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A COMPREHENSIVE REVIEW ON MOLECULAR DOCKING & ITS SOFTWARE

Author's Name- Guru Prasad Gupta*, Pandey Hardik Anil, Piyush Singh, Swapna Sahu, Smita Verma

Nirmala Devi Pharmacy College, Nayansand, Gaurabadshahpur, Jaunpur

Abstract:

Drug development, structural biology, and studies of biomolecular connections employ the operational computing approach known as molecular docking.
To distinguish between low-affinity as well as high-affinity ligands were and find drugs of interest that could move forward for additional experimental validation, a scoring system is essential when comparing and evaluating different ligand-receptor form to binding energy values using a computational tool called Molecular Docking. Molecular docking is also widely employed in a number of other Drug Progress applications, including virtual testing, lead improvement, as well as reasonable structure-based development of drugs. Molecular docking has seen a proliferation of methods developed expressly to tackle the unique challenges of drug development based on structure as well as bimolecular interaction investigations.

Keywords: CADD, molecular docking, types of molecular docking, docking mechanism, software.

Introduction:

In the discipline of computer-assisted drug design (CADD), several computational tools are employed to identify, generate, and develop new medicinal compounds. CADD makes it feasible to improve active ligands in discover novel drugs, and investigate processes in biology at the basic level [1]. Furthermore, the application fields of CADD techniques are growing as advances in physiological as well as pharmacological data, data processing capabilities, drug targets identification, and data availability are made [2].

Molecular docking is an ever-evolving and dynamic discipline that enables us to comprehend the recognition of molecules. Molecule docking is an approach that will be increasingly important as technology develops and our knowledge of biological systems expands, both in terms of finding new therapies and comprehending intricate molecular interactions. Being able to navigate through each of the major stages with ability and choose the right model, software, docking type, and strategy for each research aim separately is essential for the full potential implementation of this computational approach. Molecular docking has to have a bright future because of the therapeutic options that are now accessible and the wider variety of productive knowledge that may lead to the most complex molecular performance involved in the maintenance of life itself.

For both academics along with pharmaceutical scientists, this computational approach that mimics interaction between ligand and receptor holds great promise. Its ability to speed up drug discovery and drastically cut down on the expenses and duration of trial screening makes it of utmost importance. The scientific field of molecular docking is showing promise for the future. With advancements in computational methods and growing comprehension of biological processes, this approach is bound to develop and broaden. The accuracy and prediction potential of molecular docking will be enhanced by the use of machine learning, artificial intelligence

(AI), and dynamical factors such as solvation during the Finally, the synergy between the two fields is shown in molecular docking.

Molecular docking is a critical technique that is going to continue to help us find novel medications as well treatments that will lead to a healthier and more energized the years to come. Its influence additionally beyond lab walls as well, changing every aspect of medicinal products and medical innovation. Its immense and limitless promise ensures that it will remain relevant in the continually changing field of pharmaceutical research. It represents the pairing of computational power alongside biological information, providing the opportunity for unlocking doors to possible treatments.

Molecular Docking:

Molecular reorganization to maximize interaction between a chemical and a receptor is called docking. A cell experiences this process, as is illustrated in Figure 1, in a matter of a few seconds, where molecules create a complex that is stable through covalent bonding.

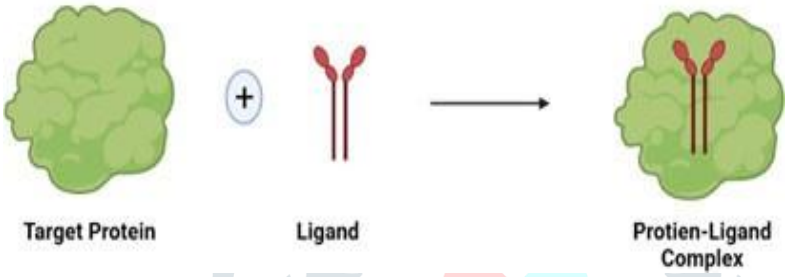

Fig.1: Molecular Docking

TYPES OF DOCKING:

Two different kinds of docking exist:

1. Rigid Docking
2. Flexible Docking.

RIGID DOCKING:

Assuming that the compounds are rigid, we are trying to find a technique to rearrange one of the compounds in three dimensions so that, in the context of a scoring system, it best fits the other compounds. The ligand can take on its shape in the presence or absence of receptor binding activity.

