Assignment: Molecular Docking

Step 1: Download the protein structure:

PDB ID: 3UMI
Classification: Metal-Binding Protein
Mutation(s): No
Resolution: 2.40 Å

Method: X-RAY Diffraction

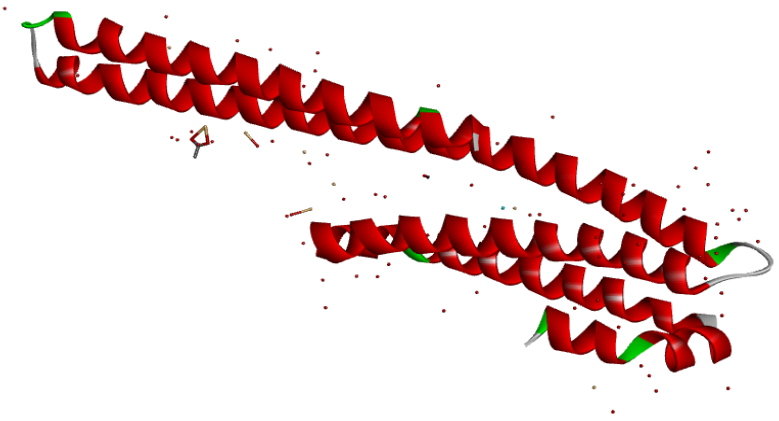

Fig-1 : 3d structure of Amyloid Precursor Protein

Step 2: Protein Preparation

According to the 3D structure of amyloid precursor protein (APP), chain A carries the suitable gene. Hence, water atoms, Ligand groups, heteroatoms, and other unessential groups are removed. After that, energy from the clean structure protein was minimized.

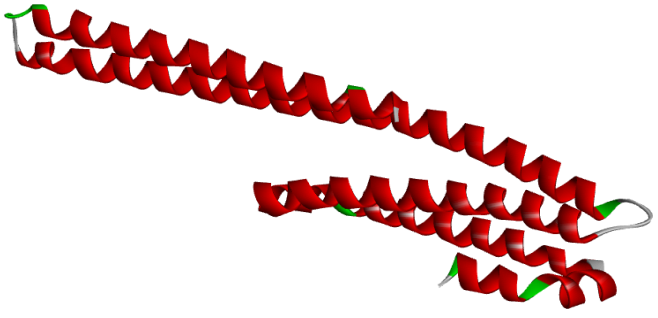

Fig-2 : Clean Protien structure

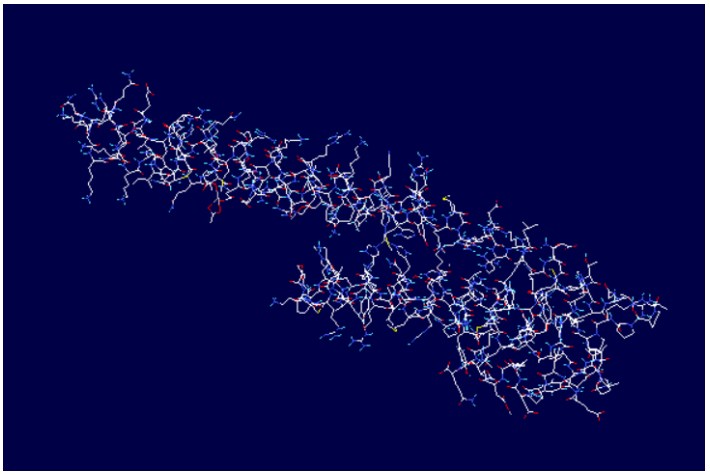

Fig-3 : Optimize Protein Structure

Step 3: Ligand Collection:

Five different ligands, including Rutin, Engeletin, Myricetin, Aspirin, and Paracetamol, were collected from the PubChem database, and their 3D structures were downloaded. Then, a ligand library is created.

