

## Open Tools of Drug Designing for Open Research

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**Abstract:** Drug detection and growth is intense, lengthy and interdisciplinary process. Traditionally, drug discovery was done by amalgamating compounds in a time-utilizing multi-step processes and then they were further investigated for their respective promising candidates. Nowadays in silico methods for drug designing have come into play, which helps in the identification of drug targets using various bioinformatics drug designing tools. They can also be used to analyze the target structures for probable binding site, generate potential molecules, examine their drug likeness, dock particular molecules with the target, rank them in accordance to their binding affinities and further amend the molecules to upgrade their binding characteristics and finally obtain potential candidates for drug discovery. As the structural information of many protein targets become available through X-Ray crystallography, NMR and bioinformatics approaches, there comes an increasing demand for the computer based tools which can recognize and inspect the active sites and suggest potential druggable unit which could specifically bind to these active sites. The major advantages of these bioinformatics drug designing tools is that they are available everywhere on internet, they have decreased support costs, decreased license costs, software integration, easy monitoring and grid calculations. For the above mentioned reasons, we compile in this review 49 online tools which could be beneficial to biotechnologist for in silico drug design.

**Keywords:** Web servers, Standalone, Binding site analysis, Pharmacophore mapping, Receptor-ligand docking.

### Introduction

The drug is a small molecule that initiates or impedes the function of a biomolecule, which in turn concomitants a medicinal protection to the victim. Therefore drug design includes the design of small molecules that interacts with the target. Drug design which depends upon computer modeling approach is usually known as computer-aided drug design (CADD) and the drug design which depends upon the understanding of the three-dimensional structure of the target is known as structure-based drug design. The most commonly used technique for drug designing is structure based drug design in which identifying a suitable target is the basic consideration. Structure based drug design imparts a magnificent platform for the recognition of novel drug targets. The first step carried out by these drug designing software is the analysis of the target site of the desired protein. Once a binding or the targeting site has been identified and analyzed, molecular building blocks or fragments need to be chosen to begin designing full molecules [1]. Structures generated using these software can be complex and difficult to synthesize therefore many packages include a method for analyzing the complexity or synthetic tractability of the designed structure. With the integration of tools and technology we can expect great amount of improvement in terms of drugs availability, cycle time reduction and mainly effectiveness of cost and productivity. Later, the growths were hinged on a conviction of ligand-receptor interactions, their influence on disease procedure,

and the ability to produce such large macromolecular proteins for restorative purposes. Small-molecule drug (SMD) finding, which employs and constructs on organic molecules as beginning materials, is also benefiting from the input of newer technologies such as combinatorial chemistry and high-throughput screening [2]. Drug discovery and expansion are costly and intrincating processes. More than 99% of exploratory compounds ultimately fail or are discarded. Of the chemicals assessed as part of drug discovery and preclinical testing, only a few advance to human clinical trials and are endorsed for marketing. Therefore, the use of online tools or software is important for the biotechnologist for the fast and easy way of prediction of potential drug targets along with their properties. Fig. 1 shows the drug designing technique followed in a standard protocol.

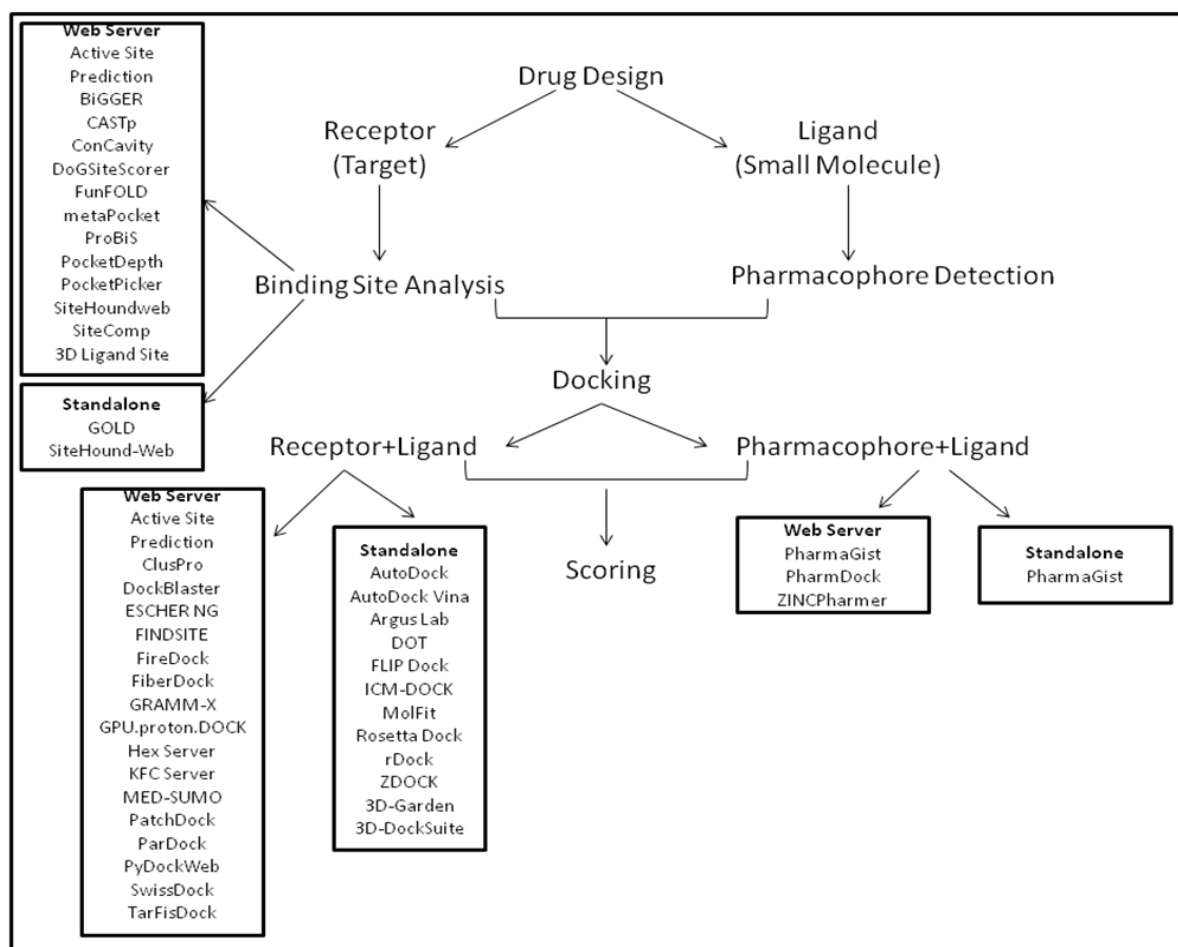


Fig. 1 The flowchart of predicting potential drugs after target-ligand and pharmacophore-ligand interaction

Table 1 shows all the tools for various steps in drug design along with their URL's, server/standalone and automation or manual scripting. Then these potential drug targets could be prepared cost effectively in wet bench and can be preclinical tested and made public.

