

Yahya Shahsavari¹, Oussama A. Dambri¹, Yaser Baseri¹, Abdelhakim Senhaji Hafid¹, and
Dimitrios Makrakis¹

¹Affiliation not available

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Integration of Federated Learning and Blockchain in Healthcare: A Tutorial

Yahya Shahsavari, Oussama A. Dambri, Yaser Baseri, Abdelhakim Senhaji Hafid, and Dimitrios Makrakis

Abstract—Wearable devices and medical sensors revolutionize health monitoring, raising concerns about data privacy in Machine Learning (ML) for healthcare. This tutorial explores Federated Learning (FL) and Blockchain (BC) integration, offering a secure and privacy-preserving approach to healthcare analytics. FL enables decentralized model training on local devices at healthcare institutions, keeping patient data localized. This facilitates collaborative model development without compromising privacy. However, FL introduces vulnerabilities. BC, with its tamper-proof ledger and smart contracts, provides a robust framework for secure collaborative learning in FL. After presenting a taxonomy for the various types of data used in ML in medical applications, and a concise review of ML techniques for healthcare use cases, this tutorial explores three integration architectures for balancing decentralization, scalability, and reliability in healthcare data. Furthermore, it investigates how Blockchain-based Federated Learning (BCFL) enhances data security and collaboration in disease prediction, medical image analysis, patient monitoring, and drug discovery. By providing a tutorial on FL, blockchain, and their integration, along with a review of BCFL applications, this paper serves as a valuable resource for researchers and practitioners seeking to leverage these technologies for secure and privacy-preserving healthcare ML. It aims to accelerate advancements in secure and collaborative healthcare analytics, ultimately improving patient outcomes.

Index Terms—Federated Learning, Blockchain Integration, Medical Data Privacy, Machine Learning in Healthcare, Decentralized Collaborative Learning, Healthcare Applications, Privacy-Preserving Machine Learning,

I. INTRODUCTION

In recent years, the rapid proliferation of wearable devices and medical sensors has unlocked remarkable possibilities for continuous health monitoring, facilitating real-time tracking of various health parameters [1], [2]. This diverse array of devices, ranging from commonly used smartwatches to highly specialized medical sensors, has significantly expanded the scope of data available for healthcare applications [3]. The voluminous and continuous streams of data generated by these devices hold immense potential for advancing personalized healthcare and contributing to medical research [4]–[6]. However, the centralized nature of medical data gathering, where data is often collected, stored, and analyzed in centralized databases or cloud servers, presents a significant challenge to

privacy [7]–[9]. This centralization poses a risk as it consolidates sensitive health information in a single location, making it an attractive target for potential breaches or unauthorized access. Concentrating such valuable and private data in one repository increases the potential impact of a security breach, jeopardizing the confidentiality and privacy of individuals' health information [8].

Medical data privacy can be compromised when used for ML, due to the centralized nature of data gathering. Concentrating sensitive health information in centralized databases or cloud servers poses a significant risk [10]. If these centralized repositories become targets for security breaches or unauthorized access, the potential impact is heightened. A security breach on such a consolidated repository becomes more attractive to malicious actors as it grants access to a wealth of valuable and private data from a diverse array of wearable devices and medical sensors [8], [11]. The centralized storage and analysis of voluminous and continuous streams of health data increase the surface area for potential privacy threats, jeopardizing the confidentiality and privacy of individuals' health information. This centralization introduces a single point of failure, making it more challenging to ensure the security and integrity of the data, thereby creating a potential avenue for compromising privacy when medical data is utilized for ML purposes. Consequently, addressing the inherent privacy challenges associated with centralized medical data gathering becomes crucial to harnessing the benefits of wearable devices while safeguarding the sensitive nature of health-related information.

FL, as an innovative decentralized learning framework, enables model training across multiple local devices while keeping raw data localized [12]–[14]. In the context of medical data, where patient confidentiality is paramount, FL emerges as a promising solution to address inherent privacy challenges [12], [15]–[17].

One of the key advantages of FL lies in its ability to facilitate collaborative model training without the need for centralized data aggregation. In conventional ML models, centralizing medical datasets raises concerns regarding unauthorized access, data breaches, and the potential for patient re-identification. FL distributes the model training process across individual devices, ensuring that raw data remains on the local device, and only model updates are shared. This decentralized approach substantially reduces the risk of privacy breaches, as sensitive patient information is not exposed beyond the confines of the local device.