FLEXIBLE DOCKING:

We use transformation in conjunction with molecular flexibility to determine confirmations for the presence of the ligand and receptor molecules in the complex depicted in Figure 4.

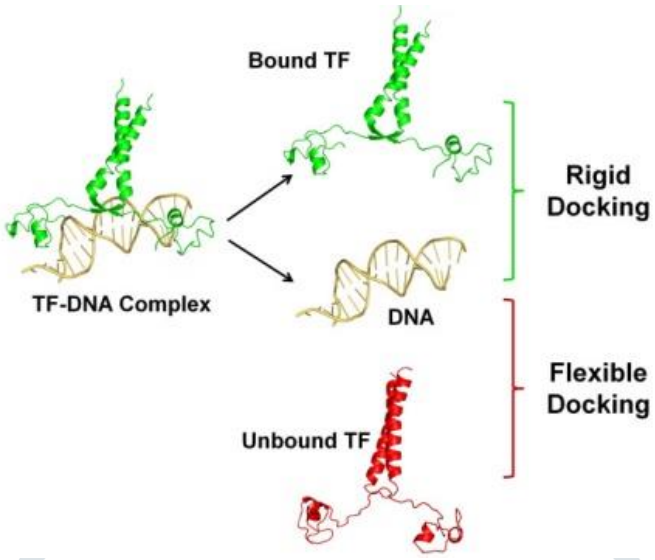

Fig. 2: Structural Images of Rigid docking & flexible docking

MECHANISM OF DOCKING

1) In order to execute a simulated docking screen, the protein of interest must first be organized. Usually, a biophysical method such as NMR crystallography or x-ray is used to determine the structure. This protein arrangement and a folder containing ligands feed a docking agenda.[11]
2) For a docking program to be successful, two procedures are required: the search algorithm and the scoring function. The investigate space is made up of the protein associated with ligand in all potential conformations and orientations [12]. With current computing capabilities, the research space cannot be thoroughly explored. At a predefined level of granularity, this would contain a list of all possible molecular distortions as well as all possible translational and rotational orientations of the ligand with respect to the protein.
3) The majority of docking programs now in use simulate a flexible ligand, and several are trying to mimic a flexible protein receptor [13].
4) Molecular docking is a process that was used to study the intermolecular communication between two molecules in insilica. The protein receptor serves as the macromolecule in this advancement. The Ligand is the tiny particle.
5) A molecule with the ability to function as an inhibitor [14].

MAJOR STEPS INVOLVED IN MECHANICS OF MOLECULAR DOCKING:

Thus, the following stages are involved in the Docking process:

STEP I – PREPARATION OF PROTEIN:

The Protein Data Bank (PDB) must be consulted in order to obtain the protein's three-dimensional structure, which must then be pre-processed. This should form side chains, stabilize the charges, allow the water molecules in the cavity to be severed, and considerably replenish the lost residue, depending on the available parameters.

STEP II – ACTIVE SITE PREDICTION:

The prediction of the active site of a protein must come first in the manufacturing process. Only the problematic active site needs to be chosen out of the many active sites in the receptor strength. Heteroatoms and water molecules are often unaffected if they are present [15,16].

STEP III – PREPARATION OF LIGAND:

Ligands may be found in many places, such as ZINC and Pub Chem, or they can be drawn using a chemical sketching tool. It is best to use LIPINSKY'S RULE OF 5 when selecting the ligand. Differentiating between chemicals that are drug-like and non-drug-like is made easier by the Lipinski Rule of Five. The computer-aided drug design and detection method is known as the CADD method. For compounds that fulfill two or more of the conforming conditions, it gives a high possibility of success or failure due to pharmacological similarities.

In order to select a ligand, let the-

Lipinsky's rule

(1) Five hydrogen bond donors in less quantity;
(2) Ten hydrogen bond acceptors in less quantity
(3) A molecular mass of 500 Da or less
(4) High lipophilicity (logarithmic not exceeding 5)
(5) The ideal range for molar refractivity is 40–130 [17].

STEP IV DOCKING:

The interactions are investigated after docking the ligand adjacent to the protein [11].