Table 1. Tools used in various steps of drug design along with their URL's, servers/standalone and automation/manual scripting

<b>Binding site analysis tools</b>			
Active site prediction	<a href="http://www.scfbio-iitd.res.in/dock/ActiveSite.jsp">http://www.scfbio-iitd.res.in/dock/ActiveSite.jsp</a>	Web Server	JAVA
BiGGER	<a href="http://centria.di.fct.unl.pt/~ludi/bigger.html">http://centria.di.fct.unl.pt/~ludi/bigger.html</a>	Web Server	HTML
CASTp	<a href="http://sts.bioe.uic.edu/castp/calculation.php">http://sts.bioe.uic.edu/castp/calculation.php</a>	Web Server	PHP
ConCavity	<a href="http://compbio.cs.princeton.edu/concavity/">http://compbio.cs.princeton.edu/concavity/</a>	Web Server	C++
DoGSiteScorer	<a href="http://dogsite.zbh.uni-hamburg.de/">http://dogsite.zbh.uni-hamburg.de/</a>	Web Server	Automatic
FunFOLD2	<a href="http://www.reading.ac.uk/bioinf/FunFOLD/FunFOLD_form_2_0.html">http://www.reading.ac.uk/bioinf/FunFOLD/FunFOLD_form_2_0.html</a>	Web Server	HTML
GOLD	<a href="http://www.ccdc.cam.ac.uk/Solutions/GoldSuite/Pages/GOLD.aspx">http://www.ccdc.cam.ac.uk/Solutions/GoldSuite/Pages/GOLD.aspx</a>	Standalone	Apache
metaPocket 2.0	<a href="http://projects.biotec.tu-dresden.de/metapocket/">http://projects.biotec.tu-dresden.de/metapocket/</a>	Web Server	Manual
PocketQuery	<a href="http://pocketquery.csb.pitt.edu/">http://pocketquery.csb.pitt.edu/</a>	Web Server	Apache
ProBiS	<a href="http://probis.cmm.ki.si/">http://probis.cmm.ki.si/</a>	Web Server	JAVA
PocketDepth	<a href="http://proline.physics.iisc.ernet.in/pocketdepth/">http://proline.physics.iisc.ernet.in/pocketdepth/</a>	Web server	Manual
PocketPicker	<a href="http://gecco.org.chemie.uni-frankfurt.de/pocketpicker/">http://gecco.org.chemie.uni-frankfurt.de/pocketpicker/</a>	Web server	JAVA
SiteHound-web	<a href="http://scbx.mssm.edu/sitehound/sitehound-web/Input.html">http://scbx.mssm.edu/sitehound/sitehound-web/Input.html</a>	Both web server and standalone	HTML
SiteComp	<a href="http://sitecomp.sanchezlab.org">http://sitecomp.sanchezlab.org</a>	Web Server	Python
3DLigandSite	<a href="http://www.sbg.bio.ic.ac.uk/3dligandsite/">http://www.sbg.bio.ic.ac.uk/3dligandsite/</a>	Web Server	Manual
<b>Pharmacophore docking tools</b>			
PharmaGist	<a href="http://bioinfo3d.cs.tau.ac.il/PharmaGist/">http://bioinfo3d.cs.tau.ac.il/PharmaGist/</a>	Both Web Server and Standalone	Ligand based approach
PharmDock	<a href="http://people.pharmacy.purdue.edu/~mlill/software/pharmdock/">http://people.pharmacy.purdue.edu/~mlill/software/pharmdock/</a>	Web Server	C, Python
ZINCPharmer	<a href="http://zincpharmer.csb.pitt.edu/">http://zincpharmer.csb.pitt.edu/</a>	Web Server	Automatic
<b>Receptor-ligand docking tools</b>			
Active site prediction	<a href="http://www.scfbio-iitd.res.in/dock/ActiveSite.jsp">http://www.scfbio-iitd.res.in/dock/ActiveSite.jsp</a>	Web Server	JAVA
AutoDock	<a href="http://autodock.scripps.edu/">http://autodock.scripps.edu/</a>	Standalone	C++, JAVA
AutoDock Vina	<a href="http://vina.scripps.edu/index.html">http://vina.scripps.edu/index.html</a>	Standalone	C++ , JAVA
Argus Lab	<a href="http://www.arguslab.com/arguslab.com/ArgusLab.html">http://www.arguslab.com/arguslab.com/ArgusLab.html</a>	Standalone	HTML
ClusPro	<a href="http://cluspro.bu.edu/login.php">http://cluspro.bu.edu/login.php</a>	Web server	PHP
DOCK Blaster	<a href="http://blaster.docking.org/">http://blaster.docking.org/</a>	Web server	Automatic
DOT 2.0	<a href="http://www.sdsc.edu/CCMS/DOT/">http://www.sdsc.edu/CCMS/DOT/</a>	Standalone	Automatic
ESCHER NG	<a href="http://users.unimi.it/dl/escherng/index.htm">http://users.unimi.it/dl/escherng/index.htm</a>	Web server	HTML
FINDSITE	<a href="http://cssb.biology.gatech.edu/findsite">http://cssb.biology.gatech.edu/findsite</a>	Web server	Structure based approach
FireDock	<a href="http://bioinfo3d.cs.tau.ac.il/FireDock/">http://bioinfo3d.cs.tau.ac.il/FireDock/</a>	Both Web Server and standalone	HTML
FiberDock	<a href="http://bioinfo3d.cs.tau.ac.il/FiberDock">http://bioinfo3d.cs.tau.ac.il/FiberDock</a>	Both Web Server and standalone	HTML
FLIP Dock	<a href="http://flipdock.scripps.edu/">http://flipdock.scripps.edu/</a>	Standalone	Automatic
GRAMM-X	<a href="http://vakser.bioinformatics.ku.edu/resources/gramm/grammx/">http://vakser.bioinformatics.ku.edu/resources/gramm/grammx/</a>	Web Server	Manual