Furthermore, FL empowers healthcare institutions to collaborate on model development without the necessity of sharing

Yahya Shahsavari, Yaser Baseri and Abdelhakim Senhaji Hafid are with Montreal Blockchain Lab, University of Montreal, Montreal, Canada. Emails: yahya.shahsavari@umontreal.ca; yaser.baseri@umontreal.ca; ahafid@umontreal.ca

Oussama A. Dambri and Dimitrios Makrakis are with the School of Electrical Engineering and Computer Science, University of Ottawa, Ottawa, Canada. E-mails: doussama@uottawa.ca; dmakraki@uottawa.ca

TABLE I: Table of Acronyms

Acronym	Explanation
AI	Artificial Intelligence
BFT	Byzantine Fault Tolerance
BFT-based consensus	Byzantine Fault Tolerant-based consensus
BC	Blockchain
BCFL	Blockchain-based Federated Learning
CAD	Computer-Aided Detection
CBC	Complete Blood Count
CNVs	Copy Number Variations
CNNs	Convolutional Neural Networks
CGM	Continuous Glucose Monitoring
CT	Computed Tomography
CPS	Cyber-Physical Systems
DApps	Decentralized Applications
DAG	Direct Acyclic Graph Tangle
DeFi	Decentralized Finance
DICOM	Digital Imaging and Communications in Medicine
DPoS	Delegated Proof of Stake
ECG	Electrocardiogram
EEG	Electroencephalogram
EMG	Electromyography
EMRs	Electronic Medical Records
EHRs	Electronic Health Records
ESR	Erythrocyte Sedimentation Rate
FTL	Federated Transfer Learning
FL	Federated Learning
FL-BETS	FL-based BC-Enabled Task Scheduling
GANs	Generative Adversarial Networks
GDPR	General Data Protection Regulation
HIPAA	Health Insurance Portability and Accountability Act
HAM10000	Human Against Machine with 10000 training samples
IBFT	Improved Byzantine Fault Tolerance
IoB	Internet of Blockchains
IoMT	Internet of Medical Things
IoT	Internet of Things
IBC	Inter-Blockchain Communication
ML	Machine Learning
MAR	Medication Administration Records
MNIST	Modified National Institute of Standards and Technology
MRI	Magnetic Resonance Imaging
NLP	Natural Language Processing
PET	Positron Emission Tomography
PCA	Principal Component Analysis
PGD	Patient-Generated Data
PoA	Proof of Authority
PoB	Proof of Burn
PoC	Proof of Capacity
PoS	Proof of Stake
PoST	Proof of Space and Time
PoW	Proof of Work
PROs	Patient Reported Outcomes
RL	Reinforcement Learning
RNA-Seq	RNA Sequencing
SNPs	Single Nucleotide Polymorphisms
SMPC	Secure Multi-Party Computation
t-SNE	t-distributed Stochastic Neighbor Embedding
VFL	Vertical Federated Learning

raw patient data. This collaborative learning paradigm allows models to be trained on diverse datasets from different sources, fostering the creation of robust and generalizable models. Importantly, by enabling the aggregation of insights from various healthcare providers, FL promotes the development of models that are representative of broader populations, thereby enhancing the efficacy and applicability of medical Artificial Intelligence (AI) solutions.

Although FL preserves the confidentiality of sensitive data by training models on decentralized devices, it introduces new vulnerabilities, such as the risk of model poisoning [18], [19], compromises to data integrity [20]–[22], and decentralized communication errors [23]. BC, with its decentralized and tamper-resistant nature, coupled with smart contracts for protocol execution, offers a robust framework to combat

malicious activities, ensure data integrity, and enhance the overall security of the collaborative learning process [24], [24]. By synergizing the strengths of FL and BC technology, we can strike a balance between privacy and security, fostering a trustworthy and resilient environment for the advancement of ML in sensitive domains such as healthcare.