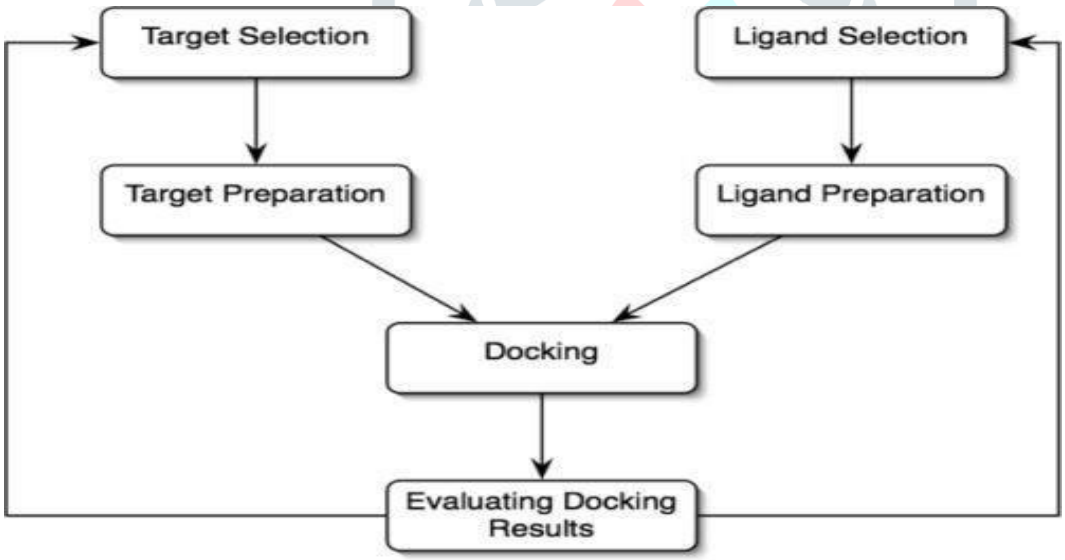

Fig.3: Flow chart for evaluating docking

MOLECULAR DOCKING PROGRAM DESIGN:

The docking of molecules has become an indispensable tool in many drug development activities, particularly in the online assessment of polyphenols or nutraceuticals are as potential treatment agents7. Docking calculations are still being refined today, having been developed for the very first time in the mid-1980s by Irwin Kuntz and colleagues of the State of California. The capability of an enzyme can be predicted and its natural substrates identified with the aid of recent advancements in docking techniques36. By focusing the search for feasible substrates and interaction types on the area where the substance relevant is discovered to belong to a certain superfamily, complicated proteins may be correctly predicted37. Techniques for diligently assigning docked components a ranking: We rate the docked molecules using many frameworks and approaches. The last section emphasizes the often utilized.

DOCK 3.5.X:

The program's basic tenet is that enzymes catalyze reactions by limiting the shift to the state that what the substrate finds most beneficial. Moreover, change state-matching bonding molecules should produce a larger signal then docking substrates since the hydrolase fam converts the protein to preserve its stiffness38. The program Glide makes it easier to arrange potential substrates in a more focused way by recognizing the enzymes that belong to specific subgroups of the enolase superfamily. Moreover, the docked complex's scoring capacity is increased and the receptor's chain segments are allowed to migrate when it is rescored and adjusted39.

HIGHLIGHTS OF MOLECULAR DOCKING SOFTWARE:

Numerous docking applications are available; this section covers some of the most well-liked ones.

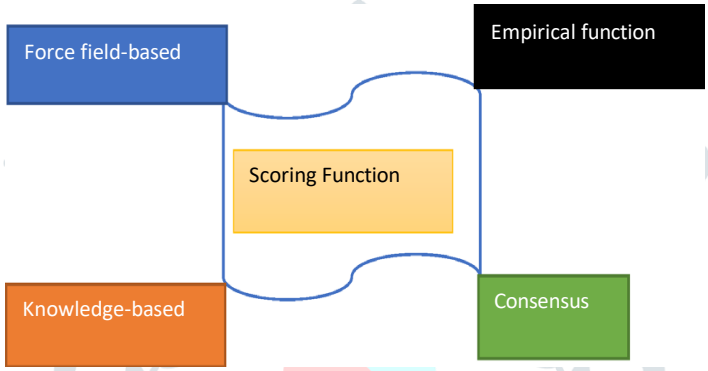

Fig. 4: Classes of scoring function mechanisms.

DOCK: http://dock.compbio.ucsf.edu.

