



Review

Artificial Intelligence: The Milestone in Modern Biomedical Research

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Abstract: In recent years, the advent of new experimental methodologies for studying the high complexity of the human genome and proteome has led to the generation of an increasing amount of digital information, hence bioinformatics, which harnesses computer science, biology, and chemistry, playing a mandatory role for the analysis of the produced datasets. The emerging technology of Artificial Intelligence (AI), including Machine Learning (ML) and Artificial Neural Networks (ANNs), is nowadays at the core of biomedical research and has already paved the way for significant breakthroughs in both biological and medical sciences. AI and computer science have transformed traditional medicine into modern biomedicine, thus promising a new era in systems biology that will enhance drug discovery strategies and facilitate clinical practice. The current review defines the main categories of AI and thoroughly describes the fundamental principles of the widely used ML, ANNs and DL approaches. Furthermore, we aim to underline the determinant role of AI-based methods in various biological research fields, such as proteomics and drug design techniques, and finally, investigate the implication of AI in everyday clinical practice and healthcare systems. Finally, this review also highlights the challenges and future directions of AI in Modern Biomedical study.

Keywords: artificial intelligence; machine learning; deep learning; neural networks; bioinformatics; biomedicine; structural biology; drug discovery; healthcare



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1. Introduction

As the century of technological advances, the 21st century is characterized by breakthroughs in informatics that have holistically changed our perception of data analysis. Although in earlier days, the primary challenge was gaining access to information, nowadays, rapidly growing datasets are available anytime in the scientific community and can be easily analyzed, shared, and stored in databases. As for the field of biomedical research, the completion of the Human Genome Project (HGP) in the early 2000s generated a tremendous amount of biological data that paved the way for the emergence of bioinformatics [1,2]. An analysis of these vast stores of information has revealed significant aspects of human genes and raised expectations about the complex nature of genomes. Hence, bioinformatics—the interdisciplinary field that harnesses computer science, biology, physics, chemistry, mathematics, and statistics—has become an indispensable part of modern biological science [3,4].

Going forward, the advent of new experimental methodologies, such as massive parallel sequencing approaches, has led to significantly increased and highly complex digital biological datasets, thus requiring in-depth analysis to understand and interpret the information. As an emerging concept and strategy, the technology of Artificial Intelligence (AI) has already been applied to modern biology and biomedicine [5]. More specifically, it refers to the ability of computers to simulate the natural intelligence displayed by humans to build intelligent systems that can function and run autonomously. AI includes a plethora of applications, such as vision, robotics, data analytics, problem-solving, Natural Language

Processing, decision science, bias, and linguistics [6,7]. Of note, AI is divided into two distinct approaches, namely, the generative or white-box approach and the discriminative or black-box approach. White-box models are interpretable, as they encompass easy-to-understand algorithms that are based on rules and patterns and show how data inputs achieve outputs. On the contrary, black-box models describe algorithms and methodologies that contain highly complicated mathematical functions and not visible inputs and operations, being confusing for observers to understand [8,9].

The technology of AI harbors multiple methods, including Machine Learning and Deep Learning, which have already delivered many commercial products, such as natural language understanding, machine translation, prognostic systems, search engines, and personal digital assistants (Table 1). Interestingly, most of these AI-based methods constitute the core of biomedical research, and the development of new computational tools has opened new vistas for both biological and medical science, which will undoubtedly enhance our efforts in systems biology and transform many aspects of healthcare [10,11]. The current review outlines the recent breakthroughs in AI-based technologies and provides a brief overview of the potential impact of AI in biological sciences that will make it attractive to researchers focusing on biomedical expert systems. In the following sections, we aim to decipher the main fields of AI that are harnessed in different aspects of life, investigate the role of AI in biomedicine, and highlight its main applications in both biology and medicine. Ultimately, the challenges associated with each widely used AI-based technology in modern medical systems are also discussed.

Table 1. List of abbreviations and acronyms.

Abbreviation	Definition
AI	Artificial Intelligence
ANNs	Artificial Neural Networks
CDI	Clostridium Difficile Infection
CNNs	Convolutional Neural Networks
CT	Computerized Tomography
CV	Computer Vision
DL	Deep Learning
DNNs	Deep Neural Networks
EHRs	Electronic Health Records
EST	Expressed Sequence Tag
FDA	Food & Drug Administration
HGP	Human Genome Project
INSIDER	INtegrated Structural Interactome & genomic Data browser
IoMT	Internet of Medical Things
ML	Machine Learning
MRI	Magnetic Resonance Imaging
MS	Mass Spectrometry
NLP	Natural Language Processing
NN	Neural Network
PA	Pulmonary Artery
QSAR	Quantitative Structure–Activity Relationship
RNNs	Recurrent Neural Networks
RVM	Relevant Vector Machine
SNNs	Stochastic Neural Networks
SRA	Sequence Read Archive
SVM	Support Vector Machine

2. Deciphering the Main Fields of AI

As an overarching computer science field, AI includes a plethora of applications that can be combined and influence almost every facet of our lives, thus improving efficiencies and augmenting human capabilities. Notably, six broad categories are worth mentioning: Machine Learning (ML), Neural Networks (NN), Deep Learning (DL), Robotics, Computer

Vision (CV), and Natural Language Processing (NLP) (Figure 1). Taken together, these computer-based approaches constitute the most demanding fields that have been extensively studied and are widely used in daily routine, expanding our toolkit of approaches in data analysis.

