SciMedCentral

Journal of Pharmacology & Clinical Toxicology

Review Article

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

Amit Joshi1 and Vikas Kaushik*

Domain of Bioinformatics, Lovely professional university, India

***Corresponding author**
Vikas Kaushik, Domain of Bioinformatics, School of Bioengineering and biosciences, Lovely professional university, Phagwara, Punjab, India, Email: vikas.14664@lpu.co.in

Submitted: 08 August 2021

Accepted: 27 August 2021

Published: 30 August 2021

ISSN: 2333-7079

Keywords
- Binding energy
- Docking
- Ligand
- Receptor
- Drug
- Vaccine

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 in Autodock tools (ADT) and install it. (From Website → 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 → Hydrogens → Add → Polar only (Ok)

6. Go to Edit → Charges → 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)

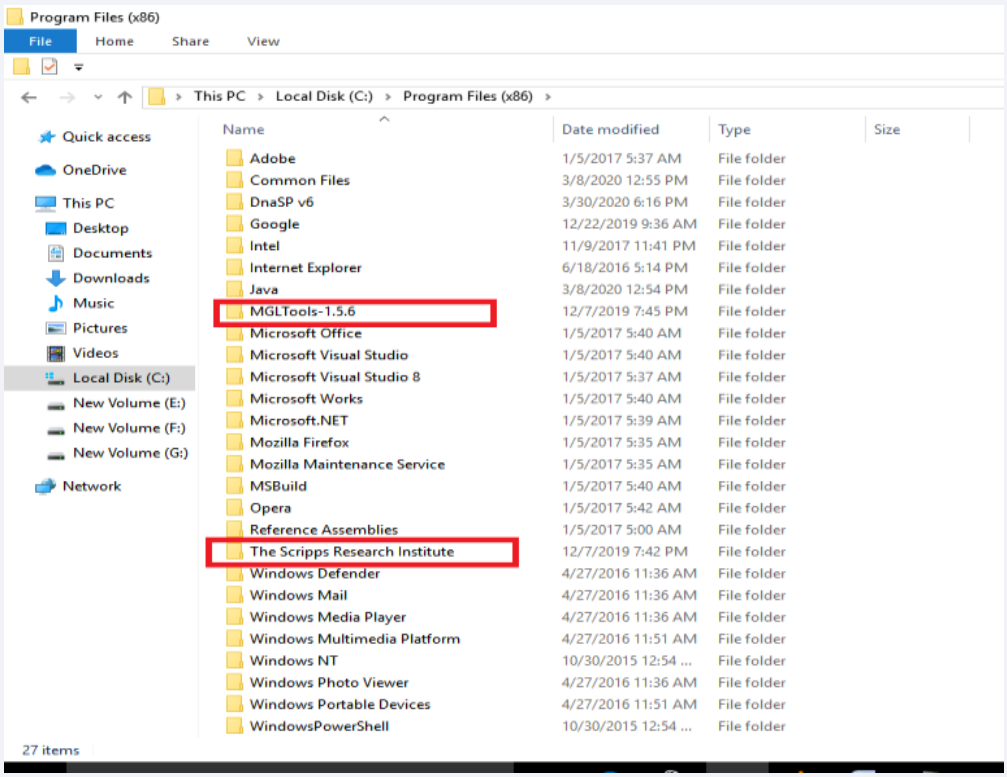

Figure 1 Important folders generated in directory after installation of autodockvina and mgltools.

