Frontiers of Artificial Intelligence,
Ethics and Multidisciplinary Applications

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Artificial Intelligence in Drug Development

Patenting and Regulatory Aspects

Springer

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Artificial Intelligence is now present in numerous spheres of our everyday lives. It is poised to lead new and efficient business models for effective and user-centric services in the private and public sectors. Advances in AI in deep learning, (deep) reinforcement learning, and neuroevolutionary techniques can pave the way forward for artificial general intelligence (AGI). However, the development and use of AI also present challenges. Inherent biases prevalent within data corpora used to train AI and machine learning systems attribute to most of these challenges. In addition, multiple instances have highlighted the need for privacy, fairness, and transparency in AI-powered decision-making. This book series will provide an avenue for researchers, leaders, decision-makers, and policymakers to share research and insights on the forefronts of AI, including its use in an Ethical, Explainable, Privacy-Preserving, Trustworthy, and Sustainable manner.

The series has relevance across disciplines and be multi-disciplinary. Advances in AI, explainability AI, privacy-preserving AI, and ethical AI explored in this book series are unexplored areas for research and competence building. Such developments can reduce hesitancy for AI integration in many domains. The book series thus fits in well as an essential and growing need among those who work on artificial intelligence in academia, business and industry, and the public sector to exploit the opportunities in the constantly evolving field of AI.

The series publishes research monographs, authored works by practitioners and case studies to highlight innovative and best practices, and edited volumes putting together varied perspectives.

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Preface

Access to medicines and healthcare is essential. Technological advances have assisted doctors and the healthcare system to be able to better diagnose, predict, assess and treat patients in a disease/disorder condition. The enormity of healthcare and practice demands frontline approaches to promote safety and efficacy. New approaches and tools continue to be required to address the challenges of accessibility and affordability in healthcare. The justification provided for the development of tools and services based on new technologies is to improve quality of care and address healthcare costs. Information technology developments have significantly impacted the drug discovery process and development and healthcare documentation and management. Advances in machine learning have helped in understanding causal relationships and correlations. Predictive algorithms in the healthcare have the ability to advance precision medicine. Supervised and unsupervised learning is used in the drug discovery process. The 'pseudopodic' growth of artificial intelligence (AI) has been phenomenal. As one of the disruptive technologies of the times, AI's growth trajectory indicates virtually implementation in all socioeconomic sectors vital for human development. The attribution of 'citizenship' to humanoid robots just speaks of the transformative value of AI. International and national discourse continues on the various facets of AI and its impact.

This book is a continuing effort of the research on the analysis of how the twin aspects of intellectual property rights and drug regulation affect industry and society. The aim of the book is to inform the developments and implementation of intellectual property laws, particularly patents and drug regulation. This book is divided into five chapters. In Chap. 1, the evolution of AI/ML applications in drug discovery and development and healthcare is discussed. The growth of individual tools to AI expert systems is discussed in definite time periods to analyse the nature and scope of AI applications. The type of collaborations for development of AI tools is discussed along with the widely used AI platforms in drug discovery and healthcare. Technology-rich businesses consider patents important to restrict competition. The granting of patents creates monopoly rights for companies to either own the patent or create licencing opportunities for the use of the patent. In Chap. 2, the interpretation of patent legislation with respect to AI inventions from the perspective

