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Original Article

A Review of Biosensors and Artificial Intelligence in Healthcare and Their Clinical Significance

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Abstract: *In the past decade, a substantial increase in medical data from various sources, including wearable sensors, medical imaging, personal health records, and public health organizations, has propelled advancements in the medical sciences. The evolution of computational hardware, such as cloud computing, GPUs, FPGAs, and TPUs, has enabled the effective utilization of this vast amount of data. Consequently, sophisticated AI techniques have been developed to extract valuable insights from healthcare datasets. This article provides a comprehensive overview of recent developments in AI and biosensors within the medical and life sciences. The review highlights the role of machine learning in key areas such as medical imaging, precision medicine, and biosensors designed for the Internet of Things (IoT). Emphasis is placed on the latest progress in wearable biosensing technologies, where AI plays a pivotal role in monitoring electrophysiological and electrochemical signals and aiding in disease diagnosis. These advancements underscore the growing trend towards personalized medicine, offering precise and cost-efficient point-of-care treatment.*

Additionally, the article delves into the advancements in computing technologies, including accelerated AI, edge computing, and federated learning specifically tailored for medical data. The challenges associated with data-driven AI approaches, potential issues arising from biosensors and IoT-based healthcare, and distribution shifts among different data modalities are thoroughly explored. The discussion concludes with insights into future prospects in the field.

Keywords: *Artificial Intelligence, Elucidatable AI, Medical Imaging, Biosensors, Federated Learning, Domain Adaptation, Analytics Of Vast Datasets, and Extensive Language Models.*

I. INTRODUCTION

Approximately 10% of the global Gross Domestic Product (GDP), equivalent to 10 trillion USD, is allocated to healthcare annually [1]. Recent technological advancements, particularly in data-driven methodologies and computational processing capabilities, have the potential to benefit both patients and the medical industry by mitigating substantial expenditures. The availability of extensive healthcare data from diverse sources, including Electronic Health Records (EHRs), genomics profiles, medical imaging, chemical and drug databases, presents an opportunity for leveraging analytical methods, particularly those based on deep learning Artificial Intelligence (AI), to create valuable clinical and medical applications capable of processing these voluminous datasets. Data-driven approaches hold promise in areas such as medical record digitization, clinical trials, diagnosis support, prognosis evaluation, and the development of optimal prevention and treatment strategies. Additionally, these methods contribute to advancements in precision medicine, drug discovery, and health policy. The evolution of computational infrastructure has empowered the generation, storage, analysis, and visualization of large, intricate, and dynamic datasets inherent in contemporary biomedical studies [2]. Clinical trials are exploring new treatment options, with artificial intelligence transitioning from theoretical studies to real-time applications over the past decade, thanks to the enhanced computational capacities of GPUs and TPUs. Methods like AutoML [4] and explainable artificial intelligence (XAI) [5] are making significant strides and have the potential to revolutionize current medical practices. However, despite these advancements, several challenges hinder the full realization of the potential of analytical methods in the healthcare sector. Critical challenges for data science in medicine include issues such as data collection, standardization of data formats, handling missing data values, establishing large and efficient computational infrastructure, and ensuring data privacy and security, among other considerations.

To address the issue of limited sample sizes in medical images, one approach involves the use of generative models to produce high-quality synthetic medical images. A specific type of neural network, known as a Generative Adversarial Network (GAN), is capable of generating synthetic data, including Magnetic Resonance Imaging (MRI) scans or positron emission tomography (PET)-scan images, by utilizing computed tomography (CT) scans. Regardless of the size, a subset of images is essentially a subset of the universal set. Generative models leverage this smaller subset to learn the probability distribution of the overall training set. Once representative features are extracted, the model can generate high-quality synthetic images by sampling from this learned probability distribution. These synthetic images, in turn, can be employed to construct generalized models for medical image analysis applicable to various clinical scenarios. The interconnected nature of biomedical data stands out as one of its paramount characteristics, often represented in the form of graphs. Employing graph machine learning enables the modeling of unstructured multimodal datasets, allowing for the exploration of more intricate relationships between diseases and patients. This approach proves valuable in understanding tumor microenvironments, predicting drug responses, and exploring repurposing possibilities. Furthermore, when coupled with attention mechanisms, graph machine learning may offer machine learning models that are more interpretable compared to conventional black-box models.

A recent groundbreaking achievement in artificial intelligence is exemplified by the Alphafold2 system, which successfully predicts the three-dimensional structure of proteins based solely on their amino acid sequences. Notably, Alphafold2 emerged victorious in the Critical Assessment of Structure Prediction (CASP), a global event for protein structure prediction held since 1994. Meta AI has also made strides in this domain, developing an AI system capable of predicting structures for approximately 600 million proteins. However, the challenge lies in translating these accomplishments to in vivo situations. While AlphaFold2 excels at predicting unbound protein structures, practical applications often require predictions for protein-drug complexes, posing an ongoing question in the field. Significant progress has occurred in processing power and biosensor technologies. For instance, the utilization of parallel processing methods and robust GPU clusters like NVIDIA-DGX enables the efficient processing of vast and intricate multi-dimensional biomedical datasets [9]. Furthermore, the integration of wearable electronics, including electronic tattoos (E-tattoos), Epidermal Electronics Systems (EES), and flexible electrochemical bioelectronics, along with machine learning algorithms, facilitates real-time monitoring of diverse biomarkers [10]. Given the active research interest in the integration of AI in healthcare, multiple surveys have explored this domain [11], [12], [13]. In [11], there is an in-depth discussion about incorporating medical sensors with artificial intelligence, covering various sensing systems and their application in medical decision-making. The survey in [12] focuses on wearable sensors for healthcare delivery, primarily examining them from a hardware perspective, and briefly touches on the advantages and challenges associated with AI. Recent work [13] delves into the utilization of AI in the Internet of Medical Things, exploring its diverse applications and algorithms, particularly in addressing various medical conditions. The survey presented in [14] centers around AutoML methods.

Given the substantial advancements in AI for healthcare in recent years, providing an updated review is crucial for the community. This article presents a comprehensive survey of recent developments in data-driven methods within the healthcare domain. The focus is specifically on practical applications of artificial intelligence, biosensors, and computational infrastructure directly impacting clinical relevance. Evaluation of emerging methods with the potential to integrate into the healthcare industry, such as AutoML [15], explainable AI [16], and Federated learning [17], is a key aspect. The article also introduces existing clinical tools and emerging AI-based start-up companies while shedding light on the prevailing challenges in AI for healthcare and proposing potential solutions. It is important to note that the scope of this review excludes the use of AI in drug discovery, nano-medicine, and medical robotics. The survey is organized into various sections, starting with Section II, highlighting machine learning applications in different healthcare sectors. Sections III, IV, and V delve into AI-based clinical tools, start-up companies, big data analytics, and biosensors, respectively. Section VI discusses computational advances, federated learning, and edge computing. The article concludes with Section VII addressing recent challenges in AI for healthcare, along with potential solutions, and Section VIII serves as the conclusion of this comprehensive review.