This paper significantly contributes to the field of decentralized ML by specifically focusing on the integration of blockchain technology with FL in the healthcare domain. Our contributions are as follows:

- 1. Motivations for Blockchain-FL Integration in Healthcare:** We analyze the need for blockchain to address data privacy, security, and trust concerns in healthcare-oriented FL systems. This analysis emphasizes the unique challenges and opportunities presented by healthcare data, setting the stage for understanding the value proposition of blockchain integration.
- 2. Exploring Integration Architectures for Healthcare FL:** We discuss three distinct integration architectures – fully coupled, semi-coupled, and loosely coupled – specifically within the context of healthcare applications. This analysis provides valuable insights for researchers and practitioners designing and implementing BCFL systems for healthcare data, considering factors like patient privacy, regulatory compliance, and data security.
- 3. Impact of Blockchain-based Federated Learning (BCFL) on Healthcare:** We delve into the emerging paradigm of FL and showcase its potential to revolutionize healthcare analytics. By demonstrating how FL frameworks can preserve patient privacy while enabling collaborative model training across healthcare institutions, this section highlights the transformative impact of FL on various healthcare domains, including disease prediction, medical image analysis, patient monitoring, and drug discovery.
- 4. Research Gaps and Future Directions in Healthcare FL:** Recognizing limitations in existing surveys, we identify key research gaps specifically at the intersection of blockchain, FL, and healthcare. We advocate for comprehensive future research endeavors encompassing regulatory, technical, and adoption aspects to guide further advancements in FL for effective healthcare solutions.
- 5. Synthesis for Advancing Decentralized Healthcare Machine Learning:** By synthesizing insights from various sections of the paper, including motivations, integration architectures, FL applications, and research gaps, we offer a comprehensive perspective on the contribution of blockchain to FL in the context of healthcare. This synthesis aims to foster collaboration, innovation, and adoption of FL specifically for healthcare applications, ultimately accelerating progress in decentralized ML for improved healthcare outcomes.

The remainder of the paper is structured as follows. Section II provides a review of medical data and their applications in ML. In Section III, we offer a brief tutorial on the application of ML and FL in medical use cases. Section IV offers a brief background on blockchain technology necessary

for understanding this paper. The integration of blockchain and FL in healthcare is discussed in Section V. Section VI presents related works on the integration of blockchain and FL in healthcare as well as currently existing surveys. Finally, Section VII concludes the paper.

II. MEDICAL DATA AND APPLICATIONS IN MACHINE LEARNING

Medical data encompasses a diverse array of information crucial for understanding, diagnosing, and treating various health conditions. This data, ranging from patient demographics and medical history to diagnostic images and genomic sequences, holds immense potential for advancing healthcare through ML applications. By harnessing the power of ML algorithms, medical data can be analyzed to extract valuable insights, predict patient outcomes, personalize treatments, and optimize healthcare delivery. However, the utilization of medical data for ML requires careful consideration of data storage and management practices to ensure compliance with privacy regulations, maintain data integrity, and facilitate seamless access for research and clinical purposes. This section explores the different types of medical data and their applications in ML.

A. Electronic Health Records

Electronic Health Records (EHRs) [25]–[28] are digital versions of patients’ paper charts in a healthcare setting. EHRs contain a patient’s medical history, diagnoses, medications, treatment plans, immunization dates, allergies, medical images (e.g., radiology images), and laboratory test results. They are designed to provide a comprehensive and up-to-date view of a patient’s health information, allowing healthcare providers to make informed decisions about a patient’s care. The key features of EHRs include:

- **Digital Format:** EHRs replace traditional paper records with electronic versions, making it easier to store, access, and share health information.
- **Interoperability:** EHRs are designed to be interoperable, meaning that they can be shared among different healthcare providers and organizations. This facilitates better coordination of care, especially when patients see multiple healthcare providers.
- **Real-Time Access:** Authorized healthcare professionals can access a patient’s EHR in real-time, providing quick access to critical health information, which is crucial, especially during emergency situations.
- **Patient Engagement:** EHRs often include features that allow patients to access their health information, schedule appointments, communicate with healthcare providers, and participate more actively in their own care.
- **Decision Support:** EHRs may include tools that provide decision support for healthcare providers, such as alerts for potential drug interactions, reminders for preventive screenings, and clinical guidelines.
- **Data Security and Privacy:** EHRs are designed with security measures to protect the confidentiality and privacy of patient information. Access to EHRs is typically restricted to authorized personnel [29]–[32].