GPU.proton. DOCK		Web server	Manual
Hex Server	<a href="http://hexserver.loria.fr/">http://hexserver.loria.fr/</a>	Both web server and standalone	PHP
HADDOCK	<a href="http://haddock.science.uu.nl/">http://haddock.science.uu.nl/</a>	Web server	Automatic
ICM-Dock	<a href="http://www.molsoft.com/docking.html">http://www.molsoft.com/docking.html</a>	Standalone	HTML
KFC server	<a href="http://kfc.mitchell-lab.org">http://kfc.mitchell-lab.org</a>	Web Server	Manual
MED-SUMO	<a href="http://medit-pharma.com/index.php?page=working-with-med-sumo">http://medit-pharma.com/index.php?page=working-with-med-sumo</a>	Web server	PHP
MolFit	<a href="http://www.weizmann.ac.il/Chemical_Research_Support/molfit/">http://www.weizmann.ac.il/Chemical_Research_Support/molfit/</a>	Standalone	Automatic
PatchDock	<a href="http://bioinfo3d.cs.tau.ac.il/PatchDock/">http://bioinfo3d.cs.tau.ac.il/PatchDock/</a>	Web Server	Automatic
ParDock	<a href="http://www.scfbio-iitd.res.in/dock/pardock.jsp">http://www.scfbio-iitd.res.in/dock/pardock.jsp</a>	Web Server	JAVA
PyDockWeb	<a href="http://life.bsc.es/servlet/pydock/home/">http://life.bsc.es/servlet/pydock/home/</a>	Web Server	JAVA
RosettaDock	<a href="http://rosettadock.graylab.jhu.edu">http://rosettadock.graylab.jhu.edu</a>	Standalone	Python
rDock	<a href="http://rdock.sourceforge.net/">http://rdock.sourceforge.net/</a>	Standalone	C++
SwissDock	<a href="http://www.swissdock.ch/">http://www.swissdock.ch/</a>	Web server	perl, php, python
SymmDock	<a href="http://bioinfo3d.cs.tau.ac.il/SymmDock/">http://bioinfo3d.cs.tau.ac.il/SymmDock/</a>	Web Server	
TarFisDock	<a href="http://www.dddc.ac.cn/TarFisDock/">http://www.dddc.ac.cn/TarFisDock/</a>	Web Server	php, html
ZDOCK	<a href="http://zdock.umassmed.edu/">http://zdock.umassmed.edu/</a>	Standalone	C
3D-Garden	<a href="http://www.sbg.bio.ic.ac.uk/3dgarden">http://www.sbg.bio.ic.ac.uk/3dgarden</a>	Web Server	Automatic
3D-Dock Suite	<a href="http://www.sbg.bio.ic.ac.uk/docking/index.html">http://www.sbg.bio.ic.ac.uk/docking/index.html</a>	Standalone	HTML

### Binding site analysis tools

The surfaces of receptors form cavities, which may be binding sites of small molecules. The deduction of these cavities on receptor surface is consequently a proviso for receptor-ligand docking [3]. Docking of small molecule or compounds into the binding site of a receptor and estimating the binding affinity of the complex is an important part of the structure based drug design process. For a thorough understanding of the structural principles as they determine the strength of a protein/ligand complex, an accurate and fast docking protocol and the ability to visualize binding geometries and interactions are necessary [4]. Computational characterization of ligand-binding sites in proteins provides preliminary information for functional annotation, protein design and ligand optimization [5]. There are various web servers or standalone tools which help in the prognostication of active sites which could be the probable sites where the ligand binds to the receptor. The choice of selection depends upon the user as per their requirements.

**Active site prediction** server predicts on the basis of physicochemical properties of functional groups interlining the cavities in the protein [6].

- *Input* – Protein structure in PDB format.
- *Output* – Various cavity points in the target protein and the results are also mailed.
- *Capabilities* – List of all cavity points in the query are generated along with the one letter code of the amino acid residues surrounding the cavity at a distance of 10Å along with the residue numbers. To visualize different cavity points download the result button needs to be clicked. The downloaded file can be graphically viewed by visualization software.
- *Application* – If the user has information from the literature regarding the amino acid residues involved in the biochemical activity of the target protein, then the user can identify the cavity of interest and dock the candidate drug molecule at that cavity.
- *Scoring function* – Monte Carlo method.

**BiGGER (Bimolecular Complex Generation with Global Evaluation and Ranking)** server predicts on the basis of three-dimensional structures of the unbound molecules [7].

- *Input* – Receptor and ligand coordinate files in PDB and mol2 format.
- *Output* – Returns few thousand of best models with the highest surface grid overlaps along with filtered out unfavourable side chain or electrostatic interactions.
- *Capabilities* – It works in two sequential steps: first, the complete 6-dimensional binding spaces of both molecules is systematically searched. In a second step, an interaction scoring function is used to rank the putative docked structures.
- *Applications* – It is used to model several biochemical systems like modulation of the proteolytic activity of matrix metalloproteinase-2 on fibrinogen [8], modeling the electron-transfer complex between aldehyde oxidoreductase and flavodoxin, etc.
- *Scoring function* – Global scoring function using weighting factors optimized through a learning process.

**CASTp (Computed Atlas of Surface Topography of Proteins) server** predicts on the basis of delineation and then quantifying concave surface parts on three-dimensional structures of proteins [9].

- *Input* – Molecular structure in PDB format.
- *Output* – Binding site pocket and the results are mailed to the user. The binding pockets are visualized using Chime plugin.
- *Capabilities* – It is used to study surface features, voids buried in the interior of proteins and functional regions of proteins.
- *Applications* – It is used for construction and defining of pockets in macromolecules [10] and ligand designing [11].
- *Scoring function* – Delaunay triangulation and the alpha complex for shape measurements.

**ConCavity** server predicts on the basis of evolutionary sequence conservation determining with structure based processes [12].

- *Input* – Protein structure in PDB format.
- *Output* – Results are given immediately in the form of predictions of both regions in space that are likely to contain ligand atoms as well as protein residues likely to contact bound ligands.
- *Capabilities* – It is able to make predictions of both regions in space that are likely to contain ligand atoms as well as protein residues likely to contact bound ligands.
- *Applications* – This server is used to aid computational function prediction, guide experimental protein analysis, and focuses on computational techniques used in drug discovery.
- *Scoring function* – Statistical scoring function Jaccard coefficient.

**DoGSiteScorer: Active Site Prediction and Analysis Server** predicts on the basis of nearest neighbour search [13].

- *Input* – PDB code or a user-specified PDB file.
- *Output* – Pockets and descriptors of PDB file provided along with the drug score which could be further analyzed according to the user's requirements.
- *Capabilities* – Prediction of potential pockets on the protein surface is based on the protein heavy atom coordinates.
- *Applications* – Used in the identification and rating of allosteric sites which can further shed light onto new pockets for the drug discovery process.

- *Scoring function* – Supervised machine learning technique.

**FunFOLD2** server predicts on the basis of continual automated model evaluation, in the ligand binding augury listing [14].

- *Input* – Protein sequence in single letter amino acid code.
- *Output* – A unique URL is generated for the output, which can be bookmarked. The results are generated in less than 24 hours and are mailed also in CASP-FN format and CAMEO-LB format. The results page contains a graphical representation of the ligand-binding site, with predicted ligands and binding site residues highlighted, which have been rendered using PyMOL.
- *Capabilities* – A list of ligand-binding site residues, predicted ligands and binding site residue propensities is provided in CAMEO format. An interactive model with predicted binding site residues and ligands can be visualized using the Jmol plug-in. A link to download a PDB file of the top model with the putative ligands is also provided.
- *Applications* – Provides an intuitive interface for the prediction of protein-ligand interactions from amino acid sequences.
- *Scoring function* – Matthews Correlation Coefficient (MCC) and Binding-site Distance Test (BDT) scores.

**GOLD** standalone tool predicts on the basis of receptor flexibility by side-chain flexibility and most particularly ensemble docking [15].