Software for molecular docking was created by the UCSF Chimera group. Small compounds may be easily docked into receptor binding sites using this straightforward approach. The ligand-receptor binding affinity is assessed by Dock using a grid-based technique. It also includes grading techniques to assign points for the positions taken throughout the docking process. PDB, molasses2, and SDF are some of the input file formats that the dock supports. You can go to the dock with this.

AUTODOCK:

Autodock, a popular molecular docking program, evolved at the Scripps Research Institute. The program may dock in an inflexible or flexible manner along with is freely available and open-source. To enhance the dispersion of ligands inside a receptor bound area, Autodock utilizes a Lamarckian evolutionary method. A number of grading systems have been included to assess how well the ligands bind to the target. Numerous file formats, which includes as PDB, MOL2, and SDF, are supported by Autodock. You may visit Auto Dock at http://autodock.scripps.edu.

ARGUS LAB 4.0.1.:

Pacific Northwestern National University in the USA hosts Argus laboratory, a molecular modeling tool built by Department of Energy researcher Mark Thomson using a mixture of quantum mechanical and traditional mechanics procedures to mimic solvent effects. Among the many tasks this application may perform includes modeling molecules, developing medications, and producing photographs. Argus Lab is available at http://www.arguslab.com.

GENETIC OPTIMIZATION FOR LIGAND DOCKING (GOLDTM).:

A program for protein-ligand docking called GOLD has a number of unique characteristics. User-defined assessment techniques are used, which may be adjusted to account for both side chain and vertebral chain

flexibility in calculations. Convergent and non-conforming contact data serve as the foundation for the energy functions. Additionally, a variety of docking methods are accessible, such as the removal of crystallographic molecules of water from the ligand attachment site. Moreover, if metal atoms are properly described in the amino acid data file, GOLD can manage them automatically. Finally, the companion tools SILVERTM or GoldMineTM allow for rapid analysis and post-processing of computer-generated high-throughput examination data.

MOLDOCK:

MolSoft LLC40 created a molecular docking program called MolDock. This docking method is fast and effective for placing tiny compounds into receptor-binding sites. MolDock assesses the affinity of ligand-receptor binding using the rapid Fourier transform (FFT) approach. Moreover, it features a scoring system that considers van der Waals forces, electrostatic interactions, and the complementary qualities of form among the substance in question and the receptor. MolDock is capable of handling many source file formats, which includes as PDB, molasses2, and SDF. Go to https://www.molsoft.com/about.html to utilize it instead.

DISCOVERY STUDIO:

BIOVIA developed a suite of tools known as the Dassault Software Discovery Studio. It is used for molecular simulations and modeling. Many tools are available for molecular docking, virtual screening, protein modeling, and analysis of molecular dynamics simulations. Molecular docking is used to predict the docking process and assess the strength of the interaction among the protein target and the ligand, or small molecule. To provide a range of potential ligand binding postures and rank those according to their predicted binding power, the Discovery Studios employs a number of parking algorithms, including CDOCKER, GOLD, and Lib-Dock.

CHIMERA:

Users may see, examine, analyze model molecular structures with Chimera, a software developed by the School of Medicine of California, San Francisco. It provides a range of tools to see the three-dimensional configurations of proteins, nucleic acids, also tiny compounds or to execute molecular docking simulations. Target the ligand and protein are prepared for docking simulations using Chimera's "Dock Prep" docking molecular module. Its tools may be used to control the ligand's placement inside the protein's binding domain by adding hydrogens, assigning charges, and forming molecular surfaces.
In addition to displaying the poses, Chimera offers analysis tools to analyze docking data, including the capacity to compute binding energies and create association maps between antagonists and protein residues.

