Computational Molecular Biology 2024, Vol.14, No.3, 115-124
http://bioscipublisher.com/index.php/cmb

Feature Review Open Access

Exploration of the Role of Computational Chemistry in Modern Drug Discovery

Xaiohua Zhang, Jianhui Li
Institute of Life Sciences, Jiyang Colloge of Zhejiang A&F University, Zhuji, 311800, Zhejiang, China
Corresponding author: jianhui li@jicat.org

Computational Molecular Biology, 2024, Vol.14, No.3 doi: 10.5376/cmb.2024.14.0014
Received: 09 Apr., 2024
Accepted: 24 May, 2024
Published: 13 Jun., 2024

Preferred citation for this article:
Zhang X.H., and Li J.H., 2024, Exploration of the role of computational chemistry in modern drug discovery, Computational Molecular Biology, 14(3): 115-124 (doi: 10.5376/cmb.2024.14.0014)

Abstract This study explores the fundamental principles of computational chemistry, such as quantum mechanics and molecular modeling, and investigates their applications in drug design, including structure based and ligand based methods. Emphasis was placed on the integration of advanced technologies such as machine learning and high-throughput virtual screening, highlighting their role in improving prediction accuracy and accelerating drug development. However, challenges such as prediction reliability, computational cost, and integration of computational data with experimental results still exist. The case study demonstrated the effectiveness of the computational method and compared it with traditional methods in developing successful candidate drugs. Looking to the future, the potential of combining computational chemistry and omics data and their role in advancing personalized medicine. Future drug discovery is likely to rely on collaborative platforms and open-source tools to push the boundaries of computational innovation.

Keywords Computational chemistry; Drug discovery; Molecular modeling; Machine learning; Structure-based design

1 Introduction

Computational chemistry has become an indispensable tool in the field of drug discovery, offering innovative solutions to complex problems and significantly reducing the time and cost associated with bringing new drugs to market. Computational chemistry encompasses a wide range of techniques and methodologies that leverage computer simulations to solve chemical problems. These techniques include molecular dynamics, quantum chemistry, machine learning, and various other modeling approaches. The integration of these methods allows researchers to predict chemical properties, optimize drug candidates, and understand molecular interactions at an unprecedented level of detail (Cova and Pais, 2019; Decherchi and Cavalli, 2020). The synergy between computational tools and experimental methods has led to significant advancements in the field, enabling the design and evaluation of new drugs with greater efficiency and accuracy (Rosales-Hernández and Correa-Basurto, 2015; Castelli et al., 2021).

The application of computational methods in drug discovery dates back over three decades, with early efforts focusing on structure-based and ligand-based approaches (Sliwoski et al., 2014). Initially, these methods were limited by computational power and the availability of biological data. However, advancements in hardware, algorithms, and the accumulation of biological and chemical data have transformed computational chemistry into a cornerstone of pharmaceutical research (Abramov et al., 2022; Blunt et al., 2022). The human genome project and the increasing knowledge of biological structures have further propelled the use of in silico tools, making them integral to various phases of the drug discovery pipeline (Cui et al., 2020).

This study provides a comprehensive overview of the current status of computational chemistry in drug discovery, investigating the latest methods, applications, and trends. We will discuss the challenges faced by researchers, such as the complexity of biological systems and the need for accurate predictive models. In addition, we will explore the prospects of emerging technologies, including quantum computing and machine learning, and their revolutionary potential for this field. Successful case studies emphasize the crucial role of computational chemistry in future drug discovery.

2 Fundamental Concepts in Computational Chemistry

2.1 Quantum mechanics and molecular modeling

Quantum mechanics (QM) and molecular modeling are foundational to computational chemistry, providing detailed insights into the electronic structure and properties of molecules. These methods are crucial for understanding the interactions at the atomic level, which is essential for drug discovery. Hybrid quantum mechanics/molecular mechanics (QM/MM) approaches are particularly valuable as they combine the accuracy of QM with the efficiency of molecular mechanics (MM). This hybrid method allows for the detailed analysis of ligand-receptor interactions, which is critical for predicting the binding affinity and specificity of potential drug candidates (Barbault and Maurel, 2015; Cascella et al., 2015). The continuous improvement in computational power and algorithm design has significantly enhanced the capabilities of QM/MM simulations, making them indispensable tools in modern drug discovery (Engkvist et al., 2018).

2.2 Molecular dynamics and simulations

Molecular dynamics (MD) simulations have become a cornerstone in the field of drug discovery due to their ability to provide dynamic structural and energetic information about biomolecular systems. MD simulations explicitly account for the structural flexibility and entropic effects of molecules, allowing for a more accurate estimation of the thermodynamics and kinetics associated with drug-target interactions (Vivo et al., 2016). These simulations are particularly useful for identifying cryptic or allosteric binding sites, enhancing virtual screening methodologies, and predicting small-molecule binding energies (Durrant and McCammon, 2011).