- *Input* – Proteins coordinate file in PDB format.
- *Output* – Output is in the form of different files like files containing initial protein and ligands, docked ligands, protein binding site geometry, ranked fitness score for an individual ligand, ranked fitness score for the set of ligands, rescore solution file, rescore log file, protein log file, ligand log file, file containing error message, process file, seed log file. It also gives information on the progress of docking runs and compares the docking solutions and also identifies different binding mode. The docked solutions are visualized in Hermes.
- *Capabilities* – It consists of three main parts: A scoring function to rank different binding modes, a mechanism for placing the ligand in the binding site and a search algorithm to explore possible binding modes.
- *Applications* – It makes confident binding mode predictions using high database enrichments. It reliably identifies the correct binding mode for a large range of test set cases. It accounts for receptor flexibility through side-chain flexibility and most importantly ensemble docking.
- *Scoring function* – Chemscore function and Goldscore function.

**metaPocket 2.0** server predicted binding sites are generated from the four methods LIGSITE (cs), PASS, Q-SiteFinder, and SURFNET [16].

- *Input* – PDB file or a PDB ID with specific chain ID.
- *Output* – The result is in the form of four downloadable files which are the PDB format of protein submitted, metapocket result with top N pocket sites, metapocket result with all pocket sites and a python script for visualization with PyMOL respectively are generated.
- *Capabilities* – As the predicted sites are generated using four methods therefore their combination improves the prediction success rate from approximately 70 to 75% at the top 1 prediction.



- *Applications* – Used for the Prediction of protein–protein interaction sites and protein–ligand binding sites.
- *Scoring function* – Different ranking scoring function on the basis of four methods so to make it comparable, a Z-score is calculated separately for each site in different methods.

**PocketQuery** server explores the premises of protein-protein interaction (PPI) admixes with a focus on the findings of propitious starting points [17].

- *Input* – PPI structures deposited in PDB and also users can upload their own custom structures for analysis.
- *Output* – Scores that range from zero to one for structures of small molecule that binds at PPI interface with zero corresponding to minimum binding at PPI interface and one corresponding to maximum binding at PPI interface.
- *Capabilities* – Small-Molecule Inhibitor Starting Points (SMISPs) from protein-ligand and protein-protein complexes in the Protein Data Bank (PDB) are extracted. These are used to train two distinct classifiers, a support vector machine and an easy to interpret *exhaustive rule* classifier which achieves 70% better results.
- *Applications* – Used in the exploration of PPI interfaces and provides key residues of the interaction.
- *Scoring Function* – Druggability score which provides an estimate of the chemical mimicry of a cluster of interface residues would result in a small-molecule inhibitor of an interaction.

**ProBiS (Protein Binding Site Detection)** server predicts on the basis of constructually homogeneous protein binding sites by local structural alignment [18].

- *Input* – Protein structure in PDB format with the chain ID. It also provides the option of advanced query in which user can select binding site.
- *Output* – Image viewed in Jmol with colors showing degrees of structural conservation from blue (unconserved) to red (structurally conserved) along with the table of similar proteins which could be further analyzed according to the users need.
- *Capabilities* – Structural similarity scores are calculated for the query protein's surface residues, and are expressed as different colors on the query protein surface.
- *Applications* – The algorithm has been used successfully for the detection of protein-protein, protein-small ligand and protein-DNA binding sites.
- *Scoring function* – Maximum clique algorithm.

**PocketDepth** server predicts on the basis of depth based clustering [19].

- *Input* – PDB format of protein.
- *Output* – Depth pocket which is used in the implementation of binding pocket identification.
- *Capabilities* – Prediction accuracies are performed using location and overlap, ranks and benchmarking, grid construction, grid cell labelling, drawing grid bars, computing depth factors, clustering and ranking.
- *Applications* – Used in finding of subspace of putative pocket in protein structure.
- *Scoring functions* – Tanimoto Quotient.
- *Real tests* – The algorithm has been tested against PDBbind and LigSiteCSC, a large curated set of 1091 proteins.

**PocketPicker** server predicts on the basis of grid-based approach that describes the shape of a probable binding-site with consideration to its buriedness [20].

- *Input* – Install PocketPicker plugin accessed via PyMol. Then load PDB-file into PyMol using PDB-loader-plugin and predict Pocket.
- *Output* – Three files are created for one computation. First, clusterinfo.txt file holding pocket-index, xyz-coordinates and buriedness of each grid probe. Second, descriptor420.txt file containing 420 dimensional shape descriptors for five biggest pockets (one descriptor per line). Third, info.txt files containing settings of the computation.
- *Capabilities* – Uses information derived from calculations of the buriedness of potential binding-sites for predicting binding sites in the query protein.
- *Applications* – Identifies ligand binding sites in proteins, and finds related binding sites by shape and a buriedness index.
- *Scoring function* – Geometric algorithm based on energy approach.
- *Real tests* – The performance of the pocket detection routine was compared to results achieved with the existing methods CAST, LIGSITE, LIGSITE<sup>CS</sup>, PASS and SURFNET.

**SiteHound-web** server and standalone tool uses carbon probe and phosphate probe for the recognition of van der Waals associations and phosphorylated ligands respectively and then uses clustering algorithm to combine distinctive affinity map points into clusters corresponding to potential binding sites [21].

- *Input* – PDB file and the specification of a probe and clustering algorithm for the calculation.
- *Output* – It has two components: an interactive web screen displaying a summary of results with a 3D representation of the putative binding sites on the protein structure; and downloadable files for offline analysis.
- *Capabilities* – This server provides two types of probes i.e. a carbon probe for the identification of binding sites for molecules that interact mainly through van der Waals contacts; and a phosphate probe which is used to identify sites that bind to phosphorylated ligands along with the clustering algorithm which determines individual affinity map points into clusters corresponding to putative binding sites.
- *Applications* – Provides information about the location and binding preference of sites in protein structures.
- *Scoring function* – Energy-based approach.

**SiteComp** server analysis ligand binding site in protein structures [5].

- *Input* – It takes input in two forms. First, compares two proteins by uploading coordinate files in PDB format. Second, analyze one protein in PDB format for molecular interaction fields.
- *Output* – Results are kept on the server privately and are deleted after 30 days. During that period the user can access the results using a unique URL generated at the time of job submission. Most output files are also available for download.
- *Capabilities* – Enables to perform binding site comparison and decomposition, and multi-probe characterization. It also calculates molecular interaction fields.
- *Applications* – Provides binding site analysis for comparison of binding sites, evaluates residue contribution to binding sites and identifies sub-sites with distinct molecular interaction properties.



- *Scoring function* – Lennard-Jones and an electrostatics term over all the atoms of the protein.

**3DLigandSite** server predicted binding sites are used to prognosticate the 3D binding sites of query protein [22].

- *Input* – Either a protein structure or sequence.
- *Output* – Split into four main sections. The first provides details of the phyre model used. The second section shows a table of the ligand clusters identified. The final two sections display the 3DLigandSite prediction.
- *Capabilities* – It utilizes protein-structure prediction to provide structural models for proteins that have not been solved. Ligands bound to structures similar to the query are superimposed onto the model and used to predict the binding site.
- *Applications* – Predicts ligand-binding sites which is used in CASP8.
- *Scoring function* – Matthew's correlation coefficient.

