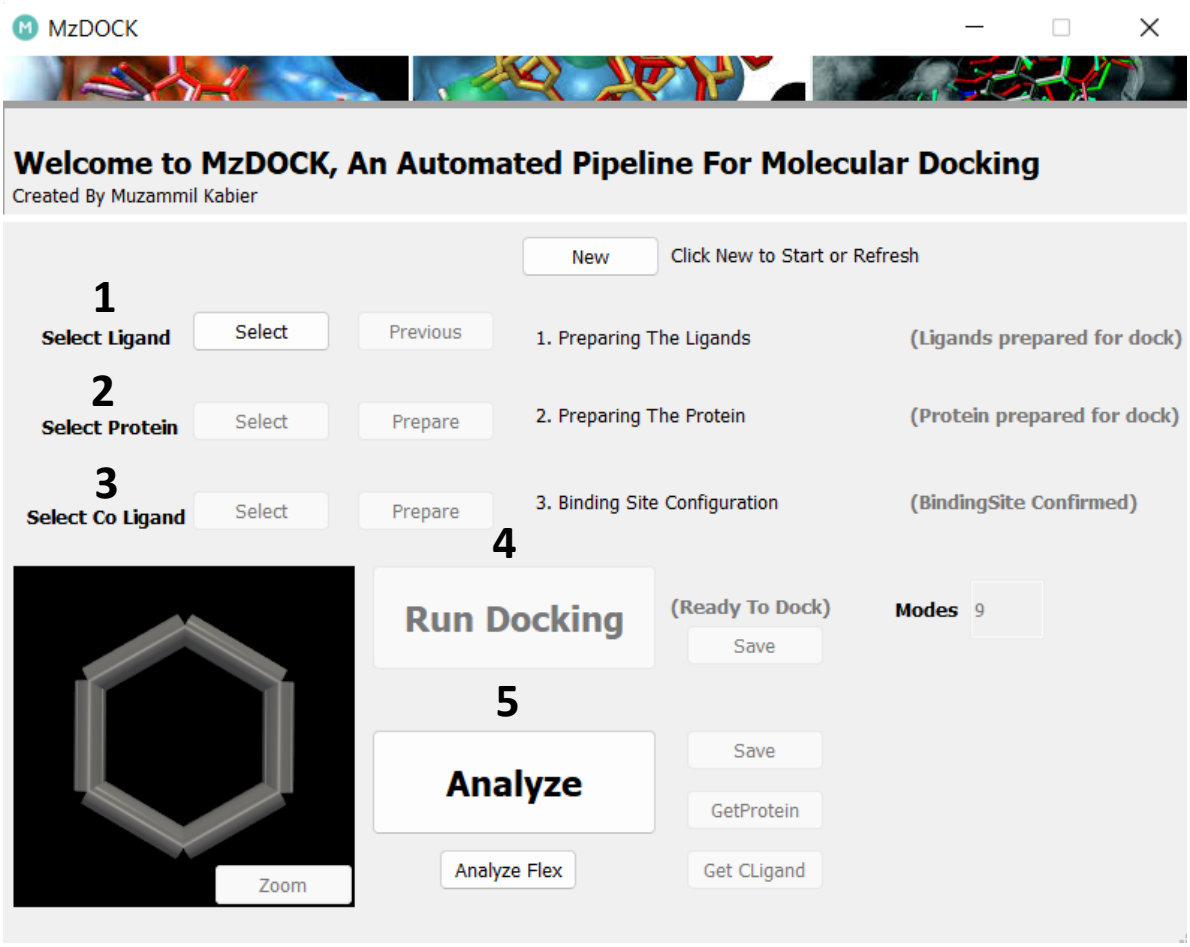
MzDOCK

MANUAL

MzDOCK GUI is simple and straightforward.