Program	Properties
AutoDock	Rigid body-flexible docking. It is used with Autodock tools. Calculation of the grid maps is automatic.
AutoDock Vina	Rigid body-flexible docking. It applies recurring local search global optimization. It is faster than AutoDock. It provides improved binding affinity prediction with a new scoring function.
Dock	Flexible docking. It is widely applied to flexible targets and flexible ligands.
LeDock	Flexible docking. Since it gives results fastly with high accuracy, its use in virtual screening is recommended.
FlexX	Rigid body-flexible docking. It can be utilized in virtual screening.
Glide	Ligands are flexible in this docking. To decrease the software search range, it uses information about the area. It has XP (extra precision), SP (standard precision), and highly efficient virtual screening modes.
GOLD	Flexible docking. The evaluation of its accuracy and reliability appeared to give good results.
Plants	It has a good balance between usage and efficiency. It allows calculating water exchange.
ICM	It gives the facility of both ligand-protein and protein-protein docking. It provides an ICM-Pro interface that makes the docking process easy.
MOE	It has a good interface and intuitive aspect. It also consists of other tools that are used in protein and ligand preparation.
Surflex	For predocking minimization and post docking optimization, it uses procedures. It makes use of morphologic similarity functions and fast pose production techniques.
LibDock	LibDock depends on the matching of the polar and apolar binding site features of the target-ligand complex. As it is driven by matching features rather than a molecular mechanics force field score, its performance attracts interest.
CDOCKER	CDOCKER (CHARMM based DOCKER) provides the advantages of full ligand flexibility, CHARMM force field, and reasonable computation time. Flexible docking.
Fitted	Fitted can deal with both macromolecule flexibility and the presence of bridging water molecules.
Molegro	The program Molegro Virtual Docker (MVD) has four search algorithms and four native scoring functions. MVD provides the opportunity of performing detailed statistical analysis of docking results when it is integrated with other programs.
Fred/Hybrid	Fred uses the target structure solely to pose and score ligands. On the other hand, Hybrid uses both the target and ligand structures to pose and score ligands. Hybrid has the ability to use multiple conformations of the target.

Table1: Molecular docking programs.

APPROACH FOR MOLECULAR DOCKING:

MONTECARLO APPROACH:

The Monte Carlo method was applied to the molecular pairing problem, determining which direction molecules would prefer to face each other while joining to form a stable structure [45]. Monte Carlo (MC) techniques use rigid-body translating, covalent rotation, or rotations at a site of action to produce ligand randomized conformation. This modification modifies how a conformation is taught and evaluated using an arsenal of energy-based standards. If all the conditions are met, it will be stored and utilized to create the next verification [46].

METROPOLIS CRITERIA:

The Metropolis criteria evaluates the need of maintaining an updated configuration. This criterion states that a new approach is adopted right away if it outperforms the old one.[47].

FRAGMENT BASED METHOD:

The fragment foundation technique, in short, involves dividing the ligand particle into separate protons or breaks down, docking each one, then reconnecting them. One can replicate the form of multiple possible attaching configurations by latching the components one at moment on targets. This method successfully avoids the enormous degree with liberty (DOF) [48].

DISTANCE GEOMETRY:

Both intra- and between-molecular measurements can be used to display a wide range of sequence characteristics. The fare geometry architecture allows these separations to be specified and suitable structures in three dimensions to be computed. Multiple attempts had been made to use distance geometry techniques to illustrate particles of various sizes, including tiny compounds, peptides, and macromolecules [49].

MATCHING APPROACH:

Complementarity is important, as the above strategies show. The arrangement of the ligand-receptor relationship may need to be changed if a ligand atom takes up a prominent position at the site. From certain perspectives, the ligand and Protein might be seen as interdependent structures with complimentary functions. Finding the ideal orientation for docking is made easier by describing the complementary nature of the target as well as ligand particles in the sense of form matching. [50].

LIGAND FIT APPROACH:

Given its speed and accuracy, "ligand fit" refers to the technique of dock ligands of small molecules onto polypeptide sites with activity while taking form complementarity into consideration. The The compound Fit docking method involves two primary stages:

(a) cavity searching to locate and choose the target amino acids region that serves as the docking active site, and

(b) docking antagonists with the selected location. (51).

Announce a comparison.

This method seeks to assess the biological geometries and pharmacological comparability of the components involved in a given interaction [52].

INVERSE DOCKING:

The automated inversion docking method can be used to connect a specific small molecule of interest to a group of receptor structures. Utilizing this technique can help identify novel chemical targeting within a related receptor family or identify distinct biological targets that could be targets for medications that are currently on the market [53]. Additionally, the technique can be used to create a digital selectivity profile to demonstrate the inhibitors' promiscuity or forecast the pharmacological profile of a drug [54].

We demonstrate 'one ligand-many targets' using an alternative docking method of computation that is structure-based.[55]. The ligand's predicted adherence (docking scores) is used to rank the listing of possible proteins to target that the reversed method produces [56].

BLIND DOCKING:
When a chemical compound gets docked onto an amino acid's whole surface without first understanding its targeted binding pocket, the process is known as blind docking.[57].

