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Mini Review

Panoramic Review on Progress and Development of Molecular Docking

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ABSTRACT

In structural molecular biology and computer-assisted drug creation, molecular docking is a crucial tool. Predicting the prevailing binding modes of a ligand with a protein having a known three-dimensional structure is the aim of ligand-protein docking. Effective docking methods use a scoring system that correctly ranks candidate dockings and efficiently explore high-dimensional spaces. Lead optimization benefits greatly from the use of docking to do virtual screening on huge libraries of compounds, rate the outcomes, and offer structural ideas for how the ligands inhibit the target. It can be difficult to interpret the findings of stochastic search methods, and setting up the input structures for docking is just as crucial as docking itself.

In recent years, computer-assisted drug design has relied heavily on the molecular docking technique to estimate the binding affinity and assess the interactive mode since it can significantly increase efficiency and lower research costs. The main concepts, techniques, and frequently utilized molecular docking applications are introduced in this work. Additionally, it contrasts the most popular docking applications and suggests relevant study fields. Finally, a brief summary of recent developments in molecular docking, including the integrated technique and deep learning, is provided. Current docking applications are not precise enough to forecast the binding affinity due to the insufficient molecular structure and the inadequacies of the scoring mechanism.

Keywords: Molecular docking; Optimization; Virtual screening; Databases

INTRODUCTION

One such structure-based drug design technique is molecular docking, which simulates molecular interaction and forecasts the binding mechanism and affinity between receptors and ligands [1]. This method has been extensively employed in the field of drug design research in recent years. In addition to making it easy for researchers to buy, manufacture, and finish further pharmacological experiments, using the compounds database to screen possible pharmacophores also significantly increases efficiency and lowers research costs. Additionally, the development of reverse molecular docking technology has the potential to dramatically enhance the ability of researchers to forecast therapeutic targets and comprehend the underlying molecular mechanisms that underlie drug design [2]. The overview concludes by briefly introducing the most recent developments and uses of molecular docking technology. This review's objective is to analyze the most recent developments in the field of molecular docking as well as the role that structural integration plays in drug discovery and medicinal chemistry.

The number of tools available for structure-based drug design is expanding quickly, driven by improvements in the determination of molecular structure. An appealing alternative to high-throughput random screening is lead discovery using molecular docking techniques to scan ligand databases [1]. When it comes to molecular docking, the scale of commercial databases places severe computational restrictions on the amount of calculational information that is allowed for each potential ligand. We discuss alternate docking philosophies that successfully handle this issue. These strategies fall within a range of models that are constrained by the Lock-and-Key and Induced-Fit theories for ligand binding with regard to the dynamic features of molecular recognition. We investigate the potential of a tolerant model for forecasting absolute ligand binding affinity vs. a rigid model for leveraging species specificity.

We emphasize this aspect of the issue throughout our validation of docking procedures because it is one of the main ways that current molecular docking approaches are constrained. Finding a suitable location and orientation for docking a tiny molecule (ligand) to a bigger receptor molecule is known as the molecular docking problem.

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REVIEW LITERATURE

Molecular docking technology

The fundamental concepts of molecular docking: In order to predict and determine the binding affinity and interactive mode between ligand and receptor, molecular docking simulates the ideal conformation in accordance with complementarity and pre-organization [1]. The original "lock-and-key model", which makes reference to rigorous docking of receptors and ligands to determine the best orientation for the "key" to open the "lock," is depicted in Figure 1A. The significance of geometric complementarity is emphasized by this model [3]. In structural molecular biology and computer-assisted drug creation, molecular docking is a crucial tool. Predicting the dominant binding mode(s) of a ligand with a protein having a known three-dimensional structure is the aim of ligand-protein docking. Effective docking methods use a scoring system that correctly ranks candidate dockings and efficiently explore high-dimensional spaces. Lead optimization benefits greatly from the use of docking to do virtual screening on huge libraries of compounds, rate the outcomes, and offer structural ideas for how the ligands inhibit the target [3]. It can be difficult to interpret the findings of stochastic search methods, and setting up the input structures for docking is just as crucial as docking itself (Figure 1).

