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INTRODUCTION

Researchers are under ever increasing pressure to discover new therapeutic compounds, as there are urgent needs to identify new molecules able to fight against life-threatening diseases. The quest for the new chemical entities and novel structural scaffolds with applications in the therapeutic areas is always at the heart of pharmaceutical chemistry. Drug discovery is however a complex and expensive endeavor that requires the use of various techniques such as experimental high-(or medium)-throughput screening (HTS), NMR, X-ray crystallography, experimental ADME (absorption, distribution, metabolism and excretion)/tox assays and combinatorial chemistry among many others [1-4]. While arriving at these structures traditionally involve arduous, careful and systematic synthesis of several putative structures or screening of natural products. Most of these efforts may be categorized as the chance discovery rather than a rational approach. The enthusiasm to embrace rational approaches is triggered in recent years following tremendous advances in the computations and protein crystallography [5-7].

To assist this highly complex process (Fig. 1), it is now well accepted that computer methods such as homology modeling, protein docking and virtual screening/de novo design can help [3, 8]. Thus in-silico approaches have gained immense popularity and have become an integral part of the industrial and academic research, directing drug design and discovery [9-13]. With regard to small ligand-receptor in silico screening methods, one can usually distinguish two main virtual screening strategies/concepts: ligand-based screening and structure-based screening [14, 15]. For ligand-based methods (similarity and substructure search, clustering, QSAR, pharmacophore matching or three-dimensional shape matching), the concept is to use information provided by compounds that are known to bind to the desired target and to use these data to identify other molecules in the databases with similar properties. For structure-based methods (SB-VLS) (Fig. 2), it is assumed that the three-dimensional (3D) structure of the target is known either by X-ray crystallography or NMR experiments or predicted by homology. The principle here is to dock all the ligands present in a database into the binding pocket of the selected target and evaluate the fit between the molecules. The quality of the fit is then used to rank the small molecules.

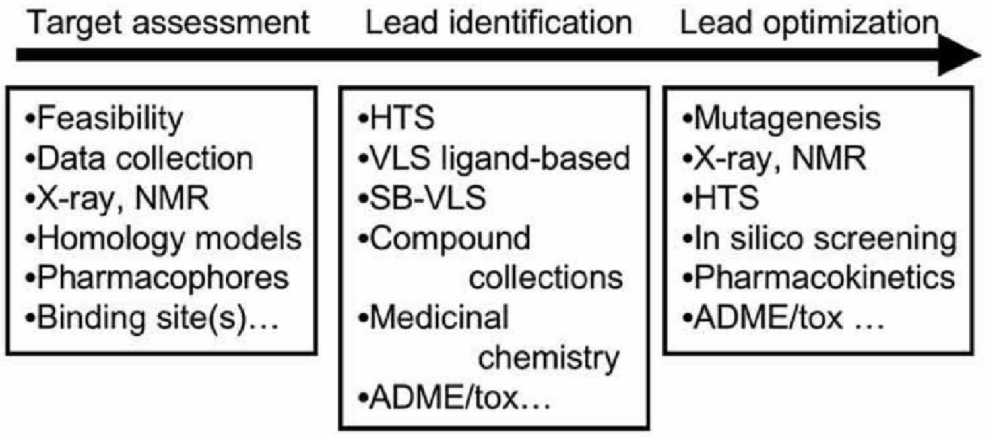


Fig.1: Some key steps in the Drug discovery process

Computational tools, which delineate the strength of interaction between a variety of ligands and targets in combination with good graphic three-dimensional visualization, are growing into important technologies to pick up lead molecules from data-bases [16, 17]. Evidently, to develop small molecular drug candidates against a given disease warrants proper under-standing of the metabolic pathways. Thus, the first and foremost task in any of the rational approaches for a given disease is to assess the various metabolic pathways and select the potential biological target [18-19]. Therefore, identification and development of potential ligands specifically for a protein target forms the primary goal in drug discovery process [20-21]. Subsequently numerous robotic and automated screening schemes (assay dependent) are available which basically allow the testing and selection of several thousands of ligands, according to their capability to interact with the biological targets for a particular disease. While computations in fact does not replace the experimental research it has been very clear that an effective interplay between the experimental and computational approaches is noticeably important to guide the prospective experimentalists in the synthesis and screening of compounds in a more rational way [22-25]. Amalgamation of random screening and rational design conventionally has shown a notable development in the drug discovery process leading to the recognition of ligands [26].

Transforming these ligands into active compounds with non-promiscuous-binding behavior, known as hits; and then refining them into a structure or series of structures with relevant biological and drug-like activity, known as leads; are the key starting points for drug discovery programs[26-27]. For those involved in drug discovery, such as medicinal and computational chemists, the strategy can be subdivided into two main tasks; Lead identification and lead optimization. It is important to begin an approach starting from a compound, which shows some activity, albeit far from the desirable extent, against a given receptor or for a given disease. This process may be referred to lead identification, normally achieved through variations of substituents by medicinal chemists [28].

Eventually, these efforts are expected to yield compounds with improved potency and enhanced efficacy. It is also important to study pharmacokinetics, and toxicological profiles in-vivo, which can be achieved by the screening procedures. However, there are sometimes other factors, which play an important role. For instance, some efflux proteins such as P-glycoprotein, affect the bioavailability of a given therapeutic which may lead to declination in its activity [29].

It is not always easy to trace the biological activity of a compound to a particular target indeed the knowledge about the other influencing phenomenon is crucial. Our experience in kinases and in the design of inhibitors for the cancer reveals the obstacles for adopting a structure based drug design [30-33]. In many cases identification of the target protein and the active site is not sufficient to reach any logical end in a drug discovery process. There are many obstructions, which come in the way of designing new drugs. In designing inhibitors for membrane proteins, which are major drug targets; the difficulties in the structure identification prompts one to employ a modeled structure [34]. Similarly, the other factors like water mediation at the interface of biomolecular complexes, and protonation states are vital in determining the drug interaction. It is also important to account for the metal ion-binding sites, the nature of the residues in the active site, and the changes that are effected to the biological receptor upon binding of

drug molecules [35-37]. Therefore it is indispensable to take account of these small and subtle factors which play a crucial role in making a drug active, or otherwise, and therefore an exhaustive computational treatment still fall short of providing a reliable answer [38]. The quest for the development of databases and interest in developing rules and concepts to categorize the chemical entities as drug like molecules is extremely important to pursue [39-40].

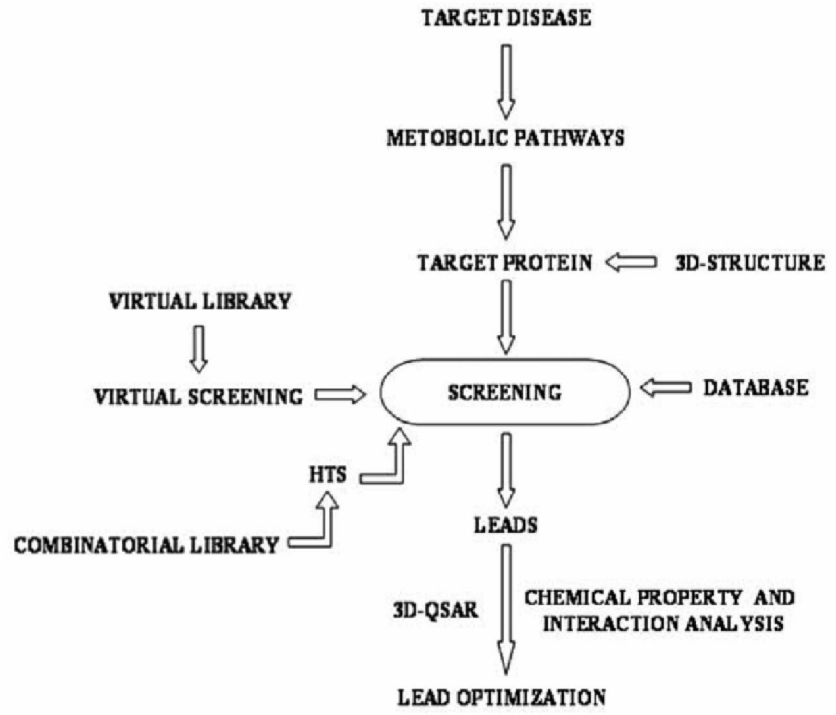


Fig.3: Schematic representation of finding a lead for a disease.

Thus quantifying drug-like nature of a given compound is also an important parameter in the virtual screening approaches. To identify hits or leads, high-throughput screening methods are normally used, in which a library containing hundreds of thousands of compounds is screened using an assay for biological activity. These approaches have been vigorously adopted by drug companies with single minded aim to churn out as many compounds as possible in search for leads, hoping that the greater the number of compounds, the greater the chance of finding hits.

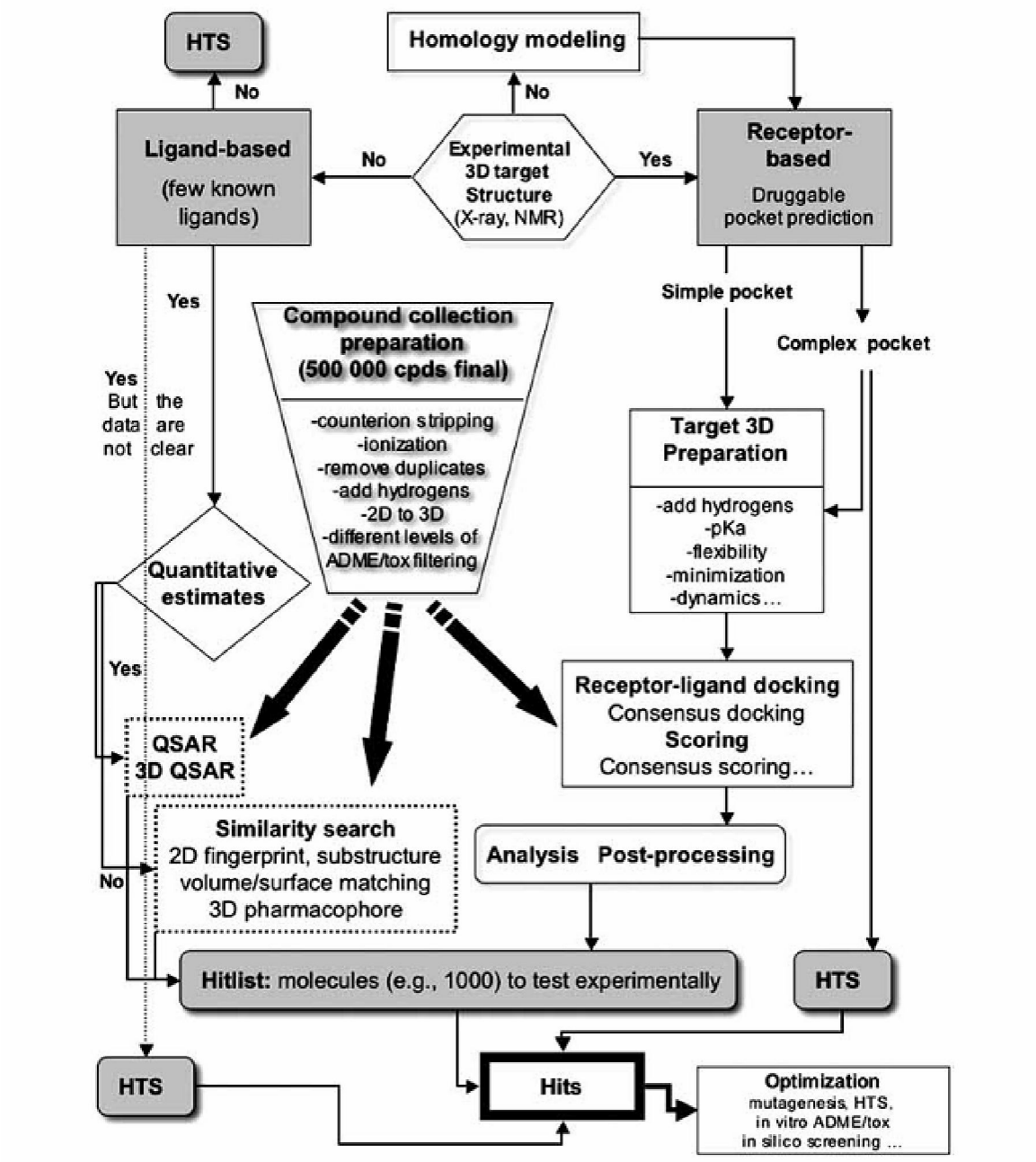


Fig.2: VLS-HTS flowchart: combining in silico screening and experimental HTS for hit finding

2. Web based resources for CADD

There are numerous websites on internet which help us in drug discovery process. Many of them are listed below [41-60] according to their use. Most of them are free resources. A short description regarding the tool is also provided. For some, the mechanism in which tool is working is also presented.

