# Computational Approaches Streamlining Molecular Modelling and Drug Designing

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**Abstract**

*As science step up digital, the importance of incorporating computational technologies into academic research and course curriculum is high-priority. Whether you need access to cutting-edge molecular Modelling for your research or you are educating the next-generation of scientists. There are so many drug designing software in the present era to designing and Modelling the biomolecule and drug for our targeted purpose . Drug designing softwares has potential role to design novel proteins or drugs in biotechnology or pharmaceutical field. The drug designing softwares are used to analyze molecular Modelling of gene, gene expression, gene sequence analysis and 3D structure of proteins. In addition to tis , drug designing area has important role in the diagnosis of diseases such as lung cancer, brain cancer, breast cancer and Alzheimer disease. This review article summarizes the structure based drug designing, ligand based behavior based drug designing softwares and their applications in the field of education, pharmacological and medical research.*

***Key words:*** *Drug designing, docking, biomolecules, disease, modelling and drug discovery.*

**1.INTRODUCTION:** Drug designing software is used to develop new pharmaceutical drugs and test whether a newly created drug will be effective in treating a particular disease. Drug discovery software automates and leverages innovative technology that significantly cuts down on the arduous process of drug development, testing, and going to market[1]-[3]. Successful drug discovery, development and launching of single new drug into the market costs about one billion dollar and it requires long time period nearly 10-12 years for accomplishing. High cost, insufficient and long time, highly risky, uncertainty

in the results, and highly complex procedures are the main challenges in the development of new drug. To overcome these problems, it is required to employ new, time effective and more cost effective drug discovery and designing methods, Figure-1 such as software and molecular docking [4]&[5].

In the US drugs need to be approved by the Food and Drug Administration (FDA).Computer aided drug design CADD or the Computer assisted drug


Figure 1: **Linear Diagram of Computer Added Drug Designing**

design or the Computer assisted Molecular-designing CAMD involve all the computer-assisted approach applied to design, discover and optimize biologically active molecules or compounds. CADD gives not only to the design of potential compounds but also many of the stepped an "Idea to Drug". It helps in finding out new leads and also optimizing them. The recent advances finding in CADD are the ligands will interact with the target site of receptor. Ligand-receptor binding involves various types of interactions viz. the hydrophobic, electrostatic and hydrogen bonding interactions. Additionally, solvation energies of the ligand and receptor site are also play important role in the binding to take place. This approach to CADD optimizes the fit of a ligand in a receptor action site, CADD approach is dependent on the quantity of data that is available on the ligand and the receptor. Three-dimensional structural information of the receptor and the receptor ligand complex are obtained from X-Ray diffraction and Nuclear Magnetic Resonance (NMR) spectral studied.

Drug designing and molecular modelling involving the identification of a compound that frame-up a biological profile and ends when the biological profile and chemical synthesis of the new chemical substance are transformed. The present review article focusing on softwares that are commonly used in new drug upshot along with their potential uses.

**1.** Drug designing is otherwise known as rational drug design and it is a method of finding new medications based on the biological receptors and target molecules. It involves the designing of small molecules which is complementary to the biological receptor to which they bind and,

**2.** Computer aided drug design CADD or the Computer assisted drug design or the computer assisted Molecular-designing CAMD involve all the computer-assisted techniques used to design, discover and optimize biologically active compounds.

## 2.DRUG DESIGNING SOFTWARE

A computer needs software for its functions such as programs. This software makes our work simpler and faster. Various companies such as BIOVIA(Accelrys is the previous name of BIOVIA), Schrodinger, Auto Dock and Argus Lab offering drug designing softwares. Accelrys is a software company with its headquarters in US, along with its organization in Europe and Japan. It provides softwares especially for drug discovery and materials science. Their products and technologies create solutions for several stages in the drug discovery and developmental process, depending upon drug action there are so many software available in domain. Some of the popular ones are:

**2.1.SANJEEVINI**: Software has been developed as a novel scientific computational pathway paving the way expressly towards automating lead design, making any number of known or new candidate molecules out of a small but versatile set of building blocks called templates, screening them for drug likeness, optimizing their geometry, determing partial atomic charges and assigning other force field parameters, docking the candidates in the active site of a given biological target , estimating the interaction/binding energy,

performing molecular dynamics simulations with explicit solvent and salt on the biomolecular target, the candidate and the complex followed by a rigorous analysis of the binding free energy for further optimization. Presently Sanjeevini coupled with AMBER and GAMESS for molecular mechanics and quantam mechanics calculations, respectively. There are total of six modules which makes Sanjeevini a complete drug design software. The source codes for all modules are written in FORTRAN, C and C++ computer languages with numerous interfacial UNIX based shell scripts which makes all the modules work like a pipeline such that output of the previous step becomes the input for the next step. The modules under Sanjeevini can also be used independent of the pathway. Software is designed to automate lead design, screen candidate molecule for drug likeness, optimize their geometry, determine partial atomic charge and force field parameters, dock the candidates in the active site of a given biological target, estimate the interaction /binding energy, perform molecular dynamic simulations with explicit solvent and salt on the bimolecular target, the candidate and complex followed by a rigorous analysis of the binding free energy for further optimization. The software contains several modules such as Drug Preparation, and scoring, and protein ligand complex. It can perform identification of potential active drug bound to protein target with binding free energy.

The software, combining principles of Chemistry and Biology with Information Technology for Genome analysis, Protein structure prediction and target directed Lead molecule design pursuing the dream of SCFBio. It play the role in biomolecule like protein target and a candidate drug. Software is perform identification of potential active sites, docking and scores the candidate drug and returns four structures of the candidate drug bound to protein target together with binding free energies.

In this software the drug molecule is uploaded with target protein. On uploading, software pops-up a window which displays the results of some essential pre-tests done based on the parameters needed for the acceptable format of the drug and protein files. The software contains following modules

such as Drug Preparation, Protein Preparation, Docking and Scoring, and Protein Ligand Complex [8] & [9].

*KEY USES*

- It is used for drug designing.
- It predicts binding affinity of biomolecule and drug.
- Prediction of protein-ligand binding affinity.

**2.2.MAESTRO**: Maestro is freely available, full-featured molecular visualization, molecular Modelling and structure designing software. Maestro is a powerful tool for interpreting, managing, and sharing the results of computational experiments. It helps for building, visualizing, and sharing 3-dimensional chemical models.

Maestro is the linchpin of Schrodinger's computational technology. It is powerful and versatile tool for the molecular Modelling in the field of computational chemistry. It manages organization and analysis of obtained data. Maestro's intuitive interface makes setting up calculations easy and straightforward. The computed results are automatically returned and incorporated into projects for further study. Maestro's provide a vast array of visualization options makes it possible to glean insight into molecular properties as well as detailed intermolecular interactions [10]&[11]..

Maestro is the portal that brings Schrödinger's physics-based tools together and helps researchers organize and analyze data. While Free Maestro lacks access to Schrödinger's physics-based applications, it provides impressive rendering capabilities, a powerful selection of chemical building tools, and an easy-to-use design that makes it a versatile visualization environment in the field of researches.

**KEY USES**:

- Visualization of vibrational modes, molecular orbital, or electron density and molecular properties.
- Quantitative structural analysis.
- It provides impressive rendering capabilities.
- A powerful selection of chemical building tools, and an easy-to-use design that makes it a versatile visualization environment in the field of researches like vibrational modes, molecular orbital, and molecular Properties.
- Maestro lays the foundation for improved treatment planning by creating accurate, easily accessible imaging data to help clinicians form a comprehensive understanding of prior therapy history and a patient's current disease.
- It is a vendor-neutral solution which leverages best-in-class image registrations and user-friendly layouts to build confidence when contouring target volumes, assessing prior treatments, and addressing tumor motion
- Create better treatment plans.

**2.3.AGRUS LAB** is indeed a molecular Modelling, graphics, and drug design program for Windows operating systems[12]. It is free software and can be easily accessed by the public.

**KEY USES**:

- **Conformational Analysis**: ArgusLab allows for conformational analysis such as geometry optimization studies[12].
- **Quantum Mechanics Principles**: ArgusLab works on the principle of quantum mechanics and helps to predict potential energies, molecular structures, geometry optimization of structure, vibration frequencies of coordinates of atoms, bond length, bond angle, and reactions pathway[12].

- **Building Molecules**: ArgusLab can be used to build molecules, build molecules using templates, to change the structure of an atom and bond types, and to build new structures from the preexisting structures[12] &[13].
- **Molecular Modelling Package**: ArgusLab serves as a comprehensive molecular Modelling package [12]-[16].

**2.4.SYBYL–X** Suite Is a molecular modelling and simulation suite a comprehensive Suite of computer added drug designing tools which boost the molecular modelling and new drug designing SYBYL-X gives information to understand and balance the competing SAR's for each of the multiple criteria which successful drug candidate must meet. It visualizes and explores relationships between multiple properties with the analysis tools in the new Molecular Data Explorer (MDE) in SYBYL-X, and obtains insights into data in least time. It provides new ways to approach life science molecular discovery projects, while extending the unrivaled.