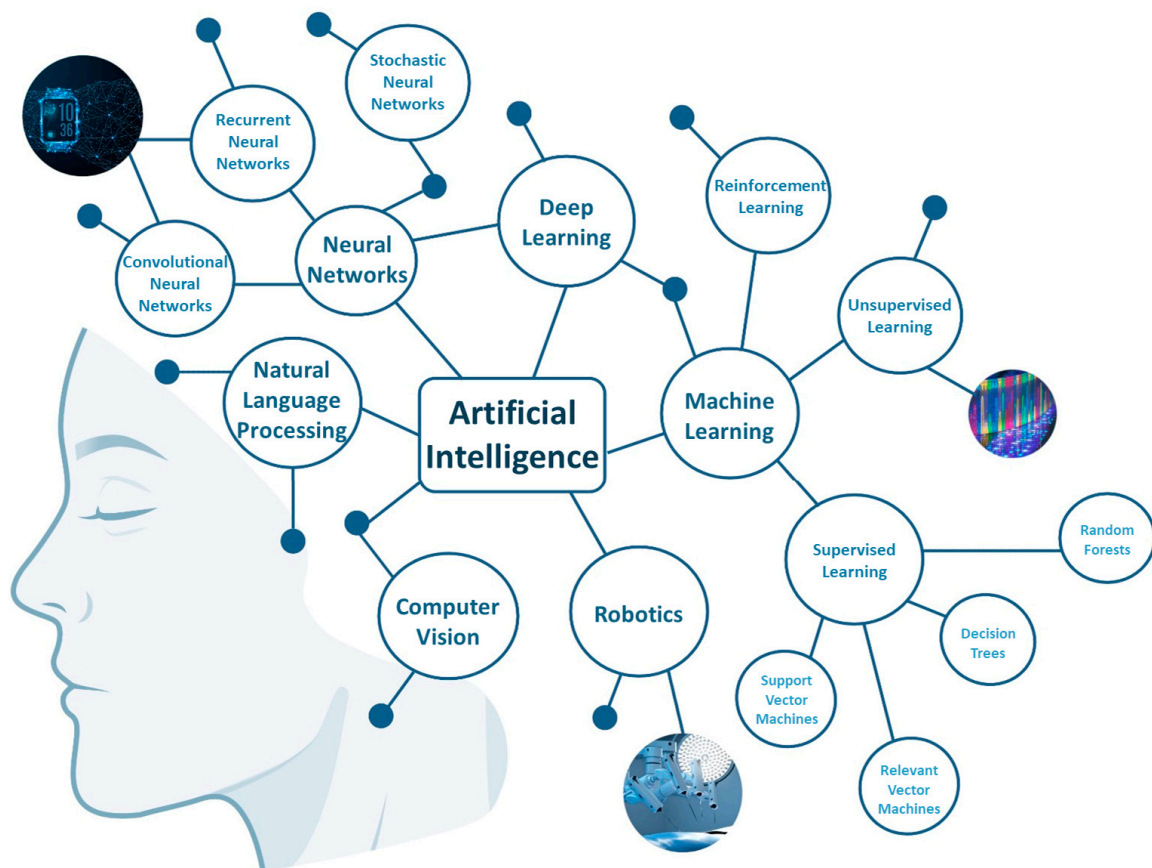


Figure 1. The six main fields of AI. ML includes three basic sub-subsets depending on the type of input and output data. NNs are divided into two distinct groups: CNN and RNN. DL combines the ML and ANNs methods. NLP, CV, and Robotics are additional types of AI.

As a scientific endeavor, ML falls within the scope of AI and constitutes an extensive and widely used method that enables computer systems to understand and self-learn from information without being explicitly programmed. ML algorithms build models based on a sample, named ‘training data’, to analyze the results, make predictions, and make decisions accordingly. Aiming to teach computers to accomplish tasks effectively, ML employs multiple approaches that can be divided into three major groups: supervised learning, unsupervised learning, and reinforcement learning (Figure 1) [12]. Algorithms that are based on supervised learning are trained with datasets in which both the input and output data are known. In this approach, the machine uses labeled datasets to classify data and build models that learn functions and can be used to predict the desired output.

Supervised learning algorithms are divided into two different types: regression and classification, based on whether the output variable is continuous or contains discrete values. Decision Trees, Support Vector Machines (SVMs), Relevant Vector Machines (RVMs), and Random Forests are additional groups of supervised learning that are commonly used in ML [13,14]. On the other hand, unsupervised machine learning algorithms use unlabeled datasets that include only inputs. Based on the features of the training data, the algorithms optimally separate the samples into classes. The unsupervised learning models perform cluster analysis, in which classification is achieved by grouping data points that share similar characteristics into clusters [15,16]. In reinforcement learning, the computer

program observes its environment and employs trial and error to come up with a solution to the problem, hence is trained to predict the features at a future step and, finally, obtain maximum reward [15,17,18].