### Pharmacophore docking tools

The IUPAC denotation of a pharmacophore is “an ensemble of steric and electronic features that is necessary to ensure the optimal supramolecular interactions with a specific biological target and to trigger (or block) its biological response” [23]. Pharmacophores can be used as queries for repossession of probable leads from structural databases (lead discovery), for intriguing molecules with particular coveting quality (lead optimization), and for determining analogy and miscellany of molecules using pharmacophore fingerprints [24]. Pharmacophore models aim to comprise the features of ligand-protein interactions that are most crucial for binding and biological activity. These models are used for virtual screening to identify potential new active targets or for generating ligand alignments for subsequent Quantitative Structure Activity Relationship (QSAR) simulations. Pharmacophore models are typically derived from structural features common to biologically active ligands that are hypothesized to be important for biological activity [25]. There are three main software which help in pharmacophore docking which could be used in accordance to the user utility.

**PharmaGist** server and standalone tool is the ligand based method in which the drug like molecule is considered pharmacophore by numerous pliable alignments of the input ligands [26].

- *Input* – Set of structures of drug-like molecules that are known to bind to the receptor.
- *Output* – Consists of candidate pharmacophores that are computed by multiple flexible alignments of the input ligands. The results are mailed to the user. The output provides for each candidate pharmacophore a 3D superposition of conformations of input ligands that share it.
- *Capabilities* – The method handles the flexibility of the input ligands explicitly and in deterministic manner within the alignment process. The method consists of four major stages: (i) ligand representation, (ii) pairwise alignment, (iii) multiple alignments and (iv) solution clustering and output.
- *Applications* – Detects candidate pharmacophores that are shared by non-predefined subsets of input ligands.
- *Scoring function* –  $S(f^p, f^t)$  is the scoring function where  $f^p$  is the function of the pivot and  $f^t$  is the function of a target ligand.
- *Real test* – The performance has been evaluated on a benchmark dataset consisting of 74 drug-like ligands divided into 12 test cases. The results show the ability of the

method to deal with different types of drug-like ligands including peptides with more than 30 rotatable bonds.

**PharmDock** server is the protein pharmacophore-based docking program [25].

- *Input* – Protein structure file in the form of PDB format.
- *Output* – Docked and simulated structures which could be visualized in PyMOL.
- *Capabilities* – It provides features of confined docking and constraint docking.
- *Applications* – Provides ligand model concept for protein flexibility and dynamics.
- *Scoring function* – Empirical scoring function.

**ZINCPharmer** server interface for discerning the buyable compounds of the ZINC database using the Pharmer pharmacophore search in which automatically a set of pharmacophore features are extracted from molecule [27].

- *Input* – Molecular structure in PDB format with a defined pharmacophore.
- *Output* – Results are returned and displayed in the results browser as they are found.
- *Capabilities* – It can automatically extract a set of pharmacophore features from molecular structure. Further the query will be refined to enhance its specificity and applicability.
- *Applications* – Users can quickly enable or disable features, adjust search tolerances and apply filters based on the results of previous searches to achieve a set of result compounds that has the desired size, specificity and chemical diversity.
- *Scoring function* – Consensus scoring scheme.

### Receptor-ligand docking tools

The docking focuses to foresee and position the structures appearing from the coalition between a specific ligand and a target protein [28]. This methodology actually aims to anticipate the fringal binding methods and empathies of small molecules inside the binding site of particular receptor and is mainly used as a gradable computational tool for lead compound optimization and virtual screening studies to find new biologically active molecules. The ability to successfully handle the intrinsic molecular flexibility of a system and to correctly describe the energetics of receptor-ligand interactions is critical to the development of predictive docking methodologies that are useful in prospective drug design studies [29]. Therefore, the user can accordingly select the tools/software in order to perform receptor-ligand docking.

**Active site prediction** server docks considering the cavity points, four docked assemblies are returned besides their corresponding binding free energies [6].

- *Input* – The cavity point, the candidate drug molecule along with its correct formal charge.
- *Output* – The results will be emailed back in the form of four docked structures along with their corresponding binding free energies in kcal/mol. The four docked structures represent the different poses of the candidate drug molecule in the active site.
- *Capabilities* – List of all cavity points in the query are generated along with the one letter code of the amino acid residues surrounding the cavity at a distance of 10Å along with the residue numbers. To visualize different cavity points download the result button needs to be clicked. The downloaded file can be graphically viewed by visualization software.

- *Application* – If the user has information from the literature regarding the amino acid residues involved in the biochemical activity of the target protein, then the user can identify the cavity of interest and dock the candidate drug molecule at that cavity.
- *Scoring function* – All atom energy based Monte Carlo method.
- *Real test* – The predicted structure and energetics of the complexes agree with experiment when tested on a data set of 170 protein-ligand complexes with known structures and binding affinities.

**AutoDock** standalone tool predicts the binding of small molecules to the receptor of known three dimensional structures [30].

- *Input* – Protein structure coordinate files in PDB format for both receptor and ligand.
- *Output* – Screened ligands and docked structures.
- *Capabilities* – It consists of two main programs: “autodock” which carries out the docking of the desired ligand to a set of grids describing the protein, and ‘autogrid’ which pre-calculates these grids. In “autodock” the ligand explores six spatial degrees of freedom, rotation and translation, and an arbitrary number of torsional degrees of freedom within the grid.
- *Applications* – Performs docking of peptides to their targets, without *a priori* knowledge of the location of the binding site. Used for drug-sized molecules [31].
- *Scoring function* – Hybrid scoring function (empirical + knowledge-based function) inspired in the X-score function.

**AutoDock Vina** standalone tool is the upgraded genre of AutoDock in which the mean exactness of the binding mode predictions is significantly enhanced. For input and output, it uses the same PDBQT molecular structure file format [32].

- *Input* – Structures of the molecules with specification of the search space including the binding site.
- *Output* – In the output some hydrogen atoms are positioned randomly. All predicted binding modes, including the positions of the flexible side chains are placed into one multimodel PDBQT file specified by the “out” parameter or chosen by default, based on the ligand file name. If needed, this file can be split into individual models using a separate program called “vina\_split”, included in the distribution.
- *Capabilities* – It significantly improves the average accuracy of the binding mode predictions. Calculates grid maps and assigns atom charges. It is designed only for receptor-ligand docking.
- *Applications* – Calculates the gradient effectively which gives the optimization algorithm a sense of direction from a single evaluation.
- *Scoring function* – Knowledge-based potentials and empirical scoring functions.

**Argus Lab** standalone tool docks the ligand to the created binding sites of the receptor automatically.

- *Input* – PDB structure along with the created ligand and binding site groups.
- *Output* – Dock the ligand into the defined binding site and analyze and save the results.
- *Capabilities* – Argus Lab is freely licensed and is a molecular modeling, graphics, and drug design program for Windows operating systems.
- *Applications* – Efficient reuse of scoring and docking grids allows user to interactively modify ligand or choose new ligand and quickly dock new structures.
- *Scoring function* – X-score.