SYBYL-X explore different insights of drug interaction mechanism with its receptor to identify potential new binding interactions that will provide 'step jumps' in potency, or to identify options for improving AMDE or physical properties without disrupting key receptor interactions [17]a, b & c.

**KEY USES**:

- Build a 3D structural model or homology model for the receptor of interest.
- Ligand Based Design.
- Identify and visualize the cavities present on target protein and the properties of protein/ligand interaction surface.
- Predict and rationalize potential drug interactions with its receptor using Surflex-Dock, docking software.
- Design fragment collections used for screening to perform virtual screening of fragment libraries, and once interesting fragments are identified, to

elaborate the fragment into structures or design a library of structures that will fit to a receptor cavity.

- Identify promising lead candidates using Surflex Dock for virtual screening of databases of in-house or commercially available compounds [18].
- Molecular Modelling from sequence through lead optimization.
- SYBYL-X Suite is also used for to build a Protein Model.

**Note:** But this software SYBYL-X Software is no longer available for purchase. June 30th, 2017 marked the end of support for SYBYL-X Software.

**2.5.SYBYL/Base** is the heart of Tripos' software suite. Touted as a "comprehensive computational tool kit for molecular design and analysis", SYBYL/Base provides essentials modelling and analysis tools for small to large molecule. The program provides facilities for building, superimposing, geometry optimization, distance geometry, docking, and interfaces to quantum mechanical and other methods[19].

**KEY USES:**

- Building and designing of small and large biomolecule.
- Structural determination of designed molecules.
- Operated with other software.
- The *Biopolymer* module provides for specialized treatment of macromolecular structures and systems summarize in Table-1

**TABLE-1**

| | |
|---|---|
| *QSAR*, Advanced *CoMFA*, *and HQSAR* modules. | Supported Quantitative Structure Activity Analyses. |
| *GASP*, *RECEPTOR*, and *DISCO* modules | Provide techniques for conformational searching and for pharmacophore recognition and analysis. |
| *ComposerTM*, *MatchMaker and* | all provide different approaches to the problems of |

| | |
|---|---|
| *GeneFold* | Protein Folding, Sequence, and Structural Similarities. |
| ProTable | *E*nhances the SYBYL "Molecular Spreadsheet" for the analysis of protein structural integrity. |
| *FlexX* and *FlexiDock* | Allow investigation of the configurations necessary for ligand binding to protein receptors. |

**2.6.PASS (PRIDICTION OF ACTIVITY FOR SUSTNCNCE):** is a software tool that predicts over 4000 kinds of biological activity, including pharmacological effects, mechanisms of action, toxic and adverse effects, interaction with metabolic enzymes and transporters, influence on gene expression, etc. It uses the structural formula of a drug-like substance as an input to obtain its estimated biological activity profile as an output.

The software can be used to find new targets (mechanisms) for some ligands and, conversely, to reveal new ligands for some biological targets. It's widely used in the field of medicinal chemistry, by both academic organizations and pharmaceutical companies. [21]-[23].

**KEY USES:**

- **Reveal new effects and mechanisms of action for known substances**: PASS can predict over 4000 types of biological activity based on the structural formula of a substance. This can help reveal new effects and mechanisms of action for known substances in your databases.
- **Find new leads with given biological activity profiles**: By predicting the biological activity profiles of compounds, PASS can help identify potential leads that match a given profile. This can be particularly useful when screening compounds from in-house and commercial databases.
- **Select the most promising compounds for high throughput screening**: The predictions made by PASS can help prioritize compounds for further testing. By identifying the compounds with the most promising predicted activity profiles, you can optimize your high throughput screening process.

**2.7.MapChecK:** The MapCheck compare absolute dose measurements of both systems with ion chamber results. It compares IMRT QA process of Sunnuclear's MapCheck and Varian's Portal Dosimetry.The MapCheck system create verification plan for each field, export calculated dose map (Frontal) to MapCheck for each field, calibrated diode array prior to collecting data. Standard deviation increases with plan complexity. The average measured dose is independent of plan complexity. It is user friendly software for data analysis, easier commissioning process and generates comprehensive report [10]&[11].

MapCHECK 3 -MapCHECK 3 is the next evolution in the MapCHECK family--the world's most chosen 2D array,provides the highest detector density, smallest detector size, and largest field size of any 2D array for IMRT QA.

**KEY USES:**

- Software allows rapid analysis of QA measurements against plan.
- MapCheck used for IMRT verification.
- Small detectors identify MLC.
- Dose based EPID IMRT QA done by using MapCheck.

**2.8.DDDPlus (DOSE DISSOLUTIN AND DISINTIGRATION SOFTWARE):** Is used to study disintegration and dissolution pattern of dosage form and active ingredients. It is an advanced computer program employed by formulation scientists to simulate in vitro disintegration and dissolution of active pharmaceutical ingredients (API) and excipients under different experimental conditions. The software developed by Simulations plus and provides a simple, intuitive user interface, model optimization ,high-quality plots and figures for reporting purposes, excellent customer support, and integration with other tools like ADMET Predictor QSAR, GastroPlus PBPK AND PBBM. The software is divided into three main tabs – 1.***formulation,*** ***2.dissolution method and 3.simulation***. In the formulation of new API, a single calibration experiment is generally required, after which DDDPlus predicts how changes in formulation or experimental parameters will affect the

dissolution rate. This software provides precise information of dissolution and disintegration rate so it is not necessary to rely on conventional 'cut and try' methods to finalize a formulation design[25].DDDPlus allow selecting from one of 5 mathematical models and 5 dosage forms employed to illustrate dissolution of a single ingredient. The mathematical models used for the in vitro dissolution simulation describes the e.ffect of following parameters on dissolution: Physicochemical properties of the formulation ingredients under study: pKa's, solubility, diffusion coefficient, and density. Main features of DDDplus.

- Manufacturing properties for immediate release dosage forms.
- Particle size distribution for each of the formulation ingredients.
- Different flow patterns and fluid velocities for each experimental apparatus.
- Interactions between the active ingredient and formulation excipients.
- Microclimate pH-dependence of solubility and dissolution/precipitation.
- Micelle-facilitated dissolution through the incorporation of surfactants in the media.

**KEY USES:**

- DDDPlus to predict API and tablet dissolution behavior in different media and rotation speeds.
- The dissolution model fitting results via DDSolver were able to differentiate between DPP and formulation influenced tablet dissolution behaviour.
- Calculates the fluid velocity automatically based on the instrument speed and apparatus type.
- DDDPlus has an optimization module that calibrates a drug's dissolution rate using a single experimental data set.

**2.9.GastroPlus: I**s a software package used for Modelling and conducting simulations of properties of drugs or chemicals. It includes features such as:

- Absorption, release rate, bioavailability, pharmacokinetics, and pharmacodynamics simulations.
- Prediction of drug-to-drug interactions.
- Prediction of drug effects on animals and virtual patient populations.
- Generation of in vitro-in vivo correlations.
- Prediction of absorption and systemic distribution/elimination for large molecules.

The software provides a simple, intuitive user interface, model customization, high-quality plots and figures for reporting purposes, and excellent customer support. It also offers integration with other tools, such as ADMET Predictor, DDDPlus, and MembranePlus. GastroPlus is used in various departments within companies, and its licensing model is flexible[88].

Software is a mechanistically based simulation software package that simulates intravenous, oral, oral cavity, ocular, intranasal and pulmonary absorption, pharmacokinetics and pharmacodynamics in human and animals.

Model parameters can be fitted to data for a single record, or across multiple records simultaneously. The program will run one simulation for each record each time and it changes the values of one or more model parameters. Typically, hundreds of iterations will be performed, each with N simulations, where N is the number of records whose observations are being used to compare predicted and observed values. Objective function weighting is user-defined, and includes the most common weighting schemes [26] & [27].

Conducting of simulations properties of drugs or chemicals including absorption, release rate, bioavailability, pharmacokinetics, and pharmacodynamics; computer software which allows for prediction of drug-to-drug interactions; computer software for the prediction of drug effects on

animals and virtual patient populations; computer software which allows researchers to adjust pharmacodynamic models to observed data and to then use the resulting fitted models to predict pharmacodynamic changes due to changes in dose, dosage form, and dosing regimen of a drug or chemical; computer software which allows for the generation of *in vitro-in vivo* correlations; computer software which allows for the prediction of absorption and systemic distribution/elimination for large molecules[28].

**KEY USES:**

- Transporter-based drug-drug interactions.
- Metabolic and/or transporter induction.
- Linked with the industry's 1-ranked dissolution/absorption (ACAT) model.
- Use with either compartmental or physiologically based pharmacokinetics (PBPKPlus).
- Apply competitive and/or time-dependent inhibition kinetics by parent and/or metabolite.
- Simulate DDIs for human and animals like cat, rat mouse , monkey rhesus cynomologous and rabbit.
- Account for enzyme expression level differences in various populations.
- Built-in tool to easily calculate the fraction metabolized from in vitro assays.

