

## Bioinformatics in Drug Development

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### Abstract

In today's world, where faster development of a new drug is crucial, not just for the patients but also for the pharmaceutical companies that are always in a competition for delivering a "new chemical entity (NCE)" to the market and the public. Bioinformatics, through various databases, web services, software and tools, has made a huge impact on the drug development process.

**Keywords:** Molecular modelling; MED-SuMo; CAVER; DTome; CHARMM

### Introduction

Bioinformatics is the science that combines the fields of computer science and biology; to apply computational methods and techniques in biological processes to facilitate in data analysis and management. Bioinformatics has its applications in life sciences including genomics, proteomics, systems biology, molecular biology, etc [1]. Drug designing, and development is an important area in life sciences as with the ever-changing times, the diseases have also greatly advanced in terms of severity and number causing more harm than ever [2]. Drug development is the process of testing a drug against a target that has been selected/identified by drug discovery. However, this whole process is classified under modern drug development approaches [3]. The approach that has always been taken for drug development is rather "slow, expansive and risky with not much efficiency. 90% of the identified drugs do not make through the rigorous trial and testing [4]. In modern drug development pipeline, various bioinformatics tools and software are applied in various areas like interaction, target identification [5], toxicity testing [6] etc. Not just tools, bioinformatics facilitates in the formulation of databases to store all the data generated from the observations and experimental analysis [6]. Several tools are used in the process of drug discovery and development. The Swiss Institute of Bioinformatics provides an easy way to access these tools from their "Click2Drug Directory of computer-aided Drug Design tools" page [7].

### Literature Review

#### Bioinformatics tools in drug development

Some of the tools and databases that are used in drug development are enlisted below.

#### Databases

**Sequence databases:** Different sequence databases like nucleotide sequence databases, protein sequence databases helps in identifying target molecules and its association with a particular disease by looking at its sequence [8]. GenBank, DDBJ, PDB, SwissProt, UniProt are some examples of sequence databases that provide data of thousands of nucleotide, mRNA and protein sequences [9].

**Expression databases:** These databases provide expression data of genes. "Gene logic" is a database which has expression data of various genes (tumor and normal expression) [10].

**Other databases:** "Comprehensive Medicinal Chemistry" is a database that has biochemical properties of various chemicals that

may be potential candidates for drugs [11]. "DrugBank" is another database which stores data about various drugs and their properties and associates them with target's data; their "sequence, structure and pathway" [12]. "PubChem" is another useful database containing of chemical compounds and is maintained by NCBI [13].

#### Web services

Various web services or online tools are also available. BLAST can be used to find similarities between sequences or proteins, which can then be selected as drug candidates, plus targets can also be identified [14]. Another web-based tool is "DTome (Drug-Target interactome tool)"; it queries in various drug and target databases and identifies a network of four different kinds of interactions, namely: "adverse drug interactions, drug-target interactions, drug-gene associations, and target-/gene-protein interactions". It showed promising and effective results when tested for a drug "clozapine" [15].

#### Visualizing software

Various visualizing and molecular modelling software are used such as "Pymol", "RasMol", "Jmol", "UCSF Chimera", "BioJava", "BioAdviser", "Molekel", "SwissPDB Viewer"etc to provide functionality for visualizing protein and other molecular structures and helps in analysis and interaction studies [16-23]. "PoseView" is a visualizing tool for protein-ligand interaction [24].

#### Molecular modelling

Modelling software which simulate interactions and dynamics are also very useful such as: "CHARMM (Chemistry at HARvard Macromolecular Mechanics)" [25], "GROMACS (GROningen MAchine for Chemical Simulations)" [26], "NAMD (Nanoscale Molecular Dynamics)" [27] are some of the tools that are used for this purpose. Molecular modelling helps us to predict the behavior and orientation of molecules. The tool "MOE" by Chemical Computing

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Group was utilized for pharmacophore modeling and searching of anti-SARS drug [28].

### Binding site prediction

Tools like “MED-SuMo” which detects surface properties of macromolecules and finds similarities among molecules [29], “CAVER” which analyzes the various tunnels and channels in the proteins [30], “FINDSITE” and “SiteMap” identifies the binding sites in the proteins (target and drug) [31,32].

## Discussion

### Screening

For screening of molecules and chemicals such as ligands, various tools are used such as Pharmer [33], LigandScout a program for virtual screening [34].

### Toxicity testing

An important process in the development of drug is toxicity testing. In conservative approach, toxicity was checked by using animal models, cell culture studies and human volunteers but that often resulted in unnecessary damage to the participants or any unknown side effects that were not known previously [35]. In the modern drug development approach, “*In-silico* toxicology” is used to identify toxicity which reduces the risk to animal and human subjects [36]. It also has the advantage that several drugs can be tested for any toxicity which cannot be done by conservative toxicity approaches. It greatly increases the scale of testing toxicity of the drug [37]. In modern toxicology, ADME (Absorption, Distribution, Metabolism and Excretion) is used for identifying toxicity related properties and effects of the drugs. This has led to more effective testing of drugs against the ADME criteria [38]. Several tools are used for this purpose, like: “QikProp” which provides rapid prediction of the ADME of the drugs [39], “VolSurf”, it identifies the ADME properties of drugs and also makes predictive models of drug’s ADME [40], “ADMET Modeler” which makes high quality predictive models of structure-property of drugs [41], “IMPACT-F” which is a program that identifies the bioavailability of drug to human candidates [42] etc.

## Conclusion

With bioinformatics, the drug development process has become much more efficient, with more rapid design and development, along with less overall cost and risk.

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