Imitating the human brain, NNs or Artificial Neural Networks (ANNs) are composed of many interconnected nodes and are aggregated into multiple layers. More precisely, NNs can receive and recognize an input, and the multiple layers filter and process the information to provide a refined output using another neuron. NNs can be trained to handle digital information of great complexity, improve decision-making, and predict the desired outcomes. Convolutional Neural Networks (CNNs), Stochastic Neural Networks (SNNs), and Recurrent Neural Networks (RNNs) are all under the umbrella of ANNs [19]. The most applied CNN algorithms are mainly used for spatial datasets and are composed of at least three fully connected layers: an input layer, an intermediate layer that performs convolutions, referred to as hidden, and an output layer, whereas in SNNs, the models are built using random variations or stochastic weights, thus mapping is performed from a set of inputs to a set of probability distributions over the outputs. The main difference between CNN and RNN models is that the latter can process temporal information, which means that they recognize sequential or time series data by using previous outputs as inputs while having hidden states [20,21]. Consequently, CNNs employ filters within layers to transform data, whereas RNNs are predictive and reuse functions from data points to generate the next output in a series. Hence, CNNs and RNNs are used for completely distinct purposes.

DL algorithms combine ML and ANNs and are based on building models that are trained by learning from processing labeled information (Figure 1). Although DL eliminates some of the data by pre-processing, which is typically related to ML, it consists of three or multiple layers, creating an additional type of ANNs named Deep Neural Networks (DNNs) [22]. Of note, for complex tasks, DL can extract high-level characteristics from raw input; thus, the more data used, the more accurate the performance will be [11,23]. Additionally, computer science involves robotics, which aims to design machines that can substitute and/or assist humans. To continue, CV uses DL models to train machines to capture and understand high-level information from the visual world to perform accurate detection and classification of objects. Depending on the task, CV includes various types, including facial recognition, pattern detection, and image segmentation [24,25]. As far as NLP is concerned, it describes the ability of computers to understand and manipulate human language as it is spoken or written. In specific, NLP algorithms enable the processing and analysis of large amounts of natural language data, mainly used in speech recognition [26,27].

Combinations of these widely used AI-based technologies are becoming accessible in various fields, offering increased insights into solving challenging problems. It should be mentioned that, in some cases, AI algorithms can perform tasks more efficiently than humans. For instance, the proper programming of AI tools can reduce human errors, and such algorithms can reach a greater degree of precision. Moreover, AI-based machines can work continuously, hence being available 24×7 , while, in the same manner, AI can be used for performing many repetitive jobs, such as sending emails or verifying certain documents for errors or typos to remove time-consuming tasks from humans. Of note, AI has opened the door to entirely new opportunities in biomedical research, with the biggest bets being on improving healthcare and medical diagnosis.

3. AI in Life Sciences

The utilization of AI approaches and modern computing has dramatically reshaped the amount of biological data available and has the potential to transform the industry of life sciences. Especially, ML is becoming integral to modern biology since it generates predictive models from biological datasets [7,28]. More precisely, building models and constructing biological networks from multi-dimensional datasets are mainly used in structural biology and can be used to study complex systems. Furthermore, a growing number of AI applications that are available for ANNs, such as Genetic Algorithms, DL,

Random Forests, SVMs, and other methods, aim to enhance genomics research, address drug development processes, and support clinical trials [29]. AI is set to reduce the high level of healthcare costs and develop faster and more efficient treatments. Advances in AI are occurring across the spectrum of the biomedical field, ranging from primary research and large-scale data to target discovery and personalized medicine [30].

3.1. Applications of AI in Biology

The increased availability of multi-omics data has opened the way for the establishment of AI methods in modern biology. Interestingly, ML techniques are broadly used in biological areas for both molecular target prediction and drug discovery [7]. As far as the area of omics is concerned, the explosion of biological sequencing data has established ML as a key tool for a plethora of fields, including genomics, transcriptomics, proteomics, and structural and systems biology (Figure 2) [31].

