Practical 3

20 August 2024

Structure based drug design: Identifying hit compounds for a kinase protein

Instructions

1. Upload your report in pdf format with the naming "roll no_p3.pdf".
2. Do not copy, it will be checked for plagiarism.

Steps:

I. Rigid Docking

1. Install Autodock
2. Obtain 3D structure of the protein with PDB ID: 1IEP
3. Obtain the structure of the given ligand (ZINC ID: ZINC126204226) from Zinc database.
4. Get 20 different orientations of the ligand in the active site using rigid docking. (Lamarckian GA algorithm)
5. Identify the best complex using interaction energy and clustering histogram and get the interactions using LigPlot.
6. Use the following active site residues and grid box dimensions for center on macromolecule
   Active site residues: Lys271, Thr315, Glu286
   size_x = 60, size_y = 46, size_z = 44
   Offset: x = -11.278, y = 18.056, z = 6.944
   Spacing (angstrom) = 0.375
   center_x = 7.025, center_y = 93.837, center_z = 61.323

II. Flexible docking

1. Assign flexible residues using select from string option (PDB: GLU64, ALA65, ASP159, PHE160, GLY161; UniProt: GLU286, ALA287, ASP381, PHE382, GLY383)
2. Classify the rigid and flexible residues using flexible residues option.
3. Get 10 different orientation of ligand (ZINC126204226) and flexible residues.
4. What type of interactions are captured in flexible docking compared to rigid docking?
5. Discuss which docking strategy (rigid/flexible) yield better result. Why?

III. Screening- Autodock Vina

1. Obtain the structures of 6 ligands with ZINC IDs from Zinc database: ZINC1283491630, ZINC49895016, ZINC118332804, ZINC31233162, ZINC235987838, ZINC295506072

2. Screen all of them using the protein structure, 1IEP and identify the ligands with lowest energy and score.
3. Tabulate the ligand interactions using ligplot/PDBSUM and discuss which ligand is binding effectively with c-Abl kinase?

Deadline: 26 August 2024