However, the actual docking procedure is so adaptable that ligands and receptors must alter their conformation to fit one another well. We create a "induced fit model" as a result (Figure 1B) [3]. The energy complementarity and pre-organization, which are based on geometric complementarity, ensure that receptors and ligands will achieve the most stable structure while minimizing the free energy [4].

According to a specific algorithm, as illustrated in Figure 2, molecular docking software can assist us in locating the best conformation and orientation. We can then use a scoring function to forecast the binding affinity and evaluate the interactive mode. Protein-DNA docking using Autodock Vina [5]. To explore intricate biological and chemical systems, pharmaceutical research has effectively incorporated a wide range of molecular modeling techniques into a number of drug development initiatives. The creation of new, promising chemicals has greatly benefited from the merging of computational and experimental methodologies. Molecular docking techniques, which are widely utilized in contemporary drug design, investigate the ligand conformations taken within the binding sites of macromolecular targets [6]. By analyzing crucial aspects of the intermolecular recognition process, this method also calculates the ligand-receptor binding free energy. Since there are numerous docking algorithms available nowadays, it is essential to comprehend the benefits and drawbacks of each algorithm before developing efficient tactics and producing pertinent outcomes

Software for molecular docking

The three primary categories of molecular docking software are listed in Figure 3. The usage of flexible-rigid docking is common. Flexible docking is typically more precise, though, therefore recent years have seen a surge in research into this area [7]. Using machine-learning techniques, several new, or at least revitalized, advancements were made in fields such nonlinear scoring functions. The recent developments in drug design, particularly in virtual screening and fragment-based drug design are the main focus of this study. The behavior of tiny molecules at the binding site of a target protein is investigated by molecular docking methods. Molecular docking is utilized more frequently as a method in drug development as more protein structures are discovered experimentally using X-ray crystallography or Nuclear Magnetic Resonance (NMR) spectroscopy. It also becomes possible for proteins whose structures are unknown to dock to homology-modeled targets [7]. For subsequent lead optimization procedures, the druggability of the compounds and their specificity against a certain target can be determined using the docking techniques.