**2.10.1.Insight II: I**s a user-friendly graphical molecular modelling program/ package developed by Accelrys Inc. (formerly a product of MSI and BIOSYM) by using this software we can design, buildup and manipulate virtually any class of molecules or molecular systems. Some of these insight II computational engines have the capacity to restart calculations from informations in the saved files that incorporates a variety of useful molecular modelling codes specifically designed for biological systems. Molecular properties can be studied through

InsightII's interface with other Biosym products such as DelPhi, DMol, and Discover[1]&[2].

**KEY USES**

- Multitude of data collection options and graphing features.
- Pre-programmed peak analysis and convenient spectral processing tools aid in sample identification and quantitation for scanning measurements.
- Multi-staged curve fitting and consecutive reaction modes provide comprehensive data fitting options for kinetics experiments.
- Sophisticated math analysis functions, including derivatives and smoothing allow custom data display.
- Merge workbooks feature allows quick and convenient comparison of data from multiple experiments.

**2.10.2.Pipeline Pilot**

Pipeline Pilot is a desktop software program developed by Dassault Systemes for processing and analyzing data. Originally used in the natural sciences, the product's basic ETL(Extract Transform, Load) and analytics capabilities have broadened over time software is now used for Data science, ETL, reporting, prediction, and analytics in a number of sectors[29]. The main key feature of the program is:-

- It provides a graphical user interface for manipulating and analyzing data.
- It allows users with limited or no coding abilities to transform and manipulate datasets.
- It has the ability to design data workflows.
- It incorporates a variety of useful molecular Modelling codes specifically designed for biological systems.
- It can be used in conjunction with other software like Discover.
- It has the capacity to restart calculations from information in saved files.

- Retrieval, filtering, analysis, and re-porting.

Data Modelling in this software is done by Modelling tools, statistical filters and clustering components optimized for large real-world data sets. One can create additional components using various technologies such as Perl, Java, SOAP and basic command line access.

**KEY USES:**

- It's used in a variety of settings, such as cheminformatics and QSAR, Next Generation Sequencing, image analysis, and text analytics[30] &[31]..
- Analyze, profile and manage the compounds in your corporate database with chemically intelligent filters and learning.
- Gene Expression focuses on visualizing, analyzing, annotating and reporting on gene expression experiments including the individual target genes.
- Mass Spectrometry offers a comprehensive set of components and example protocols to create and automate customized proteomics and metabolomics workflows
- Sequence analysis
- Materials Modelling and Simulation
- Focused on chemical product has been expanded to include general Extract, Transform, Load (ETL) capabilities.
- Data visualization and analytics and data processing collections for many scientific and engineering disciplines.
- Used for ETL, analytics and machine learning in the chemical, energy, and consumer goods, aerospace, automotive and electronics manufacturing industries [32]-[25].

**2.10.3.Discovery Studio:** is a comprehensive software suite developed and distributed by Dassault Systèmes BIOVIA[36]-[37]. It's used for simulating small molecule and macromolecule systems, making it a valuable tool in the field of computational chemistry[36] biotherapeutics, developability and life science and into more common environment. Here are some of its key features:

- **Molecular Structures Analysis and Modelling**: Discovery Studio provides tools for analyzing and Modelling molecular structures, sequences, and other data relevant to life science researchers[38].
- **Visualization**: It includes a commercial-grade graphics visualization tool, BIOVIA Discovery Studio Visualizer, for viewing, sharing, and analyzing protein and Modelling data[25].
- **Drug Design**: Discovery Studio offers a wide range of powerful tools that enable computational chemists and computational structural biologists to engineer stable and optimized novel biotherapeutics and small molecule drugs with desired safety profiles.
- **Simulations**: It provides protocols for state-of-the-art molecular dynamics simulations.
- **Structure-based Design**: Discovery Studio supports structure-based and fragment-based design [40].
- **Ligand- and Pharmacophore-based Design**: It offers tools for de novo drug design, multi-target drug design, and activity profiling[40].
- **Biotherapeutics and Antibody Modelling**: Discovery Studio has a rich set of in silico tools to support the design of biotherapeutics
- **Macromolecule Design and Analysis**: It provides a comprehensive portfolio of validated scientific tools for every aspect of macromolecule-based research.
- **QSAR, ADMET & Predictive Toxicology**: Discovery Studio includes tools for designing therapeutics with favorable pharmacokinetic properties and safety profiles[40].

**KEY USES:**

- **Discovery Studio this** software provide mechanics simulation to small molecule and macromolecule systems
- Macromolecule design, validation and engineering.
- It's widely used for 3D molecular Modelling, simulation, and visualization.
- **User-Friendly Interface**: Discovery Studio has an easy-to-use graphical interface, making it accessible for life science researchers[41].
- **Drug Design and Protein Modelling**: It offers powerful tools for drug design and protein Modelling.
- **Sequence Analysis**: Discovery Studio uses tools like BLAST (Basic Local Alignment Search Tool) for sequence analysis.
- **Pharmacophore Analysis**: It's capable of performing pharmacophore analysis.
- **Structure-Based Design**: Discovery Studio is providing a structure-based and ligand-based designing software.
- **3D Molecular Structures Visualization**: It provides a visualizing tool, ActiveXcontrol, for viewing 3D molecular structures and sharing scientific results.
- **Protein Modelling**: Discovery Studio uses DS Modeller for protein Modelling.
- **Cross-Platform Compatibility**: It can be operated on different operating systems such as Linux and Windows [42].
- **ADME-Predictive toxicity**

**2.10.4.BIOVIA Discovery Studio** is a comprehensive suite of software developed and distributed by Dassault Systèmes BIOVIA. It is designed for simulating small molecule and macromolecule systems[44]. The software

integrates over 30 years of peer-reviewed research and world-class in silico techniques such as molecular mechanics, free energy calculations, biotherapeutics developability, and more[43]b.

BIOVIA Discovery Studio provides researchers with a complete toolset to explore the nuances of protein chemistry and catalyze the discovery of small and large molecule therapeutics from Target ID to Lead Optimization. It offers a wide range of powerful tools that enable computational chemists and computational structural biologists to engineer stable and optimized novel biotherapeutics and small molecule drugs with desired safety profiles [43]b. In addition to this, BIOVIA Discovery Studio Visualizer is a free, feature-rich molecular Modelling application for viewing, sharing, and analyzing protein and small molecule data. It allows experts and their colleagues to seamlessly and efficiently exchange results, without loss of either time or scientific information[45]. This leading visualization tool is ideal for viewing, sharing, and analyzing protein and Modelling data[43]a.

BIOVIA Discovery Studio offers a wide range of powerful tools that support different areas of drug discovery[46].

**KEY USES:**

- **Molecular Dynamics Simulation**: BIOVIA Discovery Studio utilizes best-in-class molecular simulation programs, NAMD and CHARMm. Furthermore, Gaussian accelerated Molecular Dynamics (GaMD) is also implemented in the latest release of Discovery Studio for simultaneous unconstrained enhanced sampling and free energy calculations[48]a-g.
- **Structure-Based Drug Designing**: Structure-Based Design (SBD) and the related Fragment-Based Design (FBD) are well-established strategies in the rational development of small molecule drugs. BIOVIA Discovery Studio delivers a comprehensive, scalable portfolio of scientific tools, including GOLD from the Cambridge Crystallographic Data Centre (CCDC), to support and assist SBD and FBD strategies from hit discovery to late-stage lead optimization[47]a-d.

- **Ligand and Pharmacophore Multi-Target Drug Designing and Activity Profiling**: BIOVIA Discovery Studio utilizes the CATALYST Pharmacophore Modelling and Analysis toolset to assist in the assessment of small molecule therapeutics with or without target-structured data. It supports the novel drug design, multi-target drug design, and activity profiling to drive small molecule R&D.
- These tools provide researchers with a comprehensive suite for exploring the nuances of protein chemistry and catalyzing the discovery of small and large molecule therapeutics[47]-[48].

**Collaborative science of BIOVIA Discovery Studio in:**

- CHARMm for force-field based simulations: Distributed with both CPU and GPU editions
- NAMD for force-field based simulations: Distributed with both CPU and GPU editions
- MODELER for protein homology Modelling
- BLAST+ for sequence searching
- GOLD for protein-ligand docking
- ZDOCK for protein-protein docking
- Catalyst for pharmacophore modelling
- AggMap and SCM for protein aggregation & viscosity prediction

The productIt is an example of visual and dataflow programming and has use in a variety of settings, such as cheminformatics and QSAR, Next Generation Sequencing, image analysis, and text analytics. It is not an 'object oriented' programming language.