II. MACHINE LEARNING IN HEALTHCARE

Data science and machine learning have demonstrated success in various computer vision domains, including self-driving cars, action recognition, image classification, and intelligent robots. These tasks are well-defined and verifiable, with known problems and solutions. However, healthcare-related applications introduce safety and security concerns, raising privacy issues. Unlike well-defined problems, healthcare tasks are often broad, complex, and challenging to verify. An example is assessing the risk of life-threatening diseases, such as those caused by the SARS-CoV-2 virus, where data science is employed to identify prognostic indicators from diverse genetic and physiological markers and symptoms [18]. Figure 1 illustrates an ecosystem for machine learning in healthcare tasks. Machine learning not only generates actionable insights for clinical practice but also offers recommendations for optimal health policies to governments and aids in expediting and enhancing drug discovery and design processes. Table 1 outlines established use cases for various machine learning applications in healthcare.

A. Explainable Artificial Intelligence

While machine learning models applied to biomedical data have the potential to yield clinically valuable insights, particularly in the case of deep learning, these models are often perceived as opaque “black boxes” that are challenging for humans to comprehend [5]. This lack of transparency creates a bottleneck in the clinical adoption of machine learning findings, as decisions directly impact patient health. One approach to enhance transparency in machine learning predictions involves emphasizing feature importance or visualizing features at different layers. This allows for analyzing each feature's significance in the prediction model, leading to a better understanding of predictions. An example of this method is the Grad-CAM visualization [19], which relies on gradients flowing into the final convolutional layer based on the target concept to construct a localization map highlighting crucial locations or heat maps in the image for concept prediction. Explainable models, or explainable artificial intelligence, are essential to instill trust among healthcare professionals. Explainable AI methods are categorized based on the complexity and extent of their interpretability, as outlined in a classification scheme [20]. The classification takes into account the level of dependencies in the AI model. Explainability encompasses various aspects, including interpretability, stability, robustness, and confidence. In an interpretable system, users can not only observe but also understand how inputs are mathematically transformed into outputs. A stable system is not easily misled by minor perturbations or noise in the input data. Confidence measures the likelihood of a particular event occurring, aiming to quantify the level of confidence in the decision-making process [21]. In the realm of complex deep learning models, interpretability tends to be lower, and there often exists a trade-off between accuracy and interpretability. Designing models that are easy to interpret is a potential avenue to address this challenge. However, this interpretability may come at the cost of compromising accuracy. In the realm of Explainable AI (XAI), highly complex and uninterpretable models with high accuracy are commonly employed, necessitating a separate set of algorithms for interpretation. Another approach to achieving explainability involves examining whether the model is agnostic or model-specific. Agnostic methods can be applied to any machine learning algorithm, including neural networks and support vector machines, while model-specific methods are tailored to interpret a specific model [22]. Considering human factors is crucial in enhancing model interpretability, involving collaboration with domain experts, such as medical professionals, to ensure the interpretability and comprehensibility of the model. The ongoing development of Explainable AI is expected to advance research in machine learning for healthcare, addressing critical challenges such as fairness, safety, security, transparency, privacy, and trust.

a) Human And Machine Interpretable Visualizations

A critical facet of Explainable AI involves employing human-interpretable visualizations that facilitate understanding the reasoning behind AI models. For instance, decision trees, rule lists, and other interpretable models can be visually presented in a manner easily comprehensible to humans. In addition to techniques for human interpretation, the integration of machine-interpretable visualization techniques is equally significant in Explainable AI. These techniques enable AI models to elucidate their predictions or decisions in a way that other AI systems can readily understand. An illustration of a machine-interpretable visualization technique is SHAP (SHapley Additive exPlanations) [23], which is employed to explain the output of complex machine learning models, including deep neural networks. However, interpreting models with billions of parameters poses challenges, as is common in deep learning models. For example, visualizing the grad-cam heatmap for a dog may reveal concentration around the dog's ears, but interpreting such patterns can be challenging for humans, as deep learning models operate differently from human cognition.

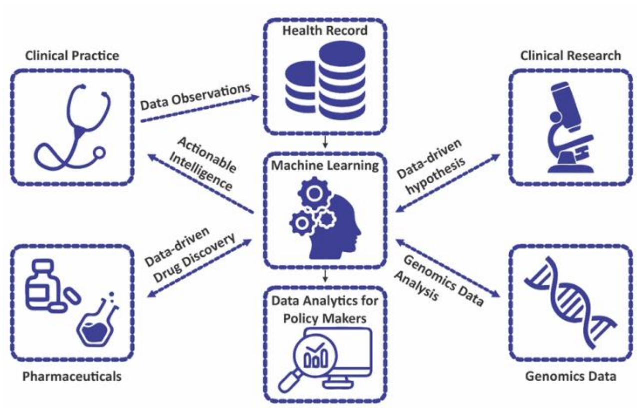

Figure 1: Machine Learning Ecosystem in the Healthcare Sector Machine learning techniques can be advantageous for pharmaceutical businesses, policy makers, and clinical decision support systems.

b) Causal Inference

Tasks related to health science require more than just predictions. In the presence of abundant data, many deep learning algorithms tend to focus solely on identifying correlations among variables, leading to predictions or classifications without providing explanations for the underlying causes. For these machine learning models to be practically applicable in daily clinical settings, it is imperative that they offer robust causal evidence. Several methods have been devised to transform the opaque nature of deep learning models into transparent ones. Examples include feature visualization [24], gradcam visualization [25], regularization through causal graph discovery [26], causal-aware imputation employing learning missing data mechanisms [27], domain adaptation [28], and tools such as Shared Interest [29] and learning generalized policies [30]. Causality can be delineated in three distinct stages. The initial stage involves association, exemplified by the relationship between a training image and its corresponding label. The second stage is intervention, where the objective is to forecast outcomes by modifying the system, such as implementing a treatment plan or altering patient conditions. The final stage is counterfactual, predicting the output in an alternative condition and environment. Causal machine learning models play a pivotal role in providing guidance for making informed and timely interventions, prompting a reconsideration of various treatment regimens and anticipated outcomes.

B. Machine Learning for Precision Medicine

Conventional medical models have historically adopted a ‘one size fits all’ approach, treating the average patient uniformly. The evolving field of precision medicine, however, embraces a personalized treatment paradigm that considers an individual patient’s distinctive clinical, genetic, epigenetic, and environmental information. This approach is gaining prominence in healthcare, facilitated by the growing volume of medical data [31]. Figure 2 illustrates a conceptual diagram depicting precision medicine leveraging various data modalities. Data encompassing a patient’s age, weight, blood pressure, medical history, and genomic sequences can be analyzed by algorithms to unveil hidden patterns and establish correlations between patient profiles and disease phenotypes. An example of a personalized drug response model is seen in the case of non-small cell lung cancer patients [32], where the binding free energy of a drug-mutant complex, along with personal patient features (such as age, sex, smoking history, and medical history), was utilized to construct a tailored drug prediction model. Extreme learning machines were employed to predict drug responses into two classes with an impressive overall accuracy of 95%, bolstered by including personal features. Personalized medicine finds application in treating complex diseases like cancer, heart disease, and diabetes [33]. If employed judiciously, this technology holds the potential to enhance healthcare performance and possibly mitigate disparities.

