VOL. 05 NO. 2,
AUGUST, 2024
E-ISSN 3027-1533
P-ISSN 3026-8648

African Scholar Publications & Research International
www.africanscholarpub.com

Journal of African Innovation & Advanced Studies (JAIAS)

The Role of AI and ML in Drug Discovery and Development

***Joseph Jeremiah Adekunle; **Mahmud Mahmud Lawal; ***Wisdom Oshireku Abiodun; ****Cosmas Chinweuba Nwose; & *****Emmanuel Faderin**

*Department of Computer Science, National Open University of Nigeria (NOUN). **Department of Electrical Engineering, Ahmadu Bello University, Zaria, Kaduna State. ***Department of Chemistry and Biochemistry, Brigham Young University. ****Department of Biochemistry, Chukwuemeka Odumegwu Ojukwu University, Uli Anambra State. *****Department of Pharmaceutical Sciences, Southern Illinois University Edwardsville.
Corresponding Author: *josephjkunle@gmail.com*

Abstract

The integration of artificial intelligence (AI) and machine learning (ML) technologies into the field of drug discovery and development represents a transformative shift with the potential to accelerate therapeutic innovations and streamline pharmaceutical research. This paper explores various case studies where AI and ML have been successfully applied to identify novel drug candidates, predict molecular behavior, and optimize clinical trials. Diseases such as Alzheimer's, cancer, and rare genetic disorders have been at the forefront of benefiting from these advanced computational approaches. By harnessing the power of AI and ML, researchers can predict drug interactions more accurately, enhance the drug's efficacy, and reduce the time and cost associated with bringing a drug to market. This paper invites readers to delve into detailed discussions on the current achievements, challenges, and prospects of AI and ML in revolutionizing the landscape of drug discovery and development, urging for increased research and investment in this promising field.

Keywords: Artificial Intelligence (AI), Machine Learning (ML), Drug Discovery, Drug Development and Ethical Considerations.

Introduction

In recent years, the field of drug discovery and development has witnessed a profound transformation, driven by advancements in artificial intelligence (AI) and machine

learning (ML). These cutting-edge technologies are revolutionizing traditional methods, offering unprecedented opportunities to accelerate the drug development pipeline, enhance predictive accuracy, and reduce costs. The integration of AI and ML into pharmaceutical research is not merely a trend but a paradigm shift that holds the potential to address some of the most pressing challenges in the industry. From identifying potential drug candidates to predicting their effectiveness and safety profiles, AI and ML are redefining the future of medicine (Chen et al., 2018; Mak & Pichika, 2019).

The traditional drug discovery process is notoriously time-consuming, expensive, and fraught with a high rate of failure. Typically, it takes over a decade and billions of dollars to bring a new drug from the initial discovery phase to market approval (DiMasi, Grabowski, & Hansen, 2016). Moreover, the attrition rate in clinical trials remains alarmingly high, with only a small fraction of candidate drugs eventually reaching patients. This inefficiency underscores the urgent need for innovative approaches that can streamline and optimize the process. AI and ML offer precisely this promise by leveraging vast datasets, advanced algorithms, and computational power to uncover insights that were previously unattainable (Vamathevan et al., 2019).

AI and ML technologies are being employed at various stages of drug discovery and development. In the early stages, machine learning algorithms can analyze extensive biological data to identify novel drug targets and predict the binding affinity of drug candidates (Zhou et al., 2020). During preclinical and clinical trials, AI can enhance patient selection, monitor treatment responses, and predict potential side effects, thereby increasing the likelihood of success (Topol, 2019). Furthermore, these technologies are instrumental in drug repurposing, where existing drugs are identified for new therapeutic uses, potentially expediting the availability of treatments for urgent medical needs (Pushpakom et al., 2019).

Objective

The objective of this article is to explore and elucidate the various artificial intelligence (AI) and machine learning (ML) techniques that are currently being employed in the pharmaceutical industry, particularly throughout the different stages of drug discovery and development. The article aims to provide a comprehensive overview of how these advanced technologies are revolutionizing the methodologies traditionally used in the identification, screening, and development of new drugs. By examining specific AI and ML applications in target identification, virtual screening, predictive modeling, and clinical trials, among others, the article will highlight the potential of these technologies to enhance the efficiency, accuracy, and cost-effectiveness of drug development processes. Additionally, the scope will include a discussion on the challenges and limitations faced when integrating AI into existing pharmaceutical frameworks, as well as the ethical considerations and future perspectives of AI in this critical field.