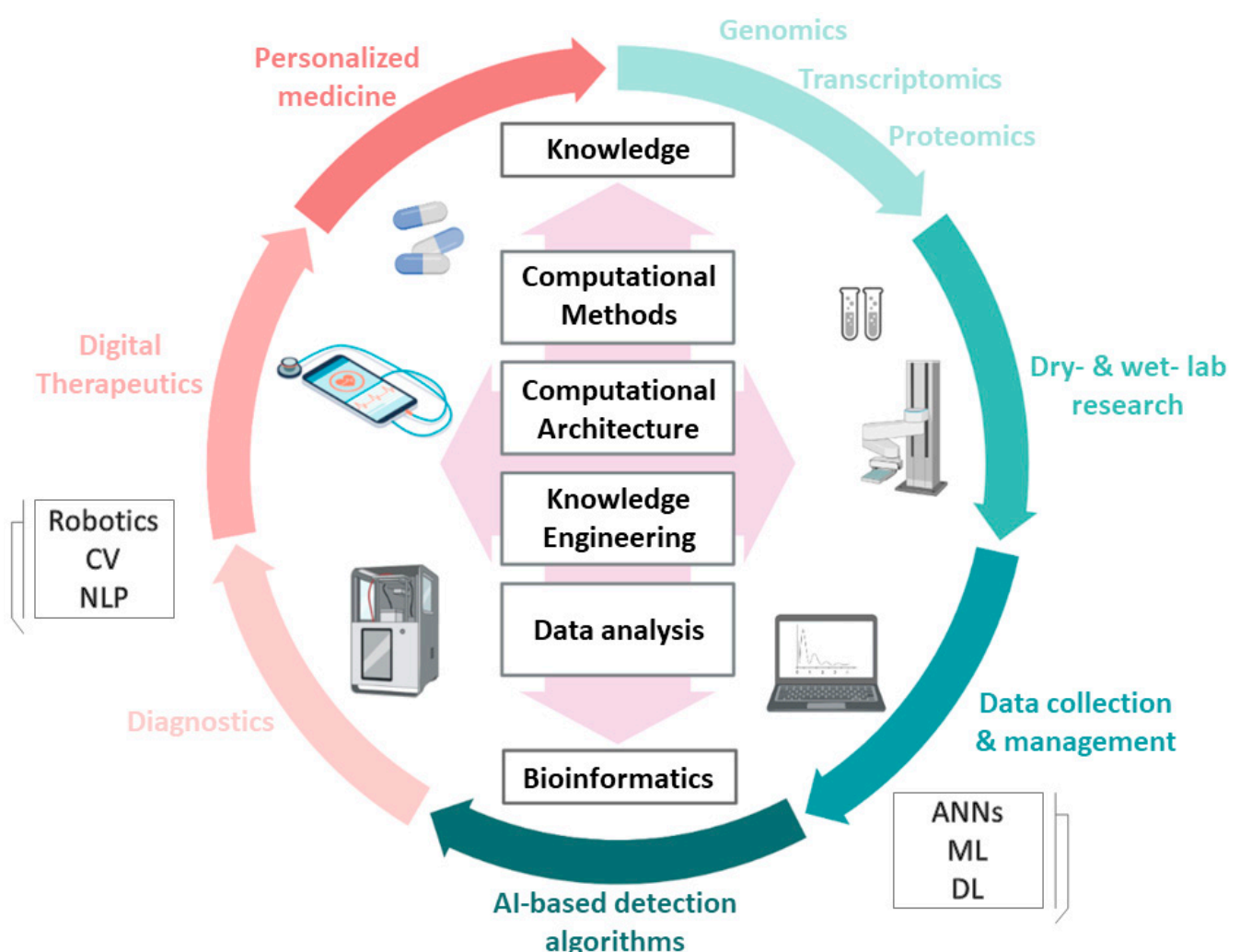


Figure 2. Illustration depicting the involvement of AI-based tools in the different levels of modern biomedicine.

Numerous computational genomics tools have been developed to recognize a given DNA sequence, predict genes, determine their functions, and estimate the location of protein-coding genes [32]. Remarkably, the Basic Local Alignment Search Tool (BLAST) is already counting 3 decades of life and still constitutes a simple and robust heuristic algorithm for the primary analysis of every DNA sequence, determining regions of similarity and mapping sequences to specific locations in a reference genome [33]. In the

same manner, Expressed Sequence Tag (EST) databases include an increasing number of raw data from the transcriptome [34], while the widely known Sequence Read Archive (SRA) database stores raw DNA, cDNA, and RNA sequencing data, as well as alignment information [35].

In recent years, the study of proteins' secondary structures, folding patterns, functions, and interactions constitutes a challenging task, and hence, both ML and ANNs have gained significant ground by providing thorough insights into the analysis of proteome and interactome [36]. Computational ML algorithms, such as SVMs and ANNs, can be categorized into two distinct groups: approaches that use sequence-based methods and approaches that employ structure-based methods [37,38]. In proteomics, ML software is used for the analysis of proteomic Mass Spectrometry (MS) data, the detection of individual proteins, and the examination of their potential as cancer biomarkers [39–41]. Notably, time-of-flight mass spectrometry (ToF-MS) constitutes a mainstream technique in which proteins are determined by measuring the ion's mass-to-charge (m/z) ratio [42]. For this purpose, a sequence-based ML tool named "ML-ToF" has been developed for recognizing MS peaks and analyzing datasets to match the generated labels to the confirmed ones, thus identifying amino acid sequences [43]. As for interactome studies, structure-based ML algorithms, such as SpotON, have already been developed for the prediction of hot-spot residues contributing to protein–protein interactions [44,45]. Moreover, Interactome INSIDER (INtegrated Structural Interactome and genomic Data browser), an additional structure-based ML tool, is also used for determining protein–protein interplays, including enriched information for mutations present in human diseases, such as cancer [46].

On the other hand, the evolving field of systems biology combines computational and mathematical analysis of complex biological datasets, aiming to identify molecular interactions and networks and understand tissue and even organism responses. Therefore, ML is used to build models that predict the binding affinity of every DNA, RNA and/or protein molecule, regulatory element, and region of interest. These regions can be derived from raw datasets generated by multiple omics sequencing approaches, such as DNA and RNA sequencing, MS approaches, formaldehyde-assisted isolation of regulatory elements with sequencing (FAIRE-seq), and self-transcribing active regulatory region sequencing (STARR-seq) [47–49].