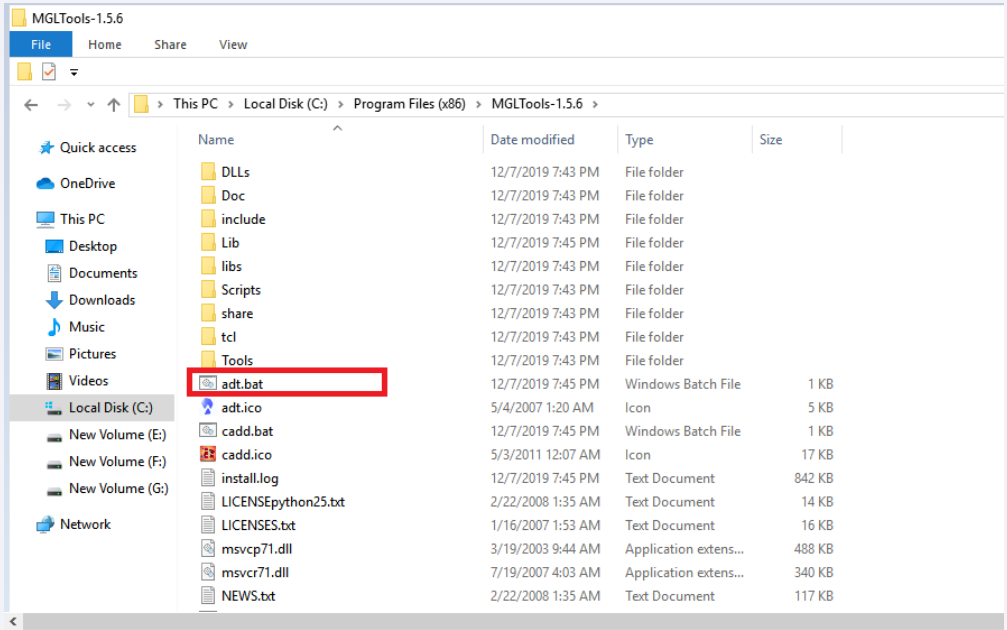

Figure 2 adt.bat file under mgltools run to make pdbqt files after analyzing ligand and protein receptor.

10. Go to Ligand → Torsion tree → detect root, this will automatically detect roots in ligand.

11. Go to Ligand → output → 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**).**

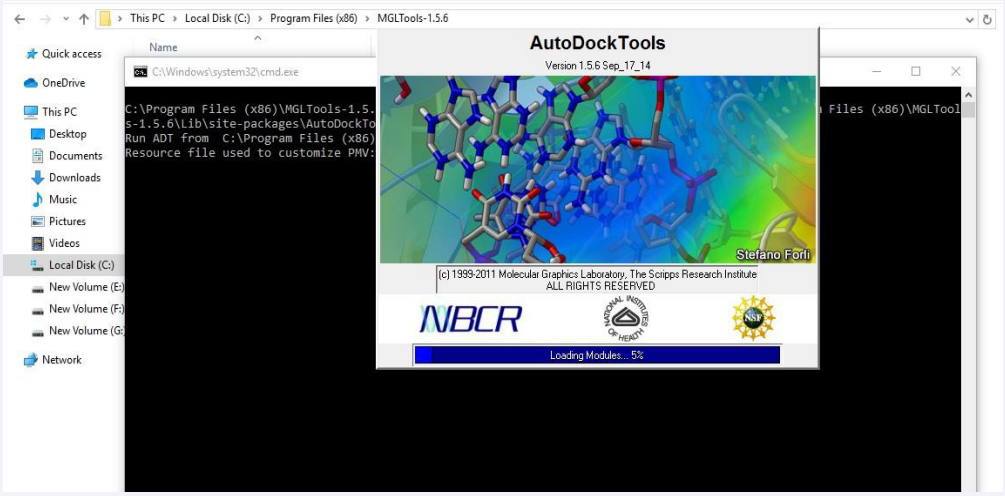

Figure 3 Autodock tools initiation after clicking adt.bat file.

