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).

(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).

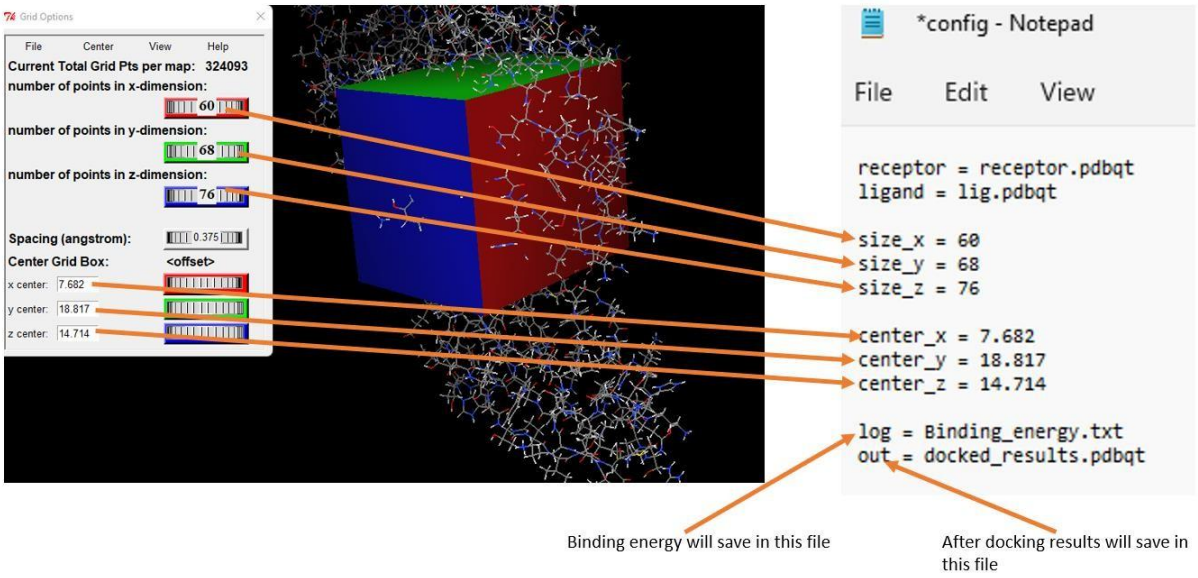
- Add hydrogens: Edit → Hydrogens →Add polar only → Ok
- Give Charges: > Edit → charges → Gasteiger charge → Ok
- Define torsions: >Ligand →Torsion tree → Choose torsion → Done
- >Ligand → Torsion tree →Set no. of torsion → Done
- Save File: >Ligand → Out put → Save as PDBQT → save → Ok
- >Edit → Delete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



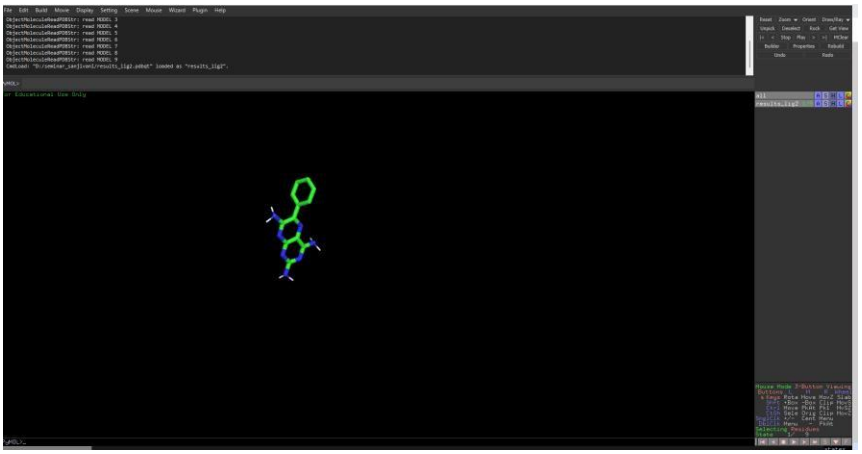
4. Docking in Autodock vina

- 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:

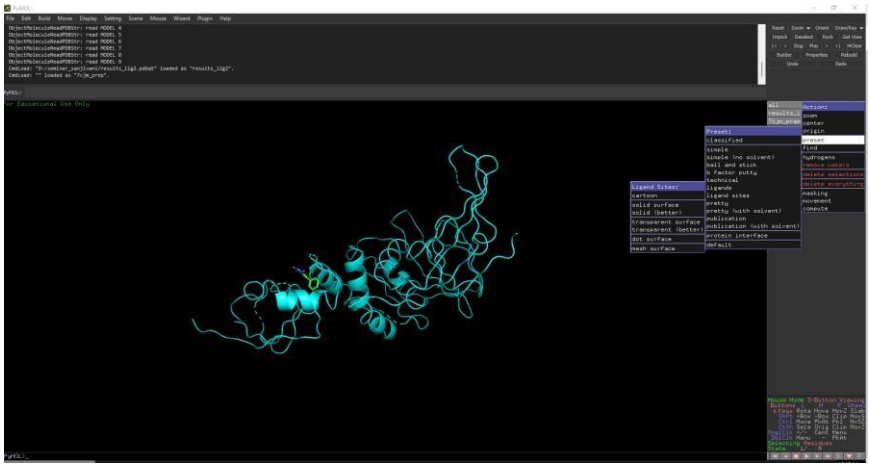
  vina --config config.txt
- If there is no error, within a few moments the docking will complete.

5. Post docking analysis

- 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

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