Advanced MD techniques, such as free-energy perturbation, metadynamics, and steered MD, are frequently employed to study drug-target binding. These methods help optimize target affinity and drug residence time, which are crucial for improving drug efficacy (Decherchi and Cavalli, 2020). Additionally, MD simulations are instrumental in investigating the pathogenic mechanisms of diseases, drug resistance mechanisms, and the role of water molecules in ligand binding and optimization (Ganesan et al., 2017; Liu et al., 2018).

The integration of MD simulations with other computational tools, such as docking and virtual screening, further streamlines the drug discovery process. This integration allows for the rapid evaluation of millions of compounds, significantly reducing the time and cost associated with drug development (Rosales-Hernández and Correa-Basurto, 2015). As computational resources continue to advance, the role of MD simulations in drug discovery is expected to grow, providing even more detailed and accurate insights into molecular interactions (Salo-Ahen et al., 2020).

3 Applications of Computational Chemistry in Drug Discovery

3.1 Structure-based drug design

Computational chemistry has revolutionized the field of drug discovery by providing tools and methods that significantly reduce the time and cost associated with the development of new therapeutics. Structure-based drug design (SBDD) relies on the three-dimensional structure of biological targets to identify and optimize potential drug candidates. This approach includes techniques such as ligand docking, pharmacophore modeling, and de novo design. SBDD is analogous to high-throughput screening, where both the target and ligand structures are crucial for the design process (Sliwoski et al., 2014). Enhanced sampling methods like metadynamics have been employed to investigate the complex mechanisms of drug binding to flexible targets, providing insights into the most probable association and dissociation pathways and the related binding free energy profiles (Cavalli et al., 2015). The integration of computational tools with experimental routines has shown a powerful impact on rational drug design, facilitating the identification of promising candidate drugs.

3.2 Ligand-based drug design

Ligand-based drug design (LBDD) uses information from known active ligands to predict the activity of new compounds. This method includes techniques such as ligand-based pharmacophores, molecular descriptors, and quantitative structure-activity relationships (QSAR). Machine learning (ML) approaches have been increasingly applied in LBDD to construct models that predict biological activity, optimize hits, and improve the prediction of

binding sites and docking solutions (Lima et al., 2016). The complementary use of SBDD and LBDD, along with their integration with experimental data, has been shown to enhance the efficiency of drug discovery processes (Macalino et al., 2015).

3.3 ADMET prediction and optimization

The prediction and optimization of absorption, distribution, metabolism, excretion, and toxicity (ADMET) properties are critical for the development of safe and effective drugs. Computational tools have been developed to automate the evaluation of ADMET properties, reducing the time and cost associated with drug discovery (Rosales-Hernández and Correa-Basurto, 2015). Recent advances in computational chemistry have enabled the accurate prediction of ADMET profiles, which is essential for optimizing lead compounds and designing novel biologically active molecules. The integration of machine learning techniques with traditional computational methods has further improved the prediction accuracy of ADMET properties, facilitating the development of drugs with favorable physiological profiles.

4 Challenges in Computational Chemistry

4.1 Accuracy and reliability of predictions

One of the primary challenges in computational chemistry is achieving high accuracy and reliability in predictions. Despite significant advancements in computational methods, accurately predicting ligand binding affinities remains difficult. For instance, free-energy calculations, which are crucial for predicting binding affinities, have seen improvements in force fields and sampling algorithms. However, achieving the necessary accuracy to guide lead optimization reliably is still challenging, limiting their widespread commercial application (Wang et al., 2015). Additionally, while methods like FEP+ (Free Energy Perturbation) have shown promise in predicting protein-ligand binding free energies with high accuracy, there are still limitations in their implementation that need to be addressed to ensure consistent reliability across different targets and ligands.

4.2 Computational costs and resources

The computational costs and resources required for advanced simulations pose another significant challenge. High-accuracy methods such as free-energy calculations and molecular dynamics simulations are computationally intensive, often requiring substantial hardware resources and time. The need for extensive computational power can be a barrier, especially for smaller research groups or institutions with limited access to high-performance computing facilities (Abel et al., 2017). Moreover, the complexity of the systems being simulated, such as large protein-ligand complexes, further exacerbates the demand for computational resources (Decherchi and Cavalli, 2020). Despite the advent of low-cost parallel computing, the resource-intensive nature of these simulations remains a critical challenge.

4.3 Integration with experimental data

Integrating computational predictions with experimental data is essential for validating and refining computational models, yet it presents its own set of challenges. Computational methods must be iteratively validated and adjusted based on experimental results to ensure their accuracy and applicability. This iterative process can be resource-intensive and time-consuming (Persico et al., 2016). Additionally, the complexity of biological systems often requires the use of multiple computational tools and methods, each with its own set of parameters and assumptions, making the integration process even more challenging (Rosales-Hernández and Correa-Basurto, 2015). Effective integration also necessitates multidisciplinary collaboration, combining expertise from computational chemistry, bioinformatics, and experimental biology to achieve meaningful and actionable insights.