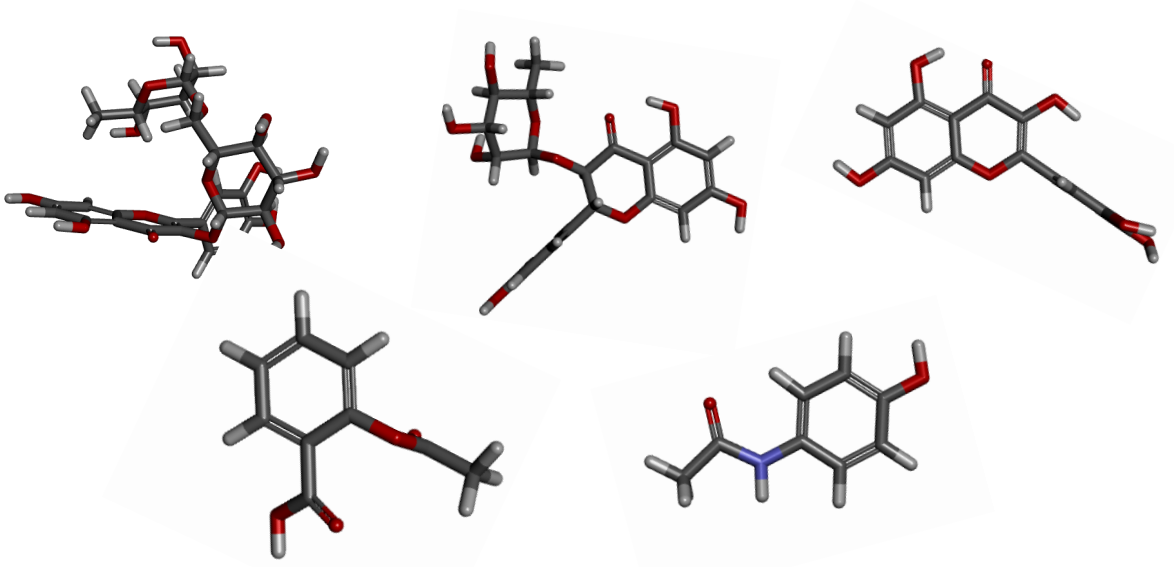

Fig -4: 3D structure of several ligands

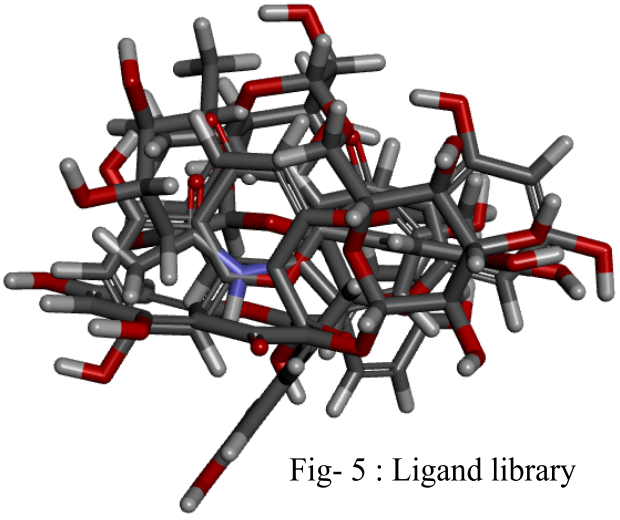

Fig- 5 : Ligand library

Step 4: Convert the protein structure into macromolecules:

In the second stage, the optimized protein structure is saved in a PDB file, which is converted into a pdbqt file (macromolecule) so that AutoDock can read it. PyRx, a molecular docking and virtual screening software, is used to create the macromolecule.