**ClusPro** server predicts putative complexes using surface complementarities then a sieving procedure is administered, selecting those structures with adept electrostatic and desolvation free energies for additional clustering giving a list of probable complexes categorized according to clustering properties [33].

- *Input* – Coordinate files of two protein structures or the PDB codes of the respective structures.
- *Output* – The program output is a short list of putative complexes ranked according to their clustering properties, which is automatically sent back to the user via email.
- *Capabilities* – The docking algorithms evaluate billions of putative complexes, retaining a preset number with favorable surface complementarities. A filtering method is then applied to set of structures, selecting those with good electrostatic and desolvation free energies for further clustering.
- *Applications* – Discriminates putative structures that have been generated by the user, using any one of the server-compatible docking algorithms.
- *Scoring function* – Electrostatic potential, pairwise shape complementarity (PSC), desolvation, and electrostatics.

**DOCK Blaster** server uses pose-fidelity, the capacity to replicate empirically noticed poses within some tolerance edge, and enhancement, the capacity to enhance actives from among a database of decoys for docking [34].

- *Input* – PDB file of the structure.
- *Output* – Reports of the screening results.
- *Capabilities* – The DOCK Blaster pipeline is composed of six modules: (a) the parser, which identifies the receptor and ligand from a PDB file, (b) the scrutinizer, which attempts to correct for problems, such as incomplete or disordered residues on the receptor, (c) the preparer, which protonates the receptor, calculates “hot spots” and scoring grids, assigns atomic parameters, including these for cofactors, post-translational modifications and metals, and prepares the ligand, decoys, and any actives and inactives for docking, (d) the calibrator, which uses supplied data to assess docking performance and suggests optimal docking parameters, (e) the docker, which manages a full database screen on the computer cluster, and (f) the assessor, which prepares reports to interpret database screening results.
- *Applications* – Helps non-specialists find new reagents for biology without the need for an expert.
- *Scoring function* – Screen score, Flex X-score, PLP-score and PMF-score.
- *Real tests* – The method is tested for pose-fidelity, the ability to reproduce experimentally observed poses within some tolerance limit, and enrichment, the ability to enrich actives from among a database of decoys, where a decoy is a member of the database that does not bind to the target.

**DOT 2.0** standalone tool executes comprehensive, systematic rigid-body forage for two macromolecules for macromolecule docking [35].

- *Input* – Protein structure in PDB format.
- *Output* – Configurations of docked structures which are further evaluated.
- *Capabilities* – It has three main steps for obtaining a list of configurations between two molecules. In the preprocessing step, the electrostatic and van der Waals properties of each molecule are calculated and DOT input files are generated. In the docking step, the DOT program maps these properties onto grids and then systematically translates and rotates one molecule (moving) around a stationary

molecule. In the evaluation step, configurations are scored, clustered, and examined for fit to experimental data [36, 37].

- *Applications* – Performs an exhaustive, rigid-body search for two macromolecules.
- *Scoring function* – Sum of electrostatic and atomic desolvation energies.

**ESCHER NG** server is used to dock unbound protein components, secondary and supersecondary structure elements and protein domains by evaluating electrostatic complementarity [38].

- *Input* – Two PDB files.
- *Output* – Generates three types of output files that can be identified by the extension. First, .pdb which is the solution extracted by the *-s* option. Second, .sol which are text files including solutions. Third, .srf which is the surface file in insight format.
- *Capabilities* – It has three modules that work in series. The first module evaluates the geometric complementarity and produces a set of rough solutions for the docking problem. The second module identifies molecular collisions within those solutions, and the third evaluates their electrostatic complementarity.
- *Applications* – It helps in the docking of protein domains, protein complexes starting from unbound components and secondary and super-secondary structure elements.
- *Scoring function* – ChemGauss2.

**FINDSITE** server is used for ligand virtual evaluation using heuristic structure cavity alignment [39].

- *Input* – Protein structure in PDB format.
- *Output* – Binding site in protein which could be used for docking.
- *Capabilities* – It is used for ligand virtual screening using heuristic structure pocket alignment [40]. They are as fast as traditional ligand-based approaches and yet overcome the limitations of traditional ligand- or structure-based approaches.
- *Applications* – A promising avenue of investigation that holds considerable promise in extending the range and scope of structure-based approaches to protein function prediction.
- *Scoring function* – Geometric methods.

**FireDock** server and standalone tool is used for fast interaction refinement in molecular docking [41].

- *Input* – There are two options for input. First, receptor and ligand coordinate files in PDB format. Second, models file in PDB format and respective chain ID's of receptor and ligand. It also provides advanced input files option.
- *Output* – The output is a table of all the input solutions, ranked by the global energy value. The refined complex structure is generated for up to 100 low-energy candidates. The user can view the complexes in the Jmol applet window and/or download the structures.
- *Capabilities* – It is the first web server for flexible refinement and scoring of protein-protein docking solutions. It includes optimization of side-chain conformations and rigid-body orientation and allows a high-throughput refinement. It also provides a user-friendly interface and a 3D visualization of the results.
- *Applications* – It is successful in refining and scoring docking solution candidates for cases taken from docking benchmarks.
- *Scoring function* – Monte Carlo method [42], [43], graph theory-based methods [44], linear programming (LP) [45].



**FiberDock** server and standalone tool is used for flexible refinement of docking solution candidates [46].

- *Input* – There are two options for input. First, receptor and ligand coordinate files in PDB format. Second, models file in PDB format and respective chain ID's of receptor and ligand. It also provides advanced input files option.
- *Output* – The output is a table of all the input solutions, ranked by the global energy value. The refined complex structure is generated for all the solutions. The user can view the complexes in the Jmol applet window and/or download the structures.
- *Capabilities* – It is capable for docking refinement which models backbone flexibility by an unlimited number of normal modes. It iteratively minimizes the structure of the flexible protein along the most relevant modes and the relevance of a mode is calculated according to the correlation between the chemical forces, applied on each atom, and the translation vector of each atom, according to the normal mode.
- *Applications* – Models backbone movements of rigid-docking models of protein-protein complexes.
- *Scoring function* – Energy function.

**FLIP Dock (Flexible Ligand-protein Docking)** standalone tool predicts interactions between a flexible ligand and a flexible receptor [47].

- *Input* – Protein structure in PDB format.
- *Output* – Docked flexible ligand molecules into active sites of flexible receptor molecules.
- *Capabilities* – The three main ingredients of a docking program are: the representation of the ligand-receptor complex, the search method, and the method for ranking putative solutions. It gives both description and encoding of docking problems using FTs and in the combination of search methods as well as scoring functions.
- *Applications* – Docks flexible ligands to receptors requiring conformational changes, including backbone motion.
- *Scoring function* – AutoDock3.05 force-field.

**GRAMM-X** server uses a fine-grid estimation of a softened Lennard-Jones potential function purposed for a probe atom for docking [48].

- *Input* – Protein structure in the PDB format.
- *Output* – Conformations of only 3 side-chains optimized during docking of unbound structures before the backbone changes become a limiting factor.
- *Capabilities* – The docking is performed by a rigid-body procedure with a smoothed potential function to accommodate conformational changes.
- *Applications* – This server maximizes the chances of the correct prediction.
- *Scoring function* – Lennard-Jones potential function for a probe, Support Vector Machine for locating correct binding site and remaining predictions are re-scored by a weighted sum of the potential terms [47].