AI-based algorithms can also focus on genomic and proteomic data analysis, with the main goal of predicting and treating diseases. Especially, ML and DL approaches can identify and target the disease mechanisms to enhance therapeutic strategies. For instance, bioinformatics analysis of the gut microbiome data from metagenomics studies has led to the identification of many host diseases, such as *Clostridium difficile* infection (CDI), toxoplasmosis and Irritable bowel syndrome [50–53], while predictive ML models, such as SVMs and Random Forests, and ANNs algorithms, such as DNNs and CNNs, have been established for the detection of microbiome–host interactions [54–56]. For instance, a plethora of AI-based tools, including DISBIOME and gutMDisorder, have been employed for connecting the gut microbiome with various human diseases, whereas publicly available databases (e.g., GMrepo v2 and gcMeta) provide a comprehensive resource of raw and processed data from metagenomic sequencing experiments [57–60]. Additionally, PopPhy-CNN is an AI-based algorithm that is used for the prediction of the host phenotype from metagenomic datasets [61]. In the same manner, Read2Pheno constitutes a deep network architecture that identifies nucleotide regions in sequencing reads and performs read-level phenotypic predictions for the accurate taxonomic classification of microbiome sequences [62].

Another discipline that encompasses massive biological datasets that are amenable to AI is the field of drug discovery. Notably, a large amount of biomedical data, containing information ranging from primary DNA sequences to complicated interaction networks, is necessary for generating novel drugs and new treatments. Indicatively, PubChem [63], DrugBank [64], and ChEMBL [65] are widely used public repositories that store a great amount of omics data. More precisely, PubChem includes chemical molecules, their special

features and their activities against biological assays, whereas DrugBank specifies the clinical applicability of both candidate and approved drugs. On the other hand, ChEMBL contains a detailed collection of the dynamic relationships between drug targets and their ligands. Furthermore, multiple studies aim to combine information from publicly available databases to detect molecules that can represent promising candidates for the development of efficient drugs for various diseases [66,67]. Interestingly, over the past decade, ML and DL methods for molecule design have evolved and been developed to address target–ligand interactions and identify potential drugs [67,68]. Specifically, ML methods manipulate the available data to perform massive permutations and combinations of datasets to design the molecular structure of a potential drug and predict its biological activity. ML is applied in all stages of the drug discovery process, starting from preliminary steps, such as designing the chemical structure of the potential drug and investigating the drug’s effectiveness, till the final FDA approval (Figure 3). Additionally, ML-based algorithms can be trained on high-throughput screening datasets to develop models that are able to predict patients’ responses to novel drugs or drug combinations [69].