- Discovery Studio
- Materials Studio
- Accord Insight II

**2.10.5.Materials Studio**

Materials studio software is the most advanced technology and is used to solve the problems in R&D process. It is designed for structural and computational researchers in chemicals and materials R&D. Materials studio provides tools for Modelling crystal structure and crystallization processes; property prediction for molecules, polymers, catalysts and for determining the structure activity relationship. They provide various ranges of quantum mechanics based tools for predicting structures, density functional methods, linear scaling and semi-empirical tools. QSAR integration in the Materials studio has wide range of descriptors such as topological and electro-topological descriptors, these helps the calculation process easier. Accord is software specially designed for cheminformatics. They can capture, manage, analyze, and mine chemical data. Accord is oracle based software used for storage, retrieval, analysis of chemical structures and related biological, chemical and inventory data. Accord is user friendly and is powered by Robust and well proven chemistry engine that can be used for any type of chemistry.

**2.10.6.BIOVIA Materials Studio** is indeed a comprehensive Modelling and simulation environment designed to allow researchers in materials science and chemistry to predict and understand the relationships of a material's atomic and molecular structure with its properties and behavior[49]a. It supports various functional areas, such as polymers, metals, semiconductors, batteries, and more, and offers an integrated, multi-scale Modelling environment with materials informatics and data-driven decision making.

Materials Studio offers an "in silico first" approach, allowing researchers to optimize their materials' performance in a relatively low cost environment prior to physical testing[49]a. This approach can:

- **Accelerate the innovation process**: Drive deeper understanding of the interactions that define material properties.
- **Reduce R&D Costs**: Minimize the number of physical experiments via "Virtually Screening" candidates.

- **Improve R&D Efficiency**: Automate and share best practices within Pipeline Pilot to reduce non-value added tasks[49]a-d.
- **Foster Data-Driven Decisions**: Complement laboratory experimentation with powerful materials informatics.

BIOVIA Materials Studio is a powerful tool for researchers in many industries who are engineering better performing materials of all types, including catalysts, polymers, composites, metals, alloys, pharmaceuticals, batteries, and more.

**2.11. SCHRODINGER SOFTWARE: I**s a powerful computational platform that provides accurate, reliable, and high-performance technology powered by physics. It is transforming the way therapeutics and materials are discovered, making the innovations of the future achievable today[51]&[54]..

The software is used by pharmaceutical companies, biotech firms, academic researchers, and supercomputing centers to simulate and model the behavior of molecules at the atomic level. This accelerates the design and development of new drugs and materials more efficiently, reducing the time and cost of bringing them to market[55].

Schrödinger software is suited for drug designing for both structure-based and ligand-based methods[50].. It offers a range of tools for quantum chemistry, molecular dynamics, and structural biology, making it an essential tool for scientists and researchers in these fields[53].

The software allows users to leverage the power of digital chemistry for materials design. Designing the next generation of materials starts at the molecular level. The software helps in designing the molecule for tomorrow's demand.

Schrödinger offers various products as part of its suite[50]. It also provides facilities to solve problems in life science research or we can say it open new world of molecular discovery. Most of the pharmaceutical companies,

biotechnology companies, government agencies, universities and supercomputing centers are using this software10[51], [52]& [54]

**KEY USES:**

- **Leverage the power of digital chemistry for materials design**
- **Designing the next generation of materials starts at the molecular level.**
- Designing the molecule for tomorrow demand
- The various products of Schrodinger are:

***Glide, Prime, Jaguar and Macro Model*** are the product of Schrödinger

**2.11.1.Glide**, a software tool used in computational chemistry for ligand-receptor docking. Here's a summary of the key points you mentioned:

- **High-throughput virtual screening (HTVS)**: Glide can screen millions of compounds quickly, making it suitable for large-scale virtual screening projects.
- **Accurate binding mode predictions**: Glide is known for its ability to reliably find the correct binding modes for a large set of test cases, achieving low RMS deviations from native co-crystallized structures.
- **Standard Precise (SP) mode**: In this mode, Glide can dock hundreds to thousands of ligands with high accuracy.
- **Extra Precision (XP) mode**: This mode further refines the results, changing false positives with advanced scoring.
- **Versatility**: Glide can exhibit an excellent range of docking accuracy across a diverse range of receptors, making it universally applicable.

It's clear that Glide offers a comprehensive solution for ligand-receptor docking, balancing speed and accuracy to meet various research needs.

**KEY USES:**

- **Ligand-Receptor Docking in Computational Chemistry**: Glide is used for ligand-receptor docking in computational chemistry. It offers high-throughput virtual screening, accurate binding mode predictions, and a range of precision modes.
- **No-Code App Development**: Glide is also a no-code app builder that transforms databases into functional apps. It's used to create custom, AI-powered apps without any coding or programming knowledge. It works with your existing business data, whether it lives in spreadsheets or databases.
- **Image Loading and Caching**: Glide is used as an image loading and caching library for Android development.

**2.11.2. Prime** is indeed a comprehensive package used for protein structure predictions. It is part of the Schrödinger software suite and is known for its user-friendly interface. Here are some key features of Prime:

1. **Complete Control**: Prime provides users with complete control over calculational settings to increase the accuracy of the results.
2. **Accurate Receptor Models**: Prime provides accurate receptor models for structure-based drug design.
3. **Homology Modelling and Fold Recognition**: Prime incorporates homology Modelling and fold recognition into a single solution [58]. It can generate accurate homology models for further structure-based studies.
4. **Threading and Fold Recognition Techniques**: Prime uses threading and fold recognition techniques in cases of low or no sequence identity.
5. **Parameter Adjustment**: Prime allows users to specify and adjust parameters to optimize the quality of predictions.

Prime is a valuable tool in the field of computational biology and drug discovery, enabling researchers to predict protein structures from sequence to

obtain a high-quality model when an experimental structure is not available[59].

Prime is a fully-integrated protein structure prediction solution that is part of the Schrödinger software suite. It incorporates homology Modelling and fold recognition into a single solution[59].

**KEY USES:**

- **Structure Prediction**: Prime includes an intuitive step-by-step interface that takes users through the workflow of structure prediction by supplying helpful default settings for each stage of the process.
- **Refinement of Experimental Structures**: Prime can refine experimental structures obtained through X-ray crystallography, NMR, or Cryo-EM for accurate and detailed starting points for subsequent simulations.
- **Prediction of Protein Structures**: Prime can accurately predict protein structures from sequence to obtain a high-quality model when an experimental structure is not available.
- **Prediction and Refinement of Side Chain Positions**: Prime can predict and refine side chain positions to create a complete, all-atom protein model.
- **Prediction of Membrane Permeability and Conformations of Macrocycles**: Prime can rapidly calculate the energetics of a system of interest using MM-GBSA.
- **Creation of Backbone Models**: Prime can create backbone models for early structural investigations or functional annotation in cases of low- or no-sequence identity.
- **Scanning of Protein Mutations**: Prime can rapidly scan thousands of protein mutations, with tight integration to FEP+ that allows for an accurate and thorough screening cascade for protein optimization[60].

**2.11.3. Jaguar** is indeed a high-performance ab initio package that is part of the Schrödinger software suite. It is designed for both gas and solution phase recreations, with a particular strength in treating metal-containing systems. Here are some key features of Jaguar: [61].

1. **Speed**: Jaguar proceeds faster than other conventional methods, making it possible to carry out more calculations at a single time.
2. **Comprehensive Calculations**: Jaguar computes a comprehensive array of molecular properties such as NMR, IR, pKa, partial charges, electron density, electrostatic potential, and NBO analysis.
3. **Potential Energy Surface**: Jaguar generates potential energy surfaces with respect to differences in the internal coordinates.

Jaguar is particularly useful in the field of computational chemistry, where it can help researchers predict structures and compute molecular properties of novel molecular systems of all sizes.

**KEY USES:**

- **Structure Prediction**: Jaguar includes an intuitive step-by-step interface that takes users through the workflow of structure prediction by supplying helpful default settings for each stage of the process[62].
- **Refinement of Experimental Structures**: Jaguar can refine experimental structures obtained through X-ray crystallography, NMR, or Cryo-EM for accurate and detailed starting points for subsequent simulations.
- **Prediction of Protein Structures**: Jaguar can accurately predict protein structures from sequence to obtain a high-quality model when an experimental structure is not available.
- **Prediction and Refinement of Side Chain Positions**: Jaguar can predict and refine side chain positions to create a complete, all-atom protein model.

- **Prediction of Membrane Permeability and Conformations of Macrocycles**: Jaguar can rapidly calculate the energetics of a system of interest using MM-GBSA.
- **Creation of Backbone Models**: Jaguar can create backbone models for early structural investigations or functional annotation in cases of low- or no-sequence identity.
- **Scanning of Protein Mutations**: Jaguar can rapidly scan thousands of protein mutations, with tight integration to FEP+ that allows for an accurate and thorough screening cascade for protein optimization[62].