1. Select Ligand
2. Select Protein
3. Define Binding Site
4. Run Docking
5. Analyze Interactions



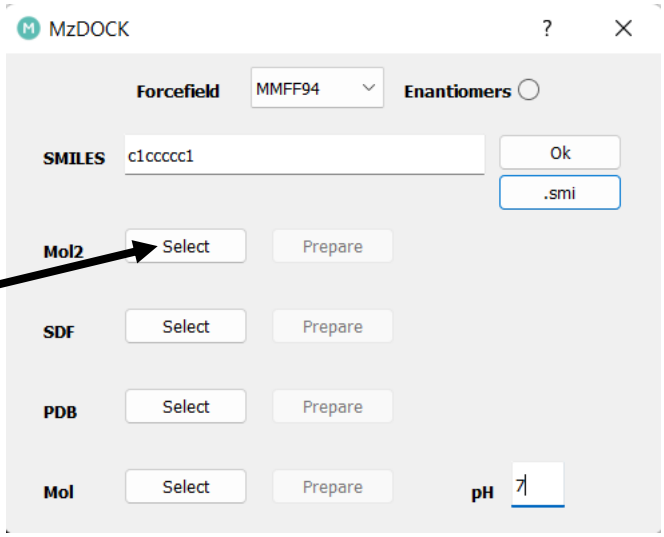
1. Ligand Preparation

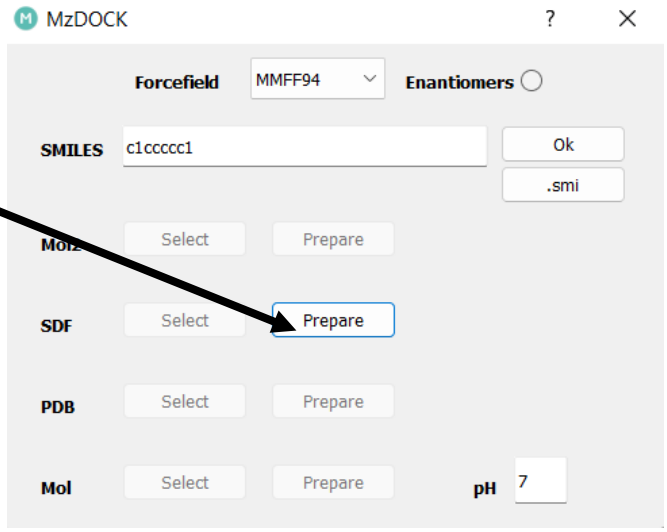
MzDOCK provides options to input various file formats such as SMILES, SDF, PDB, MOL2 and MOL.

Click on 'select' for respective file format the user requires for ligand input and choose your multiple files. Next click on 'prepare' to prepare your ligand

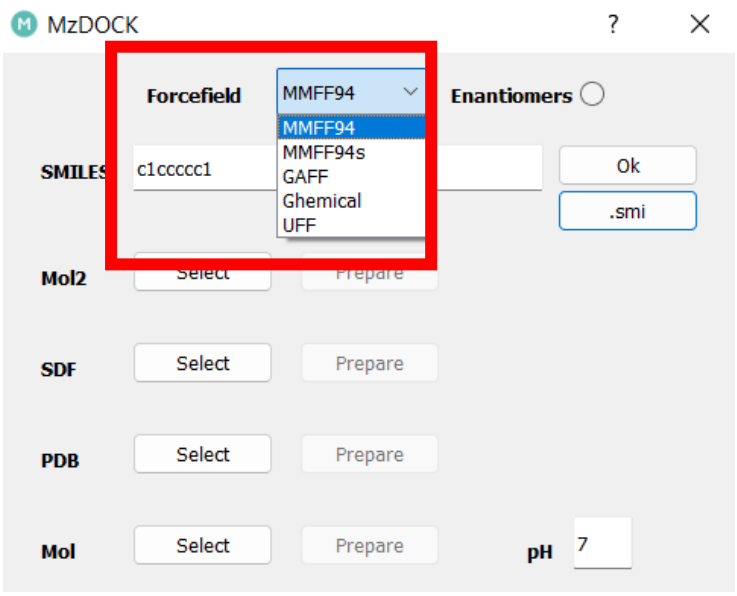
For SMILES, there is input line to give a single SMILES notation , for multiple SMILES '.smi' option can be chosen which should have a format of :

(SMILES) (name)