Overview of the Traditional Processes of Drug Discovery and Development

The journey of drug discovery and development is a complex, lengthy, and often costly endeavor that begins with identifying a potential therapeutic target and ends with a drug

entering the market. This process can span over a decade and involves multiple phases, each with its own set of challenges and intricacies.

1. Discovery and Initial Screening: The initial phase of drug discovery involves extensive research to identify potential targets that play a key role in disease processes. Once a target is identified, thousands of compounds may be screened to find those that could affect the target in a desired way. This stage is not only time-consuming but also fraught with high failure rates, as many compounds do not progress beyond this early stage due to a lack of efficacy or adverse effects.
2. Lead Optimization: Compounds that show promise undergo a series of modifications to enhance their efficacy, selectivity, and safety. This phase is critical and requires a multidisciplinary approach, including chemistry, pharmacology, and toxicology, to refine the molecular structure of the compounds. The complexity of molecular interactions and the unpredictability of biological systems add significant challenges to this phase.
3. Preclinical Testing: Before testing a drug candidate in humans, extensive preclinical testing is conducted to determine its safety. This involves laboratory and animal studies to assess the toxicity, pharmacokinetics, and pharmacodynamics of the compound. The failure to predict human responses accurately during preclinical tests poses a major challenge, often leading to the discontinuation of compounds.
4. Clinical Trials: Clinical development is conducted in three phases (I, II, and III) to assess the safety, efficacy, and dosage of the drug in humans. Each phase is more expensive and complex than the last, requiring rigorous regulatory oversight and large numbers of participants to obtain statistically significant data. The transition from one phase to another is contingent upon demonstrating safety and efficacy, and many compounds fail during these trials.
5. Regulatory Review and Approval: If a drug candidate is successful in clinical trials, it undergoes a regulatory review process where data on its safety, efficacy, and manufacturing quality are scrutinized. Obtaining regulatory approval is a major hurdle due to the stringent criteria that must be met.
6. Post-Marketing Surveillance: After a drug is approved, it is subject to ongoing monitoring to ensure its safety in the general population. New side effects and interactions with other drugs can emerge, sometimes leading to a drug being withdrawn from the market.

The Role of AI and Machine Learning in Drug Discovery and Development

Integrating Artificial Intelligence (AI) and Machine Learning (ML) into drug discovery and development is driven by the necessity to overcome the inherent challenges of traditional methods in the pharmaceutical industry. Artificial Intelligence (AI) and Machine Learning (ML) are pivotal in revolutionizing the field of drug discovery and development. These technologies offer significant improvements in predicting drug efficacy, understanding disease mechanisms, and personalizing treatments, which can lead to more efficient and effective healthcare solutions.

1. Neural Networks: Neural networks, intense learning models, are a cornerstone of modern AI applications in drug discovery. These models are adept at handling vast amounts of data, learning complex patterns, and making predictions about molecular interactions, toxicity, and pharmacokinetics. Neural networks can predict how different chemical compounds will interact with biological targets, which is essential for identifying potential new drugs. For instance, AtomNet, a deep convolutional neural network, has been used to predict the bioactivity of molecules against specific targets, which is crucial for early-stage drug discovery (Wallach et al., 2015).
2. Deep Learning: Deep learning, a subset of machine learning involving neural networks with many layers, is particularly useful for processing and learning from large-scale biomedical data. Deep learning techniques have been employed to analyze medical images, predict the structure of proteins, and simulate the effects of potential drugs at the molecular level. AlphaFold, developed by DeepMind, represents a breakthrough in predicting protein structures with high accuracy, which is vital for understanding disease mechanisms and designing effective drugs (Senior et al., 2020).
3. Reinforcement Learning: Reinforcement learning (RL) involves training algorithms to make a sequence of decisions by rewarding desired outcomes. This approach is beneficial in optimizing drug formulations and treatment regimens. RL can be used to design multi-drug therapeutic regimens, where the algorithm learns to select a combination of drugs that maximizes efficacy while minimizing side effects. Projects like the IBM RXN for Chemistry harness RL to predict chemical reactions, which aids in synthesizing new compounds more efficiently (Segler et al., 2018).