**GPU.proton.DOCK: Genuine Protein Ultrafast proton equilibria consistent DOCKing** server predicts protein-protein interactions through meticulous and ultrafast docking code [49].

- *Input* – The atomic coordinate files in PDB format. The advanced user is provided with a special input section for addition of non-polypeptide charges, extra ionogenic groups with intrinsic pKa values or fixed ions.



- *Output* – Comprised of docked complexes in PDB format as well as interactive visualization in a molecular viewer.
- *Capabilities* – Provides stringent account of electrostatic interactions self-consistency and proton equilibria mutual effects of docking partners. It is the first server offering such a crucial supplement to protein docking algorithms – a step toward more reliable and high accuracy docking results.
- *Applications* – Favors to whom needs fast and comprehensive analysis of protonation-dependent docking results as well as *in silico* charge mutagenesis effects on the interaction mechanisms.
- *Scoring function* – The Fast Fourier Transform (FFT) bottleneck and electrostatic fields computation.

**Hex Server** is the FFT-based protein docking server, mechanized by graphics processors [50].

- *Input* – Two protein structures in PDB format, i.e. one for receptor and another for ligand.
- *Output* – Produces a ranked list of up to 1000 docking predictions. The first 20 predictions may be accessed individually, and a single file of all predicted orientations may be downloaded as a compressed multi-model PDB file.
- *Capabilities* – Provides additional shape plus electrostatic calculations.
- *Applications* – Users may quickly and easily obtain a list of high quality docking predictions for subsequent refinement and analysis.
- *Scoring function* – Electrostatic contribution, shape, electrostatics and an atomic contact model of desolvation.

**HADDOCK** server is the data-driven approach to docking, with assistance for a broad range from the experimental material [51].

- *Input* – Requires only the structures of the individual components and a list of interacting residues. Additional web interfaces allow the more advanced user to exploit the full range of experimental data supported by HADDOCK and to customize the docking process.
- *Output* – Docked structures acquired after different restraints.
- *Capabilities* – The server has access to the resources of a dedicated cluster and of the e-NMR GRID infrastructure [52].
- *Applications* – This protocol facilitates the modeling of biomolecular complexes for a wide community [53].
- *Scoring function* – The HADDOCK energy scores i.e. chemical shift score and SAXS score.

**ICM-Dock** standalone suite is used for automatic ligand-protein docking, peptide-protein docking, and protein-protein docking [54].

- *Input* – PDB file, then convert PDB, move the ligand out of the pocket, check the ligand, set up the receptor and dock and finally adjust the position of the probe.
- *Output* – Output is in the form of binded ligands and virtually screened ligand.
- *Capabilities* – The ICM-Pro desktop modeling GUI interface offers a step-by-step docking menu that makes docking easier than ever.
- *Applications* – Generates multiple poses that include experimentally solved near native conformations.
- *Scoring function* – Monte Carlo method.

**KFC (Knowledge-based FADE and Contacts) server** predicts bided hot spots, or the subset of residues that report for most of a protein interface's binding free energy [55].

- *Input* – Protein-protein or protein-DNA interface.
- *Output* – The user can visualize the results using an interactive job viewer able to quickly highlight predicted hot spots and surrounding structural features within the protein structure.
- *Capabilities* – Characterizes local structural environment and compares that environment to the environments of experimentally determined hot spots and predicts if the interface residue is a hot spot.
- *Applications* – Guides molecular recognition experiments, predicts residues whose mutation can significantly disrupt an interaction and designs a protein with *improved* affinity for its binding partner.
- *Scoring function* – Machine learning approach.

**MED-SUMO** server is used for target based drug designing [56].

- *Input* – A macromolecular structure database with up to hundreds of thousands structure.
- *Output* – Ligand are aligned, shown in the graphical user interface and output as they are defined in the original PDB file.
- *Capabilities* – Predictions are essentially based on experimental data from the PDB.
- *Applications* – Used in functional annotation, binding site characterization, fragment based drug design, and bio-isoteric replacement.
- *Scoring function* – Biochemical function and shape overlaps.

**MolFit** standalone tool allows geometric, geometric-electrostatic, geometric hydrophobic and weighted-geometric docking [57].

- *Input* – Receptor and ligand files in PDB and mol format respectively.
- *Output* – Docked structure in the order of scoring function.
- *Capabilities* – MolFit is very sensitive and can identify acceptable solutions for each target.
- *Applications* – Gives multibody, multistage docking of rigid fragments, which retains the advantage of fast and simple computations that are used in cases where hinge movements occur.
- *Scoring function* – Up-weighted or down-weighted functions [58].

**PatchDock server** predicts structure of protein-protein and protein-small molecule complexes [59].

- *Input* – Protein PDB codes or protein structures with the chain IDs.
- *Output* – The solutions are presented in a table, a row for each solution. A link to a PDB file that presents the docking solution is also available in each line. There is also an option to view additional, lower ranking solutions by pressing the “next 20 solutions” button at the lower right corner of the table. In the solutions page an option to download the top scoring solutions is available. The solutions are downloaded as a compressed file in ZIP format. This compressed file contains the PDB files of the top scoring solutions.
- *Capabilities* – The algorithm divides the Connolly dot surface representation of the molecules into concave, convex and flat patches.
- *Applications* – Allows large scale docking experiments which are very efficient.
- *Scoring function* – Geometric fit and atomic desolvation energy.

**ParDock** server is based on all atom energy based Monte Carlo docking for protein-ligand complexes [60].

- *Input* – Protein with ligand and candidate molecule to dock.
- *Output* – Results are mailed to the user in the form of docked structures ranked in accordance to the scoring function.
- *Capabilities* – Center of Mass (COM) of the reference ligand is calculated. The best energy structure is selected based on energy points. The RMSD difference between crystal structure and energy minimized docked structure.
- *Applications* – Used in rigid protein Ligand docking.
- *Scoring function* – Monte Carlo method.
- *Real test* – Tested on a dataset of 226 protein-ligand complexes.

**PyDockWeb** server is used for rigid-body docking prediction of protein-protein complex structures [61].

- *Input* – Protein coordinate file in PDB format or PDB code.
- *Output* – Top 10 docked models scored by pyDock are displayed using Jmol.
- *Capabilities* – Uses a new version of the pyDock scoring algorithm. A new custom parallel FTDock implementation, with adjusted grid size for optimal FFT calculations is done.
- *Applications* – Gives best docking orientations after protein-protein docking.
- *Scoring function* – Electrostatics and desolvation energy.

**RosettaDock** standalone tool recognizes low-energy structures of a protein-protein interaction near a given starting arrangement by optimizing rigid-body placement and side-chain arrangement [62].