2.1 Chemistry tool kits, Graphics and Utilities

Cheminformatics: A list of freely available molecular datasets, incorporating information on QSAR, Toxicity, Metabolism, Permeability etc.
http://www.cheminformatics.org/

SoMFA:
http://bellatrix.pcl.ox.ac.uk/

E-Dragon:
http://146.107.217.178/lab/edragon

World wide molecular matrix, provide several services, including OpenBabel online Chemistry tools
http://wwmm-svc.ch.cam.ac.uk/wwmm/html/?cid=observer

Mol2 file format (2D or 3D) Mol2 format (Chemistry)
http://www.tripos.com/mol2/mol2_format2.html

The Protein Data Bank, see section describing the PDB format Macro-molecule 3D structures
http://www.rcsb.org/pdb

Information about different chemical structure file formats including SDF:
http://pubs3.acs.org/acs/journals/toc.page?incoden=jcisd8&indecade=1&involume=32&inissue=3

OpenBabel: File format conversion Chemistry tools
http://openbabel.sourceforge.net/babel.shtml
http://www.es.embnet.org/Services/MolBio/babel/
http://vcclab.org/lab/babel/

FAF-Drugs: OpenBabel online
http://bioserv.rpbs.jussieu.fr/Help/FAFDrugs.html

iBabel: File format conversion and other chemistry tools (essentially for Mac or Linux/Unix) Chemistry tools
http://www.macinchem.fsnet.co.uk/applescripts.htm

Tutorial for SMILES and chemistry toolkit SMILES format (Chemistry)
http://www.daylight.com/cheminformatics/tutorials/index.html

MMFF validation suite Simulation tools
http://www.ccl.net/cca/data/MMFF94s/

Chemistry toolkit- Chemistry tools
http://sourceforge.net/projects/perlmol
http://www.perlmol.org

IUPAC International Chemical Identifier project Chemistry tools
http://www.iupac.org/dhtml_home.html

GIF/PNG-creator with SMILES input Compound drawing
http://www2.chemie.uni-erlangen.de/services/gifcreator/

Computational chemistry package Chemistry tools
http://www-ra.informatik.uni-tuebingen.de/software/joelib/
http://sourceforge.net/projects/joelib/

Computational chemistry package- Chemistry tools
http://www.uku.fi/~thassine/ghemical/
http://www.uiowa.edu/~ghemical/osx.shtml

Chemical Development Kit
http://almost.cubic.uni-koeln.de/cdk/

Molecular Modeling Toolkit
http://starship.python.net/crew/hinsen/MMTK/

JME: Java Molecular Editor draws small molecules and get SMILES Compound drawing
http://www.molinspiration.com/jme/

Computer tools for chemistry Marvin is a suite of Java based chemistry software that have different forms: Marvin Applets, Marvin Beans, MarvinSketch-Chemistry tools
http://www.chemaxon.com/products.html

CDK: Chemistry development kit-Chemistry tools
http://sourceforge.net/projects/cdk/

Chemistry toolkit:
http://sourceforge.net/projects/frowns

A C++ toolbox for chemoinformatics- Chemistry tools
http://chemcpp.sourceforge.net/html/index.html

SketchEI: Chemical structure sketching tool Compound drawing
http://sourceforge.net/projects/sketchel

Online SMILES translator and structure generator Compound drawing
http://cactus.nci.nih.gov/services/translate/

The SDF toolkit (in Perl) essentially for small molecules Chemistry tools
http://cactvs.cit.nih.gov/SDF_toolkit/

To display and rotate macromolecules and small molecules in a single internet browser Molecular graphics
http://www.umass.edu/microbio/chime/index.html

MOLMOL: molecular graphics program for the structure of biological macromolecules Molecular graphics
http://hugin.ethz.ch/wuthrich/software/molmol/index.html

Cn3D: displays structures of macromolecules and performs sequence alignments Molecular graphics
http://www.ncbi.nlm.nih.gov/Structure/CN3D/cn3d.shtml

DINO: 3D viewer essentially for macromolecules-Molecular graphics
http://cobra.mih.unibas.ch/dino/intro.php

DisMol: Java applet viewer for macromolecules and small molecules Molecular graphics
http://www.rahul.net/pcm/dismol/

MolScript: creates molecular graphics image of macromolecules and small molecules-Molecular graphics
http://www.avatar.se/molscript/doc/molscript.html
http://www.strubi.ox.ac.uk/bobscript/

Colorado3D: web server for the visual analysis of protein structures Molecular graphics Structural analysis
http://asia.genesilico.pl/colorado3d/

Pymol: molecular graphics system to look at macromolecules and small molecules Molecular graphics
http://pymol.sourceforge.net/

VMD: molecular visualization program for displaying, animating, and analyzing large systems Molecular graphics
http://www.ks.uiuc.edu/Research/vmd/

MolWorks: graphic tool for drawing and sketching molecules Chemistry tools
http://www.molworks.com/en/

ChemSpotlight: metadata importer pluging for Mac OS X, which reads common chemical file formats (PDB, Mol2, SDF...) Chemistry tools
http://geoffhutchison.net/projects/chem/

DRAWNA: program for drawing schematic views of nucleic acids Molecular graphics
http://www-ibmc.u-strasbg.fr/upr9002/westhof/

ICM browser: biomolecular modeling package (can read many different file formats) Molecular graphics
http://www.molsoft.com/icm_browser.html

OpenEye Vida : molecular modeling package for macromolecules and small molecules (can read many different file formats) Molecular graphics
http://www.eyesopen.com/products/applications/vida.html

PovChem is a chemical visualization and illustration program, it can calculate and display hydrogen bonds Molecular graphics
http://www.chemicalgraphics.com/PovChem/

gOpenMol: allows visualization and analysis of small molecules, and to lesser extent protein structures, of chemical properties, total electron densities and molecule orbitals- Molecular graphics
http://www.csc.fi/gopenmol/

KMovisto: is a 3D molecule viewer essentially for Linux. It can import and export OpenBabel files Molecular graphics
http://mitglied.lycos.de/PageOfMH/

YASARA: is a molecular-graphics, -modeling and -simulation program-Molecular graphics & modeling
http://www.yasara.org/

GDIS: is a program for the display and manipulation of isolated molecules and periodic systems Molecular graphics
http://gdis.seul.org/
http://gdis.sourceforge.net/

KDrawChem and XDrawChem are molecular structure drawing programs Compound drawing
http://kemistry.sourceforge.net/kdrawchem.php
http://xdrawchem.sourceforge.net/

BKchem: is a chemical drawing program Compound drawing
http://bkchem.zirael.org/index.html

UCSF Chimera: biomolecular modeling package Molecular graphics & modeling
http://www.cgl.ucsf.edu/chimera/index.html

Tautomer generator is a program that generates a set of molecules (tautomers) from a molecular core and number of hydrogen atoms Simulation tools
http://sourceforge.net/projects/tautgen

Moloc: Roche Biostructural modeling package for small and large molecules Chemistry tools
http://www.moloc.ch/about.html

Open source molecule viewer Molecular graphics
http://www.jmol.sourceforge.net
http://www.jmol.org

JChemPaint: is a program for drawing 2D chemical structures Compound drawing
http://sourceforge.net/projects/jchempaint

MayaChemTools: is a growing collection of Perl scripts to support day-to-day computational discovery needs Chemistry tools
http://www.mayachemtools.org/index.html

A Java Chemical Structure Editor- Compound drawing
https://sourceforge.net/projects/mcdl

Links to Free Molecular Visualization and Modeling Software Molecular graphics & modeling
http://molvis.sdsc.edu/vis-res/molvisfw/author_no_descriptions.jsp

Bioclipse: is a Java-based visual platform for chemo- and bioinformatics Molecular graphics
http://bioclipse.net/index.php?option=com_content&task=view&id=2&Itemid=4

Information about SDF format SDF format
http://www.epa.gov/ncct/dsstox/MoreonSDF.html

2.2 ADME/tox Prediction and Databases

AlogP: Tools to predict logP (with several methods):
http://vcclab.org/lab/alogps
http://146.107.217.178/lab/alogps/

ADME/tox based on CDK:

http://blue.chem.psu.edu/~rajarshi/code/java/

ZINC:
http://zinc.docking.org

Find compound properties:
http://edetox.ncl.ac.uk/

ADME/tox computations:
http://sourceforge.net/projects/solubility/

Some online servers for ADME/tox calculations
http://www.eyesopen.com

http://www.molinspiration.com/

http://www.molsoft.com/mprop (also for 2D to 3D conversions)

http://www.chemaxon.com/products.html

http://www.mol-net.de/

FAF-Drugs: ADME/tox online
http://bioserv.rpbs.jussieu.fr/Help/FAFDrugs.html (also compound database)

Compute logP, retrieves experimental logP for over 13,000 compounds ADME/tox
http://www.syrres.com/esc/est_soft.htm
http://www.syrres.com/esc/est_kowdemo.htm

DBFILTER can check the mol2 format of compounds in a database and pick out problematic structures for the docking package DOCK. It can also compute ADME/tox properties (12 kinds of filters):
http://home.pchome.com.tw/team/gentamicin/mol/mol.htm

Xscore : logP computation tool:
http://sw16.im.med.umich.edu/software/xtool/

Compute logP ADME/tox
http://www.logp.com/

PHYSPROP: database, contains chemical structures, names and physical properties for over 25,000 compounds Chemistry Database
http://www.syrres.com/esc/physdemo.htm

The MetaSite has been developed to predict the site of metabolism (i.e., the place in a molecule where the metabolic reaction occurs) for substrates of 2C9, 2D6, 3A4, 1A2 and 2C19 cytochromes:
http://www.moldiscovery.com/soft_metasite.php

Metabolomic databases, which detail information on biological pathways and their workings are available as-Human Metabolite DataBase
http://www.metabolomics.ca/

MDL: Metabolite Database:
http://www.mdl.com/products/predictive/metabolite/index.jsp

jlogp/ logP prediction:
http://intro.bio.umb.edu/downloads/

Artificial neural network based approach, using atomic fragmental descriptors, to predict logP on a wide range of organic compounds and other ADME/tox tools (Demo)
http://www.compudrug.com/

PreADMET: is a web-based application for predicting ADME data
http://preadme.bmdrc.org/preadme/index.php

Chemical Effects in Biological Systems (CEBS) knowledge base (application of systems biology to ADME/Tox):
http://www.niehs.nih.gov/nct/cebs.htm

Toxicoinformatics database at the FDA (application of systems biology to ADME/Tox)
http://www.fda.gov/nctr/science/centers/toxicoinformatics/index.htm

EDGE: scientific resource for toxicology-related gene expression information (application of systems biology to ADME/Tox)
http://edge.oncology.wisc.edu/

cMolP: compute molecular properties
http://cgl.imim.es/biochemoinformatic.htm

PETRA: physicochemical properties of the compounds
http://www2.chemie.uni-erlangen.de/services/petra

OSIRIS: Log P, solubility, toxicity, drug likeness
http://www.organic-chemistry.org/prog/peo

DART, ADME-AP, TRMP, TTD: databases for facilitating the search for drug Absorption, Distribution, Metabolism, Excretion associated proteins Databases for ADME/tox:
http://bidd.nus.edu.sg/group/bidd.htm

Lazar: tool for the prediction of toxic activities of chemical structures
http://www.predictive-toxicology.org/lazar/form.php

Compumime: tool for the prediction of ADME properties
http://www.compumine.se/adme/adme.jsp

Biocatalysis/biodegradation database: tool for prediction of microbial catabolic reactions involving chemical structures ADME/tox
http://umbbd.msi.umn.edu/predict/

MolWorks: many tools including methods for estimating the properties of small molecules ADME/tox
http://www.molworks.com/en/

Distributed Structure-Searchable Toxicity (DSSTox) Database Network:
http://www.epa.gov/ncct/dsstox/index.html

Databases on toxicology, hazardous chemicals, environmental health, and toxic releases Databases & ADME/tox
http://toxnet.nlm.nih.gov/

2.3 Free Compound Collections, Target-Ligand Databases and Utilities

ChemBank: Free collections and utilities, known drugs, many annotated molecules, molecules with druglike and non-druglike properties Compound Database, Compound searching
http://chembank.med.harvard.edu

PubChem: An information resource linking chemistry and biology- Compound Database
http://pubchem.ncbi.nlm.nih.gov/

Chemical thesaurus: database including chemical entities, interactions, reactions, processes
http://www.chemthes.com/index.html

Chemical suppliers and collections-Compound Database
http://www.chemnet.com/

Web directory about compound collections and many related links, database search Compound Database, Compound searching
http://www.bioscreening.com/compound_libraries.htm

Free collections -Compound Database
http://www.cermn.unicaen.fr/chimiotheque

Free collections- Compound Database
http://www.genome.ad.jp/dbget/ligand.html

NMRShiftDB - Free collection, some molecules are in 3D-Compound Database
http://www.nmrshiftdb.org
http://sourceforge.net/projects/nmrshiftdb