5 Advances in Computational Methods

5.1 Machine learning and ai in drug discovery

5.1.1 Applications of AI in drug design

Artificial intelligence (AI) has significantly transformed the landscape of drug discovery by enabling the efficient identification of new chemical entities with desirable properties. AI algorithms, particularly deep learning, have been applied to various stages of drug discovery, including structure- and ligand-based virtual screening, de novo

drug design, and the prediction of physicochemical and pharmacokinetic properties (Yang et al., 2019). These applications have expedited the early drug discovery process by predicting protein structures, drug-target interactions, and molecular properties such as drug toxicity. AI has also been instrumental in drug repurposing and optimizing drug design by leveraging large datasets and complex models(Figure 1) (Jiménez-Luna et al., 2021).

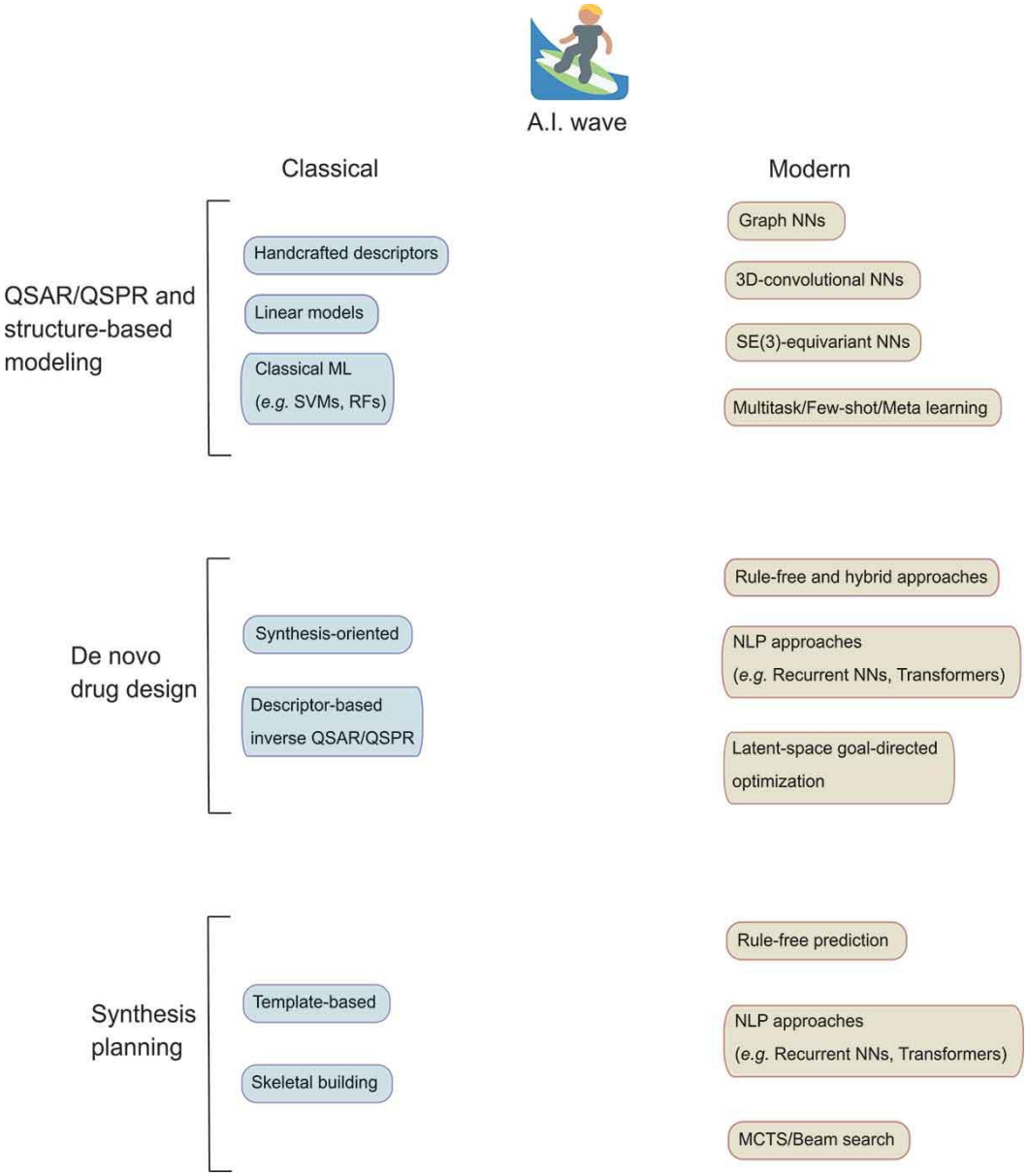

Figure 1 Schematic diagram of the transition between classical and modern methodologies for some relevant problems in drug discovery, such as QSAR/QSPR modeling, de novo drug design, and synthesis planning. Abbreviations: ML, machine learning; SVM, support vector machine; RF, random forest; QSAR/QSPR, quantitative structure-activity/property relationship; NN, neural network; SE(3), special Euclidean group in three-dimensions; NLP, natural language processing; MCTS, Monte Carlo tree search (Adopted from Jiménez-Luna et al., 2021)

The study of Jiménez-Luna et al. (2021) highlights the evolution from classical to modern approaches in drug discovery, particularly in QSAR/QSPR modeling, de novo drug design, and synthesis planning. Classical methods rely on handcrafted descriptors, linear models, and traditional machine learning techniques like SVMs and RFs. In contrast, modern methods integrate advanced neural networks, such as graph NNs, and natural language processing (NLP) techniques, enabling rule-free predictions, multitask learning, and latent-space optimization. This transition represents the growing influence of artificial intelligence (AI) in enhancing the accuracy, efficiency, and scalability of drug design and synthesis processes.