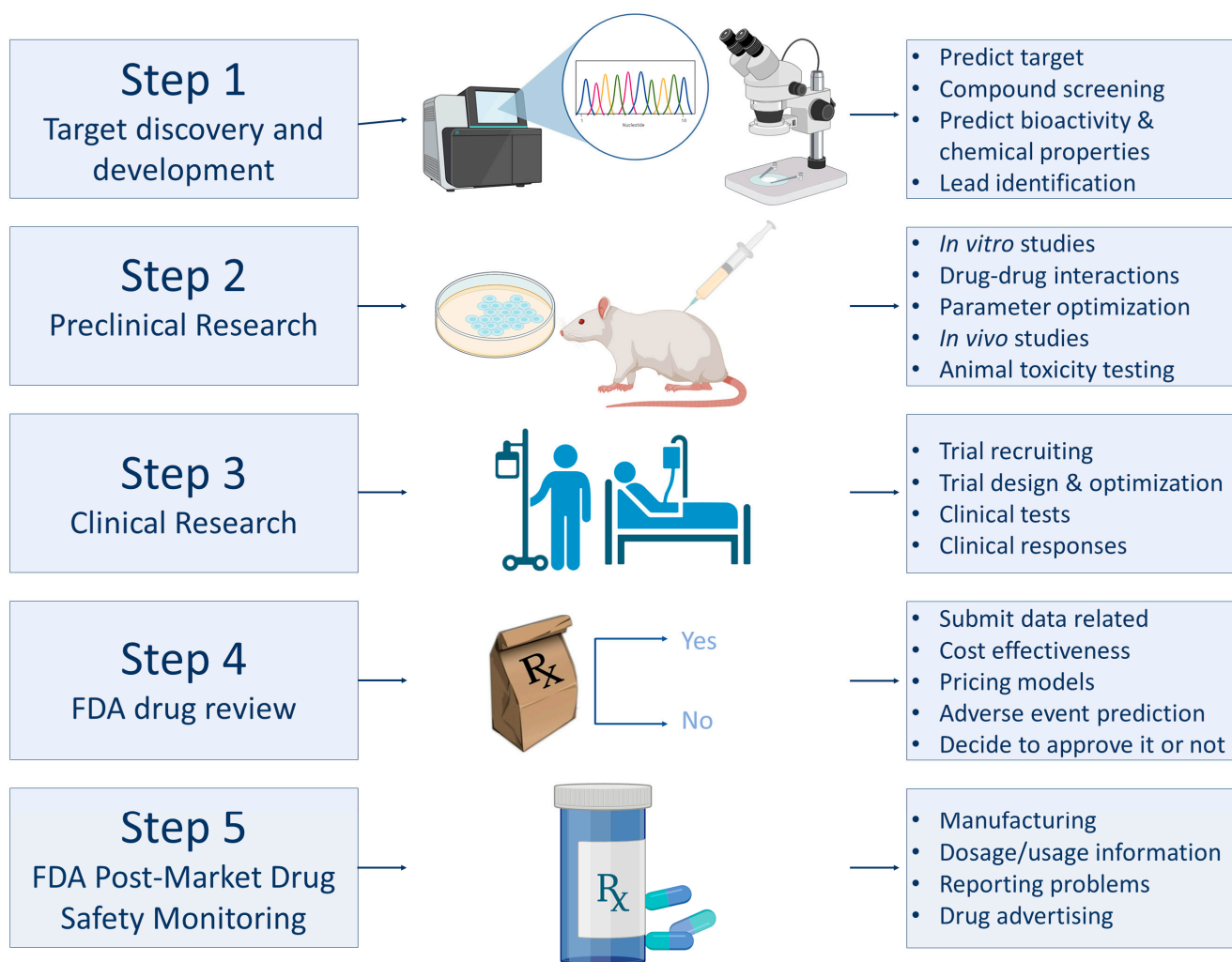


Figure 3. The 5 phases of drug design and development process. The phases are divided into the basic research and the early discovery phase (step 1), pre-clinical trials (step 2), the clinical development phase (step 3), the FDA review process (step 4), and finally the post-marketing surveillance phase (step 5).

Finally, one of the most popular computer-aided approaches for prediction model development is the quantitative structure–activity relationship (QSAR) method [70], which

constitutes a widely accepted predictive and diagnostic tool used for finding associations between chemical structures and biological activity [71,72]. Specifically, QSAR modeling has been developed to predict the physicochemical properties of biomolecules. This information can then be used to generate *in silico* models, which can estimate the functions and activities of novel molecules prior to their synthesis [73]. Overall, different AI tools eliminate the challenges of traditional drug design by manipulating biomedicine data across various applications, including QSAR analysis and *de novo* drug design, to reduce risk failures, improve decision-making, and retrieve accurate outcomes [74].

Ultimately, the goal of computational biology is the combination of different levels of genetic information to uncover hidden aspects of cellular mechanisms. Under the prism of disease biology, AI-based methods contribute to early detection and diagnosis, whereas ML and DL tools will encourage further drug design studies that will achieve both effectiveness and safety in future therapeutic strategies.

3.2. Applications of AI in Medicine

Spurred by the astonishing cascade of biological data, the constant advances in computational power and storage, as well as the ground-breaking improvements in ML approaches, AI is losing its science-fictional hypostasis and, apart from biological research, is also dynamically infiltrating the medical realm. Even though the roots of the first clinical-decision AI systems date back to the 1970s, in recent years, DL has constituted the most dominant approach that aspires to ensure accurate and rapid diagnosis, assist decision-making, reduce human errors, facilitate medical procedures, and globally improve the efficiency of health systems [75].

First and foremost, improving medical diagnosis through image analysis represents one of the most radical and successful applications of AI in medical practice. Over the years, a wide array of algorithms has been proposed, primarily utilizing DNNs, such as ANNs with multiple hidden layers, which are capable of examining diverse medical scans and detecting numerous pathological conditions in less time and with higher accuracy compared to human experts [76]. Beyond a shadow of a doubt, radiology is the field that has made the most of AI's unprecedented capabilities so far due to the need for more trained readers to cope with the skyrocketing amount of imaging data and the fact that both input and output data are already digital and ready-to-be-used by DL [77,78]. Therefore, X-rays, computed tomography (CT) scans, mammographies, and magnetic resonance imaging (MRI) images can be interpreted by DL algorithms and be used to carry out complicated diagnoses, including lung diseases [79–82], lung nodules [83], bone fractures [84], brain hemorrhages [85], breast masses [81,86], and cancer [87].

Apart from that, the advent of whole-slide imaging (WSI) and, consequently, the rise of digitalized histopathology slides allows the implementation of AI in the precise detection, classification, and prognostic evaluation of a vast number of cancer types [88], whereas electrocardiograms and dermatological, ophthalmological, and endoscopy images can also be analyzed for the accurate and rapid characterization of cardiomyopathies [89], skin lesions [90], eye conditions [91], and colon polyps [92], thus broadening the applications of DL in an ever-increasing range of medical fields (Table 2).

Robotics represents another rapidly developing application of AI, which during recent decades, has gained more and more ground in the surgical branch of medicine. Initially introduced in 1985, surgical robotic systems are constantly entering operating rooms, mainly assisting surgical procedures and providing accuracy and stability in surgical motions while still being manipulated or supervised by human experts [93]. For instance, the FDA-approved da Vinci[®] Surgical System (Intuitive Surgical, Sunnyvale, CA, USA) constitutes one of the most encountered robotic systems in minimally invasive surgeries, which through multiple robotic arms remotely controlled by a console, can mirror a surgeon's hand movements and offer precision in motions and the filtering of tremors (Table 2) [94]. Moreover, great progress is being made toward the development of autonomous robots that can carry out specific tasks on their own, thus aiding and saving valuable time in surgical

practice. Remarkably, robots that can autonomously perform suturing and cochleostomy have already been developed and, hopefully, further progress in DL and CV will result in the beneficial automation or semi-automation of numerous medical procedures [95,96].

Furthermore, the immense volume of available clinical data can be successfully processed by ML and DL algorithms to foresee clinical outcomes, monitor patients in real time, estimate risk factors, and diminish medical errors in health centers [97]. For instance, by using information from electronic health records (EHRs), such as medical history, medications or lab results, AI can make predictions on whether a patient would benefit from a specific medical procedure (e.g., surgery) or therapy (e.g., chemotherapy) and estimate the potential risk of experiencing post-surgical complications [98], developing specific diseases [99], experiencing septic shock [100], and being readmitted to the hospital or even predict hospital inpatient mortality [101].