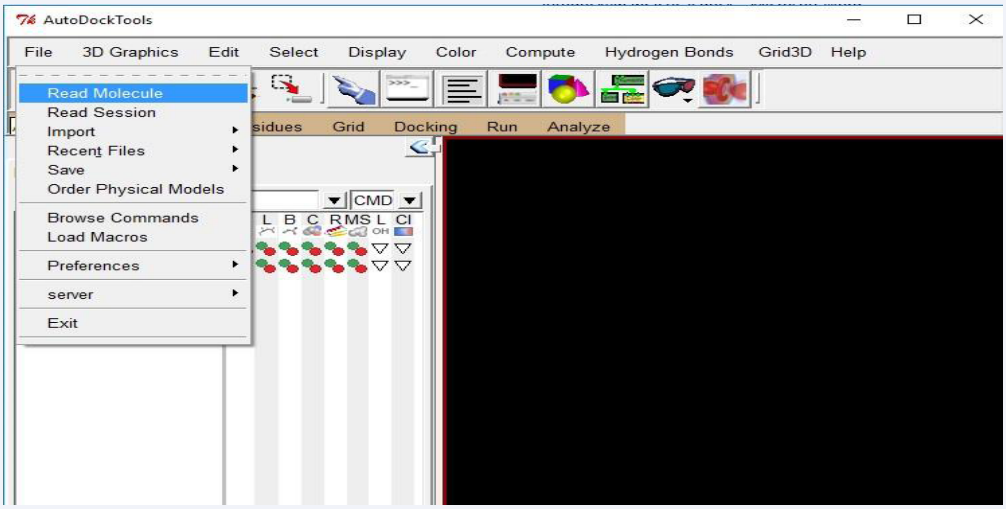

Figure 4 Autodock tools getting receptor loaded: file → Read molecule.

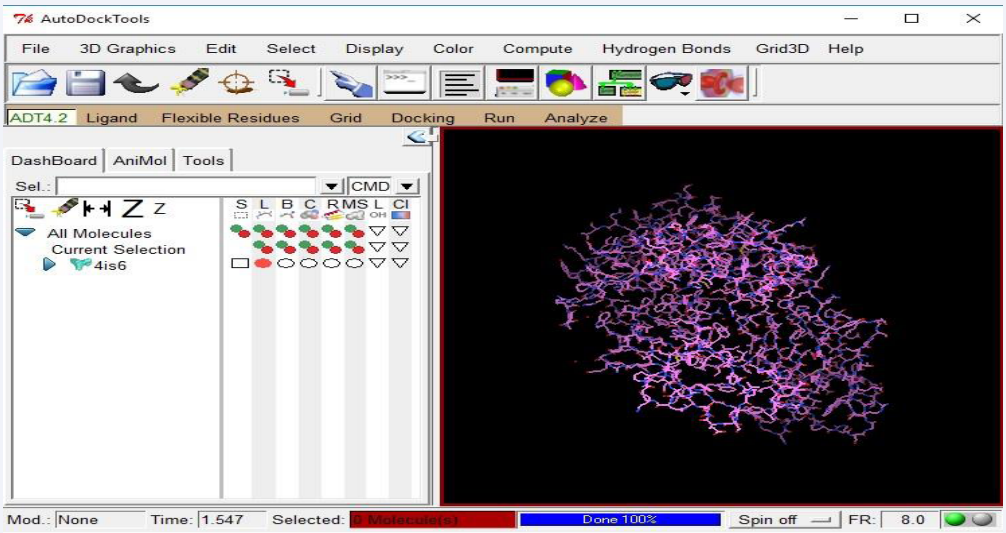

Figure 5 Opening of new receptor or protein file in Autodock tools.

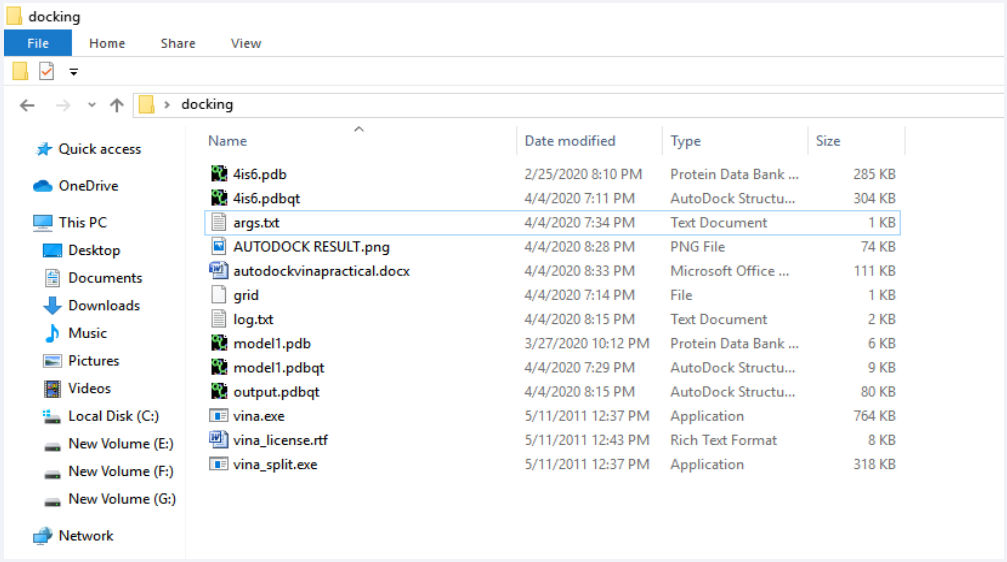

Figure 6 Working folder (named as "docking") construction having all essential files.