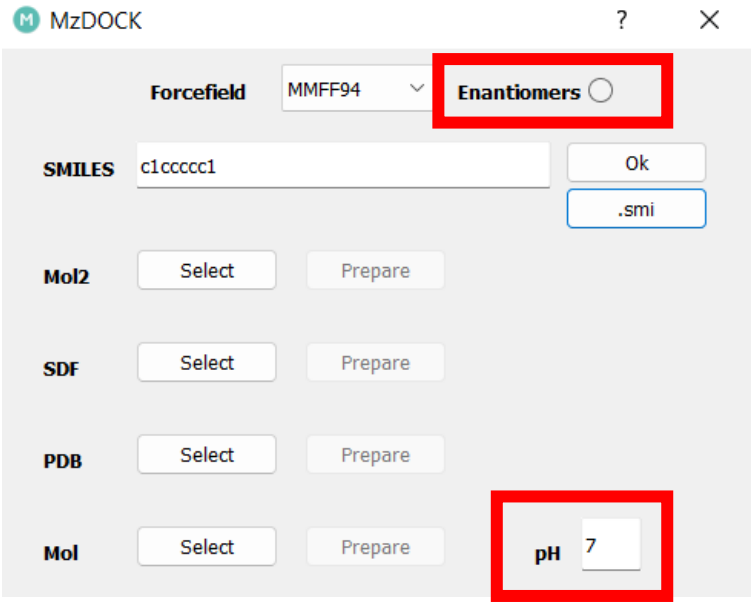




Another Interesting Thing about MzDOCK is that it energy optimizes the ligands chosen, There is a dropdown box present where user can choose the preferred forcefield for energy optimization (MMFF94, MMFF94s, GAFF, UFF and Ghemical)

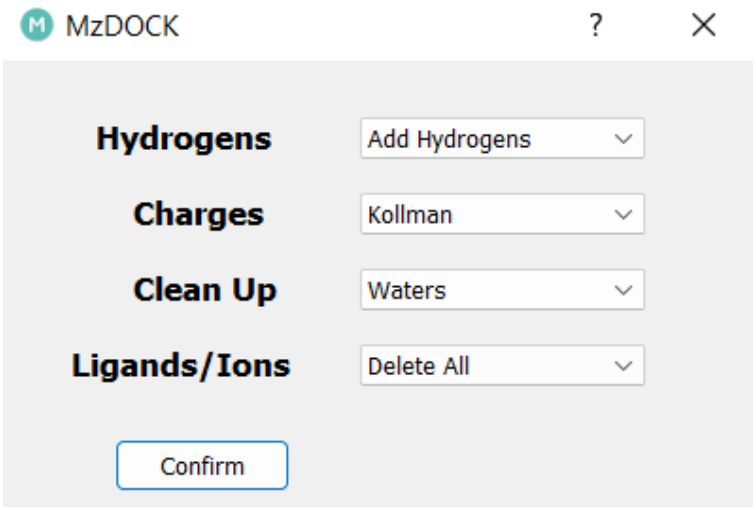


Enatiomer radiobutton generates enantiomer if possible for the SMILES provided.The pH line input provide the protonation state required

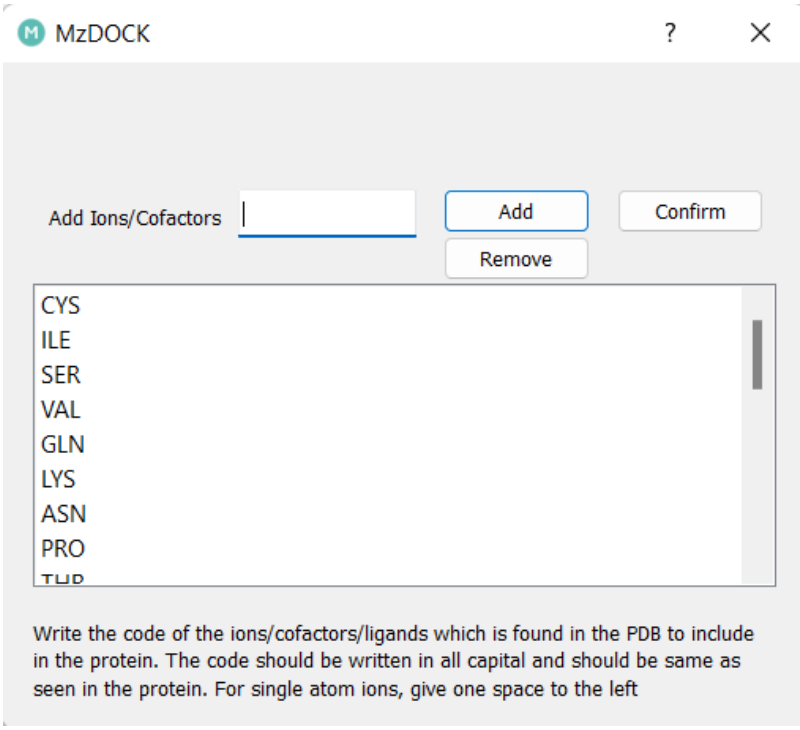


2. Protein Preparation

After Selecting the protein, and when the prepare button is clicked , the protein preparation dialog box appears where there is option to **add hydrogen**, **choose charges**(Gasteiger, Kollman), remove or keep water and option to keep, remove or selective retention of ions/ligands/cofactors.