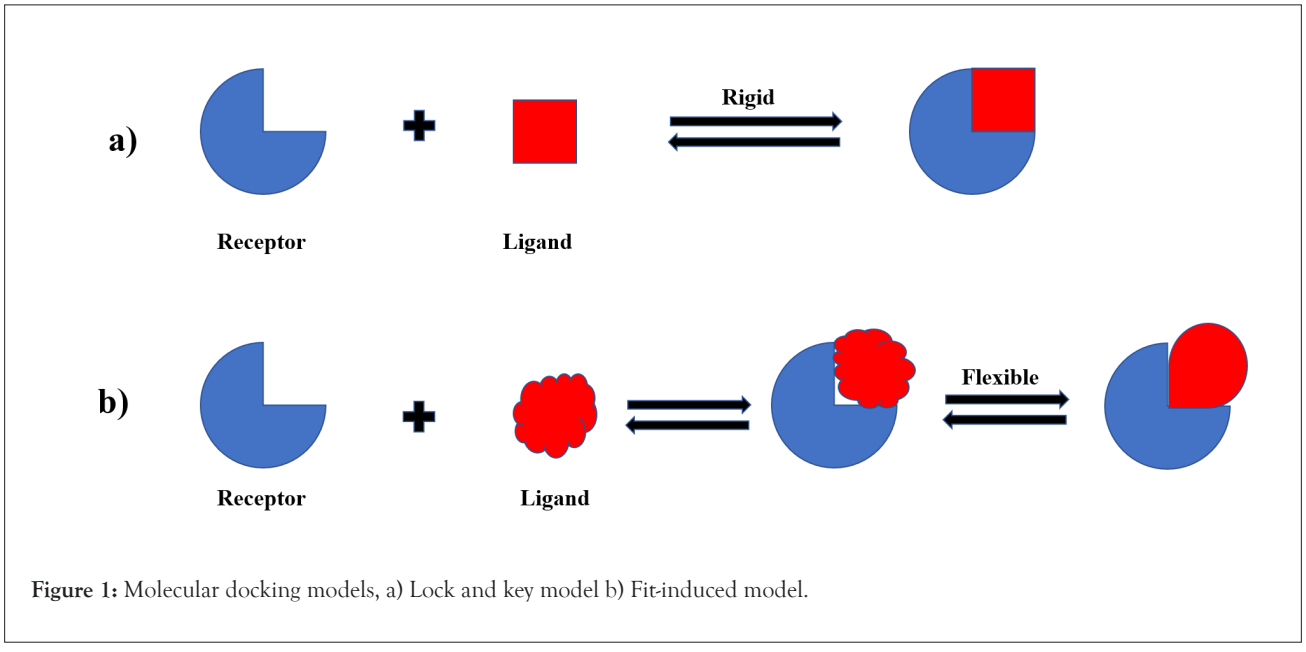

Figure 1: Molecular docking models, a) Lock and key model b) Fit-induced model.

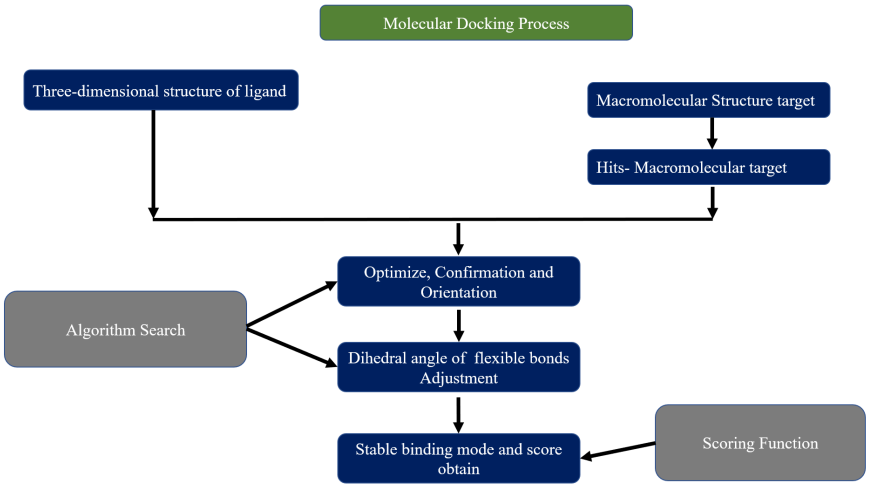

Figure 2: Molecular docking process.

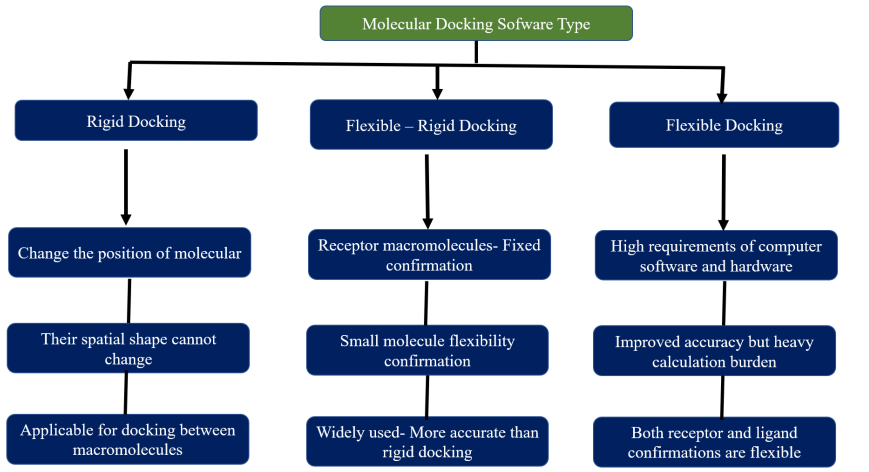

Figure 3: Molecular docking software type.

