Protocol to execute Molecular Docking

1. Create a separate folder for docking.
2. Download the protein structure from Protein Data Bank in .pdb format in that directory.
3. Download Folic acid structure from Pubchem in .sdf format and save it in that directory.
4. Convert the file in .sdf format in .pdb format using openbabel.
5. Remove ligand and all other heteroatoms from the protein structure using pymol and save the modified structure in .pdb format.
6. Copy autodock4.exe and autogrid4.exe from the following path in your system:
   "C:\Program Files (x86)\The Scripps Research Institute\Autodock\4.2.6"
7. Open Autodock and set the path where ligand.pdb and protein.pdb is saved.
   File → Preferences → Set
   Enter the path of your directory in the "Startup directory" section. Click on "Set" and the click on "Make default".
8. Open the protein molecule in Autodock. Go to file and click on "read molecule".
9. Remove water molecules from the protein structure.
   Edit → Delete water
10. Check if any residue is missing or not.
    Edit → Misc → Check for missing atoms
    Click on "Select all Residues" and then click on "Dismiss".
11. Repair missing atoms
    Edit → Misc → Repair missing atoms
    Click on "Save as 2 sets" and "Dismiss"
12. Then add hydrogen.
    Edit → Hydrogen → Add
    Click on "Polar only"
13. Edit → Charges → Add Kollman charges
    Click on "ok"
14. Now read ligand.pdb.
    Ligand → Input → Open
15. Save the ligand molecule.
    Ligand → Output → Save as pdbqt

16. Now create a Grid box. For blind docking create a grid box in such a way entire protein molecule comes within it.

    Grid → Macromolecule → choose → select protein molecule → click select molecule

    Accept the pop-up if appears on your screen.

    Save the protein molecule as "protein.pdbqt" in your working directory.
17. Grid → Set Map types → Choose ligand → select the ligand molecule → select ligand
18. Grid → Grid Box

    Adjust the number of points in the x, y, and z directions. If necessary change the size of the grid box using "Spacing (angstrom)" in the Grid options window.

    Go to the file and click on close saving current.
19. Grid → Output → Save GPF

    Save the file as "grid.gpf".
20. Run → Run autogrid

    In the program pathname section browse the "autogrid4.exe" file.

    In "parameter filename" section browse "grid.gpf" file. Once you enter .gpf file you will see .glg file in "Log Filename" section. Click on "Launch". A popup window will be there during the run time named "Autodock Process Manager". Once .gpf file is converted to .glg file the popup will disappear. The successful completion of the process can be verified by opening "grid.glg" file where "Successful Completion" and CPU time will be mentioned.
21. Docking → Macromolecule → Set rigid filename.

    Open "protein.pdbqt" file.
22. Docking → Ligand → Choose → Select ligand → Click Accept
23. Docking → Search Parameters → Genetic Algorithm → Click Accept
24. Docking → Output → Lamarckian GA (4.2)

    Save the file as "dock.dpf"
25. Run → Run AutoDock

    In the "Program pathname section" browse the "autodock4.exe" file. In the "parameter filename section" browse the "dock.dpf" file. Once you enter the .dpf file you will the see .dlg file in the "Log Filename" section. Click on "Launch". A popup window will be there during the run time named "Autodock Process Manager". Once the .dpf file is converted to a .dlg file the popup will disappear.
26. To analyze docking results.

    Analyze → Dockings → Open

Open the “dock.dlg” file.

Analyze → Macromolecule → Open

Analyze → Confirmations → Play, rank by energy

Also confirm binding energy of the docking result from .dlg file.

Note: While you are saving your file write the name of the file with the extension. For example, write “ligand.pdbqt” instead of writing only “ligand” and save the .pdbqt file in your working directory. This process should be maintained to save .pdbqt, .dpf, .gpf files.