C. AI in Remote Patient Monitoring

The integration of edge artificial intelligence (machine learning on edge devices) with the Internet of Things (IoT) has facilitated the implementation of remote healthcare systems. These systems have the capability to monitor a patient’s vital signs and other physiological parameters in real time, allowing patients to stay at home while the data is transmitted to the cloud [34]. Incorporating AI into smart devices democratizes healthcare by bringing AI-enabled health services, such as AI-based clinical decision support, directly into patients’ homes or remote healthcare settings [35]. The centralized data collected from patients can be utilized for knowledge discovery, enhancing disease prognosis, or enabling doctors to monitor patients and make/update prescriptions. Numerous commercial wearable devices offer services for measuring physiological parameters, including heart rate, ECG, and other variables, through smartwatches and biosensors. Targeted systems have also been proposed for various health conditions, such as diabetes [36], where devices can assist in insulin management [37], cardiac disease through ECG [38], sleep apnea monitoring [39], or generic monitoring platforms like smart-monitor [40] that provide a flexible system based on the patient’s health circumstances. Machine learning methods can then be applied to these physiological signals to enable predictive health management.

III. CLINICAL AI TOOLS AND EMERGING AI HEALTHCARE COMPANIES

The central inquiry revolves around the timing of the integration of AI tools into routine clinical practice, specifically for addressing real-time health challenges such as enhancing diagnostic capabilities and clinical decision support systems [41]. While AI holds significant promise in overcoming crucial healthcare challenges, several issues need addressing regarding its implementation. This section explores some pragmatic AI tools within clinical settings, along with emerging healthcare companies leveraging AI-based solutions.

A. AutoML

Machine learning models have proven beneficial in the healthcare sector, leading to cost reductions and improved outcomes. However, the current utilization of these models remains limited, with only a few hospitals incorporating them [4]. The likely reason is that healthcare professionals often lack the expertise needed to build, deploy, and integrate these models into clinical workflows. Addressing this challenge, AutoML [42] has been developed to streamline the deployment of machine learning models in daily healthcare operations. AutoML automates essential steps, including feature selection, model selection, and hyper-parameter optimization. It reduces the dependency on data scientists or machine learning engineers and makes it more accessible for health professionals to develop machine learning models for clinical data. Typically, around 80% of a data scientist’s time is dedicated to data preparation and feature engineering, tasks that often require domain knowledge experts [43]. The goal is to identify the most discriminative features that offer insights into the problem and address learning situations that are challenging for classifiers. Various machine learning frameworks have been created to streamline feature engineering processes involving selection, ranking, and optimization [44]. One widely used approach is expand-reduce, which applies transformation functions to obtain optimal features, as implemented in [45]. Genetic programming, inspired by the concept of natural evolution and survival functions, has also been employed for feature construction and selection.

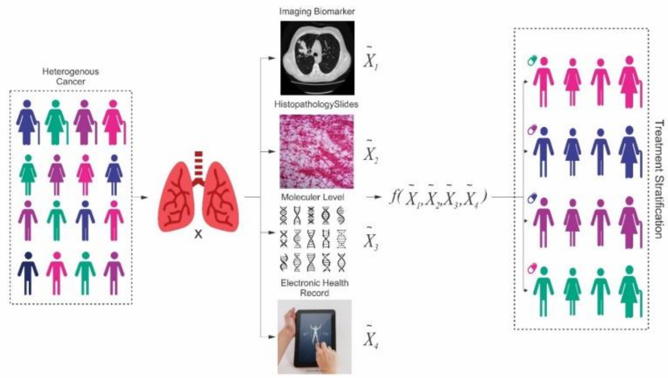

Figure 2: A Conceptual Picture for Precision Medicine that shows How Many Data Modalities are Combined to Identify Characteristics and Treatment Strategies Unique to Each Patient

B. AI Tools and Companies for Clinics

The significant advancements in the era of machine learning and the development and implementation of computer-aided diagnosis or AI tools in clinical practice face several challenges. Medical imaging [47] stands as a crucial diagnostic tool for various disorders, employing diverse modalities such as X-ray imaging, whole slide imaging, computed tomography (CT), ultrasound, Magnetic Resonance Imaging (MRI), and positron emission tomography (PET). Furthermore, numerous publicly available imaging and biological databases provide excellent opportunities for building AI systems. For instance, PathAI [48] utilizes AI methods to support pathologists in clinical diagnostics, clinical trials, and clinical translational research. Similarly, Viz.ai [49] is an AI-powered computer application designed to enhance care coordination by reducing time delays in clinical workflows. It employs AI to generate alerts promptly sent to clinicians for timely intervention. Additionally, Freenome [50] leverages AI for cancer screening, diagnostics, prevention, and improved cancer management. Table 2 enumerates companies entirely reliant on AI tools, empowering medical professionals to enhance patient outcomes.

Table 1: AI's broad classifications and uses in the healthcare sector.

Category	Specific Application
Patient care	• Diagnosis and Prognosis • Real-time case prioritization • Personalized medication • Electronic health records, Smart health
Medical Imaging	• Tumor segmentation and Detection • Early diagnosis and Imaging Biomarkers • Treatment effect monitoring
Management	• Public Health Policy • Market research • Forecasting (Pandemics)
Biosensors	• Remote health care • Real-time health monitoring • Soft computing
Computational Biology	• Drug Discovery and efficacy analysis • Single-cell analysis • Multi-omics data analysis

a) SaMD: Software as a Medical Device

SaMD [51], Software as a Medical Device, is designed for one or more medical purposes and is distinct from physical medical equipment. Since 1995, the FDA has approved over 500 software packages/applications to aid doctors in various healthcare issues [52], significantly focusing on analyzing radiology images. In numerous medical imaging tasks, AI algorithms have demonstrated superior performance compared to humans, leading innovative companies to develop AI-based systems for analyzing radiology images and digital pathology slides. For instance, Chan et al. [53] developed a computer-aided diagnosis system for identifying micro-calcifications on mammograms, conducting pioneering observer performance research that illustrated the tool's enhancement of breast radiologists' ability to detect micro-calcifications. Refer to Table 1 for additional examples. AI researchers and developers must have a comprehensive understanding of how clinicians prefer assistance in different clinical tasks. Constructing efficient AI solutions and producing interpretable results while considering practical considerations in clinical settings is imperative. If appropriately designed, validated, and implemented, effective data analytics from AI technologies can complement and support doctors' intelligence, enhancing accuracy, workflow, and, ultimately, patient care.