**2.11.4. MacroModel** is indeed a complete molecular Modelling package. It uses leading force fields to provide accurate results[63]. Here are some key features of MacroModel:

- **Force Field Molecular Modelling**: MacroModel is used to examine molecular conformations, molecular motions, and intermolecular interactions such as ligand-receptor complexes[63].
- **Molecular Dynamics**: MacroModel can perform molecular dynamics at constant temperatures using a mixed Monte Carlo algorithm and stochastic dynamics.
- **Wide Range of Searching Methods**: MacroModel supports a wide range of searching methods and can handle systems ranging from small molecules to entire proteins.
- **Support for Different Force Fields**: MacroModel supports different types of force fields such as MM2, MM3, AMBER, AMBER 94, MMFF, and OPLS-AA[1], enabling it to be used for a wide range of research applications[63].

**2.12.AutoDock**

AutoDock is a suite of automated docking tools. It is designed to predict how small biomolecules, such as substrates or drug candidates, bind to a receptor of

known 3D structure. Over the years, it has been modified and improved to add new functionalities, and multiple engines have been developed. It performs docking of the ligand with the target molecule which is a protein.

2. Auto Grid pre calculates this binding of the ligand with the target molecule. This type of study can help in designing better binders. Auto DockTools (ADT) has been developed to set up which type of bonds is rotatable in the ligand to analyze the docking.

- Xray crystallography
- Structure based drug design
- Lead Optimization
- Virtual Screening (HTS)

Current distributions of AutoDock consist of two generations of software:

**1.** AutoDock 4

**2.** AutoDock Vina

**3.** AutoDock-GPU, is an accelerated version of AutoDock4 is more recently, developed, software that is hundreds of times faster than the original single-CPU docking code.

**2.12.1**.**AutoDock 4:** actually consists of two main programs: autodock performs the docking of the ligand to a set of grids describing the target protein; autogrid pre-calculates these grids.In addition to using them for docking, the atomic affinity grids can be visualised. This can help, for example, to guide organic synthetic chemists design better binders.

**2.12.2.AutoDock Vina:** does not require choosing atom types and pre-calculating grid maps for them. Instead, it calculates the grids internally, for the atom types that are needed, and it does this virtually instantly.ADT AutoDock tools helps to set up which bonds will treated as rotatable in the ligand and to analyze dockings. AutoDock has following application in the area of:-

- X-Ray crystallography
- Structure-Based drug designing
- Lead optimization
- Virtual screening(HTS)
- Combinational library design
- Protein-Protein Docking
- Chemical mechanism studies

**2.12.3.AutoDock-GPU:** is a software tool for molecular docking and virtual screening, which uses GPUs and other accelerators to speed up the process of finding the best binding pose of a ligand-protein complex. It is based on AutoDock 4., but it has several features and improvements, such as gradient-based local search methods, batched ligand pipeline, and support for Cuda and OpenCL platforms2. AutoDock-GPU is developed by the Forli lab at Scripps Research.

**2.13.QSARProis: is** most comprehensive and powerful **advanced new molecular drug designing software based on prediction and accurate** for the indirect approach to drug designing using QSAR. QSARpro not only predicts activity but also allows researchers to optimize leads with insights from QSAR results and generate focused molecular libraries. QSAR Modelling typically involve activities such as descriptor choice and calculation, statistical evaluation of the calculated descriptors, training and test set assignment, regression and results analysis. It evaluate multiple options for classes of descriptors, test set, choice of linear or nonlinear regression and choice of regression technique to determine the option that is most suitable to a particular project [47], [48].In addition to multiple 2D/ 3D QSAR methods, QSARpro also provides:

- VLife's patent pending GQSAR technology for fragment based QSAR approach to obtain site specific design clues which are critical for lead optimization

- Novel kNN-MFA methodology which creates robust 3D QSAR models by considering non-linear relationships between molecular properties and its activity
- A wide array of over 40 method options for building QSAR models for prediction of activity and activity based profiling of a molecular dataset
- A comprehensive collection of 1000+ molecular descriptors including 2D, 3D, alignment dependent and alignment independent for building robust QSAR models
- It is employed to evaluate more than 1000 molecular descriptors including physicochemical, topological and electro-topological, information theory based, quantum mechanical, electrostatic and hydrophobic, alignment independent, MMFF atom types and so on.
- QSARpro has a wide choice of statistical methods to suit requirements of the most demanding datasets. Allowing researchers to combine model building with variable selection, QSARpro provides over 40 options for researchers to choose from.
- QSARpro providing accurate predictions it has 1000+ molecular descriptors which significantly contribute to building a robust QSAR model. These include 2D, 3D, alignment dependent and alignment independent descriptors.

**KEY USES:**

- Explore and exercise various combinations of variable selection methods and regression methods.
- Aligning given set of molecules in the protein active site with respect to the co-crystal ligand to develop a basis for the placement of ligand.
- Protein-protein interaction studies.

**2.14.Flex X:** Is our modern, ultra-high speed approach to ligand docking. Screen whole compound libraries within minutes to identify promising binders. The Flex X docking functionality in See SAR places a ligand into a binding site. It is based on an incremental construction algorithm. It is another fragment-based method using exible ligands and rigid proteins. It uses MIMUMBA torsion angle database for the creation of conformers. The MIMUMBA is an interaction geometry database used to exactly describe intermolecular interaction patterns. For best scoring, the Boehm function (with minor adoptions necessary for docking) is applied that was delivered to user. On the contrary to DOCK which performs well with a polar binding sites, Flex X shows totally opposite behaviour. It has a bit lower hit rate than DOCK but provides better estimates of Root Mean Square Distance for compounds with correctly predicted binding mode. There is an extension of Flex X called Flex E with exible receptors, which has shown to produce better results with significantly lower running times.

**Advantages**

- Docking for non-experts: no more receptor preparation – simply dock!
- Accurate binding mode prediction
- Dock gigantic libraries by using ultra-high-speed docking (< 1 s/ligand)

**KEY USES:**

- Simple Docking Common Substructure (MCS) between the template and the compound-to-dock.
- Template-based docking is performed by determining the Maximum

**2.15.GOLD:** Is indeed a protein-ligand docking software expert of drug discovery that is trusted by scientists globally. It uses a genetic algorithm to provide docking of exible ligands and proteins with exible hydroxyl groups. Otherwise, the protein is considered to be rigid. This makes it a good choice when the binding pocket contains amino acids that form hydrogen bonds with the ligand. Here are some key features of GOLD:

1. **Screening and Lead Optimization**: GOLD is used for virtual screening through to lead optimization.
2. **Pose Prediction**: GOLD is trusted by scientists globally for pose prediction.
3. **Scoring Function**: GOLD uses a scoring function that is based on favorable conformations found in the Cambridge Structural Database and on empirical results on weak chemical interactions.
4. **Comprehensive Validation Test Sets**: GOLD has one of the most **Virtual** comprehensive validation test sets[65].

**KEY USES:**

- **Protein-Protein Docking**: GOLD can be used for protein-protein docking.
- **Chemical Mechanism Studies**: GOLD can be used for studying chemical mechanisms.

**2.16.UCSF: Chimera** is an extensible program for interactive visualization and analysis of molecular structures and related data. It's developed by the Resource for Biocomputing, Visualization, and Informatics (RBVI) at the University of California, San Francisco (UCSF). Here are some of its key features[66]:

**3D Visualization**: Chimera excels at the 3D visualization of proteins, nucleic acids, small molecules, electron densities, surfaces, and trajectories.

**KEY USES**

- **Molecule Editing**: It allows users to edit molecules, which can be crucial in the process of drug design.
- **Ray Tracing and Movie Making**: Chimera can perform ray tracing to create high-quality images and animations, which can be useful for presentations and publications.

- **Molecular Modelling**: Chimera is used for various molecular modelling tasks, including protein-ligand modelling and molecular simulations.
- **Drug Screening**: It can also be used for drug screening, helping researchers identify potential drug candidates.
- **Python Plugin Tools**: Chimera's Python-based software allows for the development of plugin tools to enhance its utilities and facilitate drug design.
- These features make UCSF Chimera a versatile and valuable tool in the field of molecular visualization and analysis [66].
- **Visualization and Analysis**: Chimera allows users to visualize and analyze molecular structures and related data, including density maps, supramolecular assemblies, sequence alignments, docking results, trajectories, and conformational ensembles.
- **3D Display and Manipulation**: Users can display and manipulate structures in 3D.
- **Image and Animation Creation**: High-quality images and movies can be created [66]. Different conformations and even different proteins can be compared by morphing from one structure to another.
- **Molecular Modelling and Simulation**: Users can perform molecular Modelling and simulation [67].
- **Use in general structural analysis[68] &[69]**
  - Automatic identification of atom
  - hydrogen addition and partial charge assignment
  - High-quality hydrogen Bond contact, and clash detection
  - Geasurements: distances, angles, surface area, volume
  - Calculation of centroids, axes, planes and associated measurements

- Amino acid rotamer libraries, protein Ramachandran plot, protein contact map
- Atructure building and bond rotation
- Molecular dynemics trajectory playback (many formats), distance and angle plots
- morphing between conformations of a protein or even different proteins
- display of attributes (B-factor, hydrophobicity, etc.) with colors, radii, "worms"
- easy creation of custom attributes with simple text file inputs
- ViewDock tool to facilitate interactive screening of docking results
- rich set of commands, powerful specification syntax
- many formats read, PDB and Mol2 written
- Web and fetch from protein data bank , CATH, or SCOP(domains), EDS (density maps), EMDB (density maps), ModBase (comparative models), CASTp (protein pocket measurements), Pub3D (small molecule structures), VIPERdb (icosahedral virus capsids),UniProt (protein sequences with feature annotations), others
- interfaces to PDB2PQR charge/radius assignment, APBS electrostatics calculations, AutoDock Vina single-ligand docking.