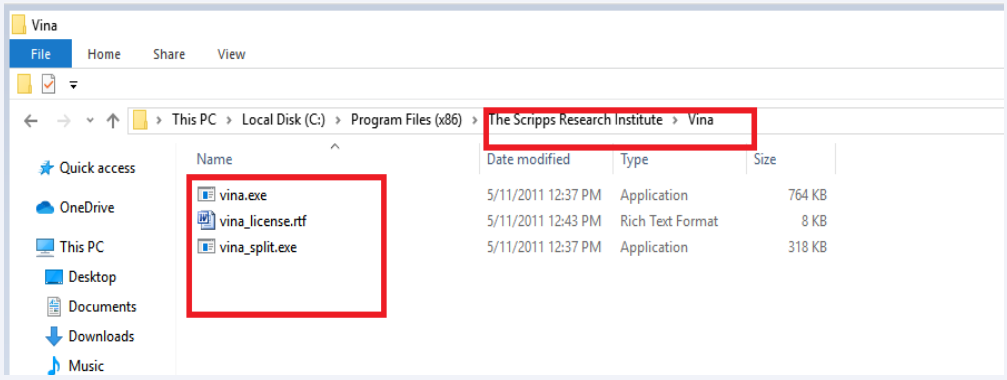

Figure 7 Essential Files under scripps institute folder that are needed to be copied in working directory.

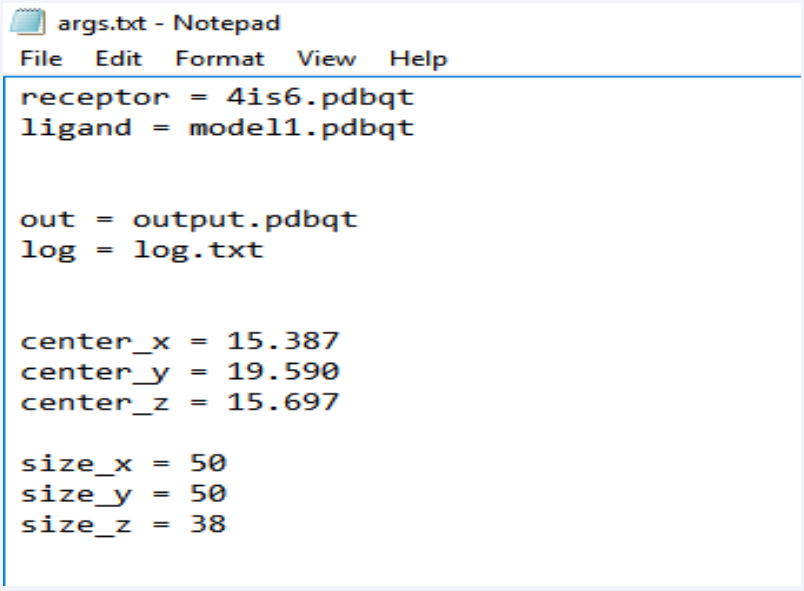

Figure 8 Designing Argument file named as args.txt.