IV. IMPLEMENTATIONS OF BIG DATA ANALYTICS IN HEALTHCARE

The healthcare system involves various stakeholders, including patients, doctors, hospitals, industry players, and policymakers, operating under stringent compliance regulations. Due to the vast amount of data generated at high speeds within the healthcare sector, it presents an ideal landscape for the application of big data analytics. Leveraging big data analytics in healthcare has the potential to facilitate personalized medicine, prompt interventions, improved health policy management, and more effective planning [65].Big data analytics systems in healthcare aim to collect, clean, extract, visualize, and analyze extensive datasets, often characterized by three key concepts: volume (large datasets), variety (highly dimensional/many attributes), and velocity (the speed at which data is generated, accessed, and analyzed). Healthcare datasets, typically large and complex, originating from diverse sources, provide valuable opportunities for big data platforms [66]. For instance, on average, a cancer patient generates 2GB of data annually in the form of images and medical records. Emerging experimental techniques like immunotherapy, targeted therapy, omics research, high throughput screening, and parallel synthesis [67] may generate even larger amounts of data, necessitating advanced data analytic methods. **I**n Figure 3, the complex, high-dimensional data from wearable sensors (ECG, Electromyograms (EMG), Electroencephalograms (EEG)), imaging data (X-rays, CT-Scans, MRI), electronic health records, and multi-omics data (genome, proteome, and microbiome) are typically collected and stored at a central repository, where pre-processing and data cleaning occur. Missing values imputation methods may be employed for further processing using statistical and machine learning methods. Centralized and mobile applications can be developed for patients, clinicians, hospitals, government agencies, and global health organizations. For example, the FDA has approved Ziopatch [68], a device measuring heart rate and ECG signals.

Multivariate statistical methods, such as principal component analysis and other clustering techniques, can be applied to identify patterns in large datasets. These patterns may reveal different disease states, mortality rates, and susceptible age groups, forecast future pandemics, and estimate economic costs [69].

A. Fusion of Multi-Modal Data: Debunking the Myth of Trash or Unearthing a Goldmine

Numerous quantities in the universe exhibit concurrent variations. Biological data, being inherently diverse, often necessitates an amalgamation of related datasets to unravel hidden dependencies within a complex biological system [70]. Nevertheless, the fusion of these multi-modal data sets can yield either valuable insights akin to a goldmine or inconclusive results akin to trash. Achieving meaningful outcomes requires a combination of domain knowledge and robust data engineering skills for efficient feature representation and subsequent analysis. For instance, a study [71] demonstrated that integrating histopathological, radiological, and clinicogenomics information enhances risk stratification for cancer patients.

a) Heterogenous Data

The extensive volumes of healthcare data generated daily, encompassing medical images, sensor data, medical histories, and genomic information, exhibit heterogeneity. Machine learning proves highly adept at analyzing multi-modal data, extracting valuable insights across three crucial domains:

i) Diagnosis:

Machine learning, when applied to health records and medical images, plays a pivotal role in aiding the diagnosis of various disease states.

ii) Prognosis:

Utilizing machine learning algorithms on the diverse data available for a patient enables the prediction of the anticipated development of a disease, particularly from its early stages.

iii) Treatment:

Machine learning algorithms, particularly when applied to multi-modal data, can generate optimal treatment plans, offering valuable insights into personalized and effective healthcare strategies.

Table 2: Hetrogenous Data

Tool/Company	Services
Viz.ai [49]	It aims to reduce delays and make the healthcare team react faster with Al solutions regarding decision-making, treatment plans, and prescription providers
PathAI [49]	It develops machine learning for pathologists to assist in diagnostics by reducing errors, specifically for cancer patients and personal treatment.

Buoy Health[54]	A chatbot attends to a patient and records the history, symptoms, and other health concerns; then, it guides the patient to the appropriate health facility. It is developed by a team at Harvard Medical School to speed up and optimize the treatment cycle.
Enlitic [55]	Enlitic creates deep-learning radiology technologies. The company's deep learning engine analyses unstructured medical data to provide clinicians with improved insight into a patient's real-time demands.
Freenome [50]	It employs Al algorithms for cancer screenings, diagnostics, and blood work to identify cancer early and suggest innovative treatments.
Beth Israel Deaconess Medical Center [56]	It employs Al to diagnose blood disorders early. The robots were taught to detect germs using 25,000 blood sample photos. Machines learned to predict hazardous blood bacteria with 95% accuracy.
Iterative Scopes [57]	It uses Al for gastrointestinal diagnosis and therapy. They have submitted the first clinical study of their Al-powered SKOUT tool to the FDA for assessment.
VirtuSense [58]	It employs Al sensors to monitor patients' activities and alert them about accidents. VST Alert can anticipate when a patient plans to get up and inform hospital services.
Caption Health [59]	It integrates Al and ultrasonography for illness detection. Al assists physicians through the scanning procedure in real time to collect early diagnosis results.
BioXcel Therapeutics [60]	It applies Al to develop immuno-oncology and neurological drugs. The company's medication initiative uses Al to uncover new uses for old pharmaceuticals.
BERG [61]	BERG is a clinical-stage, Al-powered biotechnology company taking a bold 'Back to Biology™' approach to healthcare.
Atomwise [62]	Atomwise utilizes Al to accelerate small molecule drug discovery and explores new undruggable targets to make them druggable.
XtalPi [63]	XtalPi's ID4 platform combines Al, the cloud, and quantum physics to anticipate small-molecule medicinal characteristics.
Deep Genomics[64]	Its Al platform finds neuromuscular and neurodegenerative medication possibilities. "Project Saturn" examines 69 billion cell molecules.

Medical data frequently encompasses various data modalities, such as images, signals, text, and molecular structures, which may share inherent relationships. The advent of new machine learning and deep learning models allows for the integration of these diverse data sources, adopting a data-harmonization approach [72] and leading to the extraction of multi-modal insights [73]. The derived multi-modal features can be employed to construct knowledge graphs, offering support for clinical decisions, understanding disease mechanisms [74], or providing visualization aids for orthopedic surgery [75], as depicted in Figure 3, illustrating diverse healthcare applications for patients, clinics, government, and global healthcare organizations. The integration of multiple data types can enhance clinicians' trust, as different data modalities contribute complementary information to describe treatment plans or disease processes. Figure 2 illustrates how various data modalities can be utilized for precision medicine. The primary objective of methods combining multimodal data is to unify data with values from different scales and distributions into a global feature space, ensuring more consistent representation [76]. It is crucial to note that, in many real-world scenarios, fusing data from diverse modalities might lead to a decrease in performance. Healthcare data are generated by highly complex systems and instruments involving biological, environmental, social, and psychological factors, among others [77]. These systems operate based on various underlying processes, dependent on a broad range of variables that may not always be accessible [78]. Additionally, the diversity among different data types, including the number of samples, scales, and research questions, complicates the learning process. In small clinical cohorts, the curse of dimensionality may also pose challenges [79].