- **Pentation in images and movies**
- high-resolution images
- visual effects including depth-cueing, interactive shadows, silhouette edges, multicolor backgrounds
- standard molecular representations (sticks, spheres, ribbons, molecular surfaces)
- pipes-and-planks for helices and strands; nucleotide objects including lollipops and ladder rungs

- ellipsoids to show anisotropic B-factors
- nonmolecular geometric objects
- renderings of density maps and other volume data (see below)
- labeling with text, symbols, arrows, color keys
- different structures can be clipped differently and at any angle
- optional raytracing with bundled Pov-Ray.
- scene export to X3D and other formats
- simple graphical interface for creating movies interactively
- scenes can be placed as key frames along an animation timeline
- alternatively, movie content and recording can be scripted; rich set of related commands
- movie recording is integrated with morphing and MD trajectory playback

- **Volume data tools**

- many formats of volume data maps (electron density, electrostatic potential, others) read, several written
- interactive threshold adjustment, multiple isosurfaces (mesh or solid), transparent renderings
- fitting of atomic coordinates to maps and maps to maps
- density maps can be created from atomic coordinates
- markers can be placed in maps and connected with smooth paths
- display of individual data planes or multiple orthogonal planes
- volume data time series playback and morphing
- many tools for segmenting and editing maps
- Gaussian smoothing, Fourier transform, other filtering and normalization

- measurements: surface area, surface-enclosed volume, map symmetry, others

- **Sequence structure tools**

- many sequence alignment formats read, written
- sequence alignments can be created, edited
- sequences automatically associate with structures
- sequence-structure crosstalk: highlighting in one highlights the other
- protein BLAST search via Web service
- Multiple sequencing alignment via Cluster Omega and MUSCLE Web services
- interfaces to MODELLER for homology Modelling and loop building
- structure superposition with or without pre-existing sequence alignment
- generation of structure-based sequence alignments from multiple super positions
- several methods for calculating conservation and displaying values on associated structures
- RMSD header (histogram above the sequences) showing spatial variability of associated structures
- user-defined headers including histograms and colored symbols
- UniPort and CDD feature annotations shown as colored boxes on sequences
- trees in Newick format read/displayed

**Note:** UCSF Chimera is legacy software that is no longer being supported. Users are strongly encouraged to try UCSF ChimeraX, which is under active development.

**2.17. UCSF ChimeraX:** (or simply ChimeraX) is the next-generation molecular visualization program from the Resource for Biocomputing, Visualization, and Informatics (RBVI), following UCSF Chimera[70]. It is developed with support from National Institutes of Health R01-GM129325, Chan Zuckerberg Initiative grant EOSS4-0000000439, and the Office of Cyber Infrastructure and Computational Biology, National Institute of Allergy and Infectious Diseases[70].

ChimeraX can be downloaded free of charge for academic, government, nonprofit, and personal use. Commercial users, please see ChimeraX commercial licensing.

The ChimeraX 1.7 production release is available as of December 19, 2023. Future Mac releases will require macOS 11 or higher[70].

ChimeraX offers features such as Matchmaker, Superposition, and RMSD, and can be used for viewing and analyzing molecular structures. It is the state-of-the-art visualization program from the RBVI at UC San Francisco[71].

Please note that ChimeraX is under active development.

**UCSF ChimeraX** is a versatile program for the interactive visualization and analysis of molecular structures and related data. Here are some of its key uses are

**KEY USES:**

- **Visualization and Analysis**: ChimeraX allows users to visualize and analyze molecular structures and associated data, such as density maps, sequences, sequence alignments, and more[73].
- **High-Performance Rendering**: It provides high-performance rendering of large structures and data[72].
- **Image and Animation Creation**: High-quality images and movies can be created[72].
- **Molecular Modelling and Simulation**: Users can perform molecular Modelling and simulation.

- **Virtual Reality Mode**: It offers a virtual reality mode for SteamVR systems.
- **ISOLDE Plugin**: It includes an ISOLDE plugin for building atomic models into low/medium-resolution density.
- **AlphaFold and ESMFold**: It supports AlphaFold and ESMFold AI-predicted protein structures[72] &[74].

Note that ChimeraX is under active development

**2.18.PyMOL**, a cross-platform molecular graphics tool, has been widely used for three-dimensional (3D) visualization of proteins, nucleic acids, small molecules, electron densities, surfaces, and trajectories. It is also capable of editing molecules, ray tracing, and making movies. This Python-based software, alongside many Python plugin tools, has been developed to enhance its utilities and facilitate the drug design in PyMOL. To gain an insightful view of useful drug design tools and their functions in PyMOL,

**KEY USES:**

- **3D Visualization**: PyMOL excels at the 3D visualization of proteins, nucleic acids, small molecules, electron densities, surfaces, and trajectories.
- **Molecule Editing**: It allows users to edit molecules, which can be crucial in the process of drug design.
- **Ray Tracing and Movie Making**: PyMOL can perform ray tracing to create high-quality images and animations, which can be useful for presentations and publications.
- **Molecular Modelling**: PyMOL is used for various molecular Modelling tasks, including protein-ligand Modelling and molecular simulations[75] &[76].
- **Drug Screening**: It can also be used for drug screening, helping researchers identify potential drug candidates.[75]

- **Python Plugin Tools**: PyMOL's Python-based software allows for the development of plugin tools to enhance its utilities and facilitate drug design.

These features make PyMOL a versatile and valuable tool in the field of drug design.

**2.19.EthoWatcher** is indeed a computational tool that is freely available for non-commercial purposes. It supports detailed ethography, video-tracking, and the extraction of kinematic variables from digital video files of laboratory animals. Here are some key features of EthoWatcher:

1. **Tracking Module**: The tracking module allows for controlled segmentation of the animal from the background in a video file, and automatically delivers image attributes that are used to calculate distance traveled, animal orientation, length and area, as well as a path graph.
2. **Ethography Module**: The ethography module allows users to build and use behavioral catalogues to record behavioral events online (from the environment) and offline (from video record files, continuously or frame-by-frame), producing time-segmented reports of duration, frequency, or latency of the recorded behaviors, as well as their temporal sequence[88].

**KEY USES:**

- **Simultaneous Use of Activity and Ethological Approaches**: EthoWatcher can be used for the simultaneous use of the activity and ethological approaches.
- **Information on Active and Specific Behavior Change in Experimental Animal**: EthoWatcher provides information on active and specific behavior change in experimental animals.
- **Extraction of Important Information on Behavioral**: EthoWatcher is useful for extracting important information on behavioral.
- **Combined Use of Ethography and Kinematic Data**: EthoWatcher provides the combined use of ethography and kinematic data[88].

**2.20.MicroTracker:** is an online, on-demand market research and versatile tool that provide a wide range particularly in the field of the right healthcare stakeholders[89] and market research . This tool can be particularly useful in the field of drug discovery for gathering insights and feedback from healthcare professionals.

**KEY USES:**

- **Market Research**: MicroTracker is an online, on-demand market research tool that connects you to the right healthcare stakeholders[12].
- **Survey Design**: It helps you design simple surveys, bringing you faster, quality data at a lower cost[12].
- **Data Collection and Analysis**: MicroTracker includes data collection and analysis services that provide crucial insights and improve the ability to collect and understand how to use high-quality, rigorous data[1].
- **Standardized Metrics**: It allows users to track program and client outcome metrics over time, and compare and benchmark using data from relevant industry peers, other organizations in a state, and the industry as a whole.
- **Nationwide Data Set**: MicroTracker provides a nationwide data set that draws from organization-submitted data and provides an overview of their activities, scale, effectiveness, and outcomes.
- **Tracking Agenda**: MicroTracker lets you set up your annual tracking agenda in minutes and gives you full, on-demand access to your data[89]

**2.21.Flare:** is a ligand and structure-based drug design software developed by Cresset, that enables chemists and researchers to design and prioritize novel small molecules[90].