5.1.2 Machine learning algorithms for predictive modeling

Machine learning (ML) algorithms, such as support vector machines, random forests, decision trees, and artificial neural networks, have been widely used for predictive modeling in drug discovery. These algorithms help in constructing models that predict the biological activity of new ligands, optimize hits, and predict the pharmacokinetic and toxicological profiles of compounds (Lima et al., 2016). ML techniques have also been employed in ligand-based and structure-based drug design studies, including similarity searches, classification models, and virtual screening. The integration of ML with traditional computational methods has improved the prediction of binding sites and docking solutions, thereby enhancing the efficiency of drug discovery.

5.1.3 Case studies of successful AI integration

Several successful case studies highlight the integration of AI in drug discovery. For instance, AI has been used to predict drug-target interactions and molecular properties, leading to the identification of potential drug candidates with high accuracy (Han et al., 2023). In another example, deep generative models have been employed to explore chemical space and expedite the drug discovery process by generating novel compounds with desired properties (Born and Manica, 2021). These models leverage multimodal data sources to map biochemical properties to target structures, demonstrating the potential of AI to revolutionize drug design. Additionally, AI-based methods have been successfully applied in virtual screening and de novo drug design, showcasing their ability to handle large datasets and complex molecular interactions (Batool et al., 2019).

5.2 High-throughput virtual screening

High-throughput virtual screening (HTVS) has become a cornerstone of modern drug discovery, allowing researchers to rapidly evaluate large libraries of compounds for potential biological activity. HTVS methods, such as molecular docking, pharmacophore modeling, and quantitative structure-activity relationship (QSAR) models, have significantly reduced the time and cost associated with drug discovery (Sliwoski et al., 2014). These methods enable the identification of promising drug candidates by simulating their interactions with target macromolecules and predicting their binding affinities. The integration of AI and ML techniques with HTVS has further enhanced its efficiency, enabling the rapid screening of vast chemical libraries and the identification of potential leads with high accuracy.

5.3 Multi-scale modeling approaches

Multi-scale modeling approaches in drug discovery involve the integration of various computational methods to study biological systems at different scales and dimensions. These approaches combine molecular dynamics simulations, quantum mechanics, and coarse-grained modeling to provide a comprehensive understanding of drug binding sites and mechanisms of action (Lin et al., 2020). By bridging different scales, multi-scale modeling allows for the detailed exploration of molecular interactions and the prediction of drug efficacy and safety. The use of AI and ML in multi-scale modeling has further enhanced its predictive power, enabling the accurate simulation of complex biological processes and the identification of potential drug candidates (Keith et al., 2021).

6 Case Studies in Drug Discovery

6.1 Successful drug candidates developed using computational chemistry

Computational chemistry has significantly contributed to the development of several successful drug candidates. For instance, the use of computer-aided drug discovery (CADD) methods has been instrumental in the development of anticancer drugs. These methods have provided valuable insights into cancer therapy, making the drug design process faster, cheaper, and more effective (Cui et al., 2020). Additionally, computational tools have been employed to identify novel antimalarial drugs, addressing the urgent need for potent treatments against drug-resistant strains of malaria (Duay et al., 2023).

Moreover, the integration of molecular docking and virtual screening techniques has led to the identification of promising drug candidates for various diseases. For example, the construction of a natural product database and subsequent molecular docking experiments have identified potential ligands targeting the androgen receptor for prostate cancer treatment (Huang et al., 2021). Similarly, computational methods have been used to screen active

components of traditional medicines for their efficacy against psoriasis. These examples highlight the successful application of computational chemistry in identifying and optimizing drug candidates, ultimately accelerating the drug discovery process.

6.2 Comparison of computational and traditional methods

The traditional drug discovery approach is often expensive, time-consuming, and labor-intensive, typically requiring around 12 years and 2.7 billion USD to bring a new drug to market. In contrast, computational methods offer a more efficient and cost-effective alternative. Techniques such as molecular docking, pharmacophore modeling, and quantitative structure-activity relationship (QSAR) models enable the rapid prediction of drug-target interactions and the identification of potential drug candidates (Figure 2) (Sliwoski et al., 2014; Hasan et al., 2022).

The study of Hasan et al. (2022) outlines a comprehensive workflow in computer-aided drug design (CADD), demonstrating both structure-based and ligand-based approaches. Key processes include pharmacophore modeling, molecular docking, and molecular dynamics simulations. These simulations help in understanding the interaction between potential drugs and target proteins, allowing for optimization of the drug candidates. The final step, involving MM-GBSA and MM-PBSA methods, provides energy calculations to assess binding affinity, which is crucial in predicting the effectiveness of the drug candidate. This workflow helps streamline drug discovery, reducing time and resources compared to traditional methods.