B. Genomics Data Analysis

Genomic datasets generated through next-generation sequencing often comprise extensive raw data [80], necessitating big data analysis and computational methods. Examples include the Encyclopedia of DNA Elements (ENCODE) [81] gene annotation and expression data, the Cancer Therapeutics Response Portal (CTRP) [82] offering insights into small molecule actions for personalized drug discovery based on predictive biomarkers, the Cancer Cell Line Encyclopedia (CCLE) [83], and the Genomics of Drug Sensitivity in Cancer (GDSC) [84] database conducting large-scale molecular screens on panels of hundreds of characterized cancer cell lines. These examples illustrate the potential of modern machine learning algorithms to develop drug response predictors from molecular profiles. However, existing data resources pose challenges for reliably predicting drug resistance or response [85]. Analyses of independent cohorts may yield different conclusions, and inconsistencies between datasets, along with missing clinical information, can impede predictions. To address missing values, data imputation techniques can be applied, and the high dimensionality of the data can be managed through feature filtering techniques or sparse principal component analysis [86].

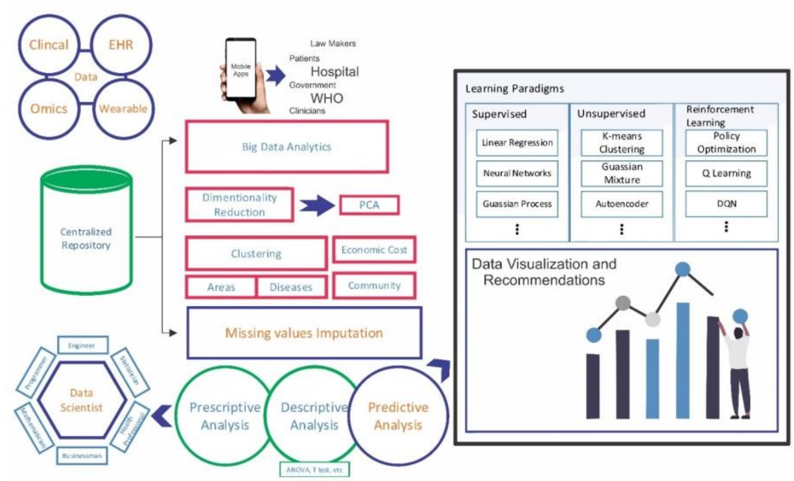

Figure 3: Healthcare Uses Big Data Analytics

Global health organizations, hospitals, doctors, governments, and patients may all benefit from learning from different data modalities in the big data world. Biomedical data can be visualized and analyzed using several machine-learning techniques.

C. Medical Imaging

Deep learning has the capability to swiftly generate magnetic resonance (MRI) images directly from sensor data with partially observed measurements. Task-oriented reconstruction enables the reconstruction of specific image portions with high quality and a confidence score. Super-resolution images, constructed using deep learning techniques like convolutional neural networks (CNNs) for single-brain MR images or generative adversarial networks (GANs) for super-resolution, enhance the quality of images built from low-resolution counterparts [87]. In Figure 4, various applications of deep learning in medical imaging are illustrated. For MRI images, image synthesis involves generating new parametric images or tissue contrasts from a set of images acquired in the same session. Generative adversarial networks [88] can act as a data augmentation tool, especially in cases where medical datasets have limited samples. They have been employed to produce synthetic abnormal MRI images for brain tumors based on techniques like pix2pix [89], [90]. Image registration, a process transforming data from multiple photographs, different sensors, views, or depths into a unified coordinate system, is enhanced through deep learning for medical image registration, leading to improved accuracy and speed. Examples include deformable image registration, model-to-image registration, and unsupervised end-to-end methods for deformable registration of 2D CT/MR images [91].

V. WEARABLE BIOSENSORS

Wearable biosensors are designed to measure electrophysiological and electrochemical signals originating from the body. These sensors capture electrical activities related to various biological processes, including heart activity (ECG), muscle activity (EMG), and sweat gland activity (Electro-Dermal Activity (EDA)). Extracting essential health information, these signals can be obtained from diagnostic machines or wearable sensors. Analytical methods applied to this data, such as principal component analysis, discrete cosine transforms, autoregressive methods, and wavelet transforms, enable the extraction of time and frequency domain features from physiological signals [92]. For instance, a bidirectional deep long short-term memory (LSTM) network, based on wavelet transform, has been utilized to classify ECG signals [93], achieving an impressive accuracy of 99.39% on the MIT-BIH arrhythmia database [94]. Another example involves a feature model based on Fourier Transform and Wavelet, applied to classify patients with Alzheimer's Disease, Mild Cognitive Impairment, and Healthy subjects using EEG signals [95].In practical scenarios, medical signal data can be collected passively using wearable sensors, such as smartphones or smartwatches [100]. Traditionally, signals have been acquired through gel-electrodes placed on the body. Recent advancements in fabrication and electronics have led to the integration of bio-sensing electrodes into various devices, including eye-glasses [101], VR head-mounted displays [102], and textiles [97].

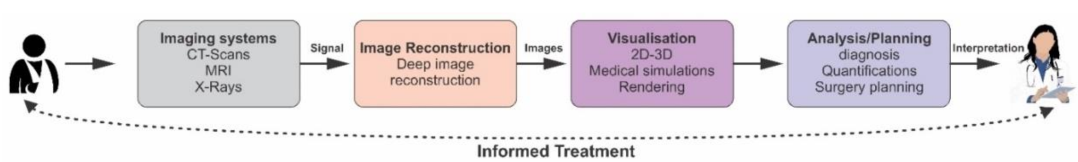

Figure 4: Medical Picture Construction can be Accelerated by Deep Learning, Which also Makes Medical Image Analysis and Visualization Easier

A. Epidermal Devices:

A new category of computing devices, called epidermal devices, enables the non-invasive capture of physiological signals through soft interactive tattoos [103], [104] (Figure 5). These devices can measure both electrophysiological signals [97], [104] and electrochemical signals in the body [105]. The availability of open-source prototyping kits and platforms, such as EMBody [106], Seeed, OpenBCI, Olimex, and BITalino, allows for the rapid prototyping of custom physiological sensing systems. Computational tools and AI-assisted approaches are actively explored to automate and customize the design of biosensing wearables. For example, Nittala et al. [98] developed a computational design tool with an integrated predictive model to optimize the design of multi-modal electrophysiological sensing devices.

B. Machine Learning Techniques on Physiological Signals:

Applying machine learning and deep learning techniques to physiological sensing is a common approach. In human-computer interaction, machine learning techniques are used to sense gestures from EMG signals [107] and identify moods from EDA, EOG, EMG, and ECG signals [102]. Deep learning approaches are commonly applied to ECG data for denoising [108], simulating signals, detecting heart-related anomalies [109], [110], emotion recognition [111], or assessing mental health by analyzing EEG signals and detecting psychiatric disorders [112]. Classen et al. [113] used machine learning to detect brain activity in clinically non-responsive, brain-injured individuals, predicting eventual recovery.