Utilities such as ligand clustering and ligand similarity search -Compound searching
http://Ligand.info

ChemDB: Free collections and utilities such as similarity search-Compound Database,
http://cdb.ics.uci.edu/CHEM/Web/

FAF-Drugs: Free collections (and ADME/tox) and utilities-
It computes the following molecular properties:
(i) Molecular weight (part of Lipinski'sRO5), (ii) Hydrogen bond donors and acceptors (part of Lipinski's RO5), Defined as the number of hydrogen bond acceptors (sum of N +O) and hydrogen bond donors (sum of OH + NH). (iii) Number of rigid bonds, (iv) Number of rings, (v) Size of the rings, (vi) Number of rotatable bond, Defined as any single non-ringbond, bounded to non-terminal heavy atom. The amide C-N bonds are not considered because of their high rotational energy barrier.(vii) Number of carbon atoms, number of hetero atoms and ratio, (viii) Number of atom with a net charge, (ix) Sum of formal charges, (x)The Topological Polar Surface Area (TPSA)

http://bioserv.rpbs.jussieu.fr/Help/FAFDrugs.html
(see also: http://www.vls3d.com/)

ZINC: Free collections (and link to commercial vendors) Compound Database, ADME/Tox, Compound searching
http://zinc.docking.org

ChemMine: Free collections and similarity search utilities
http://bioweb.ucr.edu/ChemMine

Available Chemicals Directory ACD-(essentially commercial) - Compound Database, Compound searching
http://www.mdli.com

Compound Database, Compound Searching
http://www.chemnavigator.com Commercial collection (in part commercial)

Dictionary of small molecules-Compound Database
http://www.ebi.ac.uk/chebi/

BindingDB: Measured binding affinities, macromolecule-ligand complexes Compound Database & Macromolecules
http://www.bindingdb.org/

PDBbind: macromolecules with co-crystallized ligands and experimental binding affinities-Compound Database & Macromolecules
http://www.pdbbind.org/

KiBank: Proteins with co-crystallized ligands and experimental binding affinities - Compound Database & Macromolecules
http://kibank.iis.u-tokyo.ac.jp/

RELIBASE: Proteins with co-crystallized ligands-Compound Database & Macromolecules
http://relibase.ebi.ac.uk

CCDC/Astex validation test set: 305 protein-ligand complexes to calibrate docking and scoring tools-Compound Database & Macromolecules
http://www.ccdc.cam.ac.uk/products/life_sciences/validate/astex/

DrugBank: Numerous data about drugs and targets including drugs already in use
http://redpoll.pharmacy.ualberta.ca/drugbank/
http://www.drugbank.ca/

AffinDB: Proteins with co-crystallized ligands and experimental binding affinities Compound Database & Macromolecules
http://www.agklebe.de/affinity

Ilib Diverse: tool to create virtual drug-like libraries- Virtual Database generator
http://www.inteligand.com/

The US National Cancer Institute collections including natural products -Compound Database
http://dtp.nci.nih.gov/index.html

Compilation of web sites that offer chemistry databases/search services, data about toxic molecules, hazardous substances…database browser Compound Database & ADME/Tox
http://cactus.nci.nih.gov/ncidb2/chem_www.html
http://cactus.nci.nih.gov/ncidb2/

A free database of commercially available solvents searchable by many properties Solvent Database
http://solvdb.ncms.org/solvdb.htm

Models of main functional groups, courses in organic chemistry… Chemistry courses
http://www.molecularmodels.ca/
http://www.molecularmodels.ca/molecule/molecule_index.html

MoFa: Molecular fragment miner- Compound searching
http://www.inf.uni-konstanz.de/bioml/research/index.html

Main chemical structures -Compound Database, View properties, purchase compounds
http://sourceforge.net/projects/chem-file/
http://chemfinder.cambridgesoft.com/
View structures and data of Open NCI DB compounds
http://nci.chemfinder.com

Find compound properties:
http://edetox.ncl.ac.uk/

LIGAND:
http://www.genome.ad.jp/dbget/ligand.html

With eMolecules you can draw your chemical structure and instantly search millions of molecules from across the Web and from chemical suppliers worldwide Compound searching
http://www.emolecules.com/

Asinex
http://www.asinex.com/

Chembridge
http://www.chembridge.com

MayBridge
http://www.maybridge.com/

sMOL
http://www3a.biotec.or.th/isl/index.php/download

Family-based focused library:
http://www.xemistry.com

wwLigCSRre:
This webserver performs ligand-based screening using a 3D molecular similarity engine.
http://bioserv.rpbs.univ-paris-diderot.fr/wwLigCSRre.html

SuperLigands: a database of ligand structures derived from the Protein Data Bank with similarity searches and other tools Compound Database from the PDB, Compound searching
http://bioinf.charite.de/superligands/

Chemistry and biology database: numerous links (databases, tools) valuable for drug design projects Compound Database, macromolecules & links to programs
http://www.qspr.pe.kr/chemdb.html

Small molecules from the PDB- Compound Database from the PDB
http://alpha2.bmc.uu.se/hicup/

ChemID Plus: chemical name, physical and toxicological properties- Compound Database, ADME/Tox
http://chem.sis.nlm.nih.gov/chemidplus/

QueryChem: searches public databases using text and structure- Compound Database, Compound searching
http://llama.med.harvard.edu/~jklekota/QueryChem.html

Compound collection and building blocks- Compound Database
http://www.zelinsky.ru/

2.4 Small Molecules 2D-to-3D, 2D or 3D Search and De Novo Ligand Builder

2D to 3D based on CDK:
http://blue.chem.psu.edu/~rajarshi/code/java/

MOPSPIN:
Conformational search that uses MOPAC
http://www.ifi.unicamp.br/gsonm/mopspin/index.html

PADRE
Analyzes the results of conformational searches and measures the similarity and differences between molecules
ftp://ftp.CCL.net/pub/chemistry/software/UNIX/PADRE/

Accelrys:
http://www.accelrys.com/dstudio

2D to 3D conversion-Small molecules 2D-to-3D
http://relibase.ebi.ac.uk

Corina: 2D to 3D

http://www.molecular-networks.com/online_demos/corina_demo.html
http://bioserv.cbs.cnrs.fr/HTML_BIO/APPLET_ACD/create_molecule.html

Omega: 2D to 3D conversion
http://www.eyesopen.com

ICM: 2D to 3D conversion
http://www.molsoft.com

XDrawChem: Possible 2D to 3D conversion with BUILD3D
http://xdrawchem.sourceforge.net/

EasyMol: A Java tool to design 2D molecules and render them in 3D
http://sourceforge.net/projects/easymol

LigBuilder: Based on the three-dimensional structure of the target protein, it can automatically build ligand molecules within the binding pocket Compound searching
ftp2.ipc.pku.edu.cn

Surflex-Sim: ligand-based method- compound searching
http://www.biopharmics.com/downloads.html

AURAmol: allows a user to take a candidate 2D or 3D molecular shape and use it to search for similarly shaped molecules in large databases-Compound searching
http://www.cs.york.ac.uk/auramol/index.html

2D to 3D conversion and other tools
http://iris12.colby.edu/~www/jme/smiledg.html
http://iris12.colby.edu/~www/jme/dg.html
http://davapc1.bioch.dundee.ac.uk/programs/prodrg/

3DFS is a program to search 3D databases for compounds matching a pharmacophore query
http://projects.villa-bosch.de/mcm/people/wang/3dfs_body.html

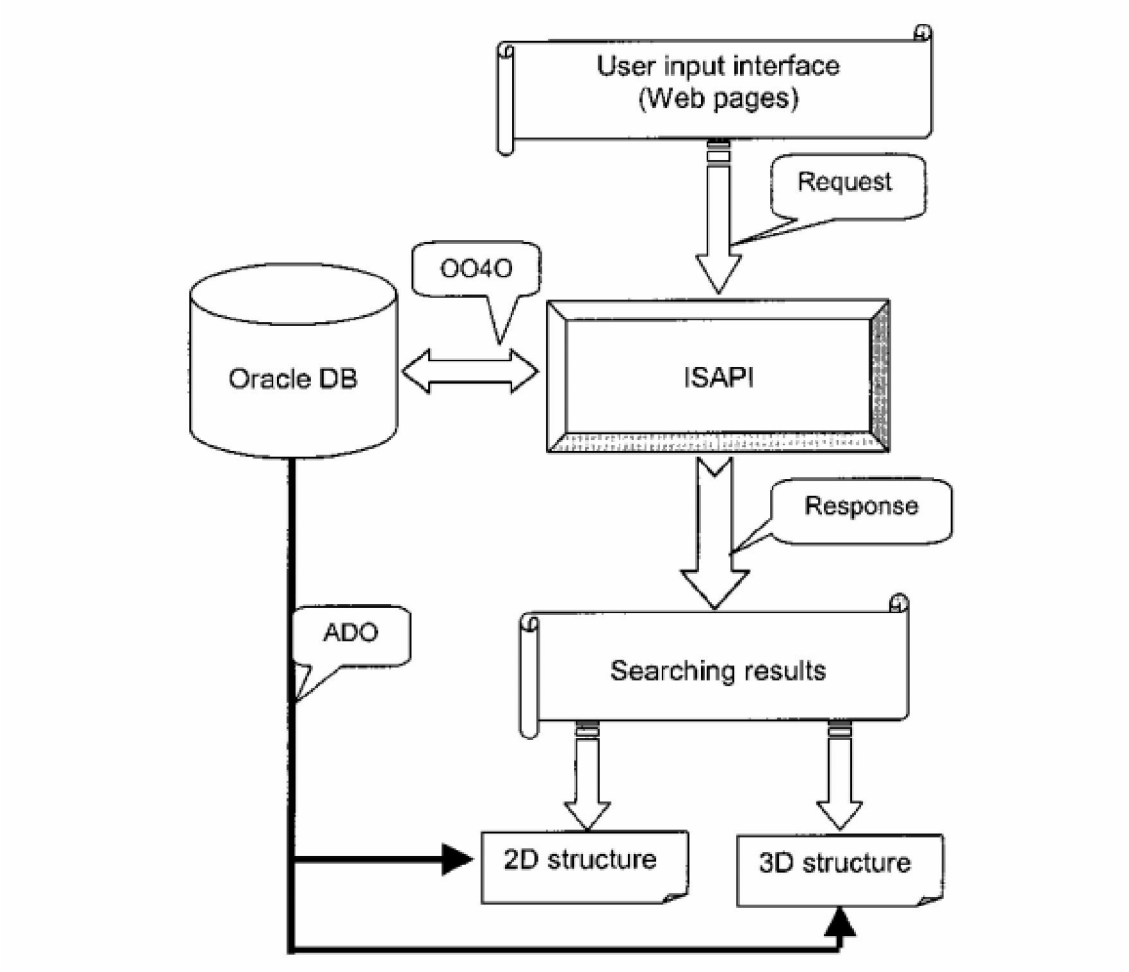


Fig.4: Architecture of web-based pharmacophore searching tool.

Frog: a free online drug 3D generator
http://bioserv.rpbs.jussieu.fr/Frog.html

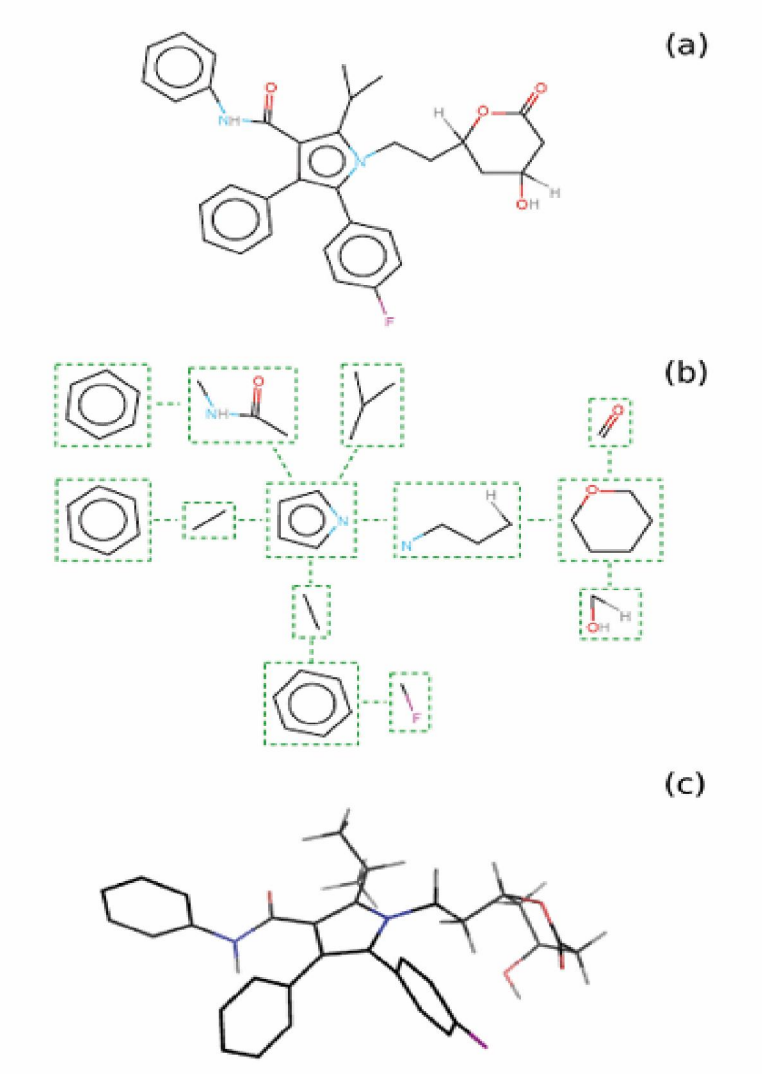


Fig.5: Flow chart of FROG processing. The compound (a) is decomposed as a graph involving rings and acyclic elements. (b)Acyclic elements are built from scratch. Ring

Conformations are extracted from library rings. Then all the elements are assembled to produce the complete compound structure (c).