Computational methods also provide a virtual shortcut in the drug discovery pipeline, reducing the need for extensive experimental screening and allowing for the prioritization of the most promising compounds (Leelananda and Lindert, 2016). For instance, virtual high-throughput screening and protein-ligand docking have been successfully employed to predict the binding affinity of compounds, thereby streamlining the drug development process (Lin et al., 2020). Additionally, the use of machine learning and artificial intelligence in computational drug design has further enhanced the predictive accuracy and efficiency of these methods (Decherchi and Cavalli, 2020).

While traditional methods rely heavily on experimental assays and animal models, computational approaches can complement these techniques by providing valuable insights into the molecular mechanisms of drug action and potential off-target effects (Agamah et al., 2019). This integration of computational and experimental methods has proven to be a powerful strategy in rational drug design, ultimately leading to more effective and safer therapeutics (Macalino et al., 2015).

7 Future Directions and Emerging Trends

7.1 Integration of computational chemistry with omics data

The integration of computational chemistry with omics data represents a significant advancement in drug discovery. Omics technologies, which include genomics, proteomics, and metabolomics, generate vast amounts of data that can be leveraged to identify and validate drug targets more efficiently. Computational platforms that utilize omics data can help in ranking disease-relevant targets by analyzing large datasets, thus expediting the drug discovery process (Paananen and Fortino, 2019). The high-throughput nature of omics technologies allows for the quantitative measurement of numerous putative targets, providing a rich dataset for computational analysis. This integration not only enhances target identification but also aids in understanding the molecular mechanisms underlying diseases, thereby facilitating the development of more effective therapeutic agents.

7.2 Personalized medicine and computational approaches

Personalized medicine aims to tailor medical treatment to the individual characteristics of each patient, and computational approaches are pivotal in achieving this goal. By integrating diverse biological data, including genetic, proteomic, and metabolomic information, computational methods can predict individual responses to drugs and identify optimal therapeutic strategies (Niazi and Mariam, 2023). Machine learning and artificial intelligence play crucial roles in analyzing these complex datasets, enabling the prediction of drug efficacy and safety on a personalized level (Yuguda et al., 2023). The convergence of computational chemistry with

personalized medicine promises to deliver tailored therapeutic solutions, although challenges such as data privacy, ethical considerations, and accessibility need to be addressed.