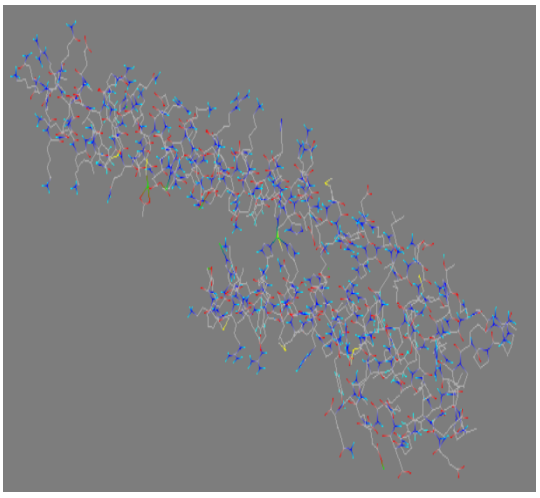

Fig- 6: Macro structure

Step 5: Converting the ligand into PDBQT file:

All the ligand files are converted to PDBQT files from SDF format.

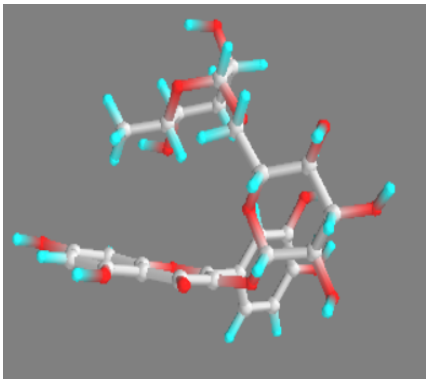

Fig-7 : Ligand file in Pdbqt format

Step 6: Docking run:

Docking is run by the Autodock Vina algorithm. After running the docking, there are some important parameters, such as the grid box parameter center (X, Y, Z) and Dimension (X, Y, Z), that should be considered. Mainly, the value of the Grid Box Parameter is more crucial for site-specific docking when a molecule binds within a particular site, and the binding sites of that protein are known. On the other hand, if the binding site is unknown, blind docking is performed so that the ligand can bind anywhere. Here, blind docking is considered, and the Maximize option is selected to finish the docking procedures successfully.

