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Review Article

Insights of Molecular Docking in Autodock-Vina: A Practical Approach

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Abstract

Computational techniques in drug discovery and vaccine prediction basically revolve around molecular docking to retrieve perfect interaction models for ligand and receptor. Binding energies can be obtained for perfectly interacting complexes. Many tools like DINC, PatchDock-Firedock, and AutoDock-Vina are deployed to conduct molecular docking in various pipelines. Discovering drug and vaccine becomes facile due to use of advanced docking techniques. Also allow researchers to screen out possible models of interaction on the basis of atomic contact energy, binding energy, and global energy. This review article provides insights to use efficient approach for docking related investigations.

INTRODUCTION

Docking is a systematic approach in which two molecules exhibits interaction due to the presence of functional groups. Lock and key binding was first described by Emil Fischer in 1894 [1]. Koshland described the further explanations for induced fit approach [2], that clearly indicates ligands have potential to induce conformational alterations in protein (Enzyme). Proteins in cellular environment orchestrated in too many conformations [3], described by an energy framework [4], and ligand entities selectively bind to lowest energy conformation [5,6]. This explanation is termed as conformational selection; the ligand provides integrity and stabilization to one of the protein conformations [7]. The conformational selection is followed by an induced fit adjustment [8]. Molecular docking opens new dimensions in practical aspects rather than theoretical understanding, as deployed in drug designing [9], and epitope based vaccine prediction.

TOOLS USED IN MOLECULAR DOCKING

The common tools that were deployed in fast docking are particularly GOLD [10,11], DINC, PatchDock-Firedock, and AutoDock-Vina [12], most of the tools are free. DINC [13], PatchDock-Firedock [14], are free webservers where investigator can directly submit pdb files of receptor and ligand to obtain results. The best tool for performing docking is AutoDock Vina, which can be freely downloaded.

STEPS TO BE FOLLOWED FOR MOLECULAR DOCKING THROUGH AUTODOCK VINA

1. Download tools a. Autodock Vina and Install it b. Mgltools

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- ReceptorDrug
- Vaccine

in Autodock tools (ADT) and install it. (From Website \rightarrow autodock.scripps.edu)

- **2.** Structure of receptor is downloaded from RCSB-PDB website in Pdb format; if ligand is in chemical form download it from ZINC15, Chembridge, Maybridge, Pubchem (NCBI) in SDF Format and convert them in to Pdb by using openbabel software.
- **3.** Go to directory where MGL-Tools were installed and click ADT.bat file. It will open autodock tools (Figure 1,2,3).
- 4. In autodock tools go to File → Read molecule → select protein (Receptor in Pdb format); it will show multiple structures in left side pan and right click on other models and keep on deleting till one model is remaining (Figure 4, 5).
- **5.** Go to Edit \rightarrow Hydrogens \rightarrow Add \rightarrow Polar only (Ok)
- **6.** Go to Edit \rightarrow Charges \rightarrow Add kollman charges
- 7. Follow {Grid → Macromolecule → choose }select protein name, click ok save as Pdbqt format.
- 8. Follow Grid → Grid box; set spacing in 1 Å, then set coordinates x, y, z. So there should be perfect fit of box on molecule (Protein/ receptor under consideration). Then under file option output grid dimension file will be present and save it as grid.txt. After that we are done with receptor.
- 9. Then go to Ligand → Input → Open, select ligand pdb file to search your ligand file (Note:- In selection window files of pdbqt will be shown by default, so please select pdb to see your ligand for selection)

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Figure 1 Important folders generated in directory after installation of autodockvina and mgltools.



- **10.** Go to Ligand \rightarrow Torsion tree \rightarrow detect root, this will automatically detect roots in ligand.
- **11.** Go to Ligand \rightarrow output \rightarrow save as pdbqt format.
- **12.** Create working folder by any name and copy all structure related files in it (Figure 6).
- 13. Also go to scripps institute → vina and copy all the three files (vina.exe, vina_licence.rtf, vina_split.exe) in it and paste it to your working folder. [This will reduce copying long paths for files all the time] (Figure 7).
- **14.** Create argument file and save as args.txt or any other name but in txt format (Figure 8).





