11DOCKING PROTOCOL

PART-I

1. Swiss model= Download protein model

Go to **swiss model** on goossgle -> paste protein sequence into box -> search for templates -> select template -> click on template id -> click on **Coordinates : PDB Format** -> file will be downloaded as **protein.pdb**

Note: If you have already a protein.pdb file then skip this step and go to next step

2. Pubchem= Download ligand model

Download **ligand.sdf** file from pubchem (note: copy and paste your ligand id into pubchem)

download -> 3D -> sdf

3. Pymol= Convert ligand.sdf to ligand.pdb

Go to pymol -> open -> ligand.sdf -> export molecule as -> generic option -> tick on the box of **original atom order -> pdb options -> save**

Note: if you have already ligand file in ligand.pdb format then skip this step

4. Autodock

Protein.pdb to Protein.pdbqt

Open autodock -> file -> read molecule -> protein.pdb -> open
edit -> delete water
edit -> delete water
edit -> hydrogen -> add -> polar only

Grid -> macromolecules -> choose -> protein -> select a molecule -> (pop window will come) save as pdbqt in your docking folder

Ligand.pdb to ligand.pdbqt

ligands -> input -> open -> ligand.pdb
ligand -> torsion tree -> detect root
ligand -> torsion tree -> choose root
ligands -> torsion tree -> choose torsion -> click on **make all bonds rotatable** (this is last option)
ligand -> output -> save as pdbqt

Delete current selections and then go for next step

Grid box over protein molecule

File -> read molecule -> protein_name.pdbqt

Grid -> grid box -> spacing angstrom set to **1 ->** adjust the box

Note: Adjust grid box around entire protein

5. Create config.txt file

Go to text editor and create a file by copy below text and paste into your config.txt file

```
receptor = protein_name.pdbqt
ligand = ligand_name.pdbqt
center_x = 6.230
center_y = 52.483
center_z = 37.837
size_x = 48
size_y = 50
size_z = 62

energy_range = 4
exhaustiveness = 8
num_modes = 10
```

copy and paste x,y,z centre from grid box values and diamention

6. Linux Terminal

Then go to terminal/ open the terminal in destination folder and enter this command
keep **vina file** in your destination folder

./vina --config **config.txt** --log **log.txt**

Note: The output of this command will give you the the **affinity values/energy of ligands**

docking first part is done

config.txt and
log.txt &
ligand_out

Above files are important

DOCKING PROTOCOL

PART-II

1. Pymol

1. Open pymol
2. open your protein **protein_name.pdbqt** file in pymol
3. open **ligand_out.pdbqt** file in pymol

Pymol command 1st

4. split_states **ligand_out**

Then

5. unselect all and keep select only **ligand_out_0001** (take that position which have lower energy: see logs.txt file or see in terminal output) and **protein_name**

Note: ligand_out_0001 is the 1st position of ligand interaction

Pymol command 2nd

6. select nhr01, **model_shubh** w. 5 of **ligand_out_0001**

Then

7. select **nhr01**
8. Go down and right corner and press **S** (sequence)
9. Note the **AA residues sequence**
10. Residues and residues between : 134, 137-146

2. Autodock

11. Open **protein_name.pdbqt** file in autodock
12. Click on **protein_name.pdbqt, click on A and** open **A**
13. Select **(residue and residues between : 134, 137-146)**
14. Then go to **select → select from string → store selection (give name eg: "flex")**
15. Residue tab -> Select name **"flex" ->** **Dismiss**
16. Flexible Residue → Input -> chooose macromolecule -> select molecule ("protein_name")
17. Flexible Residue →Choose Torsions in Residue → close
18. Flexible Residue → Output →Save Flexible PDBQT (flex.pdbqt)
19. Flexible Residue →Output →Save Rigid PDBQT (rgd.pdbqt)
20. select on **R** infront of **model_shubh** panel
21. Redraw the grid:

Grid -> Grid box

Go to **flex.pdbqt** file in your docking folder
Select x, y, z centre of any one amino acid to place grid box to proper position
select centre x, y, z values and copy paste into grid box

Adjust grid around active site (around yellow portion only. Not over entire ribbon)

Grid -> grid box -> spacing angstrom set to **1 ->** adjust the box

Note down the coordinates values given in drid box

3. Create config.txt file

Create new file config1.txt and edit it config1.txt file

Go to text editor and create a file by copy below text and paste into your config.txt file

receptor = rgd.pdbqt
flex = flex.pdbqt
ligand = **ligand.pdbqt**

center_x = -9.401
center_y = 47.936
center_z = 45.296

size_x = 52
size_y = 50
size_z = 46

energy_range = 4
exhaustiveness = 8
num_modes = 10

then go to terminal and enter this command
./vina --config **config** --log **log.txt**

docking is done
config and log.txt & ligand_out files are important