APPLICATION:
An enzyme may be activated or inhibited as a result of the adsorption contact between a small molecule mediator and an enzyme protein. If the amino acids is a receptor in order then ligand binding can result in the production of a stimulant or antagonist. Docking is mostly used in the drug design sector. Given that most drugs are composed of small compounds of chemicals, docking has the following applications:

HIT IDENTIFICATION:
Large datasets of potential medications may be rapidly screened in silico to find compounds that are likely to bind to proteins and attract attention by using a docking collective with a scoring function [26].

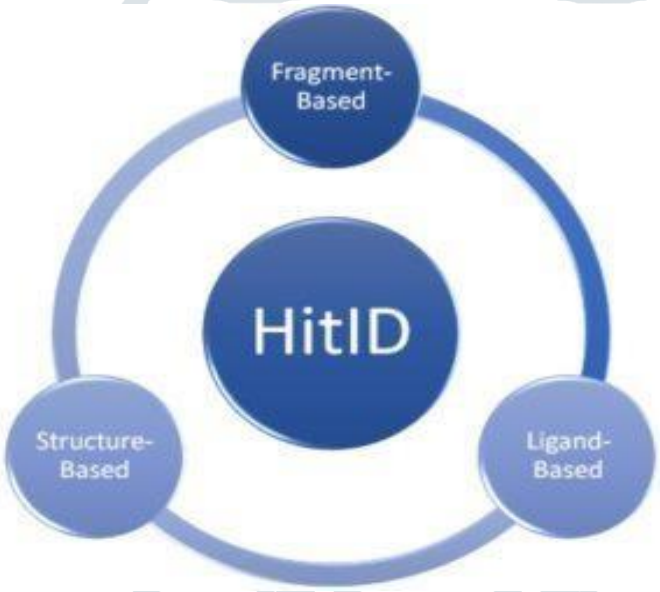

Fig.5. Hit identification

LEAD OPTIMIZATION:
Docking, also known as the binding mode or posture, can be used to determine the direction and location of a ligand's binding to a protein. This change might be used to create stronger, more concentrated analogues [27].

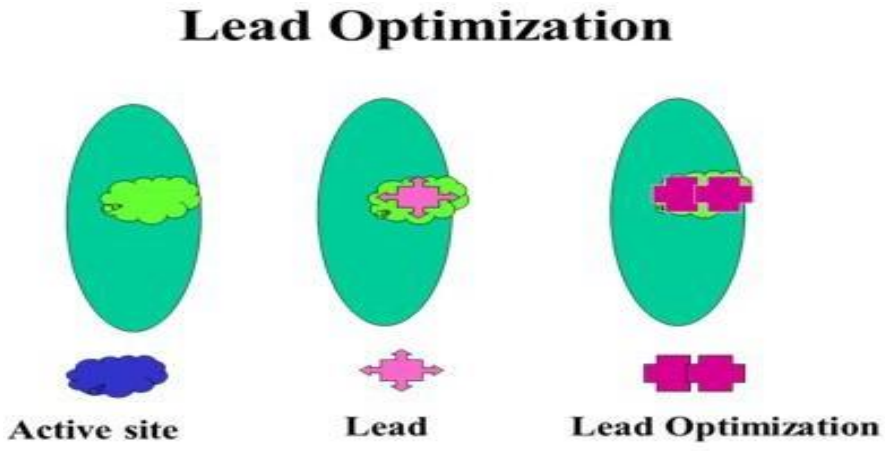

Fig.6. Lead optimization

Bioremediation:
The process of molecular docking is utilized in the bioremediation to forecast a tiny molecule's attraction for binding to the organisms that break down contaminants in the environment. By assisting in the creation of these enzymatic' activators or inhibitors, anchoring can improve the effectiveness of bioremediation. [30]

Remediation:
The degradation of certain toxins by enzymes may be additionally predicted via protein-ligand docking. With the aid of this instrument, you may locate the ideal spot and obtain the most potent medication.[31] Protein identities and modes of activity can be ascertained with the support of molecular docking techniques. The relationships between various proteins can also be ascertained using it. Filtering molecules efficiently is the remediation method's application.[32]

ADMET prediction:

The ADMET, which stands (absorption, transportation, metabolism, excretion, and toxicity) characteristics of tiny drugs can also be predicted via docking. It is possible to use the expected ADMET attributes to filter out compounds with undesired qualities early in the process of developing drugs.[3] The Schrödinger Suite, GOLD (Genetic Optimization with Ligand The docking), Glide, and AutoDock Vina are a few noteworthy instances. These computer programs offer sophisticated methods and computational techniques for successful models of ligand-receptor docking, which enable the determination of possible therapeutic targets and the calculation of binding affinities. Additionally, they have ADMET prediction modules that enable assessment of the drug's behavior with respect to its likely poisoning, metabolism, excretion, redistribution in the bloodstream, and absorption.