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Figure 7 Essential Files under scripps institute folder that are needed to be copied in working directory.

```
args.txt - Notepad
                   File Edit Format View Help
                   receptor = 4is6.pdbqt
                   ligand = model1.pdbqt
                   out = output.pdbqt
                   log = log.txt
                   center_x = 15.387
                   center_y = 19.590
center_z = 15.697
                   size_x = 50
                   size_y = 50
                   size_z = 38
Figure 8 Designing Argument file named as args.txt.
```

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Select C:\Windows\System32\cmd.exe
Microsoft Windows [Version 10.0.10586] (c) 2015 Microsoft Corporation. All rights reserved.
C:\Users\me\Desktop\docking>vina.execonfig args.txt ###################################
#
O. Trott, A. J. Olson,
<pre># AutoDock Vina: improving the speed and accuracy of docking # # with a new scoring function, efficient optimization and # # multithreading, Journal of Computational Chemistry 31 (2010) # # 455-461 # #</pre>
DOI 10.1002/jcc.21334
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Please see http://vina.scripps.edu for more information.
WARNING: The search space volume > 27000 Angstrom^3 (See FAQ) Detected 4 CPUs Reading input done. Setting up the scoring function done. Analyzing the binding site done. Using random seed: -1134301952 Performing search 0% 10 20 30 40 50 60 70 80 90 100% **********
mode affinity dist from best mode (kcal/mol) rmsd l.b. rmsd u.b.
1 -6.3 0.000 0.000
2 -6.2 4.174 14.278
3 -0.1 4.495 13.375 4 -6.1 4.201 15.205
5 -6.1 4.998 14.276
6 -6.1 5.219 15.600
7 -6.0 4.006 14.770
8 -5.9 3.647 8.156
9 -5.9 5.114 15.154

Figure 9 Working Result of docking 4IS6 PDB ID Protein to EPITOPE MIGLLSSRI Protein. (The practical docking example- downloaded pdb file from RCSB-PDB database id 4IS6 with epitope MIGLLSSRI whose structure is designed using PEPFOLD 3.5 server [15]).

- **15.** Open CMD in working directory by typing cmd in explorer mode under address bar.
- **16.** Put command: **vina.exe –config args.txt** [we will get results and it will also save in log.txt file] (Figure 9)
- **17.** Output.pdbqt file can be observed in pymol for better orientations of ligand. Then in pymol go to File \rightarrow Open and load protein file in pdbqt to view better interaction picture (Figure 10).
- 18. In the same cmd window, we can use [vina_split -input output.pdbqt] command, this will help in generating all possible ligand models. The best model will be output1. pdbqt, and then we can open it in pymol and again go to open and find the protein /receptor pdb file so click on it. Now as both structures are present in visual you can go to export image (for getting png picture) or export molecule (for saving in pdb). Another way to get docked file is by opening best ligand pdbqt file in notepad ++ and copy receptor/protein pdb file text to paste below ligand text, and save as pdb file.

APPLICATION OF MOLECULAR DOCKING

Molecular docking methods are applied for epitope based vaccine crafting and also for drug discovery approaches [16]. Molecular docking can be conducted by various web servers, and parameters like Atomic contact energy, Global energy and binding scores are usually determined. In many recent vaccine based studies, like vaccine prediction for Zika virus [17], SARSCov2 [18], Dengu virus [19], Nipah Virus [20], Hepatitis C virus [21], and *Tropheryma whipplei* [22] bacterium docking was found to be key determinant for molecular H-bond interaction analysis. Molecular predictions was successfully deployed in computational drug discovery pipelines like piperazine linked thiohydantoin derivatives as novel androgen antagonist in prostate cancer treatment [23], and also in finding anti-inflammatory role of biochanin a and genistein with 9 omega-



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3-fatty acids using complex docking analysis with ppar γ and gpr120 [24]. Recently natural compounds were tested for pharmacoactive properties against SARSCov2, on the basis of molecular docking and found to be effective [25]. Autodock vina was found to be best tool to obtain molecular docking results and to analyze interaction patterns between ligand and receptor molecules.

CONCLUSION

Best docking results and affinity is generated by deploying autodock vina and mgl tools. It is the efficient method for docking ligands to receptors/ proteins. In modern era it opens many dimensions for fast computer aided drug designing and Vaccine prediction.

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