In addition to improving clinical decision-making and personalized healthcare, analyzing EHRs and predicting the duration of hospital stay and the probability of discharge, readmission, or mortality can also assist in estimating waiting times in emergency rooms, allocating hospital resources, and better preparing for patients' hospitalizations, hence efficiently facilitating hospital management and healthcare quality [102,103]. In addition, data on patients' vital signs collected by health monitoring devices in intensive care units, coronary care units, operating rooms, other hospital wards, or even remotely from home can be analyzed by AI algorithms in order to detect abnormalities, predict risk situations (e.g., cardiac arrest, sepsis, hypoxemia, etc.), and alert clinicians so as to immediately provide the appropriate medical care, thus rendering AI life-saving in clinical emergencies [104,105].

Table 2. Examples of U.S. Food & Drugs Administration (FDA)-approved AI applications in the field of medicine.

	AI Algorithm	Description	Applications	Reference
Medical image analysis	Arterys Cardio DL	Automated analysis of cardiac MRI scans	Radiology Cardiology	[106]
	Arterys Oncology DL	Detection of liver lesions and lung nodules on MRI and CT scans	Radiology Oncology	[107]
	EchoMD Automated Ejection Fraction Software	Echocardiogram analysis for evaluation of the left ventricular ejection fraction	Radiology Cardiology	[108]
	HealthPNX	Assessment of chest X-rays for signs indicative of pneumothorax	Radiology	[109]
	icobrain	Analysis of brain CT and MRI scans of patients with brain injuries and neurological disorders	Radiology Neurology	[110,111]
	IDx-DR	Analysis of retinal images for diabetic retinopathy detection	Ophthalmology	[112]
	OsteoDetect	Analysis of wrist X-rays for fracture diagnosis	Radiology	[113]
	ProFound™ AI Software V2.1	Analysis of breast density and detection of malignant lesions using mammograms	Radiology Oncology	[107,114]
	QuantX™	Diagnosis of breast lesions through MRI scans analysis	Radiology Oncology	[115]
	Viz LVO	Detection of signs of stroke using CT angiography scans	Radiology Neurology	[116]

Table 2. Cont.

	AI Algorithm	Description	Applications	Reference
Surgical robotics	Da Vinci® Surgical System	Telemanipulated minimally invasive robotic system with robotic arms that translate user's hand movements, providing precision and filtering of tremors	Prostatectomies, gynecological, urological, gastrointestinal, cardiothoracic surgeries	[94]
	Flex® robotic System	Flexible robotic endoscope that allows surgeons to access and visualize anatomical areas which normally are inaccessible by minimally invasive approaches	Minimally invasive surgeries of larynx, oropharynx and hypopharynx	[117]
	FreeHand® v1.2	Robotic camera controller that provides steadier images, better control of camera movements and reduced surgical time	Minimally invasive and laparoscopic surgeries (gynecological, urological, thoracic, general)	[118]
	NAVIO™ Surgical System	Handheld robotic system that offers real-time bone mapping, planning of implant positioning and robotic-assisted bone preparation	Knee arthroplasty	[119]
	NeoGuide™ Endoscopy System	Computer-assisted colonoscope that enables visualization of the lower gastrointestinal (GI) tract, adjusting to colon's shape and thus decreasing looping	Colonoscopy	[120]
	Senhance® Surgical System	Remotely controlled robotic system with three robotic arms, providing improved visualization and haptic feedback	Laparoscopic surgeries (abdominal, gynecological, urological)	[121]
	Sensei® X Robotic Catheter System	Remotely manipulated cardiac catheter that translates surgeon's hand motions, providing stability during catheter positioning	Catheter positioning	[122]
Remote patient monitoring	ADAMM Intelligent Asthma Monitoring	Wearable device attached to the torso that monitors asthma symptoms and alerts in cases of significant deviations	Pulmonology	[123]
	CardioMEMS™ HF System	Wireless monitoring system that records pulmonary artery (PA) pressure in patients with heart failure through an implantable PA sensor. The daily data are sent and assessed by the healthcare provider	Cardiology	[124]
	Confirm Rx™ Insertable Cardiac Monitor	Insertable device that monitors patients' heart rhythms, detects signs of arrhythmia and transmits data to clinicians	Cardiology	[125]
	ReDS™ System	Device that rapidly and non-invasively measures the absolute fluid content in the lungs of heart failure patients.	Cardiology	[126]
	Triggerfish®	Contact lens, embedded with a microsensor, that monitors (for 24 h) ocular dimensional alterations and thus intraocular pressure variations in patients with glaucoma	Ophthalmology	[127]

Table 2. Cont.