2.5 Protein Data Bank, Receptor 3D Structures, Homology Modeling, 2D/3D Structure Prediction of the Receptor and Macromolecular Interaction Databases

The Protein Data Bank [106] Macromolecule database
http://www.rcsb.org/pdb

The RCSB PDB
www.pdb.org

The Macromolecular Structure Database at the European Bioinformatics Institute (MSD-EBI:
www.e-bi.ac.uk/msd

PDB Japan
www.pdbj.org

The BioMagResBank of the University of Wisconsins Madison, BMRB:
www.bmrb.wisc.edu

The Entrez Structure Database- Macromolecule database
http://www.ncbi.nlm.nih.gov/Structure/MMDB/mmdb.shtml

PDBCat can be used to manipulate and process PDB files using commonly available tools such as Perl, awk, etc. Tools to manipulate PDB files
http://www.ks.uiuc.edu/Development/MDTools/pdbcat/

Atlas of protein side-chain interactions within known protein structures and interactions with DNA- Macromolecule interaction database
http://www.biochem.ucl.ac.uk/bsm/sidechains/

BIND: The Biomolecular Interaction Network Database-
http://www.bind.ca/Action

DIP: Database of interacting proteins
http://dip.doe-mbi.ucla.edu/hold/main.html

MINT database [245] stores data on functional interactions between proteins
http://mint.bio.uniroma2.it/mint/Welcome.do

ProtCom : a collection of protein-protein transient complexes
http://www.ces.clemson.edu/compbio/protcom/

Many structural bioinformatics tools- to analyze macromolecules
http://www.expasy.org/

Many tools for structural bioinformatics, loop prediction, simulation, small molecules- Macromolecule interaction database
http://bioserv.rpbs.jussieu.fr/

The UCLA-DOE Structure Evaluation server is a tool designed to help in the refinement of crystallographic structures and models- Validate protein structure
http://nihserver.mbi.ucla.edu/Verify_3D/

ERRAT is a protein structure verification algorithm-Validate protein structure
http://nihserver.mbi.ucla.edu/ERRATv2/

SCWRL3.0 is the most recent version of the SCWRL program for prediction of protein side-chain conformations- Predict protein side chain conformation
http://dunbrack.fccc.edu/SCWRL3.php

SCit is a web server providing services for protein side chain conformation analysis and side chain positioning- Predict protein side chain conformation
http://bioserv.rpbs.jussieu.fr/SCit

Bodil: biomolecular modeling package
http://www.salilab.org/modeller/modeller.html

Modeller: software package for homology or comparative modeling of protein 3D structures
http://www.abo.fi/fak/mnf/bkf/research/johnson/bodil/about.php

Jackal: protein structure modeling package
http://trantor.bioc.columbia.edu/programs/jackal/index.html
http://honiglab.cpmc.columbia.edu/cgi-bin/jackal/nest.cgi

Wurst: web server for protein structure prediction with a structural scoring function, sequence profiles and optimized substitutions matrices Protein structure prediction
http://www.zbh.uni-hamburg.de/wurst/

PSIPRED: web servers performing secondary structure prediction, transmembrane topology prediction or protein fold recognition Protein structure prediction
http://bioinf.cs.ucl.ac.uk/psipred/psiform.html

PredictProtein: webserver for homology modeling and protein function prediction
http://www.predictprotein.org/newwebsite/

Prospect-PSPP: automatic computational pipeline for protein structure prediction
http://csbl.bmb.uga.edu/protein_pipeline/login.php

Robetta: web server for protein structure prediction and analysis
http://robetta.bakerlab.org/
SPACE: suite of tools for protein structure prediction and analysis based on complementarity and environment
http://ligin.weizmann.ac.il/space/

Java Protein Dossier: web-based visualization tool including large collections of physico-chemical parameters describing proteins' structure, stability, function and interaction with other macromolecules
http://trantor.bioc.columbia.edu/SMS/index_s.html

Consolv: Tool to analyze protein-water interaction- Protein structure analysis
http://www.bch.msu.edu/labs/kuhn/web/software.html

CAMPO, SCR_FIND, CHC_FIND: web tools to analyze evolutionary conserved residues, structurally conserved regions and conserved hydrophobic contacts Protein structure analysis
http://schubert.bio.uniroma1.it/SCR_FIND/
http://schubert.bio.uniroma1.it/CHC_FIND/
http://schubert.bio.uniroma1.it/CAMPO/

PRED-TMBB/ Pred-TMBB: web server for predicting the topology of beta-barrel outer membrane proteins
http://bioinformatics.biol.uoa.gr/

PDBS_V2.php ProteinDBS: web server for detection of similar protein tertiary structures
http://proteindbs.rnet.missouri.edu/

FATCAT: web server for flexible structure comparison and structure similarity searching
http://fatcat.burnham.org/

PreBi: Server for predicting biological homo protein-protein interfaces in crystal protein structures Protein structure analysis, Interface search
http://pre-s.protein.osaka-u.ac.jp/~prebi/

CaspR: web server for automated molecular replacement, method of choice for X-ray crystallography structure determination when structural homologues are available in PDB
http://www.igs.cnrs-mrs.fr/Caspr2/index.cgi

PREDITOR: Program for predicting dihedral angles from chemical shifts and/or sequential homology
http://wishart.biology.ualberta.ca/shiftor/cgi-bin/preditor_current.py

Protein Peeling: Tool for splitting a 3D protein structure into protein units which are an intermediate level of protein structure description between protein domains and secondary structures
http://www.ebgm.jussieu.fr/~gelly/index.html
OPAAS: web server for optimal, permuted and other alternative alignments of protein structures
http://opaas.ibms.sinica.edu.tw

Localizome: server for identifying transmembrane topologies and TM helices of eukaryotic proteins using domain information- Protein structure prediction
http://localizome.org/

PBE: platform for protein structure analysis using well defined library of short structural motifs (SSMs) known as structural alphabets-Protein structure prediction
http://bioinformatics.univ-reunion.fr/PBE/

SABBAC: online structural alphabet-based protein backbone reconstruction from alpha-carbon trace- Protein structure prediction
http://bioserv.rpbs.jussieu.fr/SABBAC.html

(PS)2: automated homology modeling server using a consensus strategy between psi-blast, impala and T-coffee with a final 3D structure modeled with Modeller
http://ps2.life.nctu.edu.tw/

ArchPRED: template based loop structure prediction server -Loop structure prediction
http://www.fiserlab.org/servers/archpred

TransFold: web server for predicting the structure and residue contacts of transmembrane beta-barrels- Protein structure prediction
http://bioinformatics.bc.edu/clotelab/transFold/

Harmony: web server for the assessment of protein structures- Protein structure validation
http://caps.ncbs.res.in/harmony/

RosettaDesign: Server for identifying low energy amino acid sequences from the backbone coordinates of the target structure- Protein structure prediction
http://rosettadesign.med.unc.edu/

CODA: combined algorithm for predicting loops
http://www-cryst.bioc.cam.ac.uk/coda/search_coda.html

ProteMiner: software package that searches the PDB for proteins containing a substructure similar to the one specified by the user
http://proteminer.csie.ntu.edu.tw/

MolProbity: web server for structure validation and all atoms contact analysis for nucleic acids and their complexes
http://molprobity.biochem.duke.edu/

ASTRAL: web server providing databases and tools useful for analyzing protein structures and their sequences
http://astral.berkeley.edu/

Decoys 'R' us: database of computer generated conformations of proteins sequences that possess some characteristics of native proteins- Database of side-chain, protein structure validation
http://dd.stanford.edu/

iSee: software package including the structural genomics workflow into one file, from DNA to protein structure, using the Molsoft ICM-browser technology Protein structure analysis, annotation
http://www.sgc.ox.ac.uk/iSee/

Automatic threading, optimization modeling and evaluation, homology modeling- Protein structure prediction
http://bioserv.cbs.cnrs.fr/

2.6 Pocket Prediction and Search for Functional Regions on Targets, Analysis of Interfaces

Server to predict binding sites, Q-site and pocketfinder
http://www.bioinformatics.leeds.ac.uk/qsitefinder
http://www.bioinformatics.leeds.ac.uk/pocketfinder

CASTp: Server to predict binding site - Binding sites and active sites of proteins and DNAs are often associated with structural pockets and cavities Binding site prediction
http://sts.bioengr.uic.edu/castp/

SCREEN: Server to predict binding site
http://interface.bioc.columbia.edu/screen

MEDock: Online tool to define binding site- Binding site prediction
http://medock.csie.ntu.edu.tw/
http://bioinfo.mc.ntu.edu.tw/medock/

Catalyst: Pharmacophore can be designed de novo based on complimentarily to a known ligand binding site.
http://www.accelrys.com/products/catalyst/

Phase: Pharmacophore can be designed de novo based on complimentarily to a known ligand binding site.
http://www.schrodinger.com/products/14/13/

MOE: Pharmacophore can be designed de novo based on complimentarily to a known ligand binding site.
http://www.chemcomp.com/software.htm

PharmaGist: Pharmacophore can be designed de novo based on complimentarily to a known ligand binding site.
http://bioinfo3d.cs.tau.ac.il/PharmaGist

ConSurf identifies functional regions in proteins- Binding site prediction
http://consurf.tau.ac.il

Rate4Site: an algorithmic tool for the identification of functional regions on proteins by surface mapping of evolutionary determinants within their homologues-Binding site prediction
http://www.tau.ac.il/~itaymay/cp/rate4site.html

PASS: Pocket detection method based upon the size, shape of buried volumes
Pocket detection
http://www.ccl.net/cca/software/UNIX/pass/overview.shtml

Voidoo: Pocket detection tool
http://xray.bmc.uu.se/usf/voidoo.html

SurfNet: Pocket detection tool
http://www.biochem.ucl.ac.uk/~roman/surfnet/surfnet.html

Gramm: Tools for protein-protein docking
http://vakser.bioinformatics.ku.edu/resources/gramm/gramm1/

GrammX: web interface of Gramm -Macromolecular docking
http://vakser.bioinformatics.ku.edu/resources/gramm/grammx

Intervor: Tools to analyze interfaces-Interface analysis
http://bombyx.inria.fr/Intervor/intervor.html

MolSurfer: a macromolecular interface navigator-Interface analysis
http://projects.villa-bosch.de/mcm/software/molsurfer

LIGIN: Molecular docking using surface complementarity. The LIGIN program is also available as part of the WHATIF software package. Macromolecular docking
http://swift.cmbi.kun.nl/swift/ligin/

Protein docking tools:
Patch Dock: webserver for macromolecules and small molecules docking based on shape complementarity criteria
http://bioinfo3d.cs.tau.ac.il/
PyDock: tool for protein-protein docking
http://mmb.pcb.ub.es/PyDock/

Crescendo: functional site prediction by the detection of protein-protein interaction sites-
http://www-cryst.bioc.cam.ac.uk/~viji/docking/

iMolTalk: On-line tools including detection of the interface between two chains of a structure Interface analysis
http://i.moltalk.org/

ClusPro : protein-protein docking webserver using 3 docking programs - DOT, ZDOCK , GRAMM Macromolecular docking
http://nrc.bu.edu/cluster/

ZDOCK: protein-protein docking software evaluating based on shape complementarity, desolvation energy and electrostatics.
Best predictions from ZDOCK are given to RDOCK where they are minimized by CHARMM Macromolecular docking
http://zlab.bu.edu/zdock/index.shtml

Protein-protein docking package
http://www.biotec.tu-dresden.de/~bhuang/bdock/bdock.html