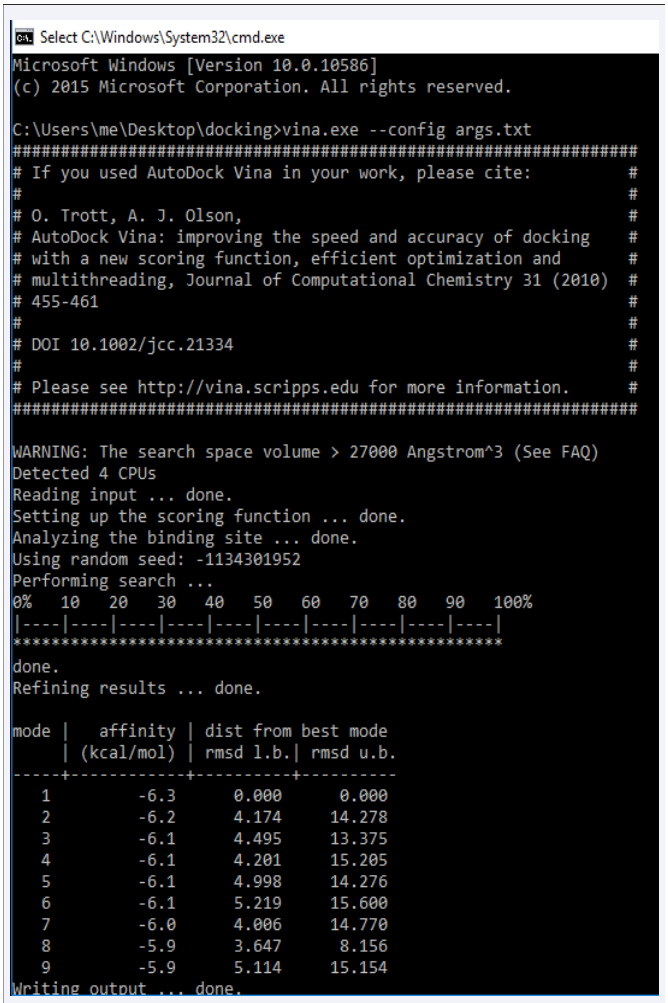

Figure 9 Working Result of docking 4IS6 PDB ID Protein to EPITOPE MIGLLSSRI Protein. (The practical docking example- downloaded pdb file from RCSB-PDB database id 4IS6 with epitope MIGLLSSRI whose structure is designed using PEPFOLD 3.5 server [15]).

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 → 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-

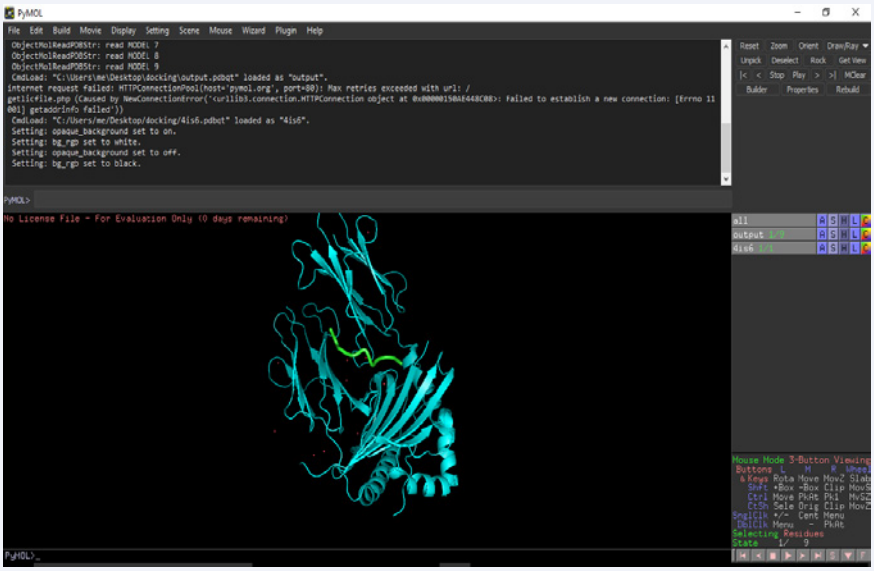

Figure 10 Pymol view of docking:- Receptor: 4IS6 PDB ID Protein to Ligand or Epitope MIGLLSSRI.

3-fatty acids using complex docking analysis with pparγ 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.