	AI Algorithm	Description	Applications	Reference
Personal biosensing devices	Eversense® E3 Continuous Glucose Monitoring (CGM) System	A system utilizing an implantable glucose sensor that regularly monitors glucose levels, a transmitter worn externally and a mobile application for real-time data display	Clinical Chemistry	[128]
	Fitbit	Smartwatch that monitors physical activities, sleep and can detect signs of atrial fibrillation	Cardiology	[129]
	KardiaMobile® 6L	Portable heart monitor that detects heart arrhythmias	Cardiology	[130]
	Study Watch with Irregular Pulse Monitor	Wearable device that records biometric information, such as heart's electrical activity, and detects irregular heart rates	Cardiology	[131]

Finally, in this era of the rapidly expanding fields of AI, Internet of Medical Things (IoMT), Big Data and biosensing, healthcare has reached a point where “taking matters into our own hands” has finally turned into reality [98]. The advent of biosensing devices (mobile, wearable or even implantable in human tissues) that can analyze a person’s physiological parameters (e.g., heart rate, blood pressure, temperature, etc.) and measure the concentration of biological analytes in body fluids (e.g., glucose, alcohol, etc.), has given people the opportunity to easily access their own health data on their smartphones, keep track of their biomedical signals, efficiently monitor symptoms, and even detect diseases at early stages [132]. For instance, continuous glucose monitoring through implantable biosensors allows the around-the-clock detection of glucose levels and their real-time display on a mobile application, thus constituting a much more time-consuming and painless alternative compared to the conventional finger-pricking method [133].

Moreover, numerous wristbands and smartwatches have already been developed for monitoring vital signs during physical activities, analyzing the sleep cycle and quality, and identifying conditions such as heart arrhythmias or sleep apnea, while several apps employing image recognition are currently being used to assess the nutritional and calorie content of food [134,135]. Particularly, due to their ease of use and cost-effectiveness, the market of wearable technology in healthcare is expected to rise even more, continuously integrating biosensors in an unimaginable scope of devices and accessories such as glasses, t-shirts, belts, socks, mouthguards, and contact lenses (Table 2). All of these are just the tip of the iceberg of what the world is going to witness in the coming years [136,137].

4. Challenges and Future Directions

Despite the widespread enthusiasm surrounding the incorporation of AI in biomedical sciences, there are still numerous non-negligible challenges lying ahead that need to be addressed. To begin with, the precision and applicability of ML algorithms in different and complex real-life scenarios are highly dependent on the quantity and quality of the datasets used to train each model. “Overfitting”, for instance, constitutes a characteristic problem in which the prolonged training on a restricted set of sample data can lead to the algorithm memorizing the noise and statistical variations of this specific sample—hence performing perfectly within this—but at the same time failing to generalize to broader and more diverse datasets [138]. In addition, low-quality training data can also reduce an algorithm’s prediction performance, underlining the need for not only utilizing larger datasets but also meticulously preparing data before training via internal or external validation and feature selection to diminish noise and eliminate the most irrelevant and/or redundant variables used for model construction [139,140].

Furthermore, the “black box problem” represents one of the major concerns regarding DL approaches. More specifically, it refers to the inability to observe the decision process of an algorithm, interpret how it arrives via numerous neuron connections at a specific outcome, and understand which of the features of the input data contributed to the final output [141]. Due to this non-transparency of how DL algorithms work, it becomes difficult to extract additional information, spot weaknesses, and make improvements to the models employed [8,142], while it also hampers AI’s implementation in daily routine, particularly in clinical practice, where interpretable AI-based systems are preferred [143]. Therefore, numerous efforts are being made towards the construction of more explainable AI models, as well as the development of methods attempting to interpret DL algorithms, for example, by visualizing CNNs’ filters or by utilizing saliency and class activation maps [144,145].

On the other hand, CV and robotics are primarily hindered by the shortage of diverse and high-quality datasets (e.g., multiple patients, different physiological and pathological conditions, a wide range of anatomical areas, different viewpoints, etc.), the need for appropriate technical and computing facilities, and the significant installation and maintenance costs [146–148]. As far as NLP is concerned, it is restricted by the small availability of open-source data, the use of jargon, slang, idioms, or synonyms in text or speech, the frequent presence of typos or mispronunciations, as well as data privacy and security issues. Moreover, a lack of consensus in the naming, definition, and relations between the concepts of specific domains pose additional obstacles to the extensive utility of NLP models, which can, however, be addressed with the establishment of standardized vocabulary and the further development of ontologies [149,150].

Finally, apart from the technical challenges concerning the integration of AI in the fields of biological research and medicine, there are also several social and legal issues coming forth. Increased ethical concerns have ensued with the advent of AI regarding matters such as the protection of privacy, patient confidentiality, biases, and inequity due to the exclusion of minorities from algorithms’ datasets and the replacement of human workers [76,151]. Moreover, the “black box” nature of AI is raising questions of accountability and medical liability (e.g., in cases of erroneous predictions), thus underlining the need for thorough validation and regulatory approval to ensure the transparency, safety, equity, and efficiency of the proposed AI tools [138]. Hence, even though bridging AI and biomedical sciences show great promise, the road ahead is still tortuous and full of a substantial number of obstacles to overcome.

5. Concluding Remarks

As global biomedical research is on the cusp of an exciting digital era, we are only in the early stage of deploying AI in life sciences. As for the field of biology, the vast amounts of multiscale data can be interpreted holistically through well-established AI-based applications to obtain a deep insight into the molecular mechanisms of the cells and tissues that are related to normal and pathological conditions. On the contrary, as far as the healthcare system is concerned, developing AI strategies is set to become widespread within the next decade, facilitating the opportunity to replace traditional and time-consuming diagnostic approaches, produce more effective drugs, and automate AI-powered surgical robots. Ultimately, although AI advances will result in broad investment across the biomedical industry and their impact will be far-reaching, AI will augment, but not replace, human expertise.

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