Literature Review of AI Applications and Technologies in Drug Development

(Technical Paper)

Discussion of the Impact of AI on Competition and Ethics in Big Pharma

(STS Paper)

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Introduction

How might the widespread adoption of AI technology change the pharmaceutical industry?

Drug development is dominated by large, multinational pharmaceutical companies(*How AI Reduces the Cost and Time of Drug Discovery and Development – NaturalAntibody*, n.d.). Commercializing a novel pharmaceutical product requires enormous upfront investment that is prohibitively high for many small, under-resourced new entrants into the pharma space. A benchmark study conducted in 2014 and reported on in *Scientific American* asserts that the cost of bringing a new drug to market has nearly doubled since the early 2000s, rising to an astonishing $2.5 billion(News, n.d.). Beyond the financial burden, drug development is an extremely risky and time-consuming venture. It can take decades for a product to go from lab to market and they are typically unsuccessful even after such a lengthy time investment. Nearly 90% of drug candidates do not pass clinical trials(*How AI Reduces the Cost and Time of Drug Discovery and Development – NaturalAntibody*, n.d.).

Successfully navigating this dangerous terrain can reap great financial rewards, which is the long-term strategy of pharma giants. AbbVie's arthritis drug Humira, for instance, saw sales revenue of nearly $21 B in 2021(Dunleavy, 2022, p. 20). These "blockbuster" drugs and the shocking revenues they return are the linchpin holding the pharmaceutical industry together. Without blockbuster medications, R&D funding for future drugs will quickly dry up. This reliance on patenting blockbusters to sustain profitable operations creates a demanding environment for new entrants and healthy competition in the pharmaceutical industry. In short, novel drug development is difficult to pursue outside of large pharmaceutical companies that can endure significant costs, risk, and time because of immensely profitable existing drugs in their portfolio.

Pharma's barriers to entry, however, do face a new challenge in the 21st century: artificial intelligence. The power of AI in drug development is clear. These algorithms can parse immense troves of data, including information on chemical compounds and structure, animal models, and patient details. AI

tools can not only help identify potential physiologic targets for future drugs, but even what molecule might be best suited for a given application(*Measuring the Risks and Rewards of Drug Development*, 2018). This prospectus seeks to identify the state-of-the-art AI tools at pharma's disposal and investigate the impact these tools may have on industry practice, competition, and ethics.

Technical Topic

What AI technology is currently being applied to drug development and how do they work?

The application of AI technology to drug development can be largely divided into two broad categories: predictive and application based. Predictive technology refers to the use of AI before any drug development occurs. Among others, predictive technology includes data mining, virtual drug screening, generative chemistry, pharmacogenomics, toxicity predictions, and drug-target predictions(*AI Is about to Remake the Pharmaceutical Industry – POLITICO*, n.d.). Application-based AI technology refers to its use after a drug has begun being developed or tested. This includes clinical trial optimization, clinical data analysis, pharmacovigilance, personalized medicine, and applications related to automating laboratory procedures or manufacturing(*AI Is about to Remake the Pharmaceutical Industry – POLITICO*, n.d.) (Vanhaelen et al., 2020).

Predictive AI Technology

One of the most powerful tools employed by pharma companies in the realm of predictive AI is called Computer-assisted Drug Design (CADD). Its application allows researchers to create an artificial, computational representation of a new drug and model its properties. This can provide information not only molecular properties such as selectivity, distribution, absorption, bioactivity, side effects, and excretion, but can help researchers optimize drug attributes entirely in silico(Vanhaelen et al., 2020). CADD is a broad term that encompasses a number of ML/AI approaches, which will be discussed in more detail in the following paragraphs.

In many cases, the ability of AI to interact with vast troves of data gives it its predictive power. One important database, called the drug-protein interaction database, contains information about the known relationships between existing drugs, their chemical structure, and the molecular mechanisms through which they interact with relevant proteins in a patient's body. Semi-supervised machine learning techniques have been successfully applied to this database and others like it to predict new drug interactions and potential side effects without ever physically testing a new pharmaceutical(Vanhaelen et al., 2020).

Deep learning techniques such as generative adversarial networks (GANs) are a new approach that goes beyond semi-supervised learning into an area referred to as AI imagination. Here the power of AI in pharmaceutical development becomes truly astounding. GANs are able to generate new objects with desired properties and have been used in several cases to generate patentable *de novo* drug candidates with clinical promise(Dara et al., 2022). Other deep learning architectures such as recurrent neural networks (RNNs), variational autoencoders (VAEs), and adversarial encoders (AAEs) have been used in additional to GANs for *de novo* drug development. These techniques differ from traditional approaches which rely on explicit chemical knowledge being built into the software or model. Deep learning approaches, such as GANs, RNNs, VAEs, or AAEs, are able to derive their own interpretations and insights from massive datasets(Dara et al., 2022). This gives them a powerful edge in inventing new compounds. There are many other examples of emerging techniques in predictive or generative tools for drug development and the field is showing promising progress in their employment. However, developing standards for the validation of *in silico* drug candidates is a significant challenge. Without a standardized, trusted, and efficient way to benchmark or compare generative chemistry models, it will be hard to fully utilize these tools. Additionally, the curation and maintenance of accessible, quality datasets is key to the successful implementation of AI in predictive drug design.