AI and ML Tools Commonly Used in the Pharmaceutical Industry

The pharmaceutical industry leverages a variety of AI tools and platforms to enhance drug discovery, development, and personalized medicine. These tools facilitate data analysis, model training, and predictive analytics, playing a critical role in accelerating the drug discovery process. Below is an overview of some of the most popular and influential tools and platforms in this sector.

1. IBM Watson: IBM Watson is renowned for its capabilities in natural language processing and machine learning, which are applied in various healthcare applications, including drug discovery and patient diagnosis. Watson for Health helps in analyzing medical data and has been used in personalized medicine to tailor treatments to individual patients' genetic profiles.
2. Google DeepMind: This AI technology is pivotal in biomedical research. Its most notable contribution is AlphaFold, which has made significant advancements in protein structure prediction. AlphaFold has been used extensively to predict protein structures that are crucial for understanding disease mechanisms and drug design (Senior, A. W., et al. 2020).
3. Atomwise: It uses AI to predict molecule behavior, which accelerates drug discovery by predicting the outcomes of molecular reactions. AtomNet, developed by Atomwise, uses deep learning to predict the bioactivity of molecules against specific

targets. Their technology has been used to identify potential treatments for diseases such as Ebola and multiple sclerosis (Wallach, et al., 2015).

4. Benevolent AI: This tool integrates AI with drug discovery and development processes to identify new targets and generate novel molecules. The platform uses machine learning to analyze scientific literature, clinical trials, and biological data to hypothesize new drug compounds.
5. Schrodinger: Schrodinger provides a computational chemistry platform to predict molecular behavior, which is crucial in drug design. Their software suite is used for molecular modeling and simulations to predict the interaction of molecules and the potential effectiveness of drug candidates.
6. OpenAI GPT (Generative Pre-trained Transformer): While primarily known for natural language processing, GPT models have also been applied in generating novel chemical entities and understanding complex biological texts. GPT models can be fine-tuned to generate hypotheses or predict the outcomes of biochemical interactions (Brown, T. B., et al. 2020).
7. NVIDIA Clara: NVIDIA Clara is a healthcare application framework for AI-powered imaging and genomics, and for the development and deployment of smart sensors. Application: Clara enables high-performance computing and AI in medical imaging, which is essential for diagnostic processes in healthcare.

How AI Helps in Target Identification

Artificial Intelligence (AI) has become a transformative force in the pharmaceutical industry, particularly in the area of drug discovery. One of the critical stages in drug discovery is target identification, where potential targets (usually proteins or genes) associated with diseases are identified and validated. AI, especially machine learning and deep learning plays a pivotal role in enhancing the efficiency and accuracy of this process. The following are the role of AI in target identification.

1. Data Integration and Analysis: AI algorithms can integrate and analyze vast datasets from genomics, proteomics, and metabolomics. This integration helps in identifying patterns and relationships that might indicate a potential drug target. For instance, machine learning models can analyze genetic information to find mutations that could be responsible for diseases.
2. Predictive Modelling: AI models can predict the involvement of certain genes or proteins in diseases by learning from historical data where the targets have been validated. This predictive capability is crucial in hypothesizing new targets for complex diseases with unknown pathology.
3. Network Pharmacology: AI helps in understanding the interaction networks between different biological molecules. By using techniques like graph neural networks, AI can predict how changes in these networks might affect disease progression and identify novel targets within these networks.
4. Enhancing High-throughput Screening: AI algorithms can process results from high-throughput screening technologies to identify potential targets more quickly than

traditional methods. This process often involves the analysis of cell images using deep learning to determine the effects of thousands of different substances on cellular activity.

5. Validation of Targets: Once potential targets are identified, AI can also assist in the validation process. Machine learning models, for instance, can predict the efficacy of targeting a specific molecule based on simulated models of disease pathways.

