Molecular docking in Autodock vina

Software Requirements

1. AutoDock Tools (ADT) - For protein and ligand preparation
2. AutoDock Vina - The main docking software (downloadable from https://vina.scripps.edu/downloads/)
3. PyMOL - For post-docking analysis and visualization
4. OpenBabel (optional) - Alternative tool for ligand preparation

Working with AutoDock-4 includes 4 steps:

1. Protein preparation
2. Ligand preparation and
3. Defining the docking parameters
4. Running the docking simulation (i.e. Docking of ligand into protein).
5. Post docking analysis using PyMOL or PLIP

(If your receptor is having different chains e.g..A, B and C chains then see whether your co-crystallized ligand is in which chain for e.g. if it is in A chain then keep A chain and delete B and C chains. Select them from the Dash board and delete them). Then save the A chain with ligand as '.pdb' format. Now we have to separate A chain and ligand and both are saved as different pdb codes.)

1. Protein preparation

- Opening file: : > File →Read molecule →Protein (pdb) Open
- Eliminate water: (Second step is to remove all the water molecules in the protein). >Select → Select from string → [write HOH* in "Residue" line and * in the "Atom" line] → Add → Dismiss → Edit
- → Delete → Delete AtomSet.
- Find missing atom and repairing them: File → Load module → [Pmv; repairCommands] → Edit
- → Misc. → Check for missing atoms → Edit → Misc. → Repair missing atoms. (IF no atom is missing then go for next step).
- Add hydrogens: Edit → Hydrogens →Add polar only → Ok
- Give Charges: > Edit → charges → Gasteiger charge → Ok
- Assigning AD4: > Edit → atom → assign AD4 type
- Saving file: > File → Save → PDBQT (or pdb).

2. Ligand preparation

- Prepare ligand as per instruction of Autodock tools (See the ligand preparation steps in manual for Autodock tools). The ligand also can be prepared using OpenBabel.

Ligand preparation through ADT:

- Make sure the ligand has all hydrogens added before working with ADT.
- Opening file: Ligand → Input → Open → All Files → [choose file] → Open.
- (ADT now automatically computes Gasteiger charges, merges nonpolar hydrogens,

and assigns Autodock Type to each atom).

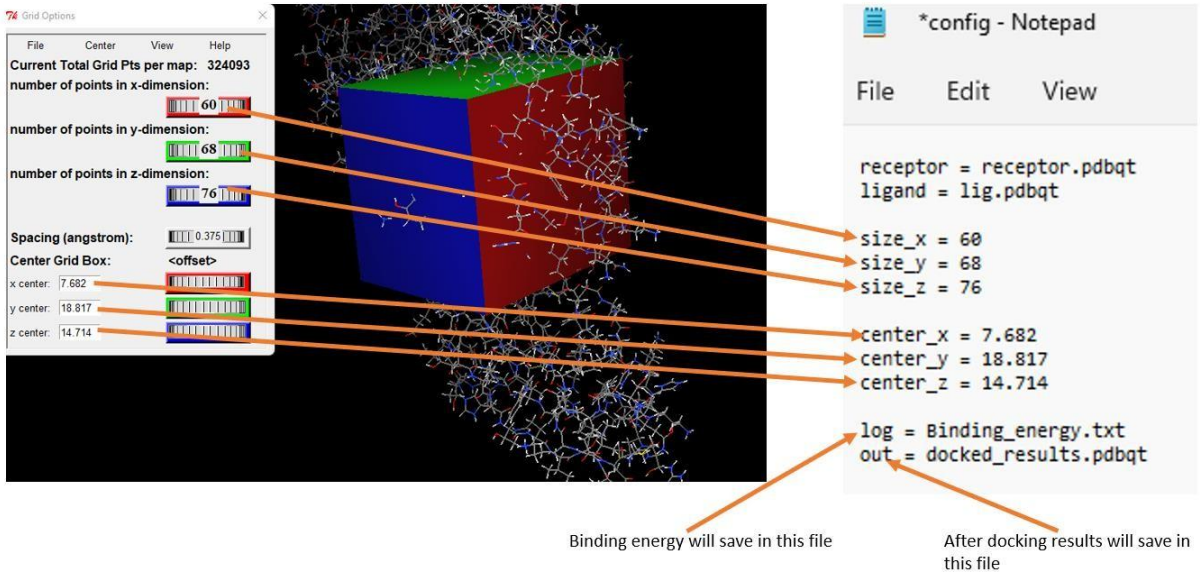
- Add hydrogens: Edit → Hydrogens →Add polar only → Ok
- Give Charges: > Edit → charges → Gasteiger charge → Ok
- Define torsions: >Ligand →Torsion tree → Choose torsion → Done
- >Ligand → Torsion tree →Set no. of torsion → Done
- Save File: >Ligand → Out put → Save as PDBQT → save → Ok
- >Edit → Delete →Delete all molecule → Continue.