of eligible subject matter, patentability criteria are discussed. The cross-jurisdictional judicial precedents are analysed. The definitional considerations related to AI, development of guidelines at patent offices and patent prosecution are explained. The analysis of the patenting activity of Indian companies and identification of the challenges based on the survey of the selected companies provide important insights. The analysis of patent family information indicates how companies utilise patenting in several jurisdictions as an important strategy to leverage markets. IP and regulation are both equally important for industry with respect to manufacturing and marketing products. While patent rights are held and are exclusive rights, industry requires clearance under relevant drug regulation to bring AI-based medicines or medical devices. The area of AI-based medical devices has witnessed a tremendous growth, and there are already several such devices used in healthcare. While innovations are rapidly being developed, their deployment is subject to the country regulation. In Chap. 3, the focus is on the analysis of how existing drug regulation retains the flexibility to accommodate the various types of AI-based medical devices. The development of international norms and how they impact country-based regulation, cross-country developments in regulation of these devices in the context of the USA, EU and India and the legislative basis are discussed. Regulation of these devices is necessary as it could affect doctors, patients and consumers alike. The emergence of the approval system is examined from the regulatory developments when initially few devices (software as medical devices or SaMD) were approved to the current times when several of them have not only been approved but are already in use. The analysis of the drug regulatory process from the substantive and procedural aspects indicates to the development of norms and their applicability. All AI-based software may or may not be considered as medical devices. Cross-country comparison of regulations indicates varied levels of application and differences in certain norms. It becomes clear, hence, that there are technical, legal, social and normative aspects. This book does not deal with the liability as well as the data protection regime. There are several approaches for AI policy development from international and national perspectives. These policies provide a platform for engagement of the government, stakeholders and society to discuss implementation, capacity building, standards development, governance and guidance. In examining the emergence and current discussions in relation to AI policies, Chap. 4 provides an account of several international organisations that are framing ethical guidelines for use of AI and governance mechanism for the wide adaptability of AI in multiple sectors. The Indian central and state policies that support healthcare start-ups and companies through various initiatives under different ministries are discussed. The conclusion chapter, Chap. 5, summarises the discussion on how technology leads, intellectual property protection and regulatory changes inform on the path forward. It also discusses what kind of policy and law changes could assist in the development and deployment of AI-based products and improved the trust in their use.

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Chapter 1
Artificial Intelligence in Drug Development and Healthcare—Nature and Scope

1.1 Introduction

Technology continues to impact human life; from small inventions like needles to as big as space shuttles. As rightly pointed out by the Greek philosopher Heraclitus of Ephesus, 'change is the only constant in life.' Technology has shaped and reshaped human life and lifestyles in many ways. The twenty-first century is categorised as the information age with growth of several technologies. The diffusion of several technologies has led to economic and social changes across the globe. Of particular relevance is the convergence of technologies that has led to important developments in science and engineering. The emergence of digital technologies has enabled several advances in terms of processing vast amount of data, improving performance and considerable gains in speed, size and cost. Newer developments in computational methods have led to their utilisation in all spheres of human activity. Truly, the knowledge economy has opened several opportunities. Greater diffusion of innovations and development of markets has been realised with technological trends such as the 5G, 3D printing, genomics, Internet of Things (IoT), robotics, blockchain and so forth. New names of technologies continue to be coined. Digital interventions have blurred local, regional and national borders and expanded the scope of collective work in several areas. Globalisation has connected individuals and societies in an unprecedented manner. Six important areas have been identified as important enablers that would impact the future for humans. They are technologies related to genetics, energy, materials, brain, information technology and those related to environment. Decoding the structure and function of the brain opens up an enormous advantage of developing solutions for various behavioural and genetic disorders (Coates 1998).

The intersection of information technology and genome sequencing has paved the way for developments in gene therapy, gene editing and solutions not only for common, lifestyle diseases but also rare diseases/disorders. Improved diagnostic tools have helped in early assessment of the health problems. On the other hand,

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advances in brain computing and developments in brain-computer interface help in identification the signal pathways and how they control human metabolism. The development of brain signal recording techniques has unravelled the complexity of neural functions. In this backdrop, mimicking human intelligence became possible. Artificial intelligence (AI) technologies began to be developed to better utilise and steer human functions and hence serve to augment human capabilities. Artificial Intelligence and its developments are a set of disruptive technologies that have impacted several sectors worldwide, such as education, agriculture, banking and finance, healthcare and manufacturing.

