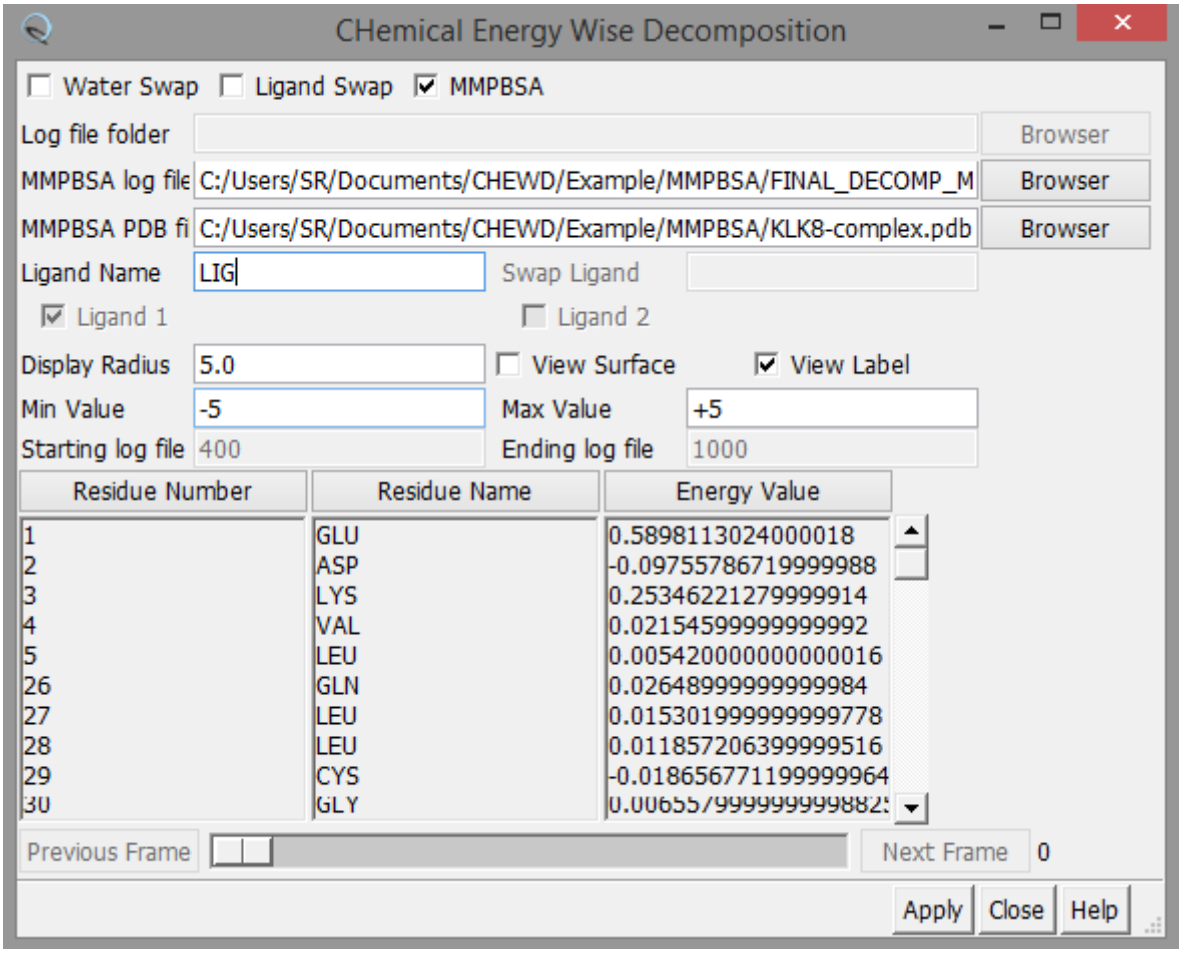
- Check the MMPBSA box at the top of the dialog box.
- Click on Browser to locate the "FINAL_DECOMP_MMPBSA.dat" file in the MMPBSA log file tab.
- Click on the final Browser to locate and select the corresponding "KLK8-complex.pdb" in the MMPBSA pdb file tab.



- The decomposition file has been written using MMPBSA.py of amber simulation package. This log output was done by setting the verbosity to 1 in the input file for MMPBSA.py.

- The results are displayed in the same way as for WaterSwap/LigangSwap





Pymol installation

- For plugin to work you would need the pymol 2.10
- Open the plugin manager from wizard tab in pymol and select "Install New Plugin" tab and browser to the CHEWD.py file.

References

1. Pettersen EF, Goddard TD, Huang CC, et al (2004) UCSF Chimera—a visualization system for exploratory research and analysis. J Comput Chem 25:1605–1612.

2. Woods CJ, Malaisree M, Hannongbua S, Mulholland AJ (2011) A water-swap reaction coordinate for the calculation of absolute protein--ligand binding free energies. J Chem Phys 134:54114.