Ligand preparation through OpenBabel:

- Use this command: obabel -ipdb .\ligand.pdb -opdbqt -h -O .\ligand.pdbqt

3. Config file generation

- Create the config.txt file with information of receptor, ligand, grid box size, grid coordinates, binding energy file name and docked result file name.
- The config file (config.txt) should look like the following figure.
- The grid size and grid coordinates can be collected from Grid generation from Autodock tool module (See the grid generation steps in manual for Autodock tools).
- The grid size and grid coordinates can be obtained from the coordinates of bound co-crystal ligand or any known amino acid from active site.



4. Docking in Autodock vina

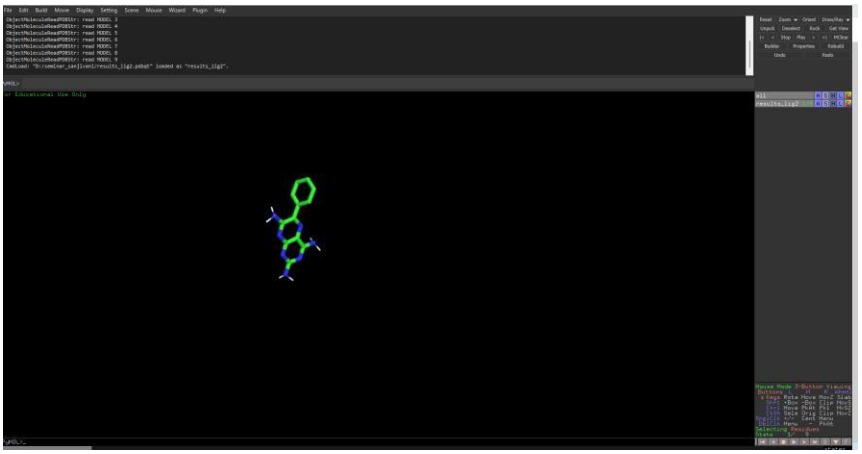
- Download and install the Autodock vina from https://vina.scripps.edu/downloads/
- During installation select default destination of installation
- After successful installation, copy the 'vina.exe' file form 'C:\Program Files (x86)\The Scripps Research Institute\Vina' to your folder where you have receptor, ligand and config.txt files.
- Open the command prompt and using 'cd' command go the folder where all the above files are there.
- Type the following command in command line:

  vina --config config.txt
- If there is no error, within a few moments the docking will complete.

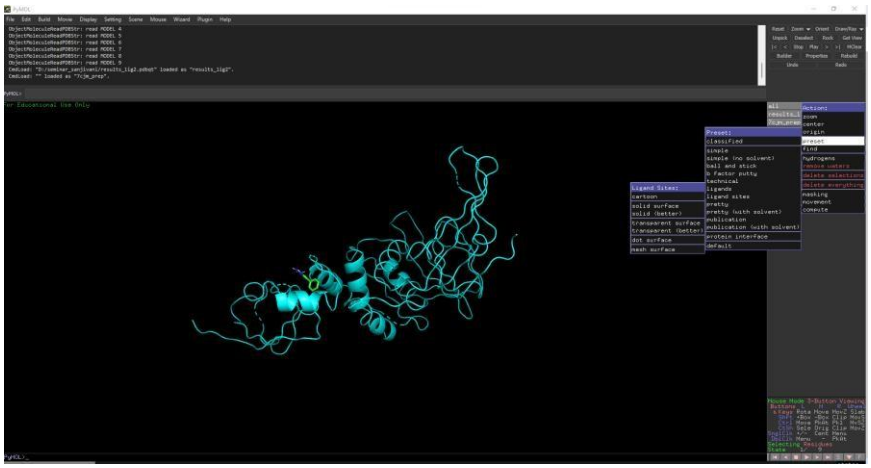
5. Post docking analysis

Using PyMOL

- Open Pymol
- Using the File menu of the Pymol, open the docked_results.pdbqt file (This is the output file after molecular docking in Autodock vina).
- You can see the number of poses at the right bottom of the Pymol window as 1/9. Its looks like as below figure.



