
## Prerequisite:

- ➢ MOE installed on your PC.

**Prerequisite terminologies:**

In order to have a thorough understanding of our main topic, you should have the basic concept of the following terminologies:

- ➢ Drug Designing.
- ➢ Ligand.
- ➢ Binding pockets of proteins.
- ➢ Binding affinities.
- ➢ Biological receptors.
- ➢ Types of Docking (Induced fit, Rigid receptor, etc).

## Introduction:

**Molecular docking** is a kind of bioinformatic modeling which involves the interaction of two or more molecules to give the stable adduct. Molecular docking is an important approach for designing new drugs and vaccines and other bioinformatics analysis as well. It predicts the three-dimensional structure of any complex depending upon binding properties of ligand and target. Molecular docking generates different possible adduct structures

that are ranked and grouped together using scoring function in the software.

**MOE** stands for Molecular Operating Environment, is a platform for drug discovery. It is a tool which integrates visualization, modeling and simulations, as well as methodology development for drug discovery, in one single package. The main applications of MOE include structure-based design, fragment-based design, pharmacophore discovery, medicinal chemistry applications, biologics applications, protein and antibody modeling, molecular modeling and simulations, cheminformatics and QSAR.

## Steps:

- Prepare a file of a suitable biological target, any protein or enzyme of your interest (e.g., PDE4B2B).
- Prepare a file of the ligand (molecular inhibitor, e.g., Rolipram) that will create an interaction with your biological target.
- Open your MOE interface and go to ‘File’ and then click on ‘Open’ and then select the file of your biological receptor.
- If you’ve any extra ligands or water molecules attached to the biological target, you need to eliminate those molecules first, this can be done by clicking on the ‘Seq’ option present on the top right corner of the menu bar.

➢ **Preparation of the receptor for Docking:**

- To protonate the receptor molecule, go to ‘Compute’, then ‘Prepare’ and then click on ‘Protonate 3D…’ and then click OK.
- For energy minimization of the receptor molecule, go to ‘Compute’ and then click on ‘Energy minimization’, change the Gradient value from 0.1 to 0.5 and click OK.

➢ **Searching for active site residues in the receptor:**

- To search the active site residues in the receptor molecule, go to ‘Compute’ and then click on ‘Site Finder’, then select the name of your biological receptor in the ‘Atoms’ field, and then click on ‘Apply’.

[It'll provide a list of the active site residues present in your biological receptor.]

- To see these residues where the ligand will be docked, on the 3D structure of the receptor molecule, click on the checkbox of 'Select Residues in SE'.
  [It'll highlight the active site residues on the biological target where the ligand will get bound to the receptor molecule.]

➢ **Ligand preparation:**

- Go to 'File' and then click on 'Open' and then select the file of your ligand molecule.
- Focus the complex in center by clicking on the 'Center' button present in the options list on the right hand side of the screen.

➢ **Docking the ligand and receptor molecules:**

- To perform the docking process on the ligand and receptor molecules, go to 'Compute' and then click on 'Dock'.
- In the pop-up window, select 'Selected Residues' in the 'Site' option to dock to the ligand against the binding site residues you've selected.
  - Select MOE format for both the receptor and ligand molecules.
  - Select MDB or SD format and then browse the file from your computer, if your ligand file is in other than MOE format.
  - Set the 'Refinement' parameter to 'Rigid Receptor' or 'Induced Fit' docking type, according to your own requirement, and leave other parameters by default.
- Enter the name of the output file and select the location to save the file on your PC, and then click on 'Run'.
- In a separate pop-up window, it'll provide you the docking results in a tabular form.
- In the first column named 'mol', it provides the poses or orientations of the ligand molecules, against which different values and scores are assigned to these orientations. The most important value in this regard is the minimum energy values present in the column named 'S'.

- Click on any pose from the first column to see where it binds to the receptor molecule.
- To change the surface of the docking complex, click on the ‘Surface’ option present on the right hand side of the screen and then click on ‘Interaction (VDW)’.
- To check the ligand interaction of the docking complex, click on the ‘Ligand’ option present on the right hand side of the screen and then click on ‘Ligand Interactions’.
- In the pop-up window, it’ll display the ligand and the active site residues interacting with the ligand molecule. At the bottom of this pop-up window, in the ‘Legend’ field, it provides the details about the interactions.
- To save this docking file, go to ‘File’ and then click on ‘Save’ and select the location on your PC and select the suitable format and click on OK.

## Summary:

In this tutorial video of molecular docking, we learned to dock a ligand molecule against a biological receptor using the MOE tool. We also got to analyze the results provided by the MOE software after docking the molecules.