VI. COMPUTATIONAL ADVANCES

Advances in computer hardware and architectures are crucial for processing highly complex scientific problems. The growth in fast processors, multicore chips, accelerators, memory designs, interconnections, FPGA-based processors, and GPUs with hundreds of cores has made computationally intensive applications, such as real-time image and video processing in healthcare, possible.

A. Accelerated Artificial Intelligence:

Deep learning systems commonly leverage multiple-core graphical processing units (GPUs) for optimizing parallel matrix operations crucial to deep neural networks. An innovative approach to faster matrix multiplication using reinforcement learning was recently discovered [114]. Google introduced the tensor processing unit (TPU), an accelerated AI processor designed especially for its TensorFlow software [115]. The acceleration of deep neural network training can be achieved by either parallelizing the training of more examples or enhancing the speed of training for each example. Operations not accelerated by GPUs or TPUs, such as early data processing stages or input-output between devices or disks, need improvement for efficient training. Techniques like data echoing [116], which reuses intermediate outputs to reclaim idle capacity, can be beneficial in addressing these challenges. In the ongoing pursuit of AI leadership, model sizes have escalated from millions to billions of parameters, as seen in OpenAI GPT models. Google reported the GLaM model with over 1 trillion parameters (compared to GPT -3's 175 billion parameters) [117]. The primary challenges associated with these massive models are training costs and their deployment on smaller devices. Potential solutions include leveraging neural network compression techniques like knowledge distillation [118] or structural sparsity [119]. In this analogy, the smaller model (student) learns from the more extensive model (teacher). A survey in [120] presents efficient hardware architectures aimed at accelerating deep convolutional neural networks.

Table 5: Wearable Biosensors: (a) tattoo-like biosensors that detect electrodermal activity (EDA) [96]. (b) a multimodal physiological sensing tattoo on the forearm that is capable of sensing ECG, EDA, and EMG signals [97]. (c) incorporating user-interface controls, such as touch buttons, into tattoos with biosensing capabilities [97]. (d) Multi-modal electrophysiological sensing device creation and optimization supported by artificial intelligence [98]. (e) Skin-conformable, ultra-thin strain sensors on a decal transfer substrate are used to identify minute changes in a person's body [99].

B. Edge Computing:

While healthcare datasets are typically large and complex, requiring significant computational resources often found in remote clusters, there is a growing need to process data locally for privacy and efficiency reasons. This local processing at the end nodes of a cluster, known as edge computing, allows edge devices or servers to handle data storage and processing. This approach can offer fast, secure, and real-time health analytics, enabling timely medical interventions. Edge computing-based AI models prove particularly beneficial in providing healthcare solutions to areas with limited connectivity and access, facilitating rapid data analysis from smart medical sensors. Ensuring the portability and compatibility of AI models for prototyping involves implementing them on low-power devices. For instance, Owais et al. [121] demonstrated the implementation of the U-Net segmentation model on the Intel Neural Compute Stick, showing that inference could be achieved on such devices with proper tuning and model modifications. While there might be a performance trade-off, experimental results on brain and heart MRI images exhibited promising segmentation performance, showcasing the potential of inference-enabled devices for real-time clinical transformations in healthcare settings.

C. Federated Learning:

Maintaining data privacy and protection is crucial for medical data, necessitating new model training frameworks that do not compromise the underlying data. Federated or Collaborative Learning [122] is one such approach, training algorithms across multiple edge devices or servers without sharing local data samples. This technique enables active collaboration among multiple parties, such as hospitals or research centers, to train algorithms without centralizing their datasets. Federated learning has proven effective in developing AI models for medical data from various locations, as demonstrated during the rapid global response to the COVID-19 pandemic. In situations where ethical and legal constraints impede the sharing of patient data across locations, federated learning serves as a viable alternative. For example, in [123], a federated learning model predicted future oxygen requirements for COVID-19 patients using clinical and radiology data without the need for centralized data sharing. Different federated learning frameworks employ various topologies, such as peer-to-peer or client-server, transforming stochastic gradient descent into federated stochastic gradient descent based on the chosen topology [124], [125].

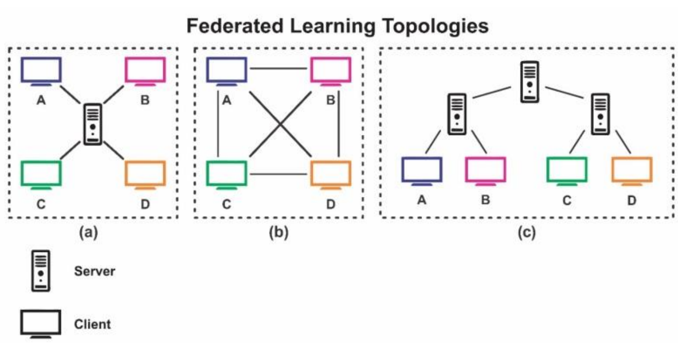

Figure 6: Shows typical federated learning topologies. (A) Client-Server. (b) A client and another client. (c) Mix topology or federation of sub-federations

All client terminals in a client-server architecture are linked to a shared server, and updates are sent through the server. Clients can exchange training updates without relying on a centralized server when using a client-client topology. Both of the above-described phenomena exist in mix topology.

VII. THE RECENT CHALLENGES IN AI FOR HEALTHCARE WITH POTENTIAL SOLUTIONS:

While AI holds tremendous promise for enhancing the healthcare industry, there exist challenges that impede its seamless integration into current healthcare systems. In this section, we delve into key issues and provide potential solutions to overcome these challenges for the betterment of healthcare.

A. Data Issues:

a) Data Availability and Access:

Ensuring success in data science within healthcare hinges on critical factors such as data availability and access. Challenges, including data quality, sample size, label disparities, and ethical concerns, must be effectively addressed to harness AI's full potential [126]. The foundational principle involves capturing clean, accurate, and properly formatted data for various healthcare applications. [127] offers insights into sharing biomedical data to fortify the role of AI.

b) Automated Data Cleaning Processes:

Employing machine learning methods aids in automated labeling, anomaly detection, missing value imputation, and other data cleaning processes [128]. For instance, in [129], deep learning identifies bleeding events from electronic health records. Automated scrubbing tools provided by IT vendors, leveraging logic rules, are another avenue for comparing, contrasting, and correcting large datasets.

c) Dataset Size and Quality:

The perception that larger datasets are necessary for accurate predictions prevails, but this overlooks the importance of data quality, proper annotations, and consultation with healthcare experts. Robust machine learning models require well-curated data generated with appropriate hypotheses and domain knowledge.

d) Data Security: Prioritizing data security in healthcare organizations is paramount. Risks, such as data breaches, hacking, and ransomware incidents, can be mitigated using machine learning to analyze patterns, preventing similar attacks and adapting to changing behaviors [132].

e) Handling Complex Data:

Dealing with imbalanced, complex, unlabeled, and poorly understood data requires careful consideration of learning paradigms and evaluation metrics. Unsupervised or semi-supervised learning can be employed to address these challenges and generate hypotheses for understanding complex diseases and signaling pathway patterns [133].

