Brief Overview

Role of Computation Biology & Bioinformatics in Drug Design

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Abstract

Drug design is used for different applications of bioinformatics tools analyze DNA, genome, and sequence target region of a small organic molecule in order to understand the molecules of disease. Bioinformatics tools are identified a newly wide research field and minimize future risks through web servers and data mining. Clinical sample test performed with the bioinformatics tools as the biomedical detective. A particular structure and configuration of protein obliging in Drug design concluded Bioinformatics. This review bioinformatics tools and webserver will discuss functions of small organic molecules according to clinical pharmacology.

Keywords: Bioinformatics, Drug Design, Small Organic Molecule, Target identification, Web-based Server

Introduction

Bioinformatics is well known for biological information or in the field of biotechnology due to various applications according to computation including biological database development, data retrieval and phylogenetic study. Computer algorithm based bioinformatics process is

used to identify the structure pattern of the target gene, design a drug with desirable properties and their therapeutic effects on specific gene. (HASAN, CHAKROBARTY, CHAKROVORTY, & NABI, 2014). There are major effects on their biochemical function through drugs on small organic molecules than altering properties of a specific gene and protein binding receptor. For human prosperity approval a new drugs are designed through a complex procedure and also require combined information for different disciplines. Major object of this review article was to provide awareness and study different effects at new research field in drug design and discover relationship between bioinformatics and their application in drug design (Ataya, 2019).

Computational biology is a widely used term that represents bioinformatics tools and databases for storing, analyzing, modeling, and administration of small organic molecules. Biological Database recognised new molecular objects that have managed the assembly of high-quality datasets and design libraries that may be boosted for molecular diversity or similarity (Song, Lim, & Tong, 2009).

Modern Computational Bioinformatics tool is easily handle to design a common drug bipolar disorder and different associated diseases. This association and interaction among the proteins of coronary heart disease, Schizophrenia and bipolar disorder helps to find a common pathway for new drug design (Habib, 2017).

Materials and Method

Web server database **in** Swiss institute of bioinformatics develops or maintains the software, database and web facilities that is related to drug design and discovery. Well known institutions administration may give software packages like ChEMBL, Swiss Similarity, Swiss Target Prediction, Some commercial software CHARMM and PyMOL are available at free recource for benefits of students and faculty (Xia, 2017).

Computation Biology & bioinformatics has wide range in the fields of energetic application and have various steps of drug discovery for drug target verification which followed by drug-target interaction and optimization of a leading organic molecule.

There are two methods of drug design:

i) **Conventional Method**

ii) **In Silico Method**

In conventional method initially desire a natural source of ingredient for treatment next used natural source of segregation for active compound, then chemical synthesis of the leading compound. Further step is experimental approach which measured the structure-activity and relationship of a leading organic molecule then generates a desirable modification to get the better drug.

In Silico method firstly separation of molecular basis disease then verification of potential drugable molecule targets which followed the screening through a database to identify "hints" of leading organic molecule. In silico structure helps the modification of lead organic molecule, docking on the target sequence and experimental authentication.

Human proteome domains for secondary, tertiary and globular structure achieved in the database. Most popular database known as Protein Data Bank (PDB). PDB contains different protein structures that are gained through an experimental method such as Cryso-Electron microscopy, NMR spectroscopy, X-ray crystallography (Thangadurai & Sangeetha, 2014).

"BLAST" also known as a web-based server against small organic molecule and retrieved similar structures for all proteins (RNA) and valuation of a function of the query protein (Xia, 2017). BLAST has different variants like BLASTN, BLASTX, BLASTP, TBLASTX, TBLASTN. Graphical overview box, a match-list and an alignment text are an output of BLAST (Xiong, 2006).