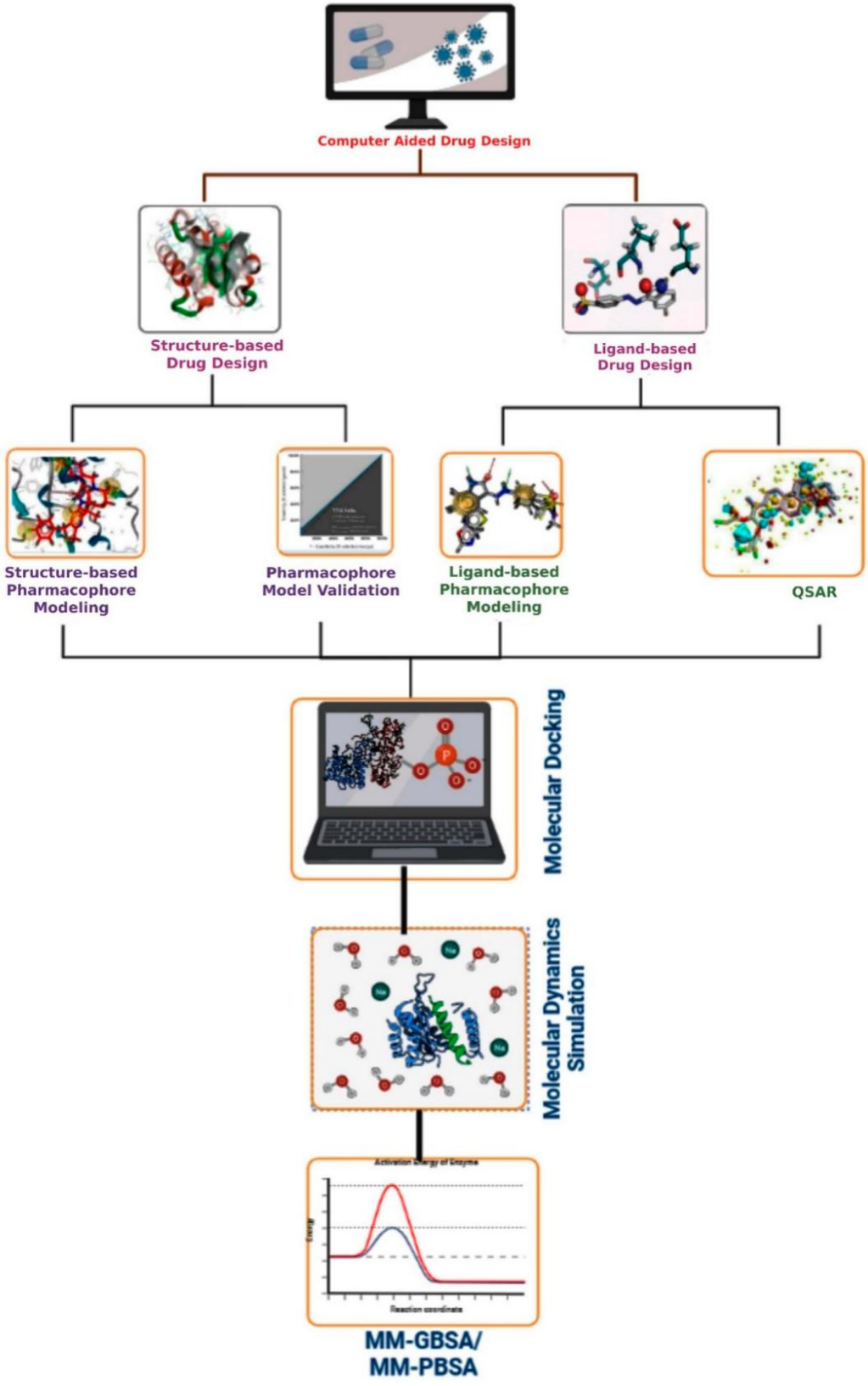

Figure 2 Representation of the basic workflow of computational drug design approaches. The CADD approaches include structure- and ligand-based drug design approaches, pharmacophore modeling, virtual screening, molecular docking, ADMET, dynamics simulation, and MM-GBSA or MM-PBSA approaches (Adopted from Hasan et al., 2022)

7.3 Collaborative platforms and open-source tools

The development and utilization of collaborative platforms and open-source tools are transforming the landscape of computational chemistry in drug discovery. These platforms facilitate the sharing of data, tools, and methodologies among researchers, thereby accelerating the drug discovery process (Cox and Gupta, 2022). Open-source applications and collaborative efforts, such as the Open-Source Malaria project, exemplify the democratization of drug discovery, making advanced computational tools accessible to a broader scientific community. Distributed computing environments and high-performance computing (HPC) resources further enhance the capabilities of these platforms, allowing for the efficient handling of complex simulations and large datasets (Banegas-Luna et al., 2018). The shift towards remote-distributed computing platforms also offers cost-effective and sustainable solutions for computational drug discovery.

8 Concluding Remarks

Computational chemistry has become a cornerstone in modern drug discovery, significantly enhancing the efficiency and effectiveness of the drug development process. It encompasses a variety of methods, including molecular docking, pharmacophore modeling, and quantitative structure-activity relationships (QSAR), which are used to predict the interaction between drugs and their targets, optimize lead compounds, and assess drug-target affinities. These techniques have been instrumental in identifying allosteric sites, understanding ligand binding mechanisms, and evaluating the thermodynamics and kinetics of drug-target interactions. The integration of computational tools has not only reduced the time and cost associated with drug discovery but also expanded the scope of research to include complex biological targets and rare events.

Despite the significant advancements, several challenges persist in the field of computational chemistry. One major issue is the accurate prediction of drug-target interactions, which is complicated by the conformational flexibility of proteins and the dynamic nature of biological systems. Additionally, the integration of various computational methods and the interpretation of complex data require substantial expertise and computational resources. To address these challenges, enhanced sampling techniques such as metadynamics have been developed to better understand the free energy landscapes and binding pathways of drug-target interactions. Moreover, the advent of machine learning and artificial intelligence offers promising solutions for automating and improving the accuracy of computational predictions. Collaborative efforts and the development of user-friendly software platforms could further streamline the application of computational methods in drug discovery.

Future research in computational chemistry should focus on several key areas to overcome existing challenges and leverage new opportunities. More complex algorithms need to be developed to accurately simulate the dynamic behavior of biomolecule systems and predict rare events; Combining machine learning technology with traditional computing methods can improve the predictive ability and efficiency of drug discovery processes; Promoting interdisciplinary collaboration between computational chemists, biologists, and pharmacologists is crucial for translating computational predictions into experimental and clinical success; Efforts should be made to establish comprehensive databases and standardized protocols to promote data sharing and reproducibility in computational drug discovery. By addressing these issues, the field of computational chemistry can continue to play a critical role in developing new and effective treatment methods.

Acknowledgments

BioSci Publisher thanks to the anonymous peer review experts for their time and feedback.

Conflict of Interest Disclosure

The authors affirm that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

References

Abel R., Wang L., Harder E., Berne B., and Friesner R., 2017, Advancing drug discovery through enhanced free energy calculations, Accounts of Chemical Research, 50(7): 1625-1632.
https://doi.org/10.1021/acs.accounts.7b00083

Abramov Y.A., Sun G., and Zeng Q., 2022, Emerging landscape of computational modeling in pharmaceutical development, Journal of Chemical Information and Modeling, 62(5): 1160-1171.
https://doi.org/10.1021/acs.jcim.1c01580

Agamah F.E., Mazandu G.K., Hassan R., Bope C.D., Thomford N.E., Ghansah A., and Chimusa E.R., 2019, Computational in silico methods in drug target and lead prediction, Briefings in Bioinformatics, 21(5): 1663-1675.
https://doi.org/10.1093/bib/bbz103

