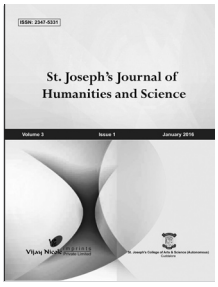
St. Joseph's Journal of Humanities and Science
ISSN: 2347 - 5331
http://sjctnc.edu.in/6107-2/



Molecular Docking: A Novel Approach a Review

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ABSTRACT

Molecular docking studies are using various docking algorithms to analyse the active site of the molecule. It explains the interaction between ligand and receptor with several intermolecular forces which involved. The scoring function and algorithm are the major sections to predict the structure of proteins. There are numerous docking programs and computational methods established to analyse the 3D structure of the protein molecule. Docking studies provides an assortment of most valuable drug design.

Keywords: Algorithm, Molecular Docking, Ligand, Docking score.

1. INTRODUCTION

Molecular docking are computational or bioinformatics approach to predict the favourable site of ligand against receptor (Protein) to make a constant complex, which involves amongst two or more integral molecules after the formation of intermolecular complex. Molecular recognition plays a crucial role in fundamental bimolecular measures such as, drug-nucleic acid interactions, drug-protein and enzyme-substrate. This technique mainly integrates algorithms like molecular dynamics, fragment based search methods, Monte Carlo stimulation [1,2].

Certain interactions such as hydrogen bonding, van der Waals are exhaustive understanding between the ligands and their protein targets to deliver an outline for scheming the expected strength and specificity of potential drug and preferred for pharmacologic agent. Docking studies gives the information of scoring functions, ligand binding position which are also working for the ligand binding affinity. The results are analysed by a scoring method which transforms interacting energy into numerical values termed as the docking score and also calculates the interacting energy. Molecular docking play a very important role in the field of drug discovery and designing [3, 4,5] **(Fig.1)**.

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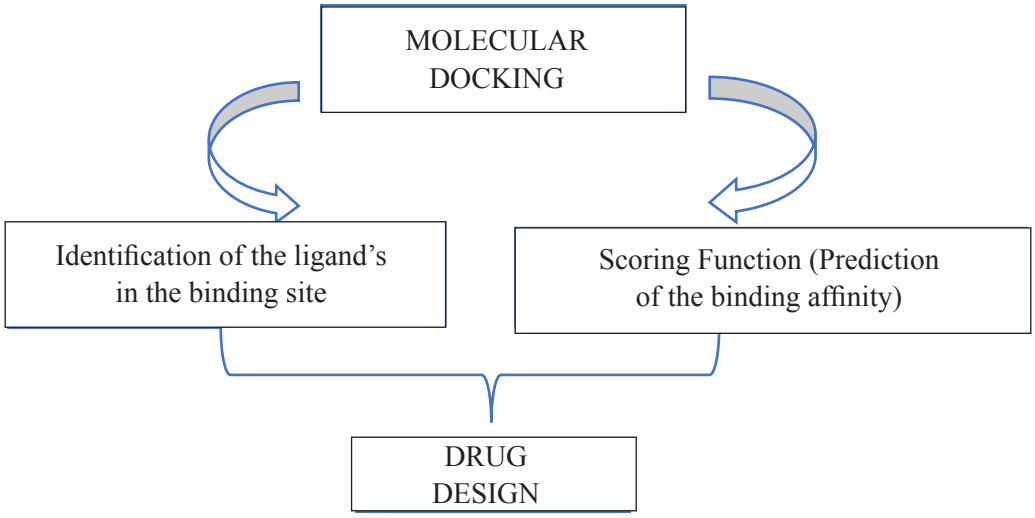

Fig.1 Molecular Docking Involved in Drug Design

2. CLASSIFICATION OF DOCKING

The major categories of docking are protein ligand, protein-protein and nucleic acid-protein. The docking systems are

- **Rigid Docking or Lock and Key–** both the interior geometry of the receptor and ligand is fixed during docking.
- **Flexible Docking or Induced fit -** both the ligand and side chain of the protein is kept stretchy and the protein is calculated by the energy for different conformations of the ligand fitting.
- **Rigid body docking:** both the receptor and small molecule are treated as rigid.
- **Flexible ligand docking:** The receptor is held rigid and the ligand is treated as flexible;
- **Flexible docking:** where both receptor and ligand flexibility is measured. [6,7]