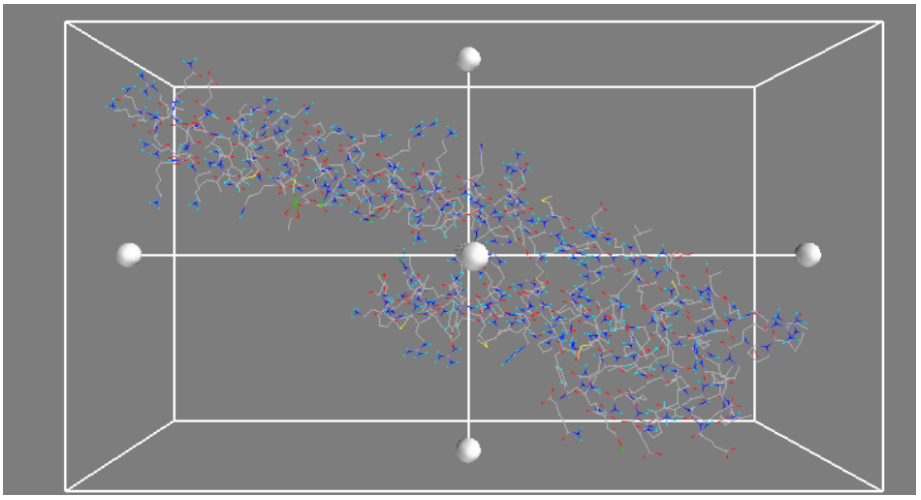

Fig-8 : Maximize the Grid Box Parameter for blind docking

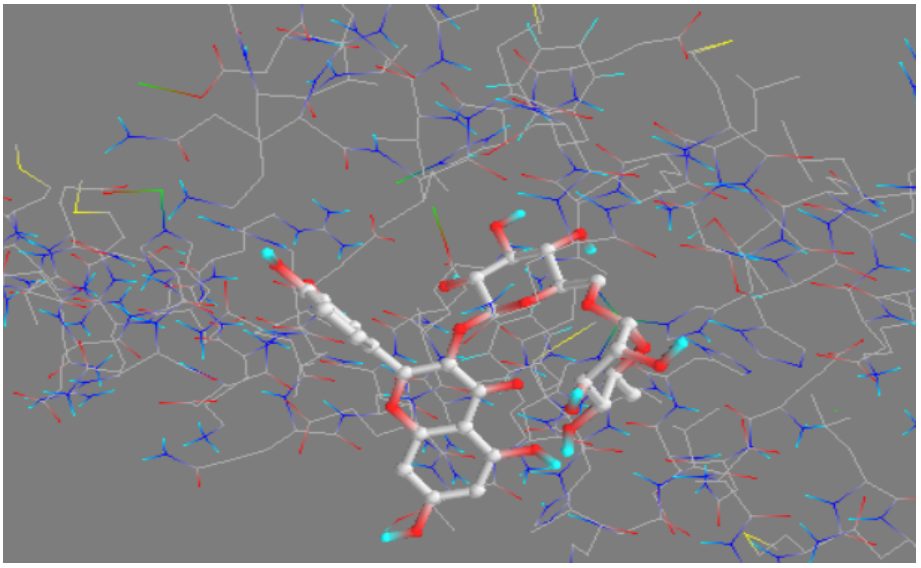

Fig- 9: Protein - Ligand binding

Step 7: Save Docking data and analysis.

After finishing the docking successfully, several data files, such as - value of the Grid Box Parameter and the ligand binding score file, are stored for further analysis.

Grid Box Parameter Value

exhaustiveness = 8

center_x = -54.6573

center_y = -35.3941

center_z = -14.3109

size_x = 90.269758482

size_y = 51.9596011734

size_z = 42.190179214

Ligand Binding Score Table

Ligand (CID)	Binding Affinity	rmsd/ub	rmsd/lb
5280805	-7.7	0	0
6453452	-6.9	0	0
5281672	-6.6	0	0
2244	-5.1	0	0
			0
1983	-4.7	0	0

According to the ligand binding score table, rutin—compound CID:5280805—has better binding affinity (-7.7). Therefore, this ligand will bind with the active site perfectly.

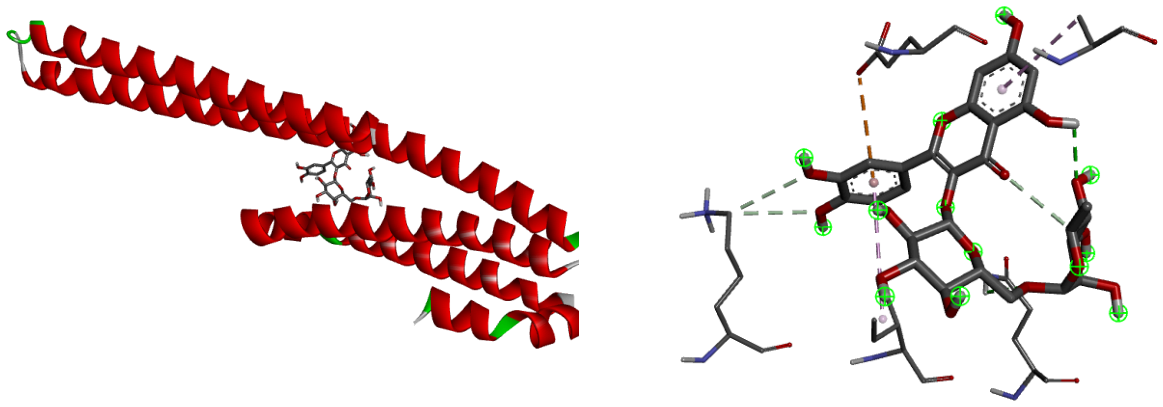

Fig :10 - Ligand -Protein interaction

Although the ligand has nine different poses (RMSD/UB, RMSD/LB = 0, 0), it has the best binding interaction, where the ligand covers glutamine, and the bond length (2.77) between this amino acid with the ligand is the lowest compared to other poses.

