International Hands-on Workshop
on
Artificial Intelligence in Drug Discovery
(21st June 2025, 10:00 am to 5:00 pm IST)

User manual
for
Molecular docking using Autodock vina

1. Software Requirements

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

2. Working with AutoDock-4 includes 4 steps:

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

(*If your receptor has different chains, such as A, B, and C, then check which chain contains your co-crystallized ligand. For example, if it is in the A chain, keep only the A chain and remove the B and C chains. You can select them from the Dashboard and delete them. After that, save the A chain with the ligand in '.pdb' format. Now, we need to separate the A chain and the ligand, saving both as different pdb files codes.*)

3. Protein preparation

- Opening file: : > File →Read molecule →Protein (pdb) Open
- Eliminate water: (The 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).

4. Ligand preparation

Prepare the ligand according to the instructions for AutoDock Tools (see the ligand preparation steps in the AutoDock Tools manual). The ligand can also be prepared using OpenBabel.

4.1 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 assign 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 → Output → Save as PDBQT → save → Ok
- >Edit → Delete →Delete all molecule → Continue.

4.2 Ligand preparation through OpenBabel:

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

5. 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 the Autodock tool module (See the grid generation steps in the manual for Autodock tools).
- The grid size and grid coordinates can be obtained from the coordinates of the bound co-crystal ligand or any known amino acid from the active site.
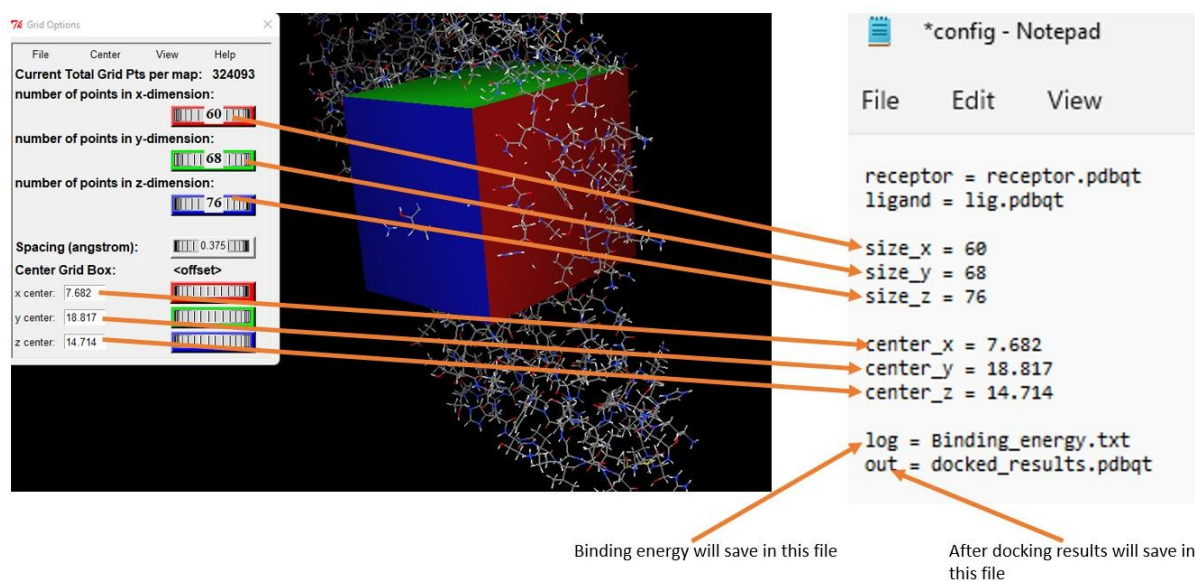
Figure 1. Details of the config.txt file from the grid box

6. Docking in Autodock vina

- Download and install the Autodock vina from https://vina.scripps.edu/downloads/
- During installation, select default destination of the installation
- After successful installation, copy the 'vina.exe' file from 'C:\Program Files (x86)\The Scripps Research Institute\Vina' to the folder where you have your 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.

7. Post docking analysis

7.1 Using PyMol

- Open PyMOL.

- Using the File menu in 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 bottom right of the PyMOL window as 1/9. It looks like the figure below.