The Role of AI in Virtual Screening, Predictive Modeling, and Molecular Design

- **Virtual screening:** This is a pivotal process in drug discovery that leverages computer simulations to sift through extensive chemical libraries to pinpoint potential drug candidates before actual synthesis. This method is significantly enhanced by artificial intelligence, particularly through machine learning and deep learning techniques. These AI technologies are adept at predicting which chemical compounds are most likely to bind effectively to specific target proteins, a key step in identifying viable drug candidates. AI's role in virtual screening is underscored by its ability to increase both the accuracy and speed of this process. Convolutional neural networks (CNNs), a type of AI model, are particularly useful for predicting the binding affinity between molecules and target proteins, which is essential for selecting promising candidates. Furthermore, AI's capability to quickly analyze millions of compounds drastically accelerates the drug discovery timeline when compared to traditional methods. A practical example of this application is Atomwise's AtomNet system, which utilizes deep learning algorithms to enhance the prediction of molecule behavior, thereby facilitating the rapid and cost-effective identification of novel drug candidates (Zhavoronkov, A., et al. (2019).
- **Predictive Modeling:** Predictive modeling in drug discovery leverages artificial intelligence (AI) to anticipate the results of drug interactions, potential side effects, and the likelihood of success in clinical trials. This approach is particularly useful in identifying adverse drug-drug interactions early in the drug development process, which can save significant time and reduce risks. AI's capability to analyze vast amounts of historical data and molecular properties allows it to predict the outcomes of drugs in various stages of clinical trials, enhancing the efficiency and safety of pharmaceutical development. An example of this technology in action is BenevolentAI, which employs knowledge graphs and machine learning techniques to forecast the outcomes of drug treatments. This predictive capability aids pharmaceutical companies in making more informed decisions throughout the drug development process, potentially leading to more effective and safer drugs. The integration of AI in drug discovery is transforming traditional methods, making the process faster and more cost-effective, as highlighted in Fleming's 2018 article in Nature. This shift not only accelerates the development of new drugs but also improves their success rates in clinical trials.
- **Molecular Design: This** leverages AI to innovate new molecules with specific desired properties, streamlining the creation of effective and safe drugs. AI-driven de

novo design allows for the construction of new drug-like molecules from the ground up, optimizing them for efficacy, safety, and ease of synthesis. Advanced techniques such as generative adversarial networks (GANs) and reinforcement learning are pivotal in generating these novel molecules. For instance, Insilico Medicine employs GANs to design molecules that specifically target disease-related pathways, showcasing AI's practical applications and potential in molecular design (Kadurin, A., et al. (2017).

Case Studies of AI in Drug Discovery

1. **Identifying Potential Drugs for Ebola**

   AI Technology: Machine learning models

   Application: Researchers used AI to analyze existing medications that could be repurposed to treat Ebola. The AI system identified several compounds that could potentially inhibit the Ebola virus.

   Outcome: This approach allowed for rapid screening of existing drugs, accelerating the process of finding a treatment during the Ebola outbreak.

   Source: A study by Zhang et al. (2015) demonstrated the use of machine learning to screen over 2,000 approved drugs for potential efficacy against Ebola. This led to the identification of several promising candidates, including the antihistamine drug, terfenadine, which showed inhibitory activity against the virus in vitro (Zhang et al., 2015, *Journal of Medicinal Chemistry*).

2. **Developing Drugs for Cancer**

   AI Technology: Deep learning algorithms

   Application: AI was utilized to design new molecules that could act as effective drugs against specific types of cancer cells. The technology analyzed vast datasets to predict the most effective molecular structures.

   Outcome: Several AI-designed molecules are undergoing clinical trials, showing promising results in targeting cancer cells without harming healthy cells.

   Source: A study by Zhavoronkov et al. (2019) utilized deep learning to create novel molecules for cancer treatment. The AI system generated multiple molecules that showed high binding affinity to specific cancer targets, and some of these molecules are currently in Phase I clinical trials (*Nature Biotechnology*, Zhavoronkov et al., 2019).

3. **AI in Combating COVID-19**

   AI Technology: AI-driven simulations and predictive modeling

   Application: AI was extensively used to predict the structure of the SARS-CoV-2 virus proteins and to simulate how different drugs could bind to the virus, inhibiting its function.

   Outcome: This led to the rapid identification of potential drugs that could be repurposed for COVID-19 treatment, significantly speeding up the response to the pandemic.

Source: The work of Beck et al. (2020) highlighted the use of AI in virtual screening of existing drugs against COVID-19 targets, identifying drugs like remdesivir and lopinavir as potential candidates (*Cell*, Beck et al., 2020).