- *Input* – Two protein structures in PDB format and a starting location for the search.
- *Output* – Generates 1000 independent structures, and the server returns pictures, coordinate files and detailed scoring information for the 10 top-scoring models. A plot of the total energy of each of the 1000 models created shows the presence or absence of an energetic binding funnel. Each model output file includes the scoring data of individual energy terms for the whole-protein complex as well as residue by-residue breakdowns and intermolecular residue-pair contributions.
- *Capabilities* – A plot of the total energy of each of the 1000 models created shows the presence or absence of an energetic binding funnel.
- *Applications* – Predicts antibody-antigen structures of therapeutic interest to provide hypotheses on a drug mechanism [63] and insights into affinity maturation [64] for complexes, where experimental structures were not available and crystallization presented challenges. It has been used on a family of rotavirus-specific antibodies and the evolution of the neutralizing antibodies was exploited to help validate the models [65]. Other examples of application targets range from calcium channels [66] and malaria proteins [67] to antibody Fc interactions [68].
- *Scoring function* – Monte Carlo based algorithm.

**rDock** standalone tool for docking ligands to proteins and nucleic acids [29].

- *Input* – Receptor in Tripos mol2 format with standard atom typing and ligands in the MDL SDF file format (SDF).
- *Output* – The result obtained is protein-ligand binding, RNA-ligand binding mode and virtually screened docked structures.

- *Capabilities* – Molecular docking program developed at Vernalis for high-throughput VS (HTVS) applications and is Evolved from RiboDock, the program can be used against proteins and nucleic acids, is designed to be computationally very efficient and allows the user to incorporate additional constraints and information as a bias to guide docking.
- *Applications* – Docks simultaneously to an ensemble of receptor coordinates to simulate receptor flexibility in an efficient way.
- *Scoring function* – Weighted sum of intermolecular, ligand intramolecular, site intramolecular, and external restraint terms.
- *Real tests* – Compares rDock to two reference programs, AutoDock Vina (open source) and Schrödinger's Glide (commercial). In terms of computational speed for VS, rDock is faster than Vina and comparable to glide. For binding mode prediction, rDock and Vina are superior to Glide. The VS performance of rDock is significantly better than Vina, but inferior to Glide for most systems unless pharmacophore constraints are used; in that case rDock and Glide are of equal performance.

**SwissDock** server is used for docking of small molecules on target proteins [69].

- *Input* – Target PDB ID, Ligand ID by specifying Zinc Database ID or structure files and docking parameters.
- *Output* – The result page has Jmol for visualization of docked structures. A predictive performance assessment can also be done using this server.
- *Capabilities* – It is based on the EADock DSS engine, combined with setup scripts for curating common problems and for preparing both the target protein and the ligand input files. This web site also provides an access to a database of manually curated complexes, based on the Ligand Protein Database.
- *Applications* – Used for drug design for small and relatively rigid ligands.
- *Scoring function* – Full fitness scoring function.

**SymmDock** server predicts the structure of a homomultimer with cyclic symmetry given the structure of the monomeric unit [59].

- *Input* – Protein PDB codes or uploaded protein structures.
- *Output* – A web page is generated to show the predicted solutions alongwith the whole multimer generated for each solution.
- *Capabilities* – The algorithm takes advantage of the special characteristics of cyclically symmetric transformations in both its search and clustering methodologies [23].
- *Applications* – Performs large-scale docking experiments with great efficiency.
- *Scoring function* – Geometry based scoring function.

**TarFisDock** server searches small molecule-protein interactions atop a substantial collection of protein structures [70].

- *Input* – Small molecule in standard mol2 format.
- *Output* – Delivered in ascending order of energy score (interaction energy). The archive file contains a list of scores, together with binding models (in mol2 format) of the small molecule tested within the binding sites of the candidate targets.
- *Capabilities* – It offers PDTD (potential drug target database), a target database containing 698 protein structures covering 15 therapeutic areas and a reverse ligand-protein docking program. In contrast to conventional ligand-protein docking, reverse

ligand-protein docking aims to seek potential protein targets by screening an appropriate protein database.

- *Applications* – Identifies potential binding proteins for small molecules such as drugs, lead compounds and natural products.
- *Scoring function* – Interaction energy composed of van der Waals and electrostatic interaction terms.

**ZDOCK** standalone tool is the FFT-based protein docking scheme which explores all feasible binding modes in the translational and rotational space between the two proteins, assessing each pose using an energy-based scoring function [71].

- *Input* – PDB files with residues for blocking from the binding site during docking, and user can also select binding site residues for filtering output predictions using an interactive Jmol-enabled interface.
- *Output* – ZDOCK output file, processed PDBs (for generating predicted models), and interactive tools to view and generate individual predictions or sets of predictions.
- *Capabilities* – It combines recently developed pairwise shape complementarity with desolvation and electrostatics.
- *Applications* – Performs a full rigid-body search of docking orientations between two proteins.
- *Scoring function* – Energy-based scoring function.

**3D-Garden** standalone tool is the suite of programs for producing and gauging models for blind or non-blind protein docking [72].

- *Input* – Structures from PDB mirror using four-character id, users may then mask out chains by label, and it will remove their heterogens.
- *Output* – Generated models which are further used for docking.
- *Capabilities* – It uses the molecular surface when constructing the initial ensemble to ensure that the interactors make at least one glancing contact, with the aim of reducing the number of models in the ensemble with substantial interpenetration.
- *Applications* – Predicts protein complexes.
- *Scoring function* – Lennard-Jones potential with explicit hydrogens but no electrostatic term.

**3D-Dock** standalone suite consists of three servers that are FTDock (Fourier Transform Dock), RPScore (Residue level Pair potential Score) and MultiDock (Multiple copy side-chain refinement Dock).

- *Input* – Protein coordinate files in PDB format [73].
- *Output* – FTDock outputs multiple predictions that can be screened using biochemical information. RPScore uses a single distance constraint empirically derived pair potential to screen the output from FTDock. A further improvement in the quality of the predictions can be gained by using MultiDock. The results of the three interfaces are in the form of the table.
- *Capabilities* – FTDock performs rigid-body docking on two biomolecules in order to predict their correct binding geometry. RPScore can reduce dramatically the list of possible complexes within which can be found a correct solution. This program is fully integrated with the present version of FTDock. A further improvement is gained by using MultiDock.
- *Applications* – With the availability of biological information, the suite yields predictions with RMSD lower than 1 Å.
- *Scoring function* – Fourier correlations accelerated with a FFT.



## Conclusion

This review provides 49 open source computational drug designing tools/software which would be helpful to the biotechnologist for identifying potential drug targets. These potential drug targets can then be developed as drug candidates. The identification of potential drug targets reduce biotechnologist labor and most importantly the cost and time period of the drug design. This review could be helpful to reader interested in further developing the algorithms for new software under the above mentioned category of docking tools/software. Researcher can manipulate, reconfigure and merge two software to develop new software for docking purpose which could further improve the quality prediction of structures to be docked. The user could directly use these computational drug designing servers through their URL's helping them to consume their time efficiently. The user has the choice of 49 servers and could use them according to their needs. Thus this review helps in reducing the burden carried by the biotechnologist and could easily use computational drug designing approach for the identification of potential drug targets.

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