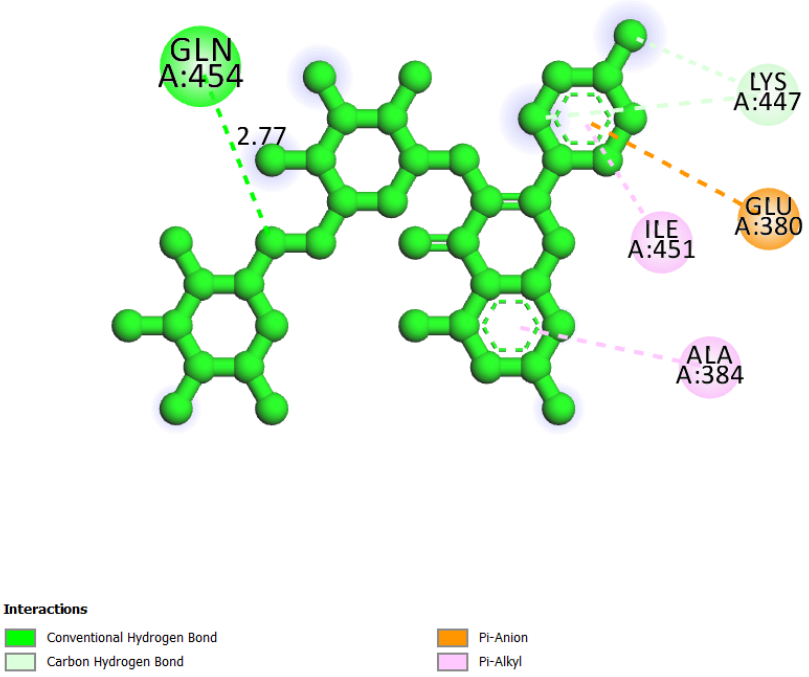

Fig- 11 : 2D structure

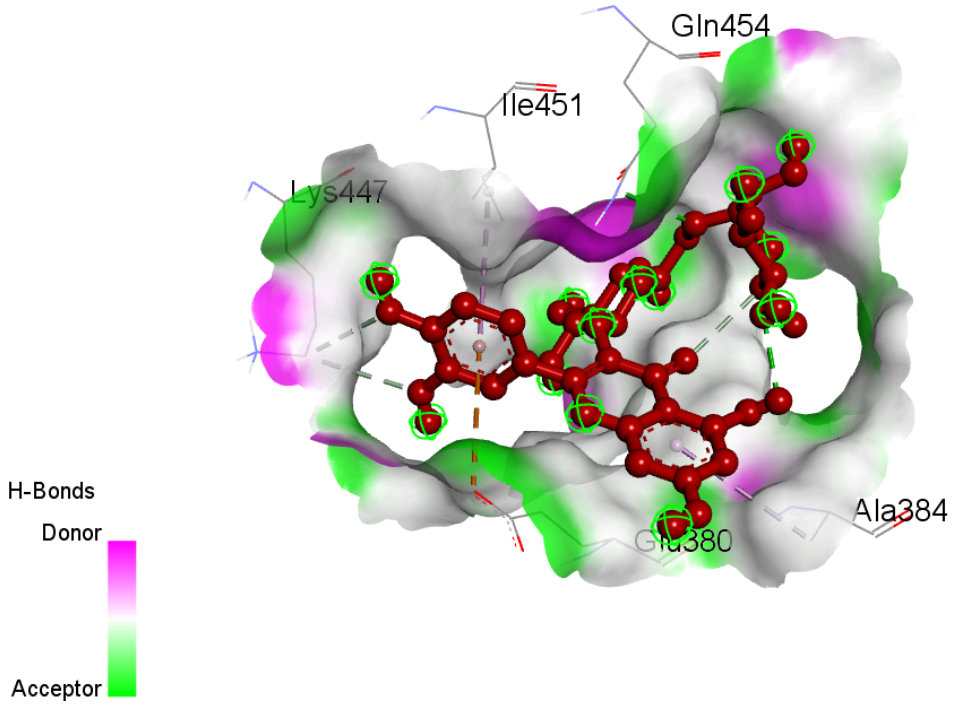

Fig -12 : 3D structure