# A Review on Molecular Docking: Novel Tool for Drug Discovery

* Abstract: - the explosion of structural informatics, genomics and proteomic plays a major role in leading the efforts towards modern era drug discovery and development.
* Molecular docking is a structure-based virtual screening (SBVS) that is used to place the computer-generated three-dimensional structures of small molecules into a target structure in a variety with a variety of applications.
* It acts as a vivacious explore domain because of its significance to structure-based drug design (SBDD), lead optimization, Evaluation of Biochemical pathways, in De Novo drug design.
* Introduction: - molecular docking is a method which anticipates the favored orientation of ligand against to make a stable complex.
* Docking is often applied to anticipate the binding orientation of drug candidates against protein targets in order to predict the affinity and activity of the drug.
* The main aim of molecular docking is to computationally simulate the molecular identification process and accomplish an optimized conformation so that the free energy of overall system is minimized.
* CADD (computer Aided Drug Discovery) Entails: -
  + Use of computational ability to streamline drug discovery and development process.
  + Advantage of chemical and biological information about ligand and/or targets to discover and optimize novel drugs.
  + Designing of in-silico filters to get rid of chemical compound with unwanted properties and select the most promising candidates.
  + Identification of novel drug targets and retrieval through database of target protein structures like the protein data bank (PDB) is being used to discover hits.
  + Virtual screening is applied to find out novel drug candidates from various chemical scaffolds by exploring databases.



* Different Types of Interactions: - interactions forces are generally separated into four classes –
  + Electrostatic forces – dipole-dipole, charge-dipole and charge-charge.
  + Electrodynamics forces – Van de Waals interactions.
  + Steric forces – Caused by entropy
  + Solvent-related forces – Hydrogen bond and hydrophobic interactions.
* Molecular Docking



* Molecular docking can be separated into two sections.
* Search algorithm: - the algorithm should create an optimum number of configurations that admit by experimentation method determining binding modes.
* These are some algorithms applied for docking analysis like Point complementary, Monte Carlo, Fragment-based, Genetic algorithm, Systematic searches, Distance geometry.
* Scoring Function: - the scoring function furnishes a mode to rank positioning of ligands proportional to some other.
* The score should correspond directly to the binding affinity of the ligand for the protein, so that the best scoring ligands are the best binders.
* Scoring is actually compiled of three different expressions applicable to docking and drug design:
  + Generated configurations ranking by the docking search.
  + Ranking different ligands against protein (virtual screening).
  + One or more ligands ranking against different proteins by their binding affinity.
* Various types of docking: - the following are the primarily applied method for docking
  + Lock and Key\Rigid Docking-Both the receptor and ligand is maintained fixed and docking is executed.
  + Induced fit\Flexible Docking-In induced fit docking both the ligand and the receptor are conformationally flexible. Every rotation the surface cell occupancy and energy is calculated; later the most optimum pose is selected.
* Major steps involved in mechanics of molecular docking: - molecular docking is the process in which the intermolecular interaction between 2 molecules was studied in In-silico.
* In this process, the Macromolecule is the protein receptor. The micro molecule is the Ligand molecule which can be acted as an inhibitor.
* Step 1- preparation of protein – three-dimensional structure of the Protein should be retrieved afterward the retrieved structure should be pre-processed.
* Step 2 - active site prediction – after protein preparation, the active site of protein should be predicted. The receptor might posses lots of active sites merely the one of the concerns should be picked out.
* Step 3 – preparation of ligand – ligand can be retrieved from several databases, while picking out the ligand the LIPINSKY’S RULE OF 5 should be utilized. The Lipinski rule of 5 assists in discerning amongst non-drug like and drug like candidates.
* For choice of a ligand allowing to the LIPINSKY’S RULE:
  + Less than five hydrogen bond donors
  + Less than ten hydrogen bond acceptors
  + Molecular mass less than 500 Da
  + High lipophilicity (expressed as LogP not over 5)
  + Molar refractivity should be between 40-130
* Step 4 – docking – ligand is docked against the protein and the interaction are analyzed. The scoring function gives score on the basis of best docked ligand complex is picked out.
* Applications of molecular docking: - molecular docking interactions may lead in activation or inhibition of the protein, whereas ligand binding may lead in agonism or antagonism.
* Molecular Docking possibly employed to:
  + Hit Identification (Virtual Screening)
  + Lead Optimization (Drug discovery)
  + Bioremediation
  + Prediction of (Biological activity?)
  + Binding site prediction (Blind docking)
  + De-orphaning of protein
  + Protein – Protein/Nucleic acid interactions
  + Searching for lead structures for protein targets
  + Studies of Structure – function
  + Mechanisms of Enzymatic reactions
  + Protein engineering
* Discussion & Conclusion: - molecular docking provides an array of valuable tools for drug design and analysis.
* Simple visualization of molecules and easy access to structural databases has become essential components on the desktop of the medicinal chemist.



* New algorithms from industry and academia are quickly incorporated into high end packages.
* Public domain packages are becoming more stable and also some of the commercial offerings computers continue to double in speed every year and a half while graphic displays became more sophisticated and intuitive.
* All of these elements make molecular docking an integral part of drug design. And it may continues to extend its role in exciting new techniques such as computational enzymology, genomics, and proteomic search engines.

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