Roadmap for screening drug design

Drug design through bioinformatics used specific tools for specific properties that depends on the choice of their accessibility and performance. Target selection sequencing of protein that founds phylogenetic analysis between sequencing and identify all members of gene families through the bioinformatics tool and interference target protein binding sites. Screening archive preparation screening through web base server and generate a 3D structure of the protein or target sequences**.**

Stereochemical quality assessment bioinformatics tools checked stereochemical quality in their sequence and recognized mutation in protein structure and sequences. Computation Modeling transfered proton on a target protein structure through a docking molecular structure. After all steps test target selectivity and modification sequences enhanced the model for drug-like properties (Song et al., 2009).

Next **e-LEA3D** is also web-based server for large spectrum applications and pharmacological tool is used to invent ideas of ligand and screening the small organic molecule of target protein. e-LEA3D served as a channel manner and accompaniments to other services devoted to a small organic molecule (Douguet, 2010).

Bioinformatics Software for Drug designing

Mostly bioinformatics software is used for different characterization of drug design such as analysis software, behavioural study, data analyzer, visualizer, image analysis, structural activity relationship, molecular modelling, molecular dynamic, ligand interactions and pharmacokinetic parameters (Jamkhande, Ghante, & Ajgunde, 2017).

Software	Key Use
1) Behavioral Study a) Ethowatcher b) MARS (Multimodal Animal Rotation System)	a) Complex behaviours of experiment animal b) Using in cell tracking software automatic and capturing of multi domain and multispectral data sets from all possible angles.
2) Data analysis a) Genespring b) QSARpPro c) REST 2009 Software	a) Identify common variation across a set of samples b) Molecular and structural analysis prediction biostatical modelling c) Quantitation of relative gene expression
3) Image analysis and Visualizers a) AMIDE (A Medical Image data Examiner) b) Discovery Studio c) Imaging Software Scge-Pro d) Xenogen Living Image Software	a) Multimodality volumetric medical image analysis b) Multi-domain protein sequences c) Structural imaging software for cytogenetic DNA damage analysis d) In vivo imaging software
4) Molecular modelling and structural action association a) Maestro b) ArgusLab c) GRAMM d) SYBYL-X Suite e) Sanjeevini f) PASS	a) Quantitative structural analysis b) Used for molecular modelling c) Using atomic coordinates of two molecules for structure prediction d) Create homology model for receptor interest e) Ligand based design f) Computational automating g) New pharmaceutical substance of lead molecule on evaluation existing library structures
5) Lignad interaction and molecular dynamic a) AutoDock b) Schrodinger c) GOLD d) Biosuite	a) Examination of results using auto docking b) Advance molecular modelling, molecular dynamics c) Proof of identity small organic molecule d) Whole genome analysis sequence analysis software
6) Pharmacokinetic parameters a) DDPlus b) GastroPlus c) MapCheck	a) Finding interaction between the active ingredient under b) Moveable drug design c) Associate dose or confience

Table 1: Software and computation biology based program used in drug designing

Computational Drug Design Tools

1. Database Binding MOAD (Mother of All Database), STITCH , SMPDB (Small Molecule Pathway Database) ChEMBL, ChemAxon and PDB (Protein Data Bank).

Binding MOAD Firstly introduced in 2004 its binding size is dual and updated in every year. Database of Binding MOAD which have all fitting protein-ligand-cofactor, Protein-cofactor, Protein ligand, and Protein-ligand Complexes. Small molecules and agonists, antagnists, co-factor, enzymatic yields those are related biologically and valid ligands. Postranslation modification of protein are not be eligible as valid ligands (Benson et al., 2007).

ChEMBL well known as bioactivity database frequently mined from the medical chemistry literature. Potential therapeutic target are used to verify too compound with many other application such as SAR data far target, examine phenotype data related like compounds and off-target effects of definite chemotypes. In the drug design ChEMBL data model used as pre-clinical and clinical phases for specific drug metabolism (Gaulton et al., 2017).

2. **Chemical structure illustrations (**PDB Hydrogen Addition, ChemMobi, OpenStructure, PyMOL, ACD/ChemSketch , Indigo, ChemDraw)

PyMOL Computation aided tool PyMOL widespread as molecular modeling programs permit researcher analysis sitmulation areas such as medical chemistry, Structural Biology and Protomics (Lill & Danielson, 2011). PyMOL is used to visualize understanding nature of life at molecular level and make rapid progress in biochemical research.