DOCK: generates many possible orientations (and more recently, conformations) of a putative ligand within a user-selected region of a receptor structure, orientations may be scored using several schemes designed to measure steric and/or chemical complementarity of the receptor-ligand complex, evaluate likely orientations of a single ligand, or to rank molecules from a database, search databases for DNA-binding compounds, examine possible binding orientations of protein-protein and protein-DNA complexes, design combinatorial libraries.
http://dock.compbio.ucsf.edu/

GRAMM: Global Range Molecular Matching, empirical approach to smoothing the intermolecular energy function by changing the range of the atom-atom potentials, requires only the atomic coordinates of the two molecules to predict the complex, structure (no binding site information needed), performs an exhaustive 6-dimensional search through the relative translations and rotations of the molecules.
http://vakser.bioinformatics.ku.edu/main/resources_gramm1.03.php

ICM-Dock: fast and accurate docking simulations, unique set of tools for accurate individual ligand-protein docking, peptide-protein docking, and protein-protein docking, including interactive graphics tools
http://www.molsoft.com/docking.html

3D-Dock Suite: incorporating FTDock, RPScore and MultiDock, FTDock (Fourier Transform Dock), performs rigid-body docking on two biomolecules in order to predict their correct binding geometry, outputs multiple predictions that can be screened using biochemical information, RPScore (Residue level Pair potential Score), uses a single, distance constraint empiricaly derived pair potential to screen the ouptut from FTDock, can reduce dramatically the list of possible complexes within which can be found a correct solution, MultiDock (Multiple copy side-chain refinement Dock)
http://www.sbg.bio.ic.ac.uk/docking/

DOT: Daughter Of TURNIP, Turnip was used to study of macromolecular docking, computation of the electrostatic potential energy between two proteins or other charged molecules.
http://www.sdsc.edu/CCMS/DOT/

ESCHER NG: enhanced version of the original ESCHER protein-protein automatic docking system, protein-protein and DNA-protein docking capability, fast surface calculation based on the NSC algorithm
http://users.unimi.it/~ddl/escherng/index.htm
http://www.ddl.unimi.it/escherng/index.htm

HADDOCK: High Ambiguity Driven protein-protein Docking, biochemical and/or biophysical interaction data such as chemical shift perturbation data resulting from NMR titration experiments or mutagenesis data introduced as ambiguous interaction restraints (AIRs) to drive the docking process, AIR - defined as an ambiguous distance between all residues shown to be involved in the interaction
http://www.nmr.chem.uu.nl/haddock/

HEX: protein docking and molecular superposition program, use spherical polar Fourier correlations to accelerate docking calculations
http://www.loria.fr/~ritchied/hex/
http://www.csd.abdn.ac.uk/hex/

BDOCK: protein-protein docking software integrating the degree of burial of surface residues into protein-protein docking
http://graylab.jhu.edu/docking/rosetta/

MolFit: protein-protein docking software estimating the extent of geometric and chemical surface complementarity
http://www.weizmann.ac.il/Chemical_Research_Support//molfit/home.html

FTDock (Fourier Transform Dock) performs rigid-body docking on two biomolecules in order to predict their correct binding geometry
http://www.bmm.icnet.uk/docking/

GRID: Tool for analysis of binding sites
http://www.moldiscovery.com/soft_grid.php

SuperStar: Tool for analysis of binding sites
http://www.ccdc.cam.ac.uk/products/life_sciences/superstar

SitesBase: Tool for analysis of binding sites
http://www.bioinformatics.leeds.ac.uk/sb/

Prism: predicts and analyzes putative protein–protein interaction sites.
http://gordion.hpc.eng.ku.edu.tr/prism

SiteEngines: recognition and comparison of binding sites and protein–protein interfaces
http://bioinfo3d.cs.tau.ac.il/SiteEngine/
http://bioinfo3d.cs.tau.ac.il/I2I-SiteEngine/

FastContact: a free energy scoring tool for protein-protein complex structures
http://structure.pitt.edu/servers/fastcontact/

2.7 Comparison of Binding Sites/Protein Functional Sites – Protein Function Prediction.

Annotated binding sites- Binding site analysis
http://smid.blueprint.org

PDBSiteScan automatically performs the best superposition of sites from PDBSite with the 3D structure of a protein under study Binding site comparison
http://wwwmgs.bionet.nsc.ru/mgs/gnw/pdbsitescan/

SiteBase: compare nucleotide and ligand binding site
http://www.bioinformatics.leeds.ac.uk/sb/

PINTS: detection of similarities between protein structures consisting of amino acids those are close in space- Structural similarity search
http://www.russell.embl.de/pints/

Tools for analysis of binding sites and to find similar motifs based on a search in the PDB- Structural similarity search
http://sumo-pbil.ibcp.fr/

SPASM: detection of similar motifs based on a search in the PDB- Structural similarity search
http://portray.bmc.uu.se/cgi-bin/spasm/scripts/spasm.pl

Catalytic site atlas: find similar catalytic sites-Structural similarity search
http://www.ebi.ac.uk/thornton-srv/databases/CSA/

pvSoar: detection of a protein surface pattern derived from a pocket or a void against all known surface patterns from the CASTp database Structural similarity search, Binding site Comparison
http://pvsoar.bioengr.uic.edu/

Sc-PDB: tool for analysis of binding sites
http://bioinfo-pharma.u-strasbg.fr/scPDB/

Pdbfun: web server for the identification of local structural similarities between annotated residues in proteins
http://pdbfun.uniroma2.it/

Ligand transposition server- Binding site comparison
http://abcis.cbs.cnrs.fr/LIGBASE_SERV_WEB/PHP/simdock.php

Docking with substructure query in a protein family- Binding site comparison
http://abcis.cbs.cnrs.fr/LIGBASE_SERV_WEB/PHP/fragamar.php

SiteEngine- recognizes regions on the surface of one protein that resemble a specific binding site of another Structural similarity search, Binding site comparison
http://bioinfo3d.cs.tau.ac.il/SiteEngine/

The ProFunc server- helps to identify the likely biochemical function of a protein from its three-dimensional structure- Binding site prediction
http://www.ebi.ac.uk/thornton-srv/databases/ProFunc/

CPASS: website for active site comparison- Binding site comparison
http://bionmr-c1.unl.edu/

eF-Site: Electrostatic surface of functional sites- Electrostatic computations, binding site search
http://ef-site.hgc.jp/eF-site

proSAT2: Features for visualizing SwissProt and PROSITE functional annotations by mapping of information on variants and mutations from the UniProt KnowledgeBase and the BRENDA enzyme information system onto protein structures Functional site visualization
http://projects.villa-bosch.de/dbase/ps2/

FeatureMap3D: tool mapping protein features such as posttranslational modifications, protease cleavage sites or exonic structure onto 3D structures of homologous proteins Functional site visualization
http://www.cbs.dtu.dk/services/FeatureMap3D/

Rasmol:
http://www.openrasmol.org
Deepview:
http://us.expasy.org/spdbv/

AstexViewer:
http://www.astex-therapeutics.com

ProKware: Integrated system containing interactive graphic interface and abundant protein property annotations a the structural level and domain-domain interaction in protein 3D structures-Functional site visualization
http://prokware.mbc.nctu.edu.tw/

Protemot: server that carries out prediction of protein binding sites based on the structural templates automatically extracted from the PDB crystals-Binding site prediction
http://protemot.csie.ntu.edu.tw/step1.cgi

2.8 Target Analysis: Flexibility, Energy Minimization, Normal Modes, Molecular Dynamics, Water Molecules in Targets, Ions, pKa and Electrostatics, Point Mutations and Related Utilities

I-Mutant 2.0: predicting stability changes upon mutation from the protein sequence or structure Analysis of mutations
http://gpcr.biocomp.unibo.it/cgi/predictors/I-Mutant2.0/I-Mutant2.0.cgi

Integrated Packages

NWChem: This program has been devoted to provide a maximum efficiency on high-performance parallel supercomputers as well as on conventional workstation clusters. The input geometry has the form of Cartesian coordinates or a Z-matrix. NWChem consists of independent modules that perform different theory options: HF (closed-shell RHF, open-shell ROHF and open-shell UHF), DFT, MP2, CASSCF, CC and CI. NWChem can perform the following operations: single point energy, evaluation of the first and second energy derivatives, geometry optimization, transition state search, molecular vibrations calculation and COSMO energy evaluation. The following properties can be computed for all wave functions that produce orbitals: multipole moments, Mulliken population analysis and bond order analysis, electrostatic potential, electric field, electric field gradient, electron and spin density, and NMR chemical shifts (only for RHF).

www.emsl.pnl.gov/docs/nwchem/nwchem.html

Ghemical: supports both quantum mechanics (semi-empirical and ab initio) and molecular mechanics models. Geometry optimization, molecular dynamics and a large set of visualization tools are currently available.
http://bioinformatics.org/ghemical/

The NIST-CCCBD: (National Institute of Standards and Technology—Computational Chemistry Comparison and Benchmark Database) is a web service that allows the comparison on line between different ab initio computational methods for the prediction of thermochemical properties. CCCBD allows geometry optimization and the calculation of vibrational frequencies, barriers of internal rotation, and electronic energy levels. In addition, enthalpies of formation, entropies, and heat corrections (integrated heat capacity) can be computed. Computed properties such as atomic charges, electric multipole moments, polarizabilities and HOMO-LUMO gaps are also available. CCCBD provides a binary decomposition products search from a starting specified molecule or more reactants. No Z-matrix is necessary, just a formulae or a CAS number. However, the program cannot use atoms with atomic number greater than 18 and cannot use more than six heavy atoms and twenty total atoms (which is very limiting).
http://srdata.nist.gov/cccbdb/

GAMESS-US: (General Atomic and Molecular Electronic Structure System) It is a well-known QM package GAMESS computes analytic energy gradients for all SCF and DFT wavefunctions, includes closed or open shell MP2 or closed shell CI, optimizes molecular geometries using the energy gradient in term of Cartesian or internal coordinates, searches transition state structures, computes normal modes, vibrational frequencies, and IR intensities. A variety of molecular properties ranging from multipole moments, electrostatic potential, electric field and electric field gradients, electron density, spin density to Mulliken and Lowding population analysis can be calculated. The COSMO model is also implemented. GAMESS has its own graphics interface and in addition a large number of codes work directly with GAMESS outputs
http://www.msg.ameslab.gov/gamess/graphics/graphics.html
http://www.msg.ameslab.gov/gamess/

Specialized DFT Program

Dacapo: is a total energy program http://www.fysik.dtu.dk/camp/dacapo.html

EMSL: (Environmental Molecular Sciences Laboratory) web service allows to extract Gaussian basis sets, and any related effective core potentials, from the Molecular Science Research Center's Basis Set Library.
http://www.emsl.pnl.gov/forms/basisform.html

Free Semi-Empirical Packages

MOPAC7:
ftp://esca.atomki.hu/mopac7/linux/
www.ccl.net/cca/software/linux/mopac7/

Free Solvation Programs:

These solvation models are used to calculate Lo'wdin partial atomic charges for gas and liquid phases and other classes of charges.
http://comp.chem.umn.edu/

OMNISOL: is a program for the estimation of solvation free energies for organic molecules in water or organic solvents, using the SM5 solvation model.
http://comp.chem.umm.edu/omnisol/

GAMESOL: is a set of modules that can be added to GAMESS; they allow the inclusion of solvation effects at the ab initio SCRF level.
http://comp.chem.umm.edu/gamesol/

AMSOL: uses solvation models ranging from SM1 to SM5.42
http://comp.chem.umm.edu/amsol/

Free Molecular Visualization Programs

gOpenMol: It can be used for the display and analysis of molecular structures, and properties, isocontour surfaces of grid data (such as molecular orbitals and electron densities) calculated with GAMESS and MOPAC for instance. The program can also be used to display electrostatic potentials generated from GAMESS.
http://www.csc.fi/gopenmol/index.phtml

WebMO: is an integrated Java 3D molecular editor, easy to use with a click-and-draw interface.
http://www.webmo.net/index.html

MOLDEN: for displaying 2D/3D outputs from GAMESS, Dalton and MOPAC packages. It is able to display molecular orbitals, electron and atomic densities. It can calculate and display the true or multipole derived electrostatic potential and atomic charges can be fitted to the electrostatic potential calculated on a Connolly surface.
http://www.caos.kun.nl/,schaft/molden/molden.html

VIZUALIZE: is a new GAMESS interface for ab initio energy calculations and surface generation. It offers some very powerful surfacing techniques. Besides just displaying molecule models and surfaces, VISUALIZE gives also access to a wide array of ab initio calculations (HF, MP2, CI, and solvation models) for both energies and geometry optimizations. However, the program supports only PDB and DAS files. To open different files, WebLab viewer (a free version of WebLab viewer Lite is available from www.msi.com) should be used to convert it into one of these two formats.
http://www.compbio.net/downloads/visualize/