REFERENCES

1. Fischer E. Einfluss der configuration auf die wirkung der enzyme. Ber Dtsch Chemischen Ges. 1984; 27: 2985-2993.
2. Koshland DE. Application of a theory of enzyme specificity to protein synthesis. Proc Natl Acad Sci USA. 1958; 44: 98-104.
3. Monod J, Wyman J, Changeux JP. ON THE NATURE OF ALLOSTERIC TRANSITIONS: A PLAUSIBLE MODEL. J Mol Biol. 1965; 12: 88-118.
4. Frauenfelder H, Sligar SG, Wolynes PG. The energy landscapes and motions of proteins. Science. 1991; 254: 1598-1603.
5. Austin RH, Beeson KW, Eisenstein L, Frauenfelder H, Gunsalus IC. Dynamics of ligand binding to myoglobin. Biochemistry. 1975; 14: 5355-5373.
6. Foote J, Milstein C. Conformational isomerism and the diversity of antibodies. Proc Natl Acad Sci USA. 1994; 91: 10370-10374.
7. Kumar S, Ma B, Tsai CJ, Sinha N, Nussinov R. Folding and binding cascades: dynamic landscapes and population shifts. Protein Sci. 2000; 9: 10-19.
8. Csermely P, Palotai R, Nussinov R. Induced fit, conformational selection and independent dynamic segments: an extended view of binding events. Trends Biochem Sci. 2010; 35: 539-546.
9. Van Drie JH. Computer-aided drug design: the next 20 years. J Comput Aided Mol Des. 2003; 21: 591-601.
10. Jones G, Willett P, Glen RC. Molecular recognition of receptor sites using a genetic algorithm with a description of desolvation. J Mol Biol. 1995; 245: 43-53.
11. Jones G, Willett P, Glen RC, Leach AR, Taylor R. Development and validation of a genetic algorithm for flexible docking. J Mol Biol. 1997; 267: 727-748.
12. Trott O, Olson AJ. AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization and multithreading. J Comput Chem. 2010; 31: 455-461.
13. Antunes DA, Moll M, Devaurs D, Jackson KR, Lizée G, and Kavraki LE. DINC 2.0: a new protein-peptide docking webserver using an incremental approach. Cancer Res. 2017; 77: e55-57.
14. Schneidman-Duhovny D, Inbar Y, Nussinov R, Wolfson HJ. PatchDock and SymmDock: servers for rigid and symmetric docking. Nucleic Acids Res. 2015; 33: W363-W367.
15. Lamiable A, Thévenet P, Rey J, Vavrusa M, Derreumaux P, Tufféry P. PEP-FOLD3: faster de novo structure prediction for linear peptides in solution and in complex. Nucleic Acids Res. 2016; 44: W449-454.
16. Kaushik V, Lahiri T, Singh J, Kumar G. Statistics of unrelated sequence properties to improve prediction of B-cell based linear epitopes" In 2018 International Conference on Engineering, Applied Sciences, and Technology (ICEAST). IEEE. 2018; 1-4
17. Sharma P, Kaur R, Upadhyay AK, Kaushik V. In-Silico Prediction of Peptide Based Vaccine Against Zika Virus. Int J Peptide Res Therapeut. 2020; 26: 85-91.
18. Joshi A, Joshi BC, Mannan MAU, Kaushik V. Epitope based vaccine prediction for SARS-COV-2 by deploying immuno-informatics approach. Informatics in Medicine Unlocked. 2020.
19. Krishnan S, Joshi A, Kaushik V. T cell epitope designing for dengue peptide vaccine using docking and molecular simulation studies. Molecular Simulation. 2020; 46: 787-795.
20. Kaushik V. In silico identification of epitope-based peptide vaccine for Nipah virus. Int J Peptide Res Therapeutics. 2019; 1-7.
21. Kaushik V, Chauhan G, Singh J. In silico peptide based vaccine design against non-structural protein 5 of hepatitis c virus. Int J Pharmacy Pharmaceu Sci. 2014; 9: 80-82.
22. Joshi A, Kaushik V. In-Silico Proteomic Exploratory Quest: Crafting T-Cell Epitope Vaccine Against Whipple's Disease. Int J Peptide Res Therapeut. 2020.
23. Bhati S, Kaushik V, Singh J. In Silico Identification of Piperazine Linked Thiohydantoin Derivatives as Novel Androgen Antagonist in Prostate Cancer Treatment. Int J Peptide Res Therapeut. 2019; 25: 845-860.
24. Rao BS, Lakshmi V, Kaushik V. An In Silico Comparative Study of Anti-inflammatory Role of Biochanin A and Genistein with 9 Omega-3-fatty Acids Using Complex Docking Analysis with PPARγ and GPR120. Int J Peptide Res Therapeut. 2020; 1-16.
25. Kar, Pallab, Neeta Raj Sharma, Bhupender Singh, Arnab Sen, and Ayan Roy. Natural compounds from Clerodendrum spp. as possible therapeutic candidates against SARS-CoV-2: An in silico investigation. J Biomolecular Structure and Dynamics. 2020: 1-12.

Cite this article

Joshi A, Kaushik V (2021) Insights of Molecular Docking in Autodock-Vina: A Practical Approach. J Pharmacol Clin Toxicol 9(1):1155.