For specific retention of ions/ligands/cofactors , choose manual option in 'Ligands/Ions' dropdown box and press 'confirm'



Here , three letter code of the specific ion/ligand/cofactor could be given and press 'add' to retain those molecule. Press 'confirm' to accept the changes. For retaining waters, in cleanup choose 'keep water' and in manual option add 'HOH'

There are additional options where user can choose specific chain from a protein.

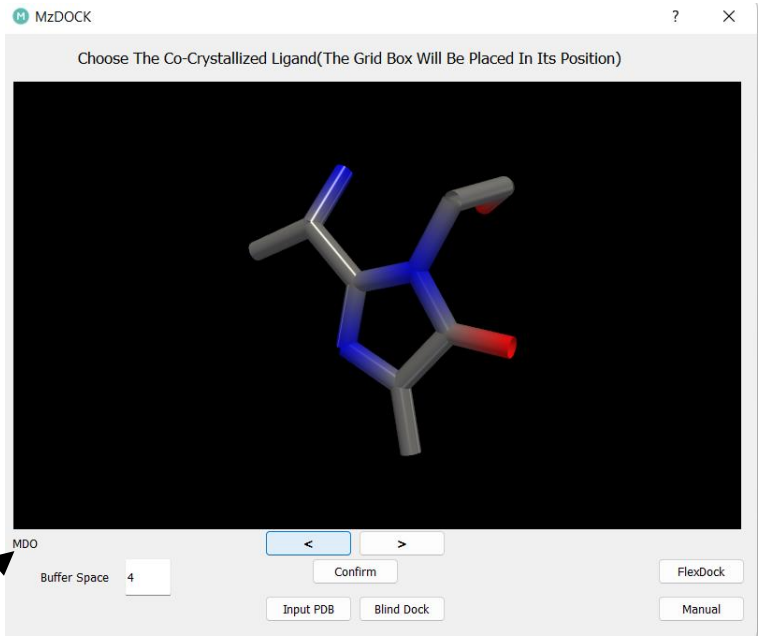
3. <u>Binding Site Defining</u>

Binding site can be defined with the help of co-crystallized ligand . swap through all the heteroatoms inside the protein which includes ions/cofactors/ligands . choose the ligand in the binding site to assign grid box there automatically

The residue name will be provided here.

the bufferspace can be given to increase search space upto 20 Angstroms.

Moreover option to 'input pdb' where some amino acid pdb could be given to assign gridbox, 'blind dock' and manual grid box assignment is possible.