- Open the receptor file (.pdb) in Pymol.
- To check the binding interactions, go to 'A' option under All in Pymol →Preset → Ligand site → Cartoon (You can see in the following figure)



- The binding interaction can be seen in dotted lines.
- To save the complex, go to File → Export molecule → Save

Using PLIP

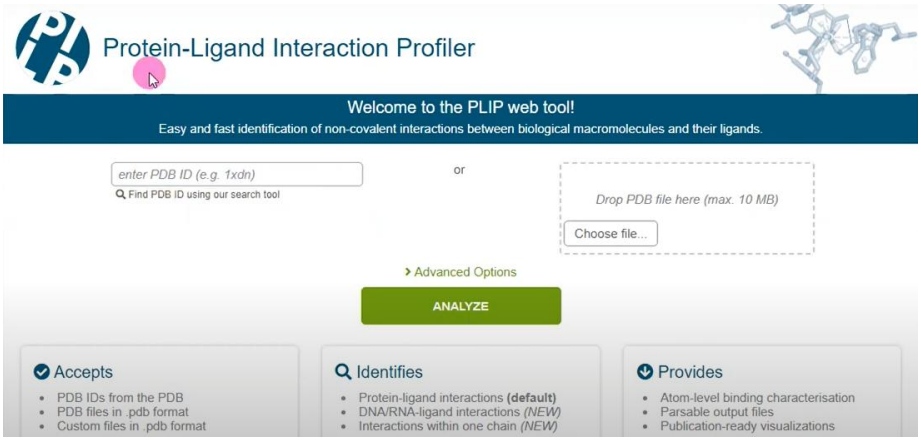
- Setting up PLIP:
  1. PLIP can be used as a standalone tool or integrated into other software like PyMOL.
  2. You'll need the PDB (Protein Data Bank) file of the protein-ligand complex after docking and the corresponding ligand file.
  3. PLIP can be run from the command line or through a graphical user interface, depending on the implementation

- Running PLIP:
  1. Command line:

     Execute the PLIP command, specifying the protein and ligand files as input.
  2. Graphical user interface

     (https://plip-tool.biotec.tu-dresden.de/plip-web/plip/index):

     Load the protein and ligand files into the PLIP interface and initiate the analysis.

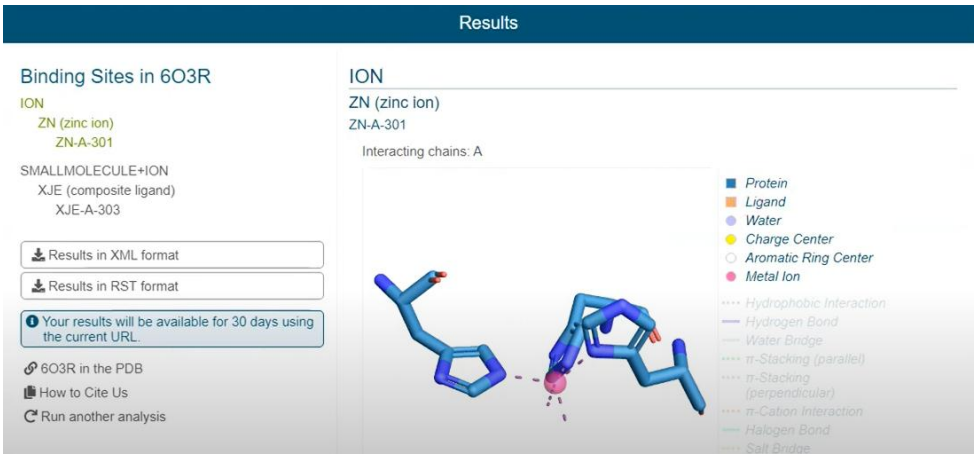


- Analyzing PLIP Output:
  1. Visualizations:

     PLIP generates visualizations, often integrated within PyMOL, that highlight the identified interactions, like hydrogen bonds, hydrophobic contacts, and salt bridges.
  2. Textual output:

     PLIP provides a detailed textual report summarizing the interactions, including distances, angles, and types of interactions.
  3. Data for further analysis:

     The textual output can be further processed using scripting languages (like Python) to extract specific information or perform statistical analysis.



****