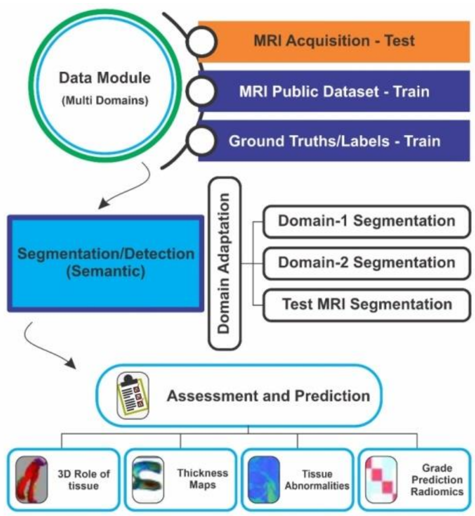

Figure 7: Domain Adaptation in Medical Imaging

f) The Difficulties with Distribution Shifts and Various Data Format

Many clinical AI systems encounter challenges due to shifts in training and testing data distributions. To address these shifts, machine learning employs domain adaptation techniques. In this process, a neural network is trained on a source dataset (X) and is expected to achieve high accuracy on a target dataset (Y) with distinct data distributions between X and Y. Domain adaptation is categorized into three types: supervised, semi-supervised, and unsupervised learning, based on the nature of the data in the training dataset. In supervised adaptation, the target dataset is considerably smaller than the source dataset because the target domain data is labeled. Unsupervised learning utilizes unlabeled data from the target domain, while semi-supervised learning incorporates both labeled and unlabeled data from the target domain. Deep domain adaptation is recommended to address challenges such as insufficient labeled data. This approach leverages deep network features to enhance model performance. The three primary strategies in deep domain adaptation are discrepancy-based, reconstruction-based, and adversarial-based techniques. These strategies aim to align and adapt the model to the differences in data distributions between the source and target datasets. Challenges arise from the delicacy of co-adaptation and representation specificity in the transferable features in the context of a discrepancy-based approach. A study referenced as [134] highlights the effectiveness of fine-tuning in enhancing generalization ability.

In the fine-tuning process applied to a deep model, a base network is trained using source data, and the target network's initial 'n' layers are directly employed. Subsequently, the remaining layers of the target network are randomly initialized and trained using a loss function based on the discrepancy. Depending on factors such as the size of the target dataset and its similarity to the source dataset, the initial layers may undergo fine-tuning or be frozen during the training procedure. Another deep domain adaptation technique, reconstruction-based domain adaptation, utilizes an autoencoder to minimize reconstruction error and acquire transferable, domain-invariant representations for aligning the discrepancies between domains. Stacked Auto Encoders (SAEs) offer a high-level representation of source and target domain data [136]. To address computational expenses associated with SAEs, a marginalized version, mSDA, which doesn't require stochastic gradient descent, was introduced in [137]. Transfer learning with deep autoencoders (TLDA) [138] employs a softmax loss to encode label information from the source domain.

In contrast, the embedding encoding layer utilizes the KL divergence to minimize the distribution distance between domains. Generative Adversarial Networks (GANs) play a crucial role in obtaining transferable and domain-invariant characteristics by minimizing distribution discrepancies between domains. GANs are also integrated into adversarial domain adaptation techniques [139]. CoGAN, proposed in [140], generates synthetic target data and associates it with synthetic source data. In [141], a method for simulated-unsupervised learning was introduced, where the focus was on minimizing adversarial and self-regularization losses. This approach utilized unlabeled real data to augment the realism of synthetic images.

B. Challenges in Medical Imaging

Medical imaging represents a highly transformative domain where AI has made significant strides, but it is not without its set of challenges [142]. One notable challenge arises from the three-dimensional nature of medical images. Processing these 3D volumes with three-dimensional convolutional neural networks (3D CNNs) demands increased memory and computational time. While researchers commonly treat 3D CNNs as stacks of 2D CNNs, introducing an additional dimension imposes additional constraints.

Privacy concerns are another critical issue in medical imaging. Although many deep learning models are constructed using anonymized public data, this approach doesn't offer a permanent solution to address privacy-related problems in medical imaging. When datasets are made public, there are inherent risks associated with potential leaks of patient privacy [143]. The high diversity of clinical scenarios adds another layer of complexity. Medical imaging serves various clinical purposes, including disease detection, localization, classification, surveillance, and even data quantification, such as pediatric bone age prediction [144]. Given the multitude of clinical activities involved in medical imaging, it becomes challenging for a single individual or model to effectively manage all these operations using current methodologies. The path forward involves developing task-aware deep-learning solutions to address these diverse clinical challenges.

Another significant hurdle in the field of medical imaging is the lack of transparency in algorithms and the challenges associated with validation and testing procedures. AI-based applications exhibit variations from data ingestion to output, and there is currently no standardized procedure in place. For instance, algorithms with comparable performance may adopt different strategies to address the same problem, necessitating specific pre-processing techniques before inference. This diversity complicates scalability, particularly in commercial AI-based products, as each application may demand its dedicated server or virtual environment. Ensuring the algorithm's transferability poses an additional challenge due to strict medical regulations in different nations. Unfortunately, no statistical method is available to evaluate the algorithm's transferability. One notable initiative addressing this challenge is Stanford University's 'medical-imagenet' project, involving petabyte-scale datasets of radiology and pathology images integrated with genomics and electronic health record information. This project aims to facilitate the rapid development of computer vision systems (Stanford-AIMI). Addressing the challenge of limited large datasets in medical imaging can be achieved through image synthesis and data augmentation. Generalization of models may be challenging as the distribution of training data, often composed of high-quality images, may differ from real-world clinical data. This discrepancy can lead to unexpected results in deep learning models. Techniques such as transfer learning, fine-tuning, or pre-training can be employed to mitigate this issue [145]. Transfer learning utilizes pre-trained weights from a network on a similar task, and greater emphasis on unsupervised machine learning models may be necessary to overcome sample size limitations. Figure 7 illustrates the applications of domain adaptation for image segmentation tasks.