MOLEKEL: is an advanced interactive 3D molecular graphics system developed at the University of Geneva and the Swiss Federal Institute of Technology. MOLEKEL uses different rendering representations, measures atom – atom distances, angles and torsion angles, and can superimpose molecules. It calculates and displays isosurfaces of electron and spin densities as well as molecular orbitals from GAMESS outputs.
http://www.cscs.ch/molekel/

ViewMol3D. ViewMol3D can draw molecules from GAMESS and MOPAC outputs.
http://members.tripod.com/~RedAndr/vm3/index.htm

SRide: server for identifying stabilizing residues in proteins- Analysis of mutations
http://sride.enzim.hu

PS13:
http://psicode.org

TINKER:
http://dasher.wustl.edu/tinker

MutDB services: interactive structural analysis of mutation data Analysis of Mutations
http://www.mutdb.org/

FoldX: empirical force field that was developed for the rapid evaluation of the effect of mutations on the stability, folding and dynamics of proteins and nucleic acids- Analysis of mutations
http://foldx.embl.de/
http://fold-x.embl-heidelberg.de:1100/cgi-bin/main.cgi

Tinker online- Molecular modeling & graphics, simulations
http://www.es.embnet.org/Services/MolBio/tinker/

AMMP is a modern full-featured molecular mechanics, dynamics and modeling program. It can manipulate both small molecules and macromolecules including proteins, nucleic acids and other polymers Molecular modeling & graphics, simulations
http://www.cs.gsu.edu/~cscrwh/ammp/ammp.html

PINY_MD is capable of performing a wide variety of molecular dynamics, electronic structure, and geometry optimization calculations. Such capabilities include force-field based simulations on system ranging in complexity from simple molecular liquids and crystals to large biomolecular systems Molecular modeling & graphics, simulations
http://homepages.nyu.edu/~mt33/PINY_MD/PINY.html

Macromolecules and small molecules modeling
http://dasher.wustl.edu/tinker/

SIFT: analyzes protein point mutations- Analysis of mutations

http://blocks.fhcrc.org/sift/SIFT.html

PolyPhen: analyzes protein point mutations- Analysis of mutations
www.bork.embl-heidelberg.de/PolyPhen/

WEBnm@: a web application for normal mode analysis of proteins to investigate for large amplitude movements. Normal modes are performed with MMTK- Molecular simulations
http://www.bioinfo.no/tools/normalmodes

Online tools to compute protein electrostatics based on MEAD: PCE (Protein Continuum Electrostatics)
http://bioserv.rpbs.jussieu.fr/PCE

H++: a server for estimating pKas and adding missing hydrogens to acromolecules Electrostatics
http://biophysics.cs.vt.edu/H++

ProPka: fast empirical method to predict pKas in proteins Electrostatics
http://propka.chem.uiowa.edu/

APBS: software package for the numerical solution of the Poisson-Boltzmann equation Electrostatics
http://sourceforge.net/projects/apbs

Open Protein Simulator (OOPS) is a program designed to serve as a test bed for different algorithms for protein folding, dynamics and structure prediction Molecular simulations
http://sourceforge.net/projects/oops-pl

Tools to analyze protein structures- Molecular modeling, structural analysis
http://somosierra.cnb.uam.es/wwwPDG/Software/software.php

Web resources for protein structure analysis, links to numerous web sites Molecular modeling, structural analysis
http://www.ysbl.york.ac.uk/~tom/structure.html

WhatIf: versatile molecular modeling package- Molecular modeling, structural analysis
http://swift.cmbi.ru.nl/whatif/

elNémo is the Web-interface to The Elastic Network Model, a fast and simple tool to compute the low frequency normal modes of a protein Molecular simulations
http://igs-server.cnrs-mrs.fr/elnemo/

GRASS: Graphical Representation and Analysis of Structure Server-Molecular surface analysis

http://honiglab.cpmc.columbia.edu/cgi-in/GRASS/surfserv_enter.cgi

PROFbval: method for predicting residue mobility based on amino-acid sequence. Identification of extremely rigid or flexible residues on the protein surface is helpful for identifying functionally important residues in proteins. A common measure of atom mobility in proteins is B-value data from x-ray crystallography structures. PROFbval is the first web server to predict normalized backbone B-values from amino-acid sequence Protein flexibility prediction
http://cubic.bioc.columbia.edu/services/profbval/

Non covalent bond finder- Structural analysis
http://www.umass.edu/microbio/chime/find-ncb/

Structural analysis of proteins- Structural analysis
http://kinemage.biochem.duke.edu/~jsr/html/anatax.2a.html

MutaProt: Tool for structural analysis of point mutations: MutaProt.Analysis of mutations
http://www.bioinfo.weizmann.ac.il/mutaprot

SVMProt: protein functional family prediction- Structural analysis
http://jing.cz3.nus.edu.sg/cgi-bin/svmprot.cgi

This program places the required number of sodium ions around a system of electric charges, e.g., the atoms of a biological macromolecule (protein, DNA, protein/DNA complex) Tools to prepare molecules for simulations
http://www.ks.uiuc.edu/Development/MDTools/sodium/

GULP: is a program for performing a variety of types of simulation on materials using boundary conditions of 0-D (molecules and clusters), 1-D (polymers), 2-D (surfaces, slabs and grain boundaries), or 3-D (periodic solids)- Molecular simulations
http://www.ivec.org/GULP/

The Biomolecule Toolkit is a library for modeling biological macromolecules such as proteins, DNA and RNA. It provides a C++ interface for common tasks in structural biology to facilitate the development of molecular modeling, design and analysis tools
http://sourceforge.net/projects/btk

Monster: web application for inferring potentially stabilizing non-bonding interactions in macromolecular structures Structural analysis, mutations
http://monster.northwestern.edu/monster.jsp

DisEMBL: computational tool for prediction of disordered/unstructured regions within a protein sequence. Structural analysis, mutations
http://dis.embl.de/

Disopred2: Prediction and functional analysis of native disorder in proteins Structural analysis, mutations
http://bioinf.cs.ucl.ac.uk/disopred/disopred.html

AVP (Another Void Program) is a new method for the analysis of voids in proteins and packing quality in a single united program Cavity search
http://www.bioinf.org.uk/software/avp/index.html

YUP: A Molecular Simulation Program for Coarse-Grained and Multiscaled Models (Python) Molecular simulations
http://rumour.biology.gatech.edu/YammpWeb/

oGNM: calculating the equilibrium dynamics of any structure submitted in PDB format, using the Gaussian network Model (GNM) Molecular simulations, flexibility
http://ignm.ccbb.pitt.edu/GNM_Online_Calculation.htm
ProtoMol: object-oriented component based framework for molecular dynamics simulations Molecular simulations
http://sourceforge.net/projects/protomol

PDB_Hydro: Tools for mutating and solvating protein structures Tools to prepare molecules for simulations
http://lorentz.immstr.pasteur.fr/pdb_hydro.php

PHEPS: fast pH-dependent electrostatic calculations for proteins Electrostatics
http://pheps.orgchm.bas.bg/home.html

PPD: an integrated, web-accessible database of experimentally determined protein pKa values Electrostatics
http://www.jenner.ac.uk/PPD

Biodrug Screening:
Ranking of predocked drug-ligand complexes data base:
http://www.biodrugscreen.org/

Super Natural: A searchable database of available natural compounds.
http://bioinformatics.charite.de/supernatural

pKD: re-designing protein pKa values for a set of point mutations Electrostatics, mutations
http://polymerase.ucd.ie/cgi-bin/pKa_Design/server_start.cgi

NOMAD-Ref: Tools using normal modes for structural refinement of large proteins Molecular simulations
http://lorentz.immstr.pasteur.fr/nomad-ref.php

UMMS: Tool using normal mode to analyze the harmonic behaviors (fluctuations) of a macromolecule around its equilibrium and elastic network interpolation to generate the anharmonic pathways for conformational transitions of two metastable conformations of the same macromolecule Molecular simulations, flexibility
http://biomechanics.ecs.umass.edu/umms.html

Readout: structure-based calculation of direct and indirect readout energies and specificities for protein-DNA recognition Analysis of protein-DNA complex and DNA structure
http://gibk26.bse.kyutech.ac.jp/jouhou/readout/

CUPSAT: server for prediction of protein stability upon point mutations by assessment of the difference in free energy of unfolding between wild-type and mutant proteins using structural environment specific atom potentials and torsion angle potential
Analysis of mutations
http://cupsat.uni-koeln.de/

FSolv: fast method for the determination of fractional contributions to solvation in proteins Solvation
http://mmb.pcb.ub.es/FSolv/

PMut: predicts the pathologic character of a punctual mutation in a protein
http://mmb.pcb.ub.es/PMut/

Qgrid: webserver for detection of charged and hydrophobic clusters in proteins
Structural analysis
http://www.netasa.org/qgrid/index.html

ILM: web server combining two algorithms, iterated loop matching and maximum weighted matching, for predicting RNA secondary structures RNA structure prediction
http://cic.cs.wustl.edu/RNA/

RDfolder: webserver for prediction of RNA secondary structure from two methods, random stacking of helical regions and helical regions distribution RNA structure prediction
http://rna.cbi.pku.edu.cn

NAMD: molecular dynamics package for simulation of large biomolecular systems Molecular simulations
http://www.ks.uiuc.edu/Research/namd/

CURVES: software package for calculating a helical parameter description for any irregular nucleic acid segment with respect to an optimal, global helical axis Nucleic acid analysis
http://www.ibpc.fr/UPR9080/Curindex.html

MANIP: interactive tool for modeling of RNA structure Nucleic acid analysis
http://www-ibmc.u-strasbg.fr/upr9002/westhof/

FANTOM (Fast Newton-Raphson Torsion Angle Minimizer) calculates low-energy conformations of polypeptides and proteins, compatible with distance and dihedral angle constraints obtained typically from NMR experiments. Protein-solvent interaction is included with a fast routine GETAREA for the calculation of accessible surface areas of individual atoms and their gradients. FANTOM is suited for the exploration of low energy conformations of cyclic peptides and of flexible loops in proteins as well. In addition to the above uses, with the newly added program EXDIS, FANTOM is an efficient tool for homology modeling of proteins [366, 367] Molecular simulations
http://www.scsb.utmb.edu/fantom/fm_home.html

CHARMM (Chemistry at HARvard Molecular Mechanics) is a program for macromolecular simulations Molecular simulations
http://www.charmm.org/

Biomer/B is a Java-based, on-line biomolecular modeling package Molecular modeling
http://www.scripps.edu/mb/case/

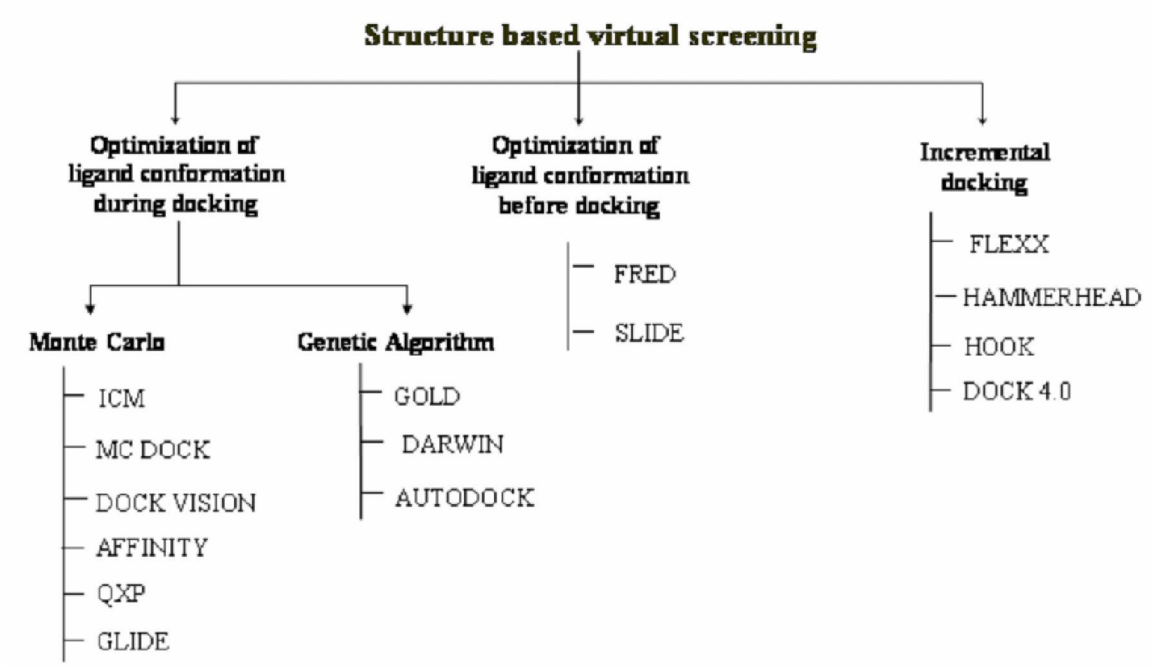
GROMACS: is a package for performing standard MD simulations, energy minimizations, NMR refinement… Molecular simulations
http://www.gromacs.org/