Molecular dynamics simulation:
Molecular docking in combination with kinetic modeling can be utilized to examine the kinetic activity of complexes consisting of protein and ligand. The long-term stability of the product and the modifications in conformation that follow ligand binding can both be better understood by simulations. Molecular docking and dynamics modeling are combined in a number of programs. A few well-known programs are Vina, AutoDock, Glide, as well as GOLD. They allow one to explore protein-ligand interactions throughout time and analyze their dynamic behavior by performing simulations using molecular dynamics in in addition to performing molecular docking.

Clarification of structure:
The structure of molecules whose structures are unknown can also be ascertained using molecular docking technique. Debugging can be employed to foresee the binding mechanism of small molecules to peptides, which can subsequently be used to build a protein topology model. To precisely estimate a proteins structure, the developed model can then be enhanced using data from experiments.[34]

CONCLUSION:

Our comprehension of the recognition of molecules is made possible by the exciting and expanding field of molecular docking. Discovering new treatments and understanding complex molecular interactions will need the application of molecule docking, which will become more and more crucial as technology advances and our understanding of the body grows. To properly utilize this computational approach, it is necessary to be able to traverse through the key steps with care along with choose the right model, applications, mooring type, and computational method for each unique study objective. With possible medicinal applications and a deeper understanding of the intricate molecular dance that underpins life itself, the prospect of docking with molecules appears bright. With the introduction of molecular docking techniques, the landscape of drug discovery has greatly evolved.

References:

1) Shoichet BK, Mcgovern SL, Wei B, Irwin JJ. Lead discovery using molecular docking. Curr Opin Chem Biol . 2002;6(4):439–85. doi:10.1016/s1367-5931(02)00339-3.
2) Huang N, Shoichet BK, Irwin JJ. Benchmarking sets for Molecular Docking. J Med Chem. 2006;49(23):6789–801. doi:10.1021/jm0608356.
3) Avinash R, Veerabhadra Rao A, et al. A review on molecular docking, Novel tool in drug design and analysis, Journal of Harmonized Research in Pharmacy. 2013; 2(4):215-218.
4) Available:https://link.springer.com/protocol/ 10.1007/978-1-59745-177-219
5) Mukesh B, Rakesh K. Molecular docking: a review, International journal of ayurveda & pharmacy. 2011;2(6):1746-1750.
6) Kitchen D, De cornez H, Furr J, Bajorath J, et al. Docking and scoring in virtual screening for drug discovery: methods and applications. International Journal of Pharma and Bioscience. 2004; 3(11):95-97.
7) McMartin C, Bohacek RS, et al. QXP: Powerful, Rapid Computer Algorithms for Structure-based Drug Design. J Comput Aid. Mol. Des. 1997;11:333-344.15.
8) Schnecke V, Kuhn LA, et al. Virtual Screening with Solvation and Ligandinduced Complementarity, Perspect. Drug Discov. 2000;20:171- 190.16.
9) Jain AN, et al. Surflex: Fully Automatic Flexible Molecular Docking Using a Molecular Similarity-Based Search Engine. J Med Chem. 2003;46: 499-511.17.
10) Kitchen, D. B., Decornez, H., Furr, J. R. & Bajorath, J. Docking and scoring in virtual screening for drug discovery: Methods and applications. Natl. Rev. Drug Discov. 3(11), 935–949 (2004).
11) Gohlke, H. & Klebe, G. Approaches to the description and prediction of the binding afnity of small-molecule ligands to macromolecular receptors. Angew. Chem. Int. Ed. 41, 2644–2676 (2002).
12) Noureldeen, A. F. H. et al. Molecular design, spectroscopic, DFT, pharmacological, and molecular docking studies of novel ruthenium(III)–Schif base complex: An inhibitor of progression in HepG2 cells. Int. J. Environ. Res. Public Health 19, 13624 (2022).
13) Xing, D. et al. Insights into protein-ligand interactions: Mechanisms, models, and methods. Int. J. Mol. Sci. 17(2), 144 (2016).
14) Venhorst, J. et al. Homology modeling of rat and human cytochrome P450 2D (CYP2D) isoforms and computational rationalization of experimental ligand-binding specifcities. J. Med. Chem. 46(1), 74–86 (2003).
15) De Azevedo, J. & Filgueira, W. MolDock applied to structure-based virtual screening. Curr. Drug Targets 11(3), 327–334 (2010).
16) Liu, M., & Wang, S. (1999). MCDOCK: a Monte Carlo simulation approach to the molecular docking problem. Journal of computer-aided molecular design, 13, 435-451.
17) Meng, X. Y., Zhang, H. X., Mezei, M., & Cui, M. (2011). Molecular docking: a powerful approach for structure-based drug discovery. Current computer-aided drug design, 7(2), 146-157.
18) Yuriev, E., & Ramsland, P. A. (2013). Latest developments in molecular docking: 2010–2011 in review. Journal of Molecular Recognition, 26(5), 215-239.
19) Liao, J. M., Wang, Y. T., & Lin, C. L. S. (2017). A fragment-based docking simulation for investigating peptide–protein bindings. Physical Chemistry Chemical Physics, 19(16), 10436-10442.
20) Spellmeyer, D. C., Wong, A. K., Bower, M. J., & Blaney, J. M. (1997). Conformational analysis using distance geometry methods. Journal of Molecular Graphics and Modelling, 15(1), 18-36.
21) Burle, S.S., Gupta, K.,Jibhkate, Y.J., Hemke, A.T., Umekar, M.J. (2023). Insights into molecular docking: A comprehensive view. International journal of pharmaceutical chemistry and analysis, 15;10(3):175–84.
22) Venkatachalam, C. M., Jiang, X., Oldfield, T., & Waldman, M. (2003). LigandFit: a novel method for the shape-directed rapid docking of ligands to protein active sites. Journal of Molecular Graphics and Modelling, 21(4), 289-307.
23) Sharma, A., Kunwar, S., Vaishali, V. A., Singh, C., Dev, M., & Sharma, N. C. (2021). Molecular docking: an explanatory approach in structure-based drug designing and discovery. databases, 11, 12.
24) Grinter, S. Z., Liang, Y., Huang, S. Y., Hyder, S. M., & Zou, X. (2011). An inverse docking approach for identifying new potential anti-cancer targets. Journal of Molecular Graphics and Modelling, 29(6), 795-799.