3. TYPES OF INTERACTIONS

The different kinds of interactions are involved in docking studies they are

- **Electrostatic forces** - interactions are charge-charge, charge dipole and dipole-dipole.
- **Electrodynamics forces**-also called as Van der Waals interactions.
- **Steric forces** – can affect chemical reactions and the free energy of a system.
- **Solvent-related forces**–chemical reactions between the solvent and protein or ligand. (hydrophilic interactions and hydrophobic interactions) [8,9]

4. MAJOR SECTIONS INVOLVED IN MOLECULAR DOCKING

There are two major sections involved in molecular docking,

- **Search algorithm** – This algorithm explains about the possible definitive conformations for a given complex like protein-protein, protein-ligand in allocation. It can also compute the energy of the resulting complex and of each individual interaction. There are numerous algorithms useful for docking analysis such as Point complementary, Genetic algorithms, Monte Carlo, Fragment-based methods, Distance geometry methods, Point complementary methods and Systematic searches [10,11].
- **Scoring function** – it is an accurate method to calculate the strength of the binding affinity between two molecules after they docked. Scoring functions have established the strength of additional kinds of intermolecular interactions [12,13]. Scoring is essentially assembled by three different expressions appropriate to docking and drug design:
  - Generated configuration ranking by the docking search.

- Position of dissimilar ligands against protein (virtual screening).
- One or more ligands position against different proteins by their binding

5. MAIN STEPS INVOLVED IN MECHANICS OF MOLECULAR DOCKING

The Docking method comprises the following stages

- **Target/Receptor selection and preparation:** The three dimensional structure of protein should be considered and retrieved from Protein data bank (PDB). The receptor must be biologically active and stable.
- **Active site prediction:** The active site inside the receptor is to be identified. The receptors have numerous active sites but the one which is interested should be selected. Typically the hetero atoms and water molecules are removed if present.
- **Ligand preparation and selection:** Ligands are found from various databases (ZINC, PubChem) or sketched using Chemsketch.
- **Docking:** Measure the interactions when the ligand is docked into the receipt for depending on the greatest fit ligand is selected for production of score.

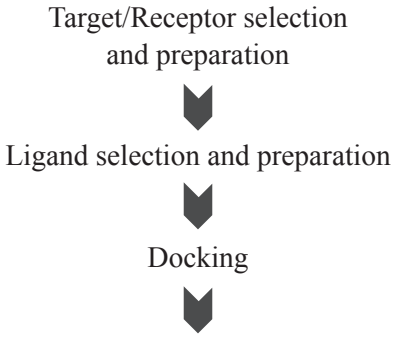

Fig.2 A Basic Stages of DOCKING

6. DOCKING SOFTWARE

Several docking programs are functioning for algorithms and scoring functions [16,17,18]. The docking programmes are accessibled for docking software or tools which are categorised based on the following criteria:

- **Scoring method** - to measure the excellence of docked complexes like knowledge-based approach, force field.
- **Molecular representation**–The way to signify the structures and properties (grid representation, atomic and surface)
- **Searching algorithm -** a well-organized search algorithm resolves, the positions to generate (Monte Carlo, exhaustive search, simulated annealing and genetic algorithms).

The major docking programs used in molecular docking are

- **AUTODOCK** – Scripps Research Institute, USA (autodock.scripps.edu/)
- **GOLD** – University of Cambridge, UK **GRAMM**
- **(Global Range Molecular Matching) Protein docking** – A Centre for Bioinformatics, University of Kansas, USA.
- **Gem Dock (Generic Evolutionary Method for Molecular Docking)** – A tool, developed by Jinn-Moon Yang, a professor of the Institute of Bioinformatics, National Chiao Tung University, Taiwan.
- **Hex Protein Docking** – University of Aberdeen, UK.

7. APPLICATIONS OF MOLECULAR DOCKING

Major applications of molecular docking are in the following important fields,

- Virtual screening (hit identification),
- Drug Discovery (lead optimization),
- Bioremediation,
- Chemical mechanism studies,
- Binding site identification,
- Protein – protein interactions, Enzyme reaction mechanisms,
- Protein engineering [19,20,21]

8. CONCLUSION

In this review, we focused on molecular docking and scoring by the description of several applications. The major goal of molecular docking is to identify explain, and to analyse the structure of intermolecular complex formed between two or more integral molecule. The molecular docking is used in the field of drug designing, therapeutic, pharmacological and various molecular based computational researches.

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