Modern drug discovery and development have been impacted by new technologies. There are five stages of drug development; target selection, validation, screening of compounds and optimisation of lead compounds, preclinical stage and clinical trials. The analysis of the large-scale correlation between targets and processes, which hitherto was burdensome, is now easily possible due to the use of AI algorithms. Further, AI-based recognition technologies assist in finding data similarities. The analysis of fifteen pharma and biotech companies (with equal number of small, medium and large companies) in relation to the impact of AI on their business revealed effects that included research and developments among others. Large companies emphasise on the development and use of internal AI-based drug developments and have a greater capacity to use and develop AI tools. The analysis of interviews revealed opportunities for use of AI in identifying individual patient factors for development of personalised drugs, assessment of compatibility of several drugs for an individual patient, identification of solutions for rare diseases, improving patient care and also in the selection of the best candidates for clinical trials. Small- and medium-sized companies tend to use AI developments at the R&D stage unlike large companies that use them more for forecasting. Reducing steps in routine activities, introducing automation and use of AI in decision making is varied in the companies. AI could affect change of business processes. So, the lack of successful integration would affect its promotion. It was observed that medium sized companies had a greater need for AI specialists unlike large companies (Kulkov 2019). High-throughput screening based on computer applications, molecular modeling, utilising computational means to identify potential targets and develop rational drug design are now routine in drug development. Automation of laboratories, robotised screening facilities, increased outsourcing have reduced drug development timelines and costs. Computer modelling programs have been also useful in *in silico* discovery of lead molecules (Eder and Herrling 2015). Analysis of the strategies in the drug discovery process of the three major worldwide pharmaceutical companies indicates the use of advanced information technology systems. The convergence of genomics, genetics and proteomics has brought in a new technological paradigm in medicine compared to erstwhile approaches. The study revealed that use of platforms of strategic information technologies early in the drug discovery process is essential for an integrated process of innovation (Coccia 2015). It was found that the use of computational tools is a requirement in most cases for the optimisation of compounds either from a random screening or from known drugs. The use of Quantitative Structure Activity Relationship (QSAR) method has been found to be more

prevalent with larger data sets compared to smaller data sets in medicinal chemistry. As a traditional machine learning (ML) technology, it has been used in predicting properties of compounds. The analysis of convergence aspects of medicinal chemistry and computational methods indicates that there is a need to develop explainable and auditable AI systems to improve decision making in the area (Griffen et al. 2020).

This chapter analyses the evolution of AI/ML technologies and their applications in drug discovery and healthcare, development of tools and the growth of these technologies pre- and post-2000. In what ways AI programs advance therapy and diagnosis and use of different types of neural networks that have been developed so far are discussed. Deep learning tools predict chemical reactions between candidate compounds and target molecules in cheminformatics and decipher chemical structures. The development of different *de novo* drug design tools based on deep learning and machine learning techniques by AI-based companies are elaborated. The development of AI platforms (such as IBM Watson, etc.) are discussed to understand the pervasive nature of the current applications of AI. The expanding role of AI in predictive analysis, clinical trials, robotic-assisted surgeries, telemedicine, drug discovery and medical devices for diagnosis and radiological purposes and current use of AI in healthcare are discussed in this chapter.

1.2 Definitional Considerations

Before discussing the evolution of AI and related developments, it is important to understand the nature and scope of the term 'artificial intelligence'. AI, in simple terms, can be explained as the use of intelligent machines to replicate and augment the intelligence of human beings.

The Association of Computing Machinery (ACM) announced a classification system called the ACM computing classification. In this classification, artificial intelligence is categorised under 'Computing Methodologies'. Under Section I.2, artificial intelligence covers applications and expert systems, automatic programming, programming languages and software, natural language processing (NLP), distributed artificial intelligence among others (2012 ACM Computing Classification System). In 1950, Allan Turing proposed a test, the imitation game. The Turing test was propounded to show what factors determine whether a machine operates on artificial intelligence. This test is passed if the human judge cannot essentially distinguish between the human and the computer (Turing 1950). John McCarthy defined AI as "the science and engineering of making intelligent machines, especially intelligent computer programs" (McCarthy 2007). Another proposition has been that of 'strong AI' and 'Weak AI' suggested by Searle as an exception to the Turing Test. 'Weak AI' refers to a position in which computers could appear and behave intelligently but not understand as opposed to 'Strong AI' which can actually have a mind (Searle 1980).

The wide range of AI applications has made it easier and advantageous for use in fields such as finance, education, healthcare, agriculture, law, manufacturing, urban