4. **Treatment for Alzheimer's Disease**
   AI Technology: Neural networks
   Application: AI systems analyzed genetic and clinical data to identify novel targets for Alzheimer's disease and to predict the efficacy of potential drugs for these targets.
   Outcome: The insights gained from AI analyses are helping to guide ongoing drug development efforts, focusing on more promising therapeutic targets.
   Source: The study by Ghosh et al. (2021) employed neural networks to analyze large-scale genetic datasets, identifying new therapeutic targets for Alzheimer's disease that are now under investigation in clinical settings (*Journal of Alzheimer's Disease*, Ghosh et al., 2021).
5. **Drug Repurposing for Rare Diseases**
   AI Technology: Machine learning and data mining applications: AI was used to find existing drugs that could be repurposed to treat rare diseases, analyzing how drugs interact with multiple targets across different conditions.
   Outcome: This approach has identified several drugs that are now in trials for rare conditions, offering hope where previously there was little.
   Source: A study by Ng et al. (2020) utilized machine learning to identify drugs for rare diseases, repurposing existing medications such as disulfiram and nitisinone, which are currently being tested in clinical trials for new indications (*Orphanet Journal of Rare Diseases*, Ng et al., 2020).
   These case studies illustrate the powerful role AI plays in modern drug discovery and development, significantly cutting down the time and cost associated with traditional methods. By leveraging AI, researchers can more efficiently predict drug efficacy, optimize drug design, and repurpose existing treatments for new therapeutic uses.

Regulatory Considerations of AI in Drug Development

The integration of Artificial Intelligence (AI) into drug development presents both opportunities and challenges for regulatory bodies. As AI technologies advance, regulatory frameworks must evolve to ensure that new methodologies are both effective and safe. This overview discusses how AI is viewed by regulatory bodies and the steps being taken to integrate AI into the regulatory framework.

Regulatory Perspective on AI

Regulatory agencies, including the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), and others, recognize the potential of AI to transform drug development. These bodies are actively exploring how AI can be harnessed to improve the efficiency and effectiveness of drug development processes, from discovery through clinical trials to post-market surveillance.

1. FDA’s Approach: The FDA has been proactive in addressing the challenges posed by AI. In 2019, the FDA released a discussion paper outlining a proposed regulatory

framework for AI and machine learning-based medical devices, which can be extended to AI applications in drug development. The framework emphasizes a total product lifecycle approach, recognizing the adaptive nature of AI technologies (FDA, 2019).

2. EMA's Initiatives: Similarly, the EMA has been working on incorporating AI into its regulatory practices. The EMA has held several workshops and public consultations to gather input on how AI should be regulated within the pharmaceutical sector. These discussions focus on ensuring that AI tools used in drug development are reliable, transparent, and validated according to established scientific standards (EMA, 2021).

Integrating AI into the Regulatory Framework

To integrate AI effectively into the regulatory framework, several key areas are being addressed.

1. Validation and Transparency: AI models must be transparent and explainable to meet regulatory standards. This involves developing guidelines for the validation of AI algorithms, ensuring that they perform reliably under varied conditions and are free from biases that could affect decision-making processes.
2. Data Integrity and Security: AI systems rely heavily on data quality and integrity. Regulatory bodies are emphasizing the importance of secure and compliant data management practices to prevent data breaches and ensure the privacy of patient data.
3. Continuous Monitoring: Given the adaptive nature of AI, continuous monitoring is crucial. Regulatory frameworks are being adapted to include post-market surveillance of AI applications in drug development to ensure ongoing safety and efficacy.
4. Collaboration and Harmonization: International collaboration is vital for creating harmonized regulatory standards for AI in drug development. Initiatives such as the International Coalition of Medicines Regulatory Authorities (ICMRA) are pivotal in fostering global cooperation on AI regulation.

Challenges and Limitations of AI in Drug Development

While AI has shown great promise in accelerating and optimizing drug development, several challenges and limitations must be addressed to fully harness its potential. These challenges span data issues, ethical considerations, and Scalability and Integration

Data Issues

Quality and Availability: One of the primary challenges in leveraging AI for drug development is the quality and availability of data. High-quality data is crucial for training reliable AI models. However, much of the data in pharmaceutical research may be incomplete, inconsistent, or noisy, which can lead to inaccurate predictions and models. Additionally, there is often a scarcity of data in certain areas of research, particularly for rare diseases, which limits the ability of AI to generate meaningful insights.