Banegas-Luna A.J., Imbernón B., Castro A., Pérez-Garrido A., Cerón-Carrasco J.P., Gesing S., Merelli I., D'Agostino D., and Pérez-Sánchez H., 2018, Advances in distributed computing with modern drug discovery, Expert Opinion on Drug Discovery, 14(1): 9-22.
https://doi.org/10.1080/17460441.2019.1552936

Barbault F., and Maurel F., 2015, Simulation with quantum mechanics/molecular mechanics for drug discovery, Expert Opinion on Drug Discovery, 10(10): 1047-1057.
https://doi.org/10.1517/17460441.2015.1076389

Batool M., Ahmad B., and Choi S., 2019, A structure-based drug discovery paradigm, International Journal of Molecular Sciences, 20(11): 2783.
https://doi.org/10.3390/ijms20112783

Blunt N., Camps J., Crawford O., Izs'ak R., Leontica S., Mirani A., Moylett A., Scivier S., Sunderhauf C., Schopf P., Taylor J., and Holzmann N., 2022, Perspective on the current state-of-the-art of quantum computing for drug discovery applications, Journal of Chemical Theory and Computation, 18: 7001-7023.
https://doi.org/10.1021/acs.jctc.2c00574

Born J., and Manica M., 2021, Trends in deep learning for property-driven drug design, Current Medicinal Chemistry, 28(38): 7862-7886.
https://doi.org/10.2174/0929867328666210729115728

Cascella M., Peraro M., and Vivo M., 2015, Computational chemistry strategies tackling function and inhibition of pharmaceutically relevant targets, Frontiers in Computational Chemistry, Bentham Science Publishers, 2015: 290-343.
https://doi.org/10.1016/B978-1-60805-865-5.50008-3

Castelli M., Serapian S., Marchetti F., Triveri A., Pirota V., Torielli L., Collina S., Doria F., Freccero M., and Colombo G., 2021, New perspectives in cancer drug development: computational advances with an eye to design, RSC Medicinal Chemistry, 12(9): 1491-1502.
https://doi.org/10.1039/d1md00192b

Cavalli A., Spitaleri A., Saladino G., and Gervasio F., 2015, Investigating drug-target association and dissociation mechanisms using metadynamics-based algorithms, Accounts of Chemical Research, 48(2): 277-285.
https://doi.org/10.1021/ar500356n

Cova T.F., and Pais A.A., 2019, Deep learning for deep chemistry: optimizing the prediction of chemical patterns, Frontiers in Chemistry, 7: 809.
https://doi.org/10.3389/fchem.2019.00809

Cox P., and Gupta R., 2022, Contemporary computational applications and tools in drug discovery, ACS Medicinal Chemistry Letters, 13(7): 1016-1029.
https://doi.org/10.1021/acsmedchemlett.1c00662

Cui W.Q., Aouidate A., Wang S.G., Yu Q.L., Li Y.H., and Yuan S.G., 2020, Discovering anti-cancer drugs via computational methods, Frontiers in Pharmacology, 11: 733.
https://doi.org/10.3389/fphar.2020.00733

Decherchi S., and Cavalli A., 2020, Thermodynamics and kinetics of drug-target binding by molecular simulation, Chemical Reviews, 120: 12788-12833.
https://doi.org/10.1021/acs.chemrev.0c00534

Duay S.S., Yap R.S.Y., Gaitano A.L., Santos J.A.A., and Macalino S.J.Y., 2023, Roles of virtual screening and molecular dynamics simulations in discovering and understanding antimalarial drugs, International Journal of Molecular Sciences, 24(11): 9289.
https://doi.org/10.3390/ijms24119289

Durrant J.D., and McCammon J.A., 2011, Molecular dynamics simulations and drug discovery, BMC Biology, 9: 1-9.
https://doi.org/10.1186/1741-7007-9-71

Engkvist O., Norrby P.O., Selmi N., Lam Y., Peng Z., Sherer E.C., Amberg W., Erhard T., and Smyth L.A., 2018, Computational prediction of chemical reactions: current status and outlook, Drug Discovery Today, 23(6): 1203-1218.
https://doi.org/10.1016/j.drudis.2018.02.014

Ganesan A., Coote M., and Barakat K., 2017, Molecular dynamics-driven drug discovery: leaping forward with confidence, Drug Discovery Today, 22(2): 249-269.
https://doi.org/10.1016/j.drudis.2016.11.001

Han R., Yoon H., Kim G., Lee H., and Lee Y., 2023, Revolutionizing medicinal chemistry: the application of artificial intelligence (AI) in early drug discovery, Pharmaceuticals, 16(9): 1259.
https://doi.org/10.3390/ph16091259

Hasan M.R., Alsaiari A.A., Fakhurji B.Z., Molla M.H.R., Asseri A.H., Sumon M.M.A., Park M.N., Ahammad F., and Kim B., 2022, Application of mathematical modeling and computational tools in the modern drug design and development process, Molecules, 27(13): 4169.
https://doi.org/10.3390/molecules27134169

Huang Z., Yao X., and Gu R., 2021, Editorial: computational approaches in drug discovery and precision medicine, Frontiers in Chemistry, 8: 639449.
https://doi.org/10.3389/fchem.2020.639449