**KEY USES:**

- **Ligand-Based Drug Design**: Flare allows users to closely examine, compare, and prioritize their molecules based on their shape,

electrostatics, and binding activity. It also includes robust QSAR models that predict the activity and ADMET properties of new compounds [91].

- **Structure-Based Drug Design**: Flare provides a variety of methods including docking and scoring, Electrostatic Complementarity, molecular dynamics, pocket analysis, and water analysis (GIST and 3D-RISM) for gaining new insights into protein-ligand binding.
- **Python API**: Thanks to the Python API, Flare features are fully customizable and expandable. Users can develop their own extensions or include one of Cresset's pre-made extensions.
- **Integration with DMTA Collaboration Tool, Torx**: Flare seamlessly connects with the DMTA collaboration tool, Torx, to streamline collaboration across the entire DMTA cycle.

Flare also offers a free version, Flare Visualizer, which allows users to produce high-resolution 3D graphics of their ligands and proteins[90]&[92].

***2.22.CDD Vault: Is CDD Is an ideally suited scientific database management system for start-up biotech,a hosted scientific data management system that helps you organize, analyzing, collaborate, and make discoveries faster. It plays a crucial role in molecular and designing drug in several ways: Main features of CDD Vault that makes it powerful tool in the field of molecular and drug designing[90].***

**Chemical Properties Calculation**: When new molecules are registered into CDD Vault, it automatically calculates a set of chemical properties for every chemical structure registered. These properties include molecular weight, log P, H-bond donors and acceptors, Lipinski Rule of Five, log D, log S, and pKa.

**Structure Searching**: CDD Vault's searching tools are extremely flexible and allow for searching over all combinations of data stored in your Vault. This includes protocols, structures, chemical properties, collections, and keywords. You can perform either a substructure, exact structure, or Tanimoto similarity search over your molecules.

**Data Management**: It helps you store both biology and chemistry data in a single, flexible system that accommodates a variety of data types and workflows.

**Research Productivity**: It enables real-time collaboration and secure data access through any web browser, so the team can spend more time making discoveries.

**Intellectual Property Protection**: It safeguards against data loss and unauthorized access, because intellectual property is your most important asset.

**AI & Machine Learning**: It structures your data to facilitate AI applications and leverages built-in generative tools to discover new leads.

**KEY USES:**

- **Protein Therapeutics**: Register peptide sequences and automatically calculate physical properties. Organize assay results as well as related entities such as expression plasmids.
- **CRISPR**: Set up genetic engineering experiments and protocols with ELN. Capture data and results and build a database of CRISPR constructs[95].
- **PROTAC**: Compare PROTACs and their bioactivities. Register the linker, E3 ligand, and warhead components as separate entities for easy cross-reference[94]
- **Antibody Drug Conjugate**: Track ADCs and their components: antibody, linker, and warhead. Define bioassay protocols to characterize candidates and visualize results.
- **Oncology Drug Screening**: Register drug combinations (mixtures) as unique entities to facilitate drug screening.
- It is used commonly used by biotech companies, CROs, academic labs, research hospitals, agrochemical and consumer goods companies[92]

**2.23.ArmChair:** Is a software that provides a suite of tools for drug discovery. It's one of the top-rated drug discovery software in 2024 according to AIMultiple. However, the specific details about its features and uses are not readily available.

**3.CONCLUSION** Drug designing software like Glide, Macro Model, Autodock, Argus lab, and Flare are used for ligand-based drug designing and molecular modelling, while Insight II, Discovery Studio, Materials Studio, Accord, Prime, and Jaguar are used for structure-based drug designing. Moreover, structurally based drug design software is utilised for gene sequence analysis, protein modelling, and molecular modelling. Software for docking ligands with target therapeutic molecules is the primary function of ligand-based drug design. With a variety of tools for quantum chemistry, molecular dynamics, and structural biology, the Schrodinger Suite is utilised in computational chemistry and materials research. Consequently, these softwares for creating drugs based on structures and ligands have potential uses in the pharmaceutical or biotechnology field to design novel drugs

**4.REFERENCES:**

[1] (a).D. Sisodiya , P. Pandey and K. Dashora, Drug Designing Softwares and Their Applications in New Drug Discover, Journal of Pharmacy Research,5(1),124-126,2012.,(b). **D.Yu**, **L. Wang** and **Y. Wang**,Recent Advances in Application in Computer- Aided Drug Design in Anti-Influenza A Virus Drug Discovery,*Int. J. Mol. Sci. 23*(9), **2022**,

[2] (a).Christoffersen, R. E., Marr J.J.; and Wolff, M.E., In Burger's Medicinal Chemistry and Drug Discovery, fifth edition, Vol.1, Principles and Practice, John Wiley and sons, Inc. New York.305, 1989.

[3] (a).G. Prasad Jamkhande , H. Mahavir . Ghante , R. Balaji , Ajgunde , Software based approaches for drug designing and development: A systematic review on commonly used software and its applications,

Bulletin of Faculty of Pharmacy, Cairo University, ,Volume 55, Issue 2, , Pages 203-210, 2017.,(**b).** Abdulilah ECE Computer-aided drug design BMC Chem. 2023 Dec; 17(1): 26. Published online 2023 Mar 24. doi: 10.1186/s13065-023-00939-w

[4] R.A. Hodos, B.A. Kidd, K. Shameer, B.P. Readhead, J.T. Dudley In silico methods for drug repurposing and pharmacology, computational approaches to drug repurposing and pharmacology WIREs Syst. Biol. Med., 186,2016.

[5] M.J. Wasko, K.A. Pellegrene, J.D. Madura, C.K. Surratt A role for fragment-based drug design in developing novel lead compounds for central nervous system targets Front. Neurol, 6, pp. 1-11, , 2015.

[6] (a). Welcome to Sanjeevini Module - Supercomputing Facility for ... ,(b). Green Marketing: A Study of Consumer Perception and Preferences in ... ,(c). A study on consumer's awareness and preference towards Green ... - JETIR

[7] M. Bhatia and A. Jain, Green Marketing: A Study of Consumer Perception and Preferences in India, Electronic Green Journal, Issue 36,ISSN: 1076-7975,. 2013

[8] http://www.scfbio-iitd.res.in/sanjeevini/sanjeevini.jsp (accessed 12.12.16).

[9] B. Jayaram, T. Singh, G. Mukherjee, A. Mathur, S. Shekhar, V. Shekhar Sanjeevini: a freely accessible web-server for target directed lead molecule discovery, BMC Bioinformatics, 13, 2012.

[10] https://www.schrodinger.com/Maestro (accessed 10.12.16).

[11] K. Sabitha, S.K.M. Habeeb. Molecular Modelling and drug discovery of potential inhibitor for anticancer target gene melk (Maternal Embryonic Leucine Zipper Knase), Int. Res. J. Pharmacy, 2, pp. 141-145,2011.

[12] ArgusLab . LSCF Bioinformatics - ArgusLab - Weizmann Institute of Science

[13] ArgusLab ·bio.tools , Mark Thompson .

[14] http://www.arguslab.com/arguslab.com/ArgusLab.html (accessed 12.12.16).

[15] A. Naz, K. Bano, F. Bano, N.A. Ghafoor, N. Akhtar, Conformational analysis (geometry optimization) of nucleosidic antitumor antibiotic showdomycin by Arguslab 4 Software, Pak. J. Pharm., 22,pp. 78-82,2009.

[16] G.E. Mathew, S. George, M. Shamnas, V.B.A. Raj, Isolation, in silico design and anti-inflammatory activity of spirosolenol from the roots of Solanumanguvi.

[17] (a). http://www.certara.com/products/molmod/sybyl-x (accessed 12.12.16).

(b). A. Dubey, S.S. Kalra, Computational comparative Modelling and visualization for HIV1 and HIV2 proteins via the software SYBYL-X, Int. J. Sci. Res. Publ., **3**,pp. 2250-3153 ,2013.

(c). G. Xu, Y. Chen, K. Shen, X. Wang, F. Li, Y. He, The discovery of potentially selective human neuronal nitric oxide synthase (nNOS) inhibitors: a combination of pharmacophore modelling, CoMFA, virtual screening and molecular docking studies, Int. J. Mol. Sci.,**15**, pp. 8553-8569,2014.

[18] SYBYL-X Software | Certara , SYBYL-X 2.1 | Scientific Computing World , SYBYL-X Suite - G6G Directory of Omics and Intelligent Software ,Sybyl - Biochemistry Computational Research Facility (BCRF)

[19] (a). SYBYL-X Software | Certara ,(b) Sybyl - Biochemistry Computational Research Facility (BCRF) ,(c). SYBYL-X Suite - G6G Directory of Omics and Intelligent Software.

[20] Way2Drug - main

[21] Pass - geneXplain

[22] PASS: prediction of activity spectra for biologically active substances ...

[23] PASS: prediction of activity spectra for biologically active substances .

[24] www.sunnuclear.com (accessed 25.12.16).