Use cases for molecular docking

To find the lead compound and the hit compound *via* virtual screening: Virtual screening has significantly increased screening efficiency over traditional screening by locating the lead chemical and hit compound from molecular databases in accordance with the scoring algorithm [8].

Virtual screening applications are frequently employed. Notably, the integrated approach thrives swiftly because to the exponential rise of high-throughput, high performance computing, machine learning, and deep learning approach [9-13]. For instance, Pereira et al. deep's learning approach was used in virtual screening to construct distributed vector representations of protein-ligand complexes by extracting pertinent features from molecular docking data. Another suggestion was made by Pyzerknapp et al. for virtual high-throughput screening [14].

Prediction of targets' potential

In order to dock with the same receptor, the aforementioned methods all use general docking techniques that use different ligands from the database. The currently used reverse docking approach is distinct from them, though. Figure 3 was used in this article to explain the reverse docking procedure [9,15]. By using a single small-molecule ligand as the probe to dock with various receptors to find potential binding holes, the reverse docking approach identifies novel targets [16,17]. The probable targets of a medicine can be predicted in this fashion. Finally, we thought that studying pertinent mechanisms of action or side effect profiles using structural biology analysis, such as the pocket analysis, could greatly aid in the development of novel drugs [6,18,19].

Molecular docking is more and more taken into account for lead discovery as the structures of more and more proteins and nucleic acids become known. Recent research takes into account the improvement of docking screens' hit rates and the precision of docking structure forecasts. As more experimentally defined protein structures are discovered, more proteins can be docked against homology-modeled targets.

One important molecular docking statistic is the enrichment of ligands among top-ranking hits. Decoys should be physically similar to ligands in order to prevent bias and ensure that enrichment is more than just the separation of superficial features, but chemically different from them in order to make it less likely that they are binders. A Directory of Usable Decoys (DUD) with 2950 ligands

for 40 different targets has been put together by us. A database of 98266 compounds is produced by the 36 decoy molecules that each ligand contains, which are physically identical but topologically distinct. With uncorrected databases like the MDDR, enrichment was at least half a log better for the majority of targets than with DUD, showing bias in the latter. These calculations also enabled 40 × 40 cross-docking, allowing specificity metric for the docking screens by comparing the enrichments of each ligand set for each of the 40 targets.

DISCUSSION AND CONCLUSION

The molecular docking score of inactive molecules will be wrongly so high that implies false positive due to the approximation capacity of the scoring function and inadequate collection of conformations. Additionally, the molecular docking score will be anomalous if the physical properties of the actual chemical and the compound in the database differ noticeably. As a result, in order to assess the accuracy of the prediction of affinity, one must either employ retrospective verification or take into consideration thermodynamic properties. Additionally, the molecular docking result cannot accurately reflect the state of the actual docking since the three-dimensional structure will have changed conformation due to being removed from its original context.

We are enhancing the conformational search method in the distant future by incorporating more flexible bonds, solvent conditions, and current biological data mining technologies into account. In general, we think that by improving the scoring function and modernizing the pertinent search algorithms, the molecular docking technique will develop into such a dependable drug-design tool that integrates the large amount of biological data.

DECLARATIONS

Consent for publication

Nil

AVAILABILITY OF DATA AND MATERIAL

Not Applicable.

AUTHOR'S CONTRIBUTIONS

All the authors have contributed to the review work and preparation of the final manuscript

CONFLICT OF INTERESTS

All the authors do not have any possible conflicts of interest

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ETHICAL DECLARATION

No animal or human subjects were used during the preparation of this manuscript.