3. **Molecular Modelling** (SwissParam, Amber, GROMACS, CHARMM)

SwissParam is a tool used as fast force field generation called SwissParam.The parameters in swissParam are generated by using Docksoftware such as EADock2 and EADock SS which describes the docking of small molecules considering proteins , they are described by CHARMM force field and allow them to extend success rate from 56 to 78% . We can use SwissParam for ligands to expand swift binding free energy and CHARMM22/7 for proteins.(Zoete, Cuendet, Grosdidier, & Michielin, 2011)

4. **Homology Modeling** (Swiss –Model, Modeller,LOMESTS)

Swiss-model is a server used for automated comparative modelling of three dimensional (3D) protein structure. It develop the subject of robotic modelling and begins in 1993. Swiss-model give various extent of user intraction by world wide interference, within " First approach mode" can build a 3D structure of protein by only amino acids. In "Alignment mode" Modelling procedure is built on a user defined target-template alignment.In "Project Mode" let the user to give in a manually optimized modelling appeal to the SWISS-MODEL server (Schwede, Kopp, Guex, & Peitsch, 2003).

5. **Binding Site Prophecy** (3DLigandSite, PockDrug, metaPocket)

PocKdrug-Server is used to predict the ability of Drug logical for one and another

a) For ligand binding closeness
b) Protein information about structure

The server provides compatible predict the ability of drug by various approximation methods. It is vigorous regarding pocket boundary and estimation unreliability so logically utilized Apo pockets are ultimatum to estimate (Hussein et al., 2015).

6. **Docking** (GOLD, SwissDock, DOCK, AutoDock)

AutoDock is a server is used to predict the interrelation of small molecules of superamolecular aims to easily break nanomolar and micromolecule binding energies by those with submicromolar binding energy and can often rate molecules with greater differences in sensitivity.AutoDock can be use to moniter the test variety of possible compounds to hunt for novel compounds with specific binding properties, or even to check the check a variety of alterations to the known compound.AutoDock is much more user-friendly server. The second step is to develop *PDBQ* Format file for target and ligand and grid and parmeter docking file. The third step is to produce a molecular docking operation by *Cygwin* and the project is defined (Rizvi, Shakil, & Haneef, 2013).