[25] (a). M. Almukainzi, A. Okumu, H. Wei, R. Lobenberg Simulation of in vitro dissolution behavior using DDDPlus ,AAPS Pharmascitech, pp. 1-2, 2014.

(b).http://www.simulationsus.com/Products.aspx?GastroPlus&grpID=3&cID=16&pID=11. (accessed 12.12.16), (c). Perun, T. J.; and Propst, C.L., In Computer Aided Drug Design, Method & Applications, Marcel Dekker, Inc, New York, **2**. 5,1989. Newall, C., In The Role of Organic Chemistry, Academic press, London, 209, 1985.

[26] T.S. Honorio, E.C. Pinto, H.V.A. Rocha, V.A.D. Esteves, T.C. Santos, H.C.R. Castro, In vitro–in vivo correlation of efavirenz tablets using GastroPlus® AAPS PharmSciTech., **14,** pp. 1244-1254,2013.

[27] http://www.simulations-plus.com/Products.aspx?DDD Plus&grpID=2&cID=14& pID=14. (accessed 10.12.16).

[28] M. Almukainzi, A. Okumu, H. Wei, R. Lobenberg, Simulation of in vitro dissolution behavior using DDDPlus, AAPS Pharmascitech, pp. 1-2, 2014.

[29] Pipeline Pilot - Wikipedia , PIPELINE PILOT OVERVIEW - Dassault Systèmes,. BIOVIA Pipeline Pilot | Dassault Systemes ,Tips for Using Pipeline Pilot as an Integration Platform .

[30] The NMITLI-BioSuite Team,BioSuite: a comprehensive bioinformatics software package (A unique industry–academia collaboration),Curr. Sci., **92** pp. 29-38, 2007.

[31] https://www.schrodinger.com/Maestro (accessed 10.12.16).

[32] Pipeline Pilot - Wikipedia

[33] BIOVIA Pipeline Pilot | Dassault Systemes

[34] PIPELINE PILOT OVERVIEW - Dassault Systèmes

[35] Tips for Using Pipeline Pilot as an Integration Platform

[36] Introduction to the Discovery Studio Visualizer

[37] Free Download: BIOVIA Discovery Studio Visualizer.

[38] BIOVIA Discovery Studio | Dassault Systèmes

[39] Discovery Studio - Wikipedia.

[40] Discovery Studio Software Applications - CD ComputaBio .

[41] S.M.D. Rizvi, S. Shakil, M. Haneef, A simple click by click protocol to perform docking: Autodock 4.2 made easy for non- Bioinformaticians, Excli. J., 12 (2013), pp. 831-857

[42] http://accelrys.com/products/discovery-studio/visualization-download.php (accessed 20.12.16).

[43] Discovery Studio - Wikipedia BIOVIA Discovery Studio | Dassault Systèmes

[44] BIOVIA Discovery Studio Visualizer | Dassault Systèmes

[45] Free Download: BIOVIA Discovery Studio Visualizer

[46] Ligand and Pharmacophore based Design | BIOVIA - Dassault Systèmes

[47] (a). Molecular Dynamics Simulations | BIOVIA - Dassault Systèmes,

(b). Structure based Design | BIOVIA - Dassault Systèmes,

(c). Pharmacophore Ligand-Based Design with Biovia Discovery Studio

(d). BIOVIA Discovery Studio Visualizer | Dassault Systèmes

[48] (a). Biotherapeutics and Antibody Modelling | BIOVIA - Dassault Systemes,

(b). Drug Design Using Biovia – Courseware :: Centurion University,

(c). ANTIBODY STRUCTURE MODELLING WITH DISCOVERY STUDIO - Dassault Systèmes,

(d). Frontiers | Enhanced utility of AI/ML methods during lead optimization ...,

(e). BIOVIA Discovery Studio | Dassault Systèmes,

(f). MOLECULAR SIMULATIONS WITH BIOVIA DISCOVERY STUDIO - Dassault Systèmes,

(g). Biovia Discovery Studio® 2019 Comprehensive Modelling - DocsLib.

[49] (a). BIOVIA Materials Studio | Dassault Systèmes,b.BIOVIA Materials Studio - Semiconductors | Dassault Systemes, c . BIOVIA MATERIALS STUDIO CASTEP - Dassault Systèmes, d. BIOVIA MATERIALS STUDIO OVERVIEW - gga.asia

[50] Schrödinger - Physics-based Software Platform for Molecular Discovery ...

[51] https://en.wikipedia.org/wiki/Schr%C3%B6dinger,_Inc

[52] Schrodinger Suite 2023-4 Free Download - FileCR

[53] Computational Platform for Molecular Discovery & Design - Schrödinger

[54] Schrödinger, Inc. - Wikipedia

[55] Schrödinger - Sherlock

[56] Life Science: Prime - Schrödinger

[57] PRIME: A program for prediction of protein-RNA complex structure

[58] Life Science: Prime - Schrödinger

[59] Jaguar for Life Science - Schrödinger , Jaguar for Materials Science - Schrödinger , New features in Jaguar: DFT corrections for improved accuracy of energy ...

[60] Jaguar (software) - Wikipedia, https://www.schrodinger.com/jaguar

[61] MacroModel - Wikipedia ,Life Science: MacroModel - Schrödinger , MacroModel Quick Start Guide - University of California, Irvine, MacroModel Reference Manual

[62] Protein–ligand Docking with GOLD | CCDC - University of Cambridge, GOLD - Docs CSC, CSD/GOLD - UKRI, GOLD: The All In One Molecular Docking Package | CCDC

[63] Download UCSF Chimera for Windows 11, 10, 7, 8/8.1 (64 bit/32 bit)

[64] Chimera User's Guide

[65] UCSF Chimera: Molecular Modelling Software for Visualization and ...

[67] Developer Tale - A brief history of UCSF Chimera - SBGrid

[68] UCSF ChimeraX Home Page

[69] Download UCSF ChimeraX, UCSF ChimeraX - I - Overview - University of Wisconsin–Madison

[70] UCSF ChimeraX: Tools for Structure Building and Analysis

[71] UCSF ChimeraX: Structure Visualization for Researchers, Educators, and ...

[72] UCSF ChimeraX Advantages

[73] Python-Based Software for Computational Drug Design

[74] Using PyMOL as a Platform for Computational Drug Design

[75] Computer-aided drug design platform using PyMOL

[76] EthoWatcher - UFSC, EthoWatcher - OpenBehavior , EthoWatcher - UFSC

[77] Best Drug Discovery Software of  based on 104 reviews - AIMultiple, 2024.

[78] Ligand and Structure-Based Drug Design Software | Flare

[79] Flare Visualizer | Free Molecular Modelling Software

[80] Licensing Flare - Computational solutions for drug discovery

[81] Chemical Properties Calculated by CDD Vault During Chemical ... , Structure Searching in CDD Vault – CDD Support ,Log D Calculated by CDD Vault During Chemical Registration

[82] Collaborative Drug Discovery - Wikipedia, Home | CDD Vault - Collaborative Drug

[83] CDD Gives Back with Open Access Data Visualization Tool - CDD Vault

[84] Best Drug Discovery Software of 2024 based on 104 reviews - AIMultiple

[85] Ligand and Structure-Based Drug Design Software | Flare

[86] B.D. Kumar,P.V. Kumar,SPBuvneshwarn and A. Mitra, AdvanceDrug Designing software and their application in Medical Research International Journel of Pharmacy and Pharmaceutical Science,Vol2(3) ,2010,16-18.

[87] I. Ajad, T. Khan, N. Ahmad, A.R. Rahman and Yusuf,Updates on Drug Designing Approach Through computational Strategies,A review ,Future Science2023.

[88] ttp://www.simulationsus.com/Products.aspx?GastroPlus&grpID=3&cID=16&pID=11. (accessed 12.12.16)..

[89] B.K. Chandrashekhar, V. Harshada, S. Swapnil M., Review Article on Drug Design and Discovery International Journal of Research Publication and Reviews, Vol 4, (3), pp 3095-3099, 2023.

[90] Li Xiang, Li Fabing and Gao Mingyu, Flare: A Fast, Secure, and Memory-Efficient Distributed Analytics Framework, Proceedings of the VLDB Endowment 16(6),1439-145, 2023.

[91] Author links open overlay panelYeon- J. pyeong, C. Yongheon , H.Sungwon , Dynamic analysis and optimization of flare network system for topside process of offshore plant, Process Safety and Environmental Protection Vol. 134, Pages 260-269, February 2020.

[92] S.Paul,Humphries, R.Bersot, J. Kincaid, E. Mabery, K. Mc Cluskie, T. Park, T.Renner, E.Riegler, T.Steinfeld, E. D. Turtle, Zhi-Liang Wei, E.Willis, Carbazole-containing sulfonamides and sulfamides: Discovery of cryptochrome modulators as antidiabetic agents, **Bioorganic & Medicinal Chemistry Letters**,Volu.26, (3).pp 757-760, 2016.