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REFERENCES

1. Morris GM, Lim-Wilby M. Molecular docking. Methods Mol Biol. 2008;443:365-382.
2. Pagadala NS, Syed K, Tuszynski J. Software for molecular docking: A review. Biophys Rev. 2017;9(2):91-102.
3. Dias R, de Azevedo J, Walter F. Molecular docking algorithms. Curr Drug Targets. 2008;9(12):1040-1047.
4. Fan J, Fu A, Zhang L. Progress in molecular docking. Quant Biol. 2019;7(2):83-89.
5. Talyzina A, Sidorov-Biryukov D, Podshivalov D, Agapova J, Rakitina T, Timofeev V. Molecular docking and molecular dynamics studies of the novel hu protein DNA binding ability inhibitors. Insights into the inhibition mechanism and selectivity. 3rd Kazan Summer School on Chemoinformatics. 2017.
6. Tripathi A, Misra KJ. Molecular docking: A structure-based drug designing approach. JSM Chemistry. 2017;5(2):1042-1047.
7. Agarwal S, Mehrotra RJ. An overview of molecular docking. JSM Chemistry. 2016;4(2):1024-1028.
8. Stanzione F, Giangreco I, Cole JC. Use of molecular docking computational tools in drug discovery. Prog Med Chem. 2021;60:273-343.
9. Yuriev E, Holien J, Ramsland PA. Improvements, trends, and new ideas in molecular docking: 2012–2013 in review. J Mol Recognit. 2015;28(10):581-604.
10. Dong D, Xu Z, Zhong W, Peng S. Parallelization of molecular docking: a review. Curr Top Med Chem. 2018;18(12):1015-1028.
11. Andrusier N, Nussinov R, Wolfson HJ. FireDock: Fast interaction refinement in molecular docking. Proteins. 2007;69(1):139-1359.
12. Saikia S, Bordoloi M. Molecular docking: challenges, advances and its use in drug discovery perspective. Curr Drug Targets. 2019;20(5):501-521.
13. Fan M, Wang J, Jiang H, Feng Y, Mahdavi M, Madduri K, et al. Gpu-accelerated flexible molecular docking. J Phys Chem B. 2021;125(4):1049-1060.
14. Pyzer-Knapp EO. Using bayesian optimization to accelerate virtual screening for the discovery of therapeutics appropriate for repurposing for covid-19. Quant Biol. 2020.
15. Pinzi L, Rastelli G. Molecular docking: Shifting paradigms in drug discovery. Int J Mol Sci. 2019;20(18):4331.
16. Aamir M, Singh VK, Dubey MK, Meena M, Kashyap SP, Katari SK, et al. In silico prediction, characterization, molecular docking, and dynamic studies on fungal SDRs as novel targets for searching potential fungicides against Fusarium wilt in tomato. Front Pharmacol. 2018;9:1038.
17. Skariyachan S, Gopal D, Chakrabarti S, Kempanna P, Uttarkar A, Muddebihalkar AG, et al. Structural and molecular basis of the interaction mechanism of selected drugs towards multiple targets of SARS-CoV-2 by molecular docking and dynamic simulation studies-deciphering the scope of repurposed drugs. Comput Biol Med. 2020;126:104054.
18. Han L, Wei X-X, Zheng Y-J, Zhang L-L, Wang X-M, Yang H-Y, et al. Potential mechanism prediction of Cold-Damp Plague Formula against COVID-19 via network pharmacology analysis and molecular docking. Chin Med. 2020;15(1):1-16.
19. Parvez MSA, Karim MA, Hasan M, Jaman J, Karim Z, Tahsin T, et al. Prediction of potential inhibitors for RNA-dependent RNA polymerase of SARS-CoV-2 using comprehensive drug repurposing and molecular docking approach. Int J Biol Macromol. 2020;163:1787-97.