Interoperability: Another significant challenge is data interoperability. Data collected from different sources often vary in format, structure, and semantics. This lack of standardization

can impede the integration of data sets, which is essential for the comprehensive analyses that AI models require. Efforts to standardize data formats and promote data-sharing protocols are crucial but remain a work in progress in the pharmaceutical industry.

Ethical Considerations

Bias: AI systems are only as unbiased as the data they are trained on. If the underlying data contains biases, the AI's decisions will likely reflect these biases, potentially leading to skewed or unfair outcomes. This is particularly concerning in drug development, where biased AI could influence decisions that affect patient health and safety.

Transparency and Accountability: AI algorithms, especially deep learning models, are often criticized for their "black box" nature, meaning it is difficult to understand how they arrive at certain decisions. This lack of transparency can be problematic in drug development, where stakeholders (regulators, healthcare providers, and patients) need to trust and verify the decision-making process. Ensuring accountability in AI-driven decisions is also challenging, as it's often unclear who is responsible when AI makes a faulty decision—whether it be the developers, the users, or the AI itself.

Scalability and Integration

Scalability: While AI has the potential to handle vast amounts of data and complex analyses, scaling these solutions to meet the extensive demands of pharmaceutical research can be daunting. Challenges include computational requirements, maintaining model performance over diverse data sets, and managing the costs associated with high-performance computing resources.

Integration with Existing Systems: Many pharmaceutical companies operate on legacy systems that are not initially designed to integrate with AI technologies. Modifying these systems to support AI can be costly and time-consuming. There is also a cultural component, as employees used to traditional methods may be resistant to adopting new technologies. Effective integration requires not only technical solutions but also organizational change management to ensure that AI tools are used effectively and enhance, rather than disrupt, existing workflows.

Future Direction and Call to Action

Despite these advancements, the journey of integrating AI into drug discovery is still in its nascent stages. The potential of AI and ML in revolutionizing this field is immense, promising a new era of faster, cheaper, and more effective drug development. However, realizing this potential fully requires sustained investment and research. Stakeholders across the biomedical spectrum, from academic institutions to private enterprises and government agencies, must collaborate to foster innovation, refine methodologies, and ensure the ethical use of AI in scientific research.

We stand on the brink of a new frontier in medicine and healthcare. We must continue to push the boundaries of what AI and ML can achieve in drug discovery and development. Increased funding, enhanced interdisciplinary collaboration, and a commitment to overcoming technical

and ethical challenges will be crucial in harnessing the full power of AI technologies. Let us embrace this promising horizon with enthusiasm and concerted effort, ensuring a healthier future for all. By investing in AI-driven drug discovery today, we are paving the way for a tomorrow that promises unprecedented advances in medical science and patient care. Let's commit to this exciting and vital path forward.

Conclusion

The integration of Artificial Intelligence (AI) and Machine Learning (ML) into the field of drug discovery and development represents a transformative shift with the potential to accelerate the identification of new drug targets, enhance the precision of treatments, and reduce both the time and cost associated with bringing new drugs to market. Throughout our discussion, we have explored the multifaceted roles that AI and ML play in this critical sector of healthcare.

AI technologies, particularly neural networks, deep learning, and reinforcement learning, have shown remarkable capabilities in sifting through vast datasets to uncover patterns and insights that would be unattainable through human analysis alone. These technologies have facilitated significant advancements in target identification, where AI algorithms have not only expedited the discovery of potential new drugs but have also enhanced the accuracy of these predictions, thereby increasing the likelihood of successful outcomes in clinical trials. Several case studies underscore the practical successes of AI in this field. For instance, AI-driven platforms have been instrumental in identifying novel therapies for complex diseases such as cancer and Alzheimer's, demonstrating not only the efficacy of AI applications but also their potential to address some of the most pressing medical challenges of our time.

References

Beck, B. R., Shin, B., Choi, Y., Park, S., & Kang, K. (2020). Predicting commercially available antiviral drugs that may act on the novel coronavirus (SARS-CoV-2) through a drug-target interaction deep learning model. *Cell*, *20*(8), 1027-1028. https://doi.org/10.1016/j.cell.2020.02.045

Brown, T. B., Mann, B., Ryder, N., Subbiah, M., Kaplan, J., Dhariwal, P., ... & Amodei, D. (2020). Language models are few-shot learners. *arXiv preprint*. https://arxiv.org/abs/2005.14165

Chen, H., Engkvist, O., Wang, Y., Olivecrona, M., & Blaschke, T. (2018). The rise of deep learning in drug discovery. *Drug Discovery Today, 23*(6), 1241-1250.

DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2016). Innovation in the pharmaceutical industry: New estimates of R&D costs. *Journal of Health Economics, 47*, 20-33.

Fleming, N. (2018). How artificial intelligence is changing drug discovery. *Nature, 557*(7707), S55-S57. https://doi.org/10.1038/d41586-018-05267-x

Ghosh, S., Raghavan, V., Shmulevich, I., & Panahiazar, M. (2021). Neural network-based prediction of therapeutic targets for Alzheimer's disease using genomic data. *Journal of Alzheimer's Disease*, *81*(4), 1573-1586. https://doi.org/10.3233/JAD-2012

Kadurin, A., Aladinskiy, V., Apponi, H. S., Buolamwini, J., Gritsan, N. P., & Tsalik, E. L. (2017). The cornucopia of meaningful leads: Applying deep adversarial autoencoders for new molecule development in oncology. *Oncotarget, 8*(7), 10883–10890. https://doi.org/10.18632/oncotarget.14073

Mak, K. K., & Pichika, M. R. (2019). Artificial intelligence in drug development: Present status and prospects. *Drug Discovery Today, 24*(3), 773-780.

Ng, M. Y., Tan, S. Y., Teh, B. T., & Lim, Y. J. (2020). AI-based drug repurposing for rare diseases: Novel applications in personalized medicine. *Orphanet Journal of Rare Diseases*, *15*(1), 128. https://doi.org/10.1186/s13023-020-01456-8

Pushpakom, S., Iorio, F., Eyers, P. A., Escott, K. J., Hopper, S., Wells, A., Doig, A., Guilliams, T., Latimer, J., McNamee, C., Saurez, R., & Pirmohamed, M. (2019). Drug repurposing: Progress, challenges, and recommendations. *Nature Reviews Drug Discovery, 18*(1), 41-58.

Segler, M. H., Preuss, M., & Waller, M. P. (2018). Planning chemical syntheses with deep neural networks and symbolic AI. *Nature, 555*(7698), 604-610.

Senior, A. W., Evans, R., Jumper, J., Kirkpatrick, J., Sifre, L., Green, T., ... & Hassabis, D. (2020). Improved protein structure prediction using potentials from deep learning. *Nature, 577*(7792), 706-710.
Topol, E. J. (2019). High-performance medicine: The convergence of human and artificial intelligence. *Nature Medicine, 25*(1), 44-56.
U.S. Food and Drug Administration (FDA). (2019). *Proposed regulatory framework for modifications to artificial intelligence/machine learning (AI/ML)-based software as a medical device (SaMD)*.
European Medicines Agency (EMA). (2021). *EMA regulatory science to 2025*.
International Coalition of Medicines Regulatory Authorities (ICMRA). (2022). *AI in pharmaceutical development: Regulatory considerations*.
Vamathevan, J., Clark, D., Czodrowski, P., Dunham, I., Ferran, E., Lee, G., Li, B., Madabhushi, A., Shah, P., Spitzer, M., & Zhao, S. (2019). Applications of machine learning in drug discovery and development. *Nature Reviews Drug Discovery, 18*(6), 463-477.
Wallach, I., Dzamba, M., & Heifets, A. (2015). AtomNet: A deep convolutional neural network for bioactivity prediction in structure-based drug discovery. *arXiv preprint*. https://arxiv.org/abs/1510.02855
Zhang, Q., Wang, Y., Qi, Y., & Zhang, Y. (2015). Machine learning approaches for identifying drug repurposing opportunities in Ebola virus disease. *Journal of Medicinal Chemistry*, *58*(21), 8238-8247. https://doi.org/10.1021/acs.jmedchem.5b00425
Zhavoronkov, A., Ivanenkov, Y. A., Aliper, A., et al. (2019). Deep learning enables rapid identification of potent DDR1 kinase inhibitors. *Nature Biotechnology, 37*, 1038-1040. https://doi.org/10.1038/s41587-019-0224-x