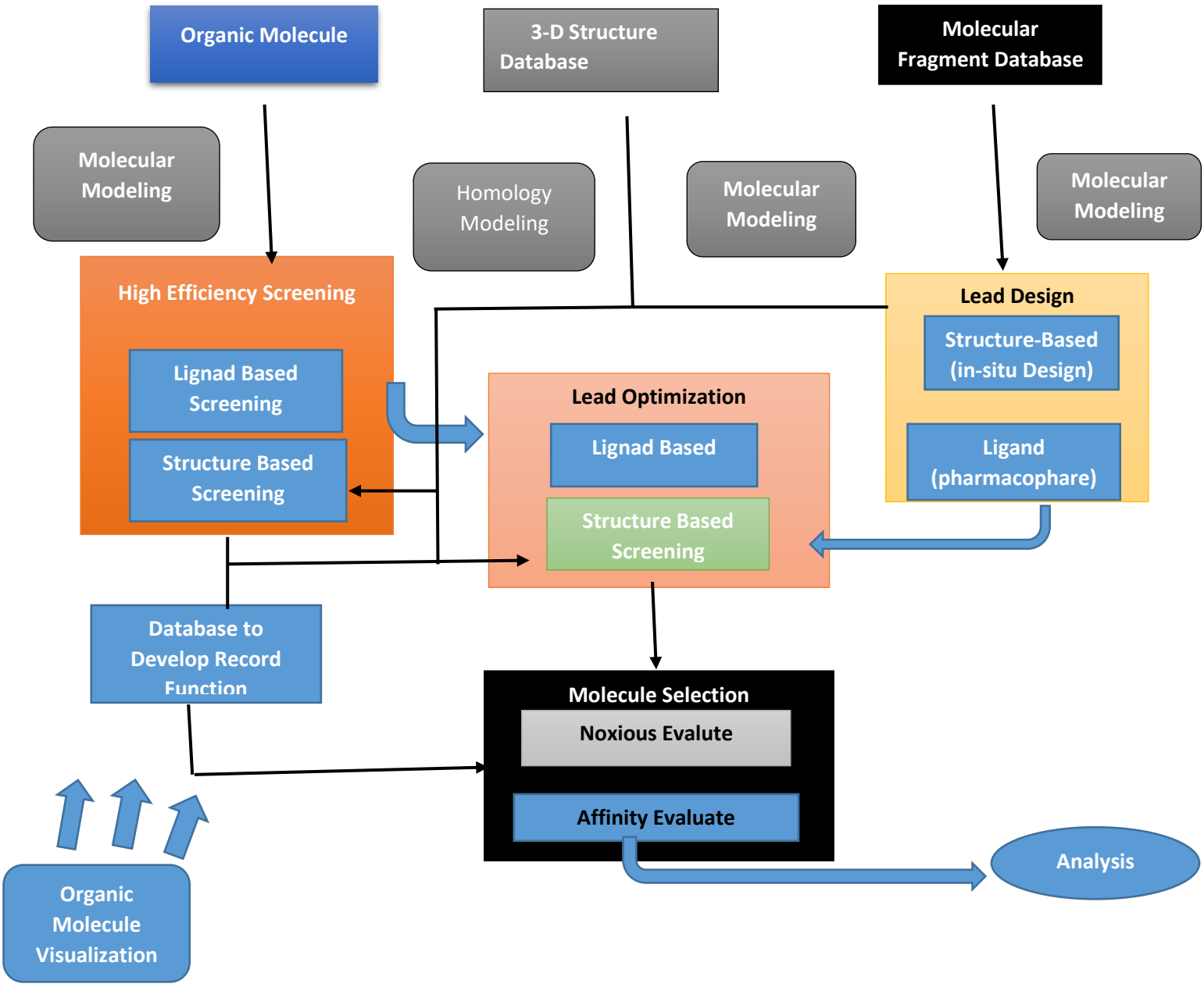

Figure 1: Docking strategy for target protein profiling overview

Clinical Review

Bioinformatics tools increase the development process of Drug design and drug discovery. Different tools successfully sequenced G-protein Couple receptors (GPCRs). Bioinformatics helps to understand complex nucleotide mechanisms of cells. Clinical pharmacology always required multidisciplinary information such as Biotechnology, Genomics, Cheminformatics, High Throughput Screening (HTS) and Bioinformatics according to clinical features. In their human determine metabolic and pharmacology activity of drug increase, increase efficacy due to normal and higher doses. There are four phases of clinical trials. Phase 1: Clinical Bioinformatics Pharmacology Evolution. Phase 2: Controlled Clinical Bioinformatics Evolution. Phase 3: Extended Clinical Bioinformatics Evolution. Phase 4: Investigation during Commercial Use The organic molecules are divided into stage clinical pharmacology linked (Human studies) (Siddharthan, Prabu, & Sivasankari, 2016)Large number of Disease needed de novo drug development that is impossible but 5% of drug compound proved first clinical trial. Conclusion new sign and target sequence of small organic molecule is called drug repurposing or re-locating. Area of Bioinformatics in pharmacology also known as Silico drug repurposing. Silico drug repurpose is changing or abundant in their existing drug identify effective drug for disease (Park, 2019).

Conclusion

Bioinformatics field which collection of biological database have primary and secondary databases of nucleic acid sequences , and protein sequences and structures. now a Drug design is based on computation biology this based on combinational approaches Protomics , Genomics ,pharmacology. Bioinformatics tool and web server show sequence of target region

and multi domians protein.Drug design is most expensive and high disappointment percentage.

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