25) Rollinger, J. M. (2009). Accessing target information by virtual parallel screening—the impact on natural product research. Phytochemistry Letters, 2(2), 53-58.
26) Wang, F., Wu, F. X., Li, C. Z., Jia, C. Y., Su, S. W., Hao, G. F., & Yang, G. F. (2019). ACID: a free tool for drug repurposing using consensus inverse docking strategy. Journal of Cheminformatics, 11, 1-11.
27) Furlan, V., Konc, J., & Bren, U. (2018). Inverse molecular docking as a novel approach to study anticarcinogenic and anti-neuroinflammatory effects of curcumin. Molecules, 23(12), 3351.
28) Hassan, N. M., Alhossary, A. A., Mu, Y., & Kwoh, C. K. (2017). Protein-ligand blind docking using QuickVina-W with inter-process spatio-temporal integration. Scientific reports, 7(1), 15451.
29) Availablehttps://www.creativebiolabs.com/drugdiscovery/therapeutics/lead-optimization4.html
30) Available:https://images.app.goo.gl/MaR4gsqoda Rmwv Y18
31) Suresh PS, Kumar A, Kumar R, Singh VP et al. An in silico [correction of in silico] approach to bioremediation: laccase as a case study. J Mol Graph Model. 2008;26(5):8459.
32) Gschwend DA, Good AC, Kuntz ID. Molecular docking towards drugdiscovery. J Mol Recognit. 1996;9(2):175–86. doi:10.1002/(sici)1099-1352(199603)9:2<175::aid-jmr260>3.0.co;2-d.
33) Dhanik, A., McMurray, J. S. & Kavraki, L. E. DINC: A new AutoDock-based protocol for docking large ligands. BMC Struct. Biol. 13(1), S11 (2013).
34) Ferreira, L., dos Santos, R., Oliva, G. & Andricopulo, A. Molecular docking and structure-based drug design strategies. Molecules 20(7), 13384–133421 (2015).