C. Biosensors and Flexible Bioelectronics: A Way Forward

Despite notable progress in recent years, several significant challenges remain to be addressed before AI biosensors for Internet of Things (IoT)-based applications reach commercial maturity. A crucial element for commercial applications is the incorporation of flexible bioelectronic materials. Given the natural elasticity and flexibility of the human body and its internal organisms, integrating electronics into platforms made of flexible materials becomes essential. Current soft wearables placed on the skin primarily rely on capturing physiological signals and transmitting them to an external computing infrastructure (e.g., mobile devices, laptops). Flexible bioelectronics offers advantages in aligning with the human body and organs (such as skin, eyes, and muscles) while minimizing mechanical damage to tissues and reducing adverse effects after long-term integration due to its exceptionally flexible mechanical properties. Medical AI biosensors are poised to play a crucial role in shaping future technologies, particularly with the aid of nanotechnology. These biosensors will continue to progress in terms of miniaturization, scalability, low power consumption, affordability, high sensitivity, multifunctionality, safety, non-toxicity, and degradation [146].

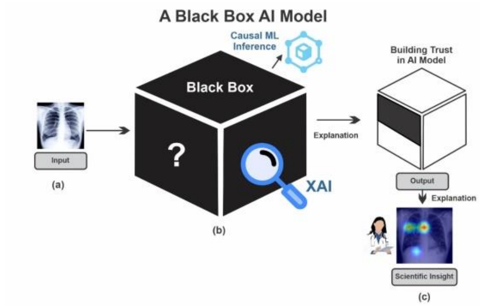

Figure 8: Black-Box Model for AI

The predictions can be interpreted using algorithms such as causal inference, feature visualisation, or Explainable AI. The Gradcams visualization can be used to highlight significant areas that can increase healthcare practitioners' trust.

D. Adaptability

A prevalent issue in the realm of ML-enhanced biosensors is the limited presence of adaptive learning capabilities. Presently, many biosensors augmented with machine learning lack the ability to adapt and learn from their surroundings, relying solely on manually input training sets. Adaptive learning in biosensors allows them to continually enhance and optimize their performance by learning from their environment, contrasting with non-adaptive systems. The adoption of adaptable models has the potential to reduce the likelihood of critical errors and erroneous outcomes, which can be a concern with fixed models. While non-adaptive ML models might excel in local performance, there is a potential trade-off in terms of generalizability, especially in clinical applications. Adaptive learning serves as a viable solution to address this conflict, providing the flexibility needed for robust and contextually relevant performance in various scenarios.

E. Big Data in Smart Sensors

Implementing a smart sensor system that relies on vast datasets and sophisticated algorithms presents a significant challenge, particularly regarding the platform for data processing and storage. Cloud computing has recently been a preferred choice for processing sensor signals due to its superior computational power and expansive data storage capabilities. Integrating cloud and biosensors is not a novel concept, especially in monitoring applications where the volume of data continually expands. However, the direct connection of numerous sensors to the cloud can be prohibitively expensive and sluggish, primarily due to the exponential growth in the number of sensors. To address this, edge computing has emerged as a solution in recent years. Unlike a centralized data center, edge computing facilitates data processing at distributed edge devices. It offers advantages such as enhanced computational efficiency, swift network processing, and cost-effectiveness. As a result, cutting-edge biosensors are likely to leverage this innovative technology.

F. Opening the Black Box of Deep Learning

A significant challenge in implementing AI lies in the opaque nature of deep learning models, particularly in critical healthcare scenarios where complete reliance on model predictions is not feasible. The need for interpretable and transparent models becomes crucial for making informed healthcare decisions. As input data traverses through the layers of a neural network, it undergoes compression, generating predictors for the target label. Max-pooling is applied at each layer, and certain neurons are dropped out in the final layers to prevent overfitting. Due to these compressed representations, explaining predictions at each level becomes challenging. However, obtaining a high-level understanding of the model's inner workings is still possible. In our opinion, complex deep learning models, comprising hundreds of millions of parameters, are nearly impossible to interpret comprehensively. In Figure 8, various methods used to elucidate the workings of deep learning models are illustrated. These methods offer an explanation of predictions to a certain extent without compromising accuracy. There exists a trade-off between accuracy and explainable AI, contingent on the specific problem at hand. An intriguing study [147] introduced the information bottleneck [148] to shed light on the functioning of deep neural networks. The information bound, a theoretical limit proposed by [148], represents the optimal point at which the model performs best given a set of features, with no further compression possible. The study suggests that during most training epochs, the model focuses on learning efficient representations of the input, and the compression of representations initiates when the training error starts to decrease. As the model converges layer by layer, the last layer retains only the most relevant features for predicting the output label.

Table 3: Healthcare Applications of ChatGPT.

Application	Description	Advantages	Disadvantages
Patient communication	ChatGPT can be used to communicate with patients and provide them with general medical advice. This can help reduce the	Provides immediate medical advice, is available 24/7, and can handle large volumes of	It may not be able to replace human interaction and empathy fully, may not be able to handle complex or critical

	workload on healthcare providers and improve patient satisfaction.	inquiries simultaneously.	cases, and raises concerns about patient privacy and confidentiality.
Telemedicine	It can facilitate virtual consultations between patients and healthcare providers. By providing patients with access to medical advice and expertise, ChatGPT can help improve healthcare access and outcomes, particularly in rural or under-served areas.	Improve healthcare access, reduce travel costs and wait times, and increase patient engagement.	It may not be suitable for all types of medical consultations, may not be able to perform physical exams or provide hands-on care, and raises concerns about patient privacy and security.
Medical education	It can be used as a tool for medical education, providing students and healthcare professionals with access to medical information and resources. By analyzing medical data and answering questions, It can improve medical knowledge and training.	Improves medical education accessibility, personalizes the learning experience, and can be used for quick reference and knowledge consolidation.	May not be able to provide hands-on training, raises concerns about patient privacy and confidentiality, may perpetuate health disparities for students or institutions who do not have access to the technology or resources.
Medical research	ChatGPT can be used in medical research to analyze large amounts of medical data and identify new patterns and trends.	Enables faster and more efficient analysis of large amounts of data to identify previously unknown correlations and patterns.	It may require significant computing resources and expertise and may not be able to fully replace human researchers and medical experts.
Diagnosis support	It can assist healthcare providers in diagnosing diseases by analyzing patient symptoms, medical history, and other data.	Improves the accuracy and consistency of diagnoses, saves time, reduces errors, and can support rare and complex cases.	It may not be able to fully replace human diagnostic skills, expertise, and all clinical factors.

G. Model Fairness and Accountability

An inherent challenge in deploying biosensors with AI lies in ensuring unbiased outcomes. Studies [149] [150] have indicated that ML algorithms may exhibit disparities in outcomes among different population groups, particularly those already marginalized in society. Addressing this challenge requires several strategic measures when developing ML applications utilizing biosensors. These may involve consciously including diversity in the data collection process and establishing robust policies for post-application performance audits to assess the impact on vulnerable communities. From a technical standpoint, it is crucial to monitor model performance logging for performance drift detection. Implementing such procedures in the deployment and monitoring of biosensors using AI applications is essential for instilling confidence in the services provided among healthcare professionals and patients.

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