Application Based AI Technology

One of the most important places where AI is employed after the identification of a drug candidate is the design and implementation of clinical trials. The standard linear, discrete format of clinical trials has changed very little of time. It does not, however, always facilitate optimal clinical trials where heterogenous patient groups, complex therapies, and difficult retention or patient monitoring contribute to a high rate of failure. AI can mitigate some of these common problems by seamlessly integrating data collection, management, storage and even trial design itself(*Intelligent Clinical Trials*, n.d.).

The utility of AI in the design and conduct of clinical trials stems largely from its ability to process large amounts of data and integrate that information across locations or databases. AI technologies have a truly unparalleled ability to collect and interpret data at scale. Analyzing and extracting patterns from current and past clinical trials, post-market surveillance, and other programs or research is a useful asset in the design of clinical trials, relieving significant burden on the company responsible for bringing a drug to market. ML and AI techniques can also be employed to identify potential trial subjects who have favorable characteristics for the study, such as population heterogeneity (often meant from a medical perspective pertaining to the treatment), patients with measurable endpoints, and patients likely to respond to the treatment(*Intelligent Clinical Trials*, n.d.). From there, AI can be used in trial data analysis, site selection for the clinical trial, and patient monitoring. The ability to integrate and interpret large amounts of data through AI will make the design and implementation of clinical trials easier.

Another important area is in pharmaceutical manufacturing. AI can help use historic data to predict maintenance needs on the manufacturing line, supply chain issues, and inventory forecasting to help optimize production rates. In these and other ways, it can be an indispensable tool in operations management.

STS Topic

In what ways will AI impact ethics, competition, and common practices in the pharmaceutical industry?

The ethical problems surrounding big pharma are some of the most controversial in medicine. Promoting ineffective drugs, covering up unflattering research, selling harmful medications, and violating antitrust laws to charge extortionary prices are but a few examples of recent multi-million-dollar settlements made by leaders in the pharmaceutical industry(Szalavitz, 2012). With a technical understanding of the application of AI in drug development, this section will explore the ethical implications of a shifting industry. AI technology has the potential to reduce drug prices, increase competition, and ultimately address some of the primary ethical shortcomings of the pharmaceutical industry and its standard of practice.

There are numerous perspectives with which to consider AI's impact. AI technology has the potential to drive down production and research costs resulting in increased competition from new entrants in the pharma space, which may drive accountability across the industry. AI, as an effective tool for the collection and analysis of data, could be used to make judgements directly and quickly on a drug's efficacy. This will make information on medication more available to the public and reduce the freedom with which drug companies suppress contradictory studies. Regulatory bodies such as the FDA can employ AI technology in their mission to ensure that only safe and effective treatments are approved. This section will focus not on AI technology itself, but on the various potential impacts it could have on industry practice, society, and government.

As a regulatory tool, automation from AI could help reduce the time required for collecting, categorizing, and standardizing data from various records, reducing the amount of human involvement throughout this process. In pharmaceuticals specifically, the regulatory process is exceedingly slow. Records and data are complex and require regular maintenance and updating. Combing the computational power of AI as a tool for automating data management and analysis with human

intelligence or guidance can dramatically relieve regulatory workload. This would maximize time for things like strategic planning of regulatory approvals and investigation into misconduct or flawed research(Patil et al., 2023). In doing so, AI could be a powerful tool for government and public oversight of pharma.

AI's potential for increased competition in the pharma space depends heavily on small biotech companies' ability to incorporate novel technologies. Currently, it is the pharma giants who are best positioned to invest in and capitalize on emerging computational approaches to drug development. For the industry to truly shift and see a significant reduction in entry barriers, smaller companies will need to focus on incorporating AI into their process(Foster, n.d.). Today, AI and ML technical talent is a rare enough resource to be dominated by big pharma companies. The future, however, is likely to see this change. In a world where AI technology is equally available to small and large pharmaceutical companies, there will be a fundamental change in how the industry operates and likely an increase in competition and accountability.

Conclusion

Artificial intelligence is a seismic force impacting nearly every industry and society. This new tool is something that will be felt by individuals across every aspect of life. Education, technology, business, social media and even relationships are to be redefined by the continued development of AI technology.

The pharmaceutical industry is one of the most powerful and important entities in American society. It is also an entity dominated by a select few major corporations. The significant cost of drug development has left their position at the top of this industry unchallenged for decades. Big pharma is, however, especially susceptible to the advent of new AI technologies. These software tools can design

clinical trials, parse immense quantities of medical data and draw conclusions, and even generate new chemical compounds for testing. Big pharma is best positioned to invest in and capitalize on this emerging technology, but as technical expertise and hardware become more available smaller biotech challengers are likely to leverage these powerful tools to compete with big pharma in new ways.

Government regulation will also be improved through the application of AI. These tools can help organizations like the FDA monitor immense amounts of medical, clinical trial, or research data. This has the potential to greatly improve the government's capacity for regulated drug development, increasing the number of new drugs that can be safely approved and assisting in post-market surveillance of released products. Either as a precursor for increased competition or as a direct tool for regulatory agencies, AI has the potential to dramatically impact ethics and accountability in the pharma industry. In many ways, AI could be the silver bullet to an industry that has become notorious for corruption, greed, and a lack of accountability.

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