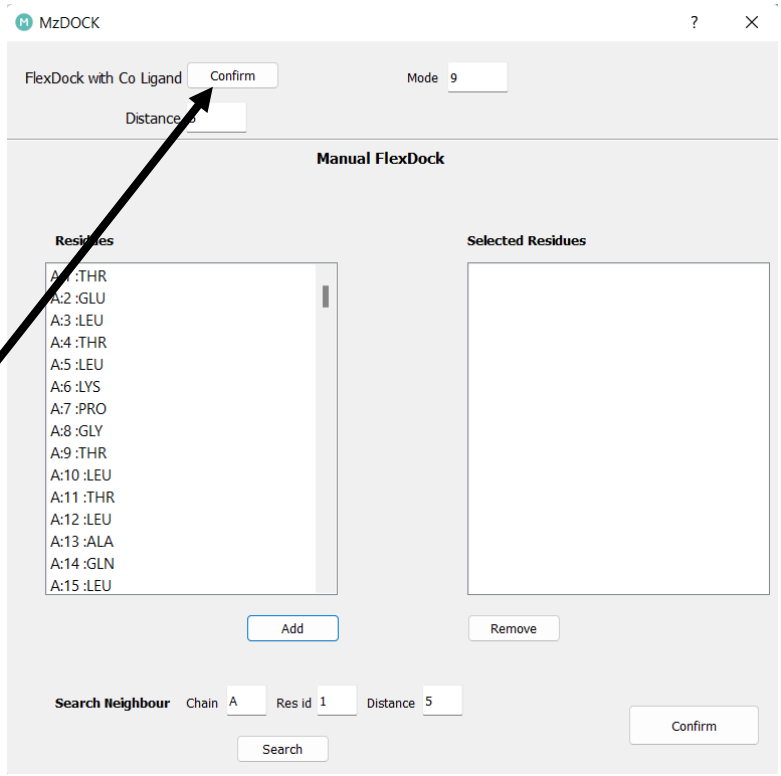


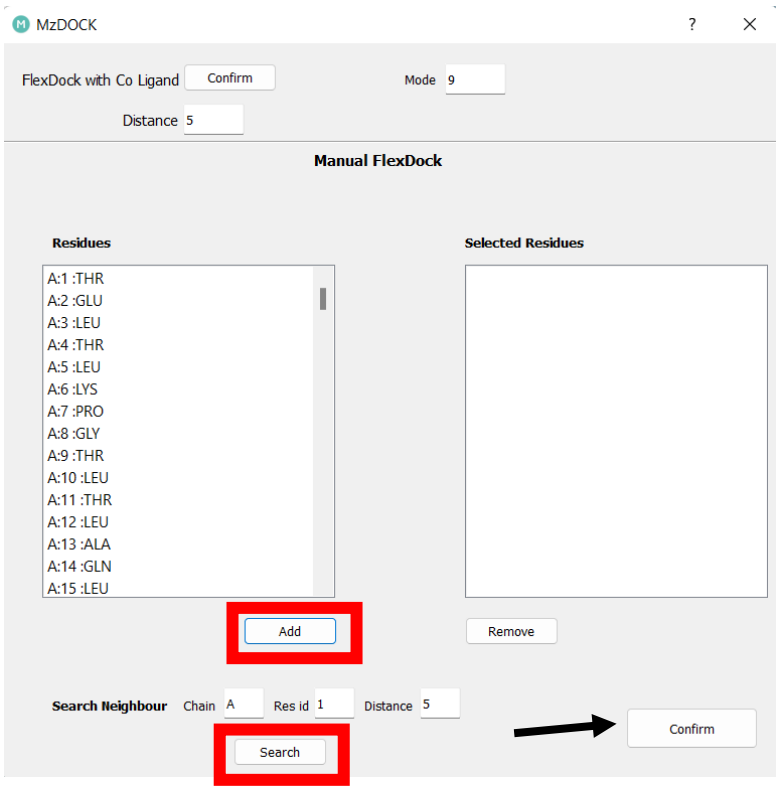
Induced Fit Docking

If there is a presence of co-crystallized ligand , the 'FlexDock' button is activated which gives access to induced fit docking.

Here there is automated induced fir docking with option 'FlexDock with Co Ligand' .click on the confirm button , change distance from the co-ligand where the amino acids are made flexible and number of modes to generate .

For Manual mode, Amino acid residue if known are choosen manually to make it flexible by clicking the residue and press 'add' to add to the selected residues . Also there is an option to search neighbour of a specific amino acid residue which adds those residues to the selected residues.

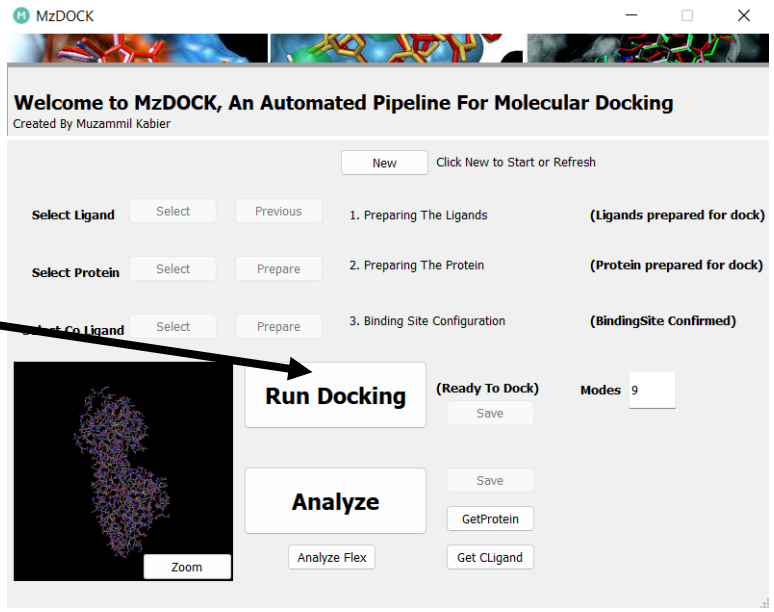




4. Run Docking

When the 'Run Docking' button is activated, click on it to run Docking.

.pdbqt and log file is generated and save the files in the directory you choose.



5. Analyze Interactions

Soon as the docking is completed, click on Analyze, and choose the output pdbqt file and choose a specific pose in the prompt which will be displayed. Then MzDOCK provides you with images, Pymol session file and a report of the binding interactions. Save in the desired directory