Jiménez-Luna J., Grisoni F., Weskamp N., and Schneider G., 2021, Artificial intelligence in drug discovery: recent advances and future perspectives, Expert Opinion on Drug Discovery, 16(9): 949-959.
https://doi.org/10.1080/17460441.2021.1909567

Keith J., Vassilev-Galindo V., Cheng B., Chmiela S., Gastegger M., Müller K., and Tkatchenko A., 2021, Combining machine learning and computational chemistry for predictive insights into chemical systems, Chemical Reviews, 121: 9816-9872.
https://doi.org/10.1021/acs.chemrev.1c00107

Leelananda S., and Lindert S., 2016, Computational methods in drug discovery, Beilstein Journal of Organic Chemistry, 66(1): 334-395.
https://doi.org/10.3762/bjoc.12.267

Lima A.N., Philot E.A., Trossini G.H.G., Scott L.P.B., Maltarollo V.G., and Honório K.M., 2016, Use of machine learning approaches for novel drug discovery, Expert Opinion on Drug Discovery, 11(3): 225-239.
https://doi.org/10.1517/17460441.2016.1146250

Lin X.Q., Li X., and Lin X.B., 2020, A review on applications of computational methods in drug screening and design, Molecules, 25(6): 1375.
https://doi.org/10.3390/molecules25061375

Liu X.W., Shi D.F., Zhou S.Y., Liu H.L., Liu H.X., and Yao X.J., 2018, Molecular dynamics simulations and novel drug discovery, Expert Opinion on Drug Discovery, 13(1): 23-37.
https://doi.org/10.1080/17460441.2018.1403419

Macalino S., Gosu V., Hong S., and Choi S., 2015, Role of computer-aided drug design in modern drug discovery, Archives of Pharmacal Research, 38: 1686-1701.
https://doi.org/10.1007/s12272-015-0640-5

Niazi S.K., and Mariam Z., 2023, Computer-aided drug design and drug discovery: a prospective analysis, Pharmaceuticals, 17(1): 22.
https://doi.org/10.3390/ph17010022

Paananen J., and Fortino V., 2019, An omics perspective on drug target discovery platforms, Briefings in Bioinformatics, 21: 1937-1953.
https://doi.org/10.1093/bib/bbz122

Persico M., Di Dato A., Orteca N., Cimino P., Novellino E., and Fattorusso C., 2016, Use of integrated computational approaches in the search for new therapeutic agents, Molecular Informatics, 35(8-9): 309-325.
https://doi.org/10.1002/minf.201501028

Rosales-Hernández M., and Correa-Basurto J., 2015, The importance of employing computational resources for the automation of drug discovery, Expert Opinion on Drug Discovery, 10: 213-219.
https://doi.org/10.1517/17460441.2015.1005071

Salo-Ahen O.M.H., Alanko I., Bhadane R.V., Bonvin A.M.J.J., Honorato R., Hossain S., Juffer A.H., Kabedev A., Lahtela-Kakkonen M., Larsen A., Lescrinier E., Marimuthu P., Mirza M., Mustafa G., Nunes-Alves A., Pantsar T., Saadabadi A.S., Singaravelu K., and Vanmeert M.U., 2020, Molecular dynamics simulations in drug discovery and pharmaceutical development, Processes, 9(1): 71.
https://doi.org/10.3390/pr9010071

Sliwoski G., Kothiwale S., Meiler J., and Lowe E., 2014, Computational methods in drug discovery, Pharmacological Reviews, 66: 334-395.
https://doi.org/10.1124/pr.112.007336

Vivo M., Masetti M., Bottegoni G., and Cavalli A., 2016, Role of molecular dynamics and related methods in drug discovery, Journal of Medicinal Chemistry, 59(9): 4035-4061.
https://doi.org/10.1021/acs.jmedchem.5b01684

Wang L., Wu Y., Deng Y., Kim B., Pierce L., Krilov G., Lupyan D., Robinson S., Dahlgren M., Greenwood J., Romero D., Masse C., Knight J., Steinbrecher T., Beuming T., Damm W., Harder E., Sherman W., Brewer M., Wester R., Murcko M., Frye L., Farid R., Lin T., Mobley D., Jorgensen W., Berne B., Friesner R., and Abel R., 2015, Accurate and reliable prediction of relative ligand binding potency in prospective drug discovery by way of a modern free-energy calculation protocol and force field, Journal of the American Chemical Society, 137(7): 2695-2703.
https://doi.org/10.1021/ja512751q

Yang X., Wang Y., Byrne R., Schneider G., and Yang S., 2019, Concepts of artificial intelligence for computer-assisted drug discovery, Chemical Reviews, 119(18): 10520-10594.
https://doi.org/10.1021/acs.chemrev.8b00728

Yuguda Y.M., Magaji Y., Unuebho I.E., and Dhanushya J., 2023, Emerging trends in computational approaches for drug discovery in molecular biology, GSC Biological and Pharmaceutical Sciences, 24(3): 202-213.
https://doi.org/10.30574/gscbps.2023.24.3.0340