Figure 2. Poses in PyMol

- 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)
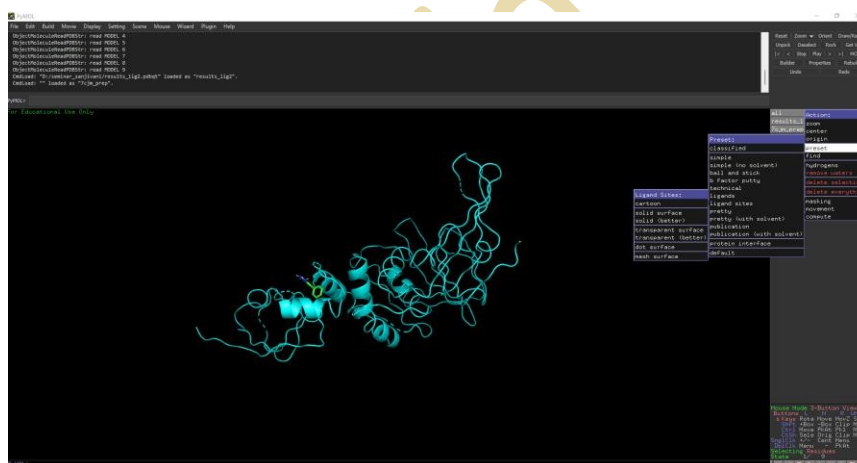

Figure 3. Binding interactions in PyMol

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

7.2 Binding interactions using PLIP

7.2.1 Setting up PLIP:

a) PLIP can be used as a standalone tool or integrated into other software like PyMOL.

b) You'll need the PDB (Protein Data Bank) file of the protein-ligand complex after docking and the corresponding ligand file.

c) PLIP can be run from the command line or through a graphical user interface, depending on

---

the implementation

7.2.2 Running PLIP:
a) Command line:
b) Execute the PLIP command, specifying the protein and ligand files as input.
c) Graphical user interface
d) (https://plip-tool.biotec.tu-dresden.de/plip-web/plip/index):
e) Load the protein and ligand files into the PLIP interface and initiate the analysis.
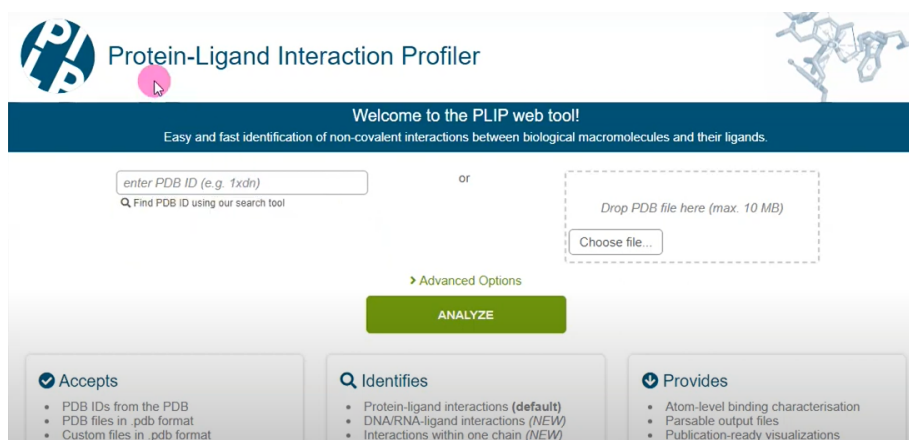

Figure 4. PLIP webpage

7.3 Analyzing PLIP Output:
a) Visualizations:

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

b) Textual output:

PLIP provides a detailed textual report summarizing the interactions, including distances, angles, and types of interactions.

c) Data for further analysis:

The textual output can be further processed using scripting languages (like Python) to extract specific information or perform statistical analysis.
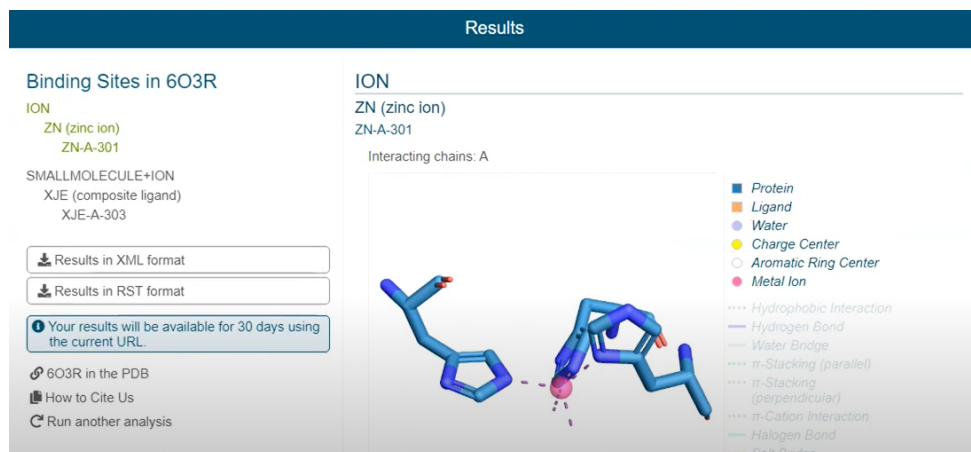
Figure 5. Binding interactions in PLIP

****