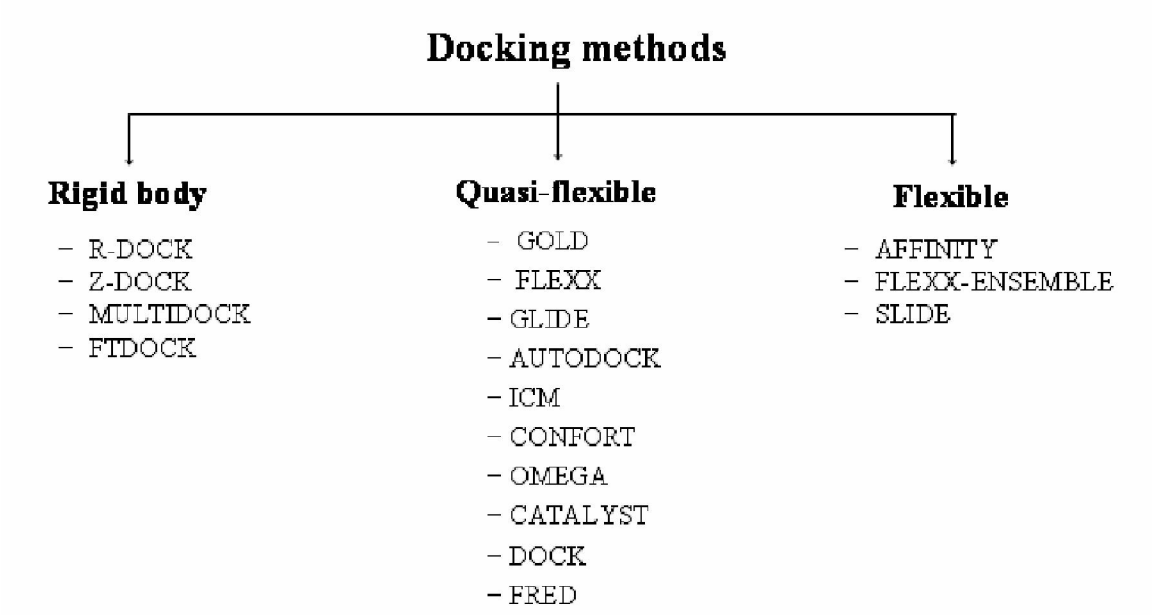
Molecular Dynamics Extended Library (Database of Molecular Dynamics Trajectories) Molecular simulation database
http://mmb.pcb.ub.es/MODEL/

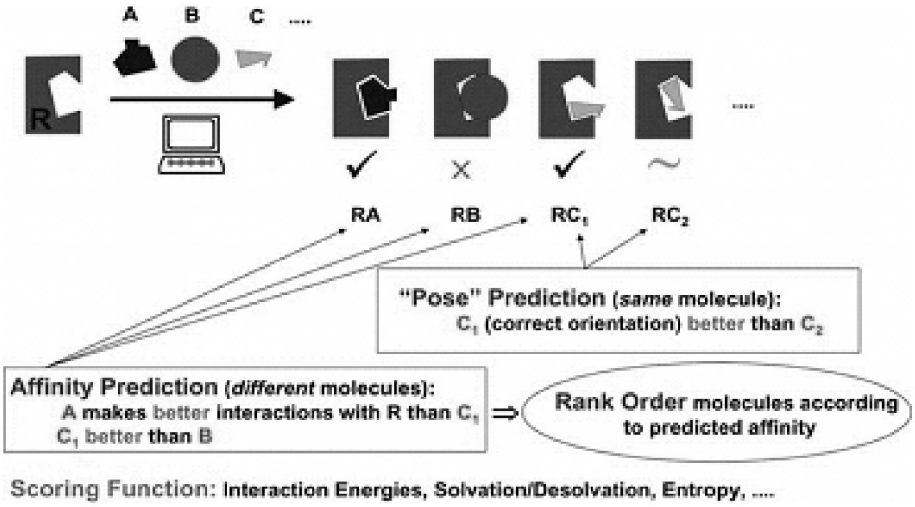
The Uppsala Electron Density Server: Protein X-ray structural analysis
http://eds.bmc.uu.se/

BioShell is a suite of programs designed for pre- and post-processing in protein structure modeling protocols Tools to prepare molecules for simulations
http://www.biocomp.chem.uw.edu.pl/services/BioShell/about.html

2.9 Docking and/or Scoring Engines for Small Molecule-Macromolecule Interactions







AutoDock- small molecule docking small molecule docking
http://www.scripps.edu/mb/olson/doc/autodock

BDT (is an easy-to-use front-end application for automation of massive docking tasks and complex docking strategies with AutoDock- Graphics interface for small molecule docking.
http://www.quimica.urv.cat/~pujadas/BDT/

Dockres (reads the log file of docking runs performed by Autodock (version 3.0.5) and extracts the top scoring poses. The extraction can be subject to various filters (e.g., the residue nearest to the ligand...). The program also calculates distributions of various properties of the ligand set (e.g., molecular weight, number of hydrogen bond donors) and the distribution of docking sites as well as the distribution of docking free energies per target residue-AutoDock postdocking processing
http://fulcrum.physbio.mssm.edu/~mezei/dockres/

eHits: Small molecule docking-Small molecule docking
http://www.simbiosys.ca/ehits/index.html

FRED: small molecule docking. See the online demos to try many OpenEye applications Small molecule docking
http://www.eyesopen.com

DOCK: Small molecule docking. Small molecule docking
http://dock.compbio.ucsf.edu/

ViewDock to analyze Dock data and tools for post-processing DOCK results Small molecule docking post-docking processing
http://www.cgl.ucsf.edu/chimera/docs/UsersGuide/index.html

Surflex: Small molecule docking-Small molecule docking
http://www.biopharmics.com

Plants: Small molecule docking- Small molecule docking
http://www.tcd.uni-konstanz.de/research/plants.php

FRED:
http://www.eyesopen.com/

PSI-DOCK: Small molecule docking. Small molecule docking
ftp://ftp2.ipc.pku.edu.cn/pub/software

PEARLS: Program for Energetic Analysis of Receptor-Ligand System Scoring
http://ang.cz3.nus.edu.sg/cgi-bin/prog/rune.pl

AutoDock: automated docking of flexible ligands to macromolecules, designed to predict how small molecules, such as substrates or drug candidates, bind to a receptor of known 3D structure

http://autodock.scripps.edu/

DockVision: docking package created by scientists for scientists by including Monte Carlo, Genetic Algorithm, and database screening docking algorithms

http://dockvision.com/

FRED: accurate and extremely fast, multiconformer docking program examines all possible poses within a protein active site, filtering for shape complementarity and optional pharmacaphoric features before scoring with more traditional functions
http://www.eyesopen.com/products/applications/fred.html

FlexiDock: simple, flexible docking of ligands into binding sites on proteins, fast genetic algorithm for generation of configurations, rigid, partially flexible, or fully flexible receptor side chains provide optimal control of ligand binding characteristics, conformationally flexible ligands, tunable energy evaluation function with special H-bond treatment, very fast run times.
http://www.tripos.com/index.php?family=modules,SimplePage,,,&page=sybyl_biopolymer&s=0

FlexX: fast computer program for predicting protein-ligand interactions, two main applications: complex prediction (create and rank a series of possible protein-ligand complexes), virtual screening (selecting a set of compounds for experimental testing), conformational flexibility of the ligand; rigid protein, placement algorithm based on the interactions occurring between the molecules (limited to low-energy structures), MIMUMBA torsion angle database used for the creation of conformers; interaction

geometry database used to exactly describe intermolecular interaction patterns, Boehm function (with minor adaptions necessary for docking) applied for scoring
http://www.biosolveit.de/FlexX/index.html?ct=1

GLIDE: high-throughput ligand-receptor docking for fast library screening, fast and accurate docking program, identifies the best binding mode through Monte Carlo sampling, provides an accurate scoring function for ranking of binding affinities, can enrich the fraction of suitable lead candidates in a chemical database - by predicting binding affinity rapidly and with a reasonable level of accuracy - will greatly enhance the probability of success in a drug discovery program
http://www.schrodinger.com/ProductDescription.php?mID=6&sID=6&cID=0

GOLD: calculating docking modes of small molecules into protein binding sites, genetic algorithm for protein-ligand docking, full ligand and partial protein flexibility, energy functions partly based on conformational and non-bonded contact information from the CSD, choice of scoring functions: GoldScore, ChemScore and User defined score, virtual library screening
http://www.ccdc.cam.ac.uk/products/life_sciences/gold/

HINT! **H**ydropathic **Int**eractions: empirical molecular modeling system with new methods for de novo drug design and protein or nucleic acid structural analysis, translates the well-developed Medicinal Chemistry and QSAR formalism of LogP and hydrophobicity into a free energy interaction model for all biomolecular systems based on the experimental data from solvent partitioning, calculates 3D hydropathy fields and 3D hydropathic interaction maps, estimates LogP for modeled molecules or data files, numerically and graphically evaluates binding of drugs or inhibitors into protein structures and scores DOCK orientations, constructs hydropathic (LOCK and KEY) complementarity maps (can be used to predict an ideal substrate from a known receptor or protein structure or to propose the hydropathic structure from known agonists or antagonists), evaluates/predicts effects of site-directed mutagenesis on protein structure and stability
http://www.edusoft-lc.com/hint/

LIGPLOT: program for automatically plotting protein-ligand interactions, generates schematic diagrams of protein-ligand interactions for a given PDB file, interactions shown are those mediated by hydrogen bonds (dashed lines between the atoms involved) and by hydrophobic contacts (represented by an arc with spokes radiating towards the ligand atoms they contact)
http://www.biochem.ucl.ac.uk/bsm/ligplot/ligplot.html

SITUS: program package for modeling of atomic resolution structures into low-resolution density maps, software supports both rigid-body and flexible docking using a variety of fitting strategies.
http://situs.biomachina.org/index.html

VEGA: calculation of ligand-receptor interaction energy
http://users.unimi.it/~ddl/vega/index.htm

GFscore: A General Non-Linear Consensus Scoring Function for High-Throughput Docking Scoring
http://gfscore.cnrs-mrs.fr/index.htm

SCORE: is an empirical method developed for estimating the binding affinity of protein-ligand complex with known three-dimensional structure Scoring.
ftp://ftp2.ipc.pku.edu.cn/

DrugScore : evaluate ligand-receptor interaction energy Scoring
http://pc1664.pharmazie.uni-marburg.de/drugscore/

FOLD-X can compute binding energy Scoring
http://fold-x.embl-heidelberg.de:1100/cgi-bin/main.cgi

CLIBE: A database of the computed ligand binding energy for ligand-receptor complexes. The energy is computed based on a molecular mechanics force field that has been used in the prediction of therapeutic and toxicity targets of drugs. This database also contains information about ligand function and other properties.
http://bidd.nus.edu.sg/group/CLiBE/CLiBE.asp

Xscore: tool to predict binding energy between ligand and receptor Scoring
http://sw16.im.med.umich.edu/software/xtool/

The goal of the CGAL Open Source Project is to provide easy access to efficient and reliable geometric algorithms to users in industry and academia in the form of a C++ library Help for docking
http://www.cgal.org/index.html

OpenMolGrid: tools to speed-up computations- Tools to speed-up computations
http://www.openmolgrid.org

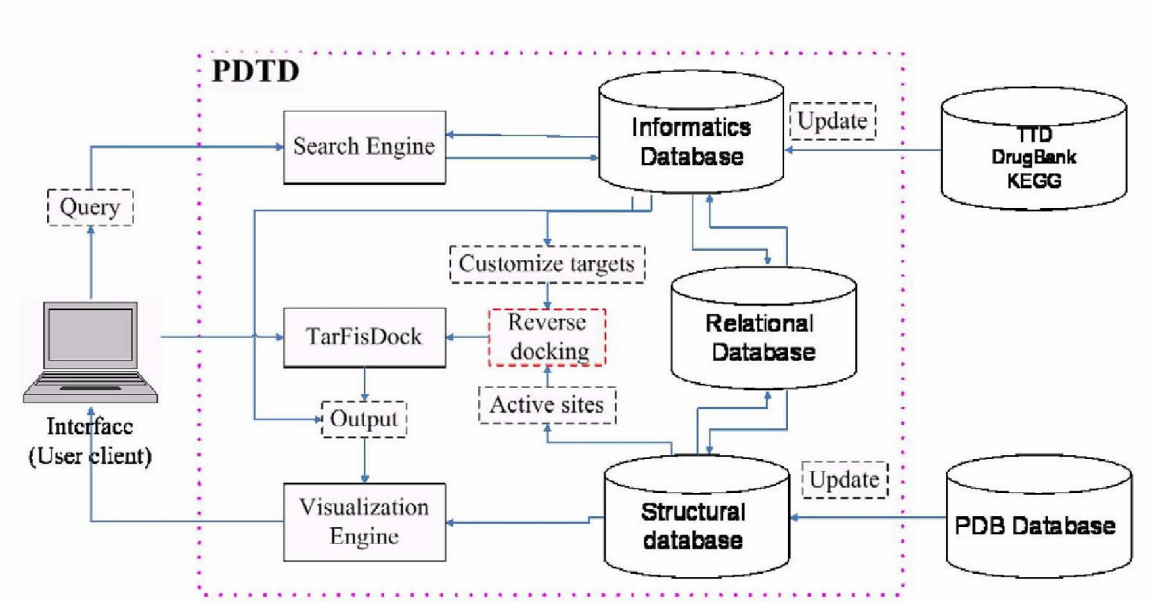
Kindock:
http://abcis.cbs.cnrs.fr/kindock/

Simdock: Tool for comparative docking of protein kinase ligands and ligand transposition server Small molecule positioning.
http://abcis.cbs.cnrs.fr/LIGBASE_SERV_WEB/PHP/simdock.php

RASSE:
A structure-based method for de novo drug design
ftp.ipc.pku.edu.cn

PyRx:
http://pyrx.scripps.edu/downloads

tarFisDock: docks ligands into the proteins targets in PDTD (Potential Drug Target Database), and outputs the top 2%, 5% or 10% candidates ranked by the energy score, including their binding conformations and a table of the related target information
Small molecule docking
http://www.dddc.ac.cn/tarfisdock/
http://dddc.ac.cn/pdtd/



GRID: A computational procedure for determining energetically favorable binding sites on molecules of known structure. It may be used to study individual molecules such as drugs, molecular arrays such as membranes or crystals, and macromolecules such as proteins, nucleic acids, glycoproteins or polysaccharides. Several different molecules can be processed one after the other.
http://www.moldiscovery.com/soft_grid.php

Vina:
http://vina.scripps.edu/manual.html

Argus Lab:
http://www.arguslab.com/index.htm

GlamDock: GlamDock, our in-house docking tool, has recently been validated on two benchmark datasets. On the smaller benchmark, on which data for other docking tools is available, GlamDock was shown to perform better than the best established docking tools (62% scoring accuracy compared to 57% for the best contender Gold, Glide 55%).

GlamDock is based on a Monte-Carlo with minimization (basin hopping) search in a hybrid interaction matching / internal coordinate search space. GlamDock is highly efficient, taking from 5 seconds (fast virtual screening settings) to ~20 seconds (high quality docking settings) on average on standard 2.8GHz Intel Xeon CPUs. Newest developments include an improved scoring function for pose recognition and virtual screening, and the introduction of protein flexibility into GlamDock. In cooperation with our partners GlamDock has been integrated in a de novo molecular design strategy.

http://www.chil2.de/Glamdock.html

DockIt:
http://www.metaphorics.com/products/dockit

Insight II Affinity and Cerius2 Ligand Fit
http://www.accelrys.com/

Sybyl including FlexE and FlexX
http://tripos.com/index.php?family=modules,SimplePage,,,&page=comp_informatics

MOE
http://www.chemcomp.com/software.htm

Conclusion:

Drug Discovery is a very complex process. It is estimated that it takes at least 10 years for a molecule to get into the market after it proves its activity. It is becoming important due to Multi Drug Resistant Diseases. Also, the sensitized body demands for more potent drug. So, the quest becomes hectic to continuously introduce a new series of potent and safe drugs. CADD comes to the rescue of medicinal chemists to a large extent. But then, it has its own limitations like: the scoring for the docking process varies with the principle used, it is possible that the ligand binds to the new site in enzyme/protein and there by elicits its action, the high-scoring ligand is very poorly active in-vivo and there is also a chance that we may loose a low-scoring ligand-which may be active in physiological conditions.

But still, it's a boon for medicinal chemists for developing safe, efficacious drugs by taking into account several of its limitations and build-up a case dependent protocol for the mathematical calculations for each ligand. An attempt has been made to create a 'repository of web-based resources used in CADD'.

References:

[1] Kubinyi, H., Nature Reviews in Drug Discovery, 2003, 2, 665-668.

[2] Kubinyi, H., Drug Discovery Today, 2002, 7, 707-709.

[3] Rupasinghe, C. N. and Spaller, M. R., Current Opinion in Chemical Biology, 2006, 10, 188-193.

[4] Harris, N. V. and Clark, D. E., GOR, 2004, 6, 27-31.

[5] Roberts, N., Martin, J., Kinchington, D., Broadhurst, A., Craig, J., Duncan, I., Galpin, S., Handa, B., Kay, J., Krohn, A., Science, 1990, 248, 358–361.

[6] Erickson, J., Neidhart, D., VanDrie, J., Kempf, D., Wang, X., Norbeck, D., Plattner, J., Rittenhouse, J., Turon, M., Wideburg, N., Science, 1990, 249, 527–533.

[7] Dorsey, B. D., Levin, R.B., McDaniel, S.L., Vacca, J.P., Guare, J.P., Darke, P.L., Zugay, J.A., Emini, E.A., Schleif, W.A., Quintero J.C., Journal of Medicinal Chemistry, 1994, 37, 3443–3451.

[8] Stoermer, M. J., Medicinal Chemistry, 2006, 2, 89-112.

[9] Schapira, M., Raaka, B.M., Samuels, H.H., Abagyan, R., Proceedings of National Academy of Sciences, 2000, 97, 1008-1013.

[10] Wang, X., Richards, N. G. J., Current Pharmaceutical Design, 2005, 11, 345-356.

[11] Colmenarejo, G., Current Computer Aided Drug Design, 2005, 1, 365-376.

[12] Jennings, A., Tennant, M., Current Pharmaceutical Design, 2005, 11, 335-344.

[13] Kalyanaraman, C. Bernacki, K., Jacobson, M.P., Biochemistry, 2005, 44, 2059-2071.

[14] Schneidman-Duhovny, D., Nussinov, R. and Wolfson, H. J., Current Medicinal Chemistry, 2004, 11, 91-107.

[15] Dror, O., Shulman-Peleg, A., Nussinov, R. and Wolfson, H. J. Current Medicinal Chemistry, 2004, 11, 71-90.

[16] Alvarez, J., Shoichet, B., ChemBioChem, 2006, 7, 389 – 390.

[17] Joseph-McCarthy, D., Pharmacology and Therapeutics, 1999, 84, 179–191.

[18] Mitcheson, J.S., Chen, J., Lin, M., Culberson, C., Sanguinetti, M.C., Proceedings of National Academy of Sciences, 97, 2000, 12329-12333.

[19] Walters, W.M., Namchuk, M., Nature Reviews in Drug Discovery, 2003, 2, 259-266.

[20] Koh, T.J., Proceedings of National Academy of Sciences, 2003, 100, 6902-6903.

[21] Evers, A., Klebe, G., Angewandte Chemie International Edition, 2004, 43, 248-251.

[22] Smith, A., Nature, 2002, 418, 453-459.

[23] Erickson, A.K., Natural Medicine, 2005, 11, 584-584.

[24] Song, H., Wang, R., Wang, S., Lin, J., Proceedings of National Academy of Sciences, 2005, 102, 4700-4705.

[25] Xu, H., Agrafiotis, D.K., Current Topics in Medicinal Chemistry, 2002, 2, 1305-1320.

[26] Pickett, S.D., McLay, I.M., Clark, D.E. Journal of Chemical Information and Modeling, 2000, 40, 263-272.

[27] Kenakin, T., Nature Reviews in Drug Discovery, 2003, 2, 429-38.

[28] Huber, W., Journal of Molecular Recognition, 2005, 18, 273–281.

[29] Srinivas, E., Murthy, J. N., Rao, A. R., Sastry, G. N. Current Drug Metabolism, 2006, 7, 205-217.

[30] Janardhan, S., Srivani, P., Sastry, G. N., Current Medicinal Chemistry, 2006, 13, 1169-1186.

[31] Janardhan, S., Srivani, P., Sastry, G. N., QSAR and Combinatorial Science, 2006, 25, 860-872..

[32] Kulkarni, R., Achaiah, G., Sastry, G. N. Current Pharmaceutical Design, 2006, 12, 2437-2454.

[33] Murthy, J.N., Rao, A. R., Sastry, G. N. Current Medicinal Chemistry, 2004, Anti-Cancer Agent, 4, 523-535.

[34] Reddy, Ch. S., Vijayasarathy, K., Srinivas, E., Sastry, G. M., Sastry, G. N. , Computational Biology and Chemistry, 2006, 30, 120-126.

[35] Chourasia, M., Sastry, G. M., Sastry, G. N., Biochemical Biophysical Research Communications, 2005, 336, 961-966.

[36] Bindu, P.H., Sastry, G.M., Sastry, G. N., Biochemical Biophysical Research Communications, 2004, 320, 461-467.

[37] Murthy, J.N., Nagaraju, M., Rao, A. R., Sastry, G. N., Journal of Computer Aided Molecular Design, 2004, 19, 857-870.

[38] Schulz-Gasch, T., Stahl,M., Journal Molecular Modeling, 2003, 9, 47-57.

[39] Dash, R., Moharana, S. S., Reddy, A. S., Sastry, G. M., Sastry, G. N. International Journal of Biological Macromolecules, 2006, 38, 65-69.

[40] Reddy, A. S., Sastry, G. M., Sastry, G. N. Proteins, 2007, 67, 1179–184..

[41] Liwei Li, Khuchtumur Bum-Erdene, Peter H. Baenziger, Joshua J. Rosen, Jamison R. Hemmert, Joy A. Nellis, Marlon E. Pierce and Samy O. Meroueh, Nucleic Acids Research, 2010, Vol.38, Data base issue D765–D773

[42] Chun Meng Song, Shen Jean Limand, Joo Chuan Tong, Briefings in Bioinformatics, Vol 10, No5, 579-591.

[43] David Cavalla, Current Opinion in Drug Discovery & Development 2004 Vol 7 No 4, 393-394.

[44] Igor V.Tetko, Drug Discovery Today, 2005, Vol 10, No 22, 1497-1500.

[45] Werner J.Geldenhuys, Kevin E.Gaasch, Mark Watson, David D.Allen and Cornelis J.Van der Schyf, Drug Discovery Today, 2006, Vol 11, No 3/4, 127-132

[46] AdamC.Leeand, GordonM.Crippen, Journal of Chemical Information and Modeling, 2009, 49, 2013–2033

[47] Johannes Kirchmair, Patrick Markt, Simona Distinto, Daniela Schuster, Gudrun M. Spitzer, KlausR. Liedl, Thierry Langer and Gerhard Wolber, Journal of Medicinal Chemistry, 2008, Vol.51, No.22, 7021-7040.

[48] CX.Chen, Z.L.Ji, D.G.Zhi, Y.Z.Chen, Computers & Chemistry, 2002, No 26, 661-666.

[49] Darby Tien-Hau Chang, Yen-Jen Oyang and Jung-Hsin Lin, Nucleic Acids Research, 2005, Vol.33, Web Server issue W233–W238.

[50] Zhenting Gao, Honglin Li, Hailei Zhang, Xiaofeng Liu, Ling Kang, Xiaomin Luo, Weiliang Zhu, Kaixian Chen, Xicheng Wang and Hualiang Jiang, BMC Bioinformatics 2008, 9:104.

[51] O.Sperandio, M.Petitjean and P.Tuffery, Nucleic Acids Research, 2009, Vol.37, Web Server issue, W504–W509.

[52] Mathias Dunkel, Melanie Fullbeck, Stefanie Neumann and Robert Preissner, Nucleic Acids Research, 2006, Vol.34, Database issue, D678–D683.

[53] Maria A.Miteva, StephanieViolas, Matthieu Montes, DavidGomez, Pierre Tuffery and Bruno O. Villoutreix, Nucleic Acids Research, 2006, Vol.34,Web Server issue, W738–W744.

[54] T.BohmeLeite, D.Gomes, M.A.Miteva, J.Chomilier, B.O.Villoutreix and P.Tuffery, Nucleic Acids Research, 2007, Vol.35, Web Server issue, W568–W572.

[55] Romano T. Kroemer, Current Protein and Peptide Science, 2007, 8, 312-328.

[56] I.M. Kapetanovic, Chemical Biological Interactions, 2008, 171(2): 165–176.

[57] Bruno O. Villoutreix, Nicolas Renault, David Lagorce, Olivier Sperandio, Matthieu Montes and Maria A. Miteva Current Protein and Peptide Science, 2007, 8, 381-411.

[59] Srinivas Reddy, S. Priyadarshini Pati, P. Praveen Kumar, H.N. Pradeep and G. Narahari Sastry, Current Protein and Peptide Science, 2007, 8, 329-351.

[60] N.Marchand-Genestesar and AJM Carpy, QSAR in Environmental Research, 2004, Vol. 15(1), 43–54.