EHRs serve as a rich source of structured and unstructured data that can be leveraged for ML applications in healthcare. Since EHRs contain comprehensive information about patients, ML algorithms can analyze this wealth of information to extract meaningful insights, predict patient outcomes, identify patterns, and improve clinical decision-making [33]–[35]. In the context of ML, EHR data can be used for a variety of tasks, including:

- **Predictive Analytics:** ML models trained on EHR data can predict the likelihood of various medical events, such as hospital readmission, disease onset or progression, adverse drug reactions, and mortality rates. These predictions enable proactive interventions and personalized care strategies [36]–[39].
- **Disease Identification and Diagnosis:** ML algorithms can analyze EHR data to assist in the early detection and diagnosis of diseases. By identifying subtle patterns and anomalies in patient data, these models can aid healthcare providers in making accurate and timely diagnoses [40]–[46].
- **Treatment Recommendations:** ML models trained on EHR data can suggest personalized treatment plans based on patients’ medical history, demographic information, genetic profiles, and responses to previous interventions. These recommendations help optimize treatment outcomes and minimize adverse effects [47]–[52].

In summary, EHRs serve as a valuable resource for ML and FL applications in healthcare, enabling predictive analytics, disease identification, personalized treatment recommendations, and collaborative model training, while ensuring patient privacy and data sovereignty.

B. Medical Imaging Data

Medical imaging data encompasses diverse visual representations of the internal structures of the human body, intended for clinical scrutiny and medical intervention. These visual depictions are acquired utilizing distinct imaging modalities [53]–[55] and play a pivotal role in the diagnosis and ongoing assessment of diverse medical conditions. Key components of medical imaging data are as follows:

- **Patient Information:** consists of basic information about the patient, including their name, identification number, age, gender, and other relevant demographic details as well as information about the patient’s medical history, current symptoms, and any relevant details that might impact the interpretation of the images.
- **Imaging Modalities:** Each imaging modality utilizes distinct principles and technologies to generate specific types of images [56]. Different imaging modalities offer complementary information, and the choice of modality depends on the specific clinical question, the type of tissue or organ under investigation, and the desired level of detail [57], [58]. Common imaging modalities include:
 - 1) *X-ray*: uses ionizing radiation to produce images of bones and some soft tissues [59]–[61].

- 2) *Computed Tomography (CT)*: combines X-rays with computer technology to create detailed cross-sectional images of the body [62]–[66].
 - 3) *Magnetic Resonance Imaging (MRI)*: Uses strong magnetic fields and radio waves to generate detailed images of soft tissues, organs, and joints [67]–[72].
 - 4) *Ultrasound*: Utilizes sound waves to create images of internal structures, commonly used for examining the abdomen, pelvis, and fetus during pregnancy [73]–[80].
 - 5) *Nuclear Medicine*: Involves the injection of radioactive substances to visualize the functioning of organs and tissues [81]–[86].
 - 6) *Positron Emission Tomography (PET)*: Combines nuclear medicine with computed tomography to provide functional information about tissues and organs, particularly in cancer diagnosis and staging [87]–[91].
 - 7) *Fluoroscopy*: Involves continuous X-ray imaging to capture real-time moving images, commonly used for procedures such as angiography and gastrointestinal studies [92]–[97].
- **Image Files**: Medical data [98] including metadata [99]–[101] such as patient information, acquisition parameters, and image details are being stored, shared, and transmitted regarding a set of technical standards [102] referred to as Digital Imaging and Communications in Medicine (DICOM) [103].
 - **Annotations and Measurements**: Annotations in medical data involve adding context, insights, or labels to enhance the interpretation of information, while measurements quantify various aspects of physiological parameters, imaging features, and laboratory results, providing objective data for diagnosis and treatment decisions. Both annotations and measurements are essential for comprehensive and accurate medical analysis and decision-making [104]–[107].
 - **Image Series**: In medical imaging, an image series refers to a sequence of images acquired during a single imaging study or examination. This sequence of images is typically obtained to capture different views, slices, or time points of a particular anatomical region or physiological process [108].
 - **Metadata**: Metadata in the context of medical imaging refers to additional information that accompanies the actual image data. This information is crucial for understanding, interpreting, and managing medical images [98]. Key components of metadata in the medical context are acquisition parameters (i.e. exposure settings, magnetic field strength, etc.), image acquisition time, patient information (i.e. patient-related data, including name, ID, age, gender, clinical history, etc.), study information (e.g. study ID, modality, etc.), image details (e.g. orientation and position, slice thickness, etc.), device information (e.g. make and model of the scanner or machine, software version), dose parameters (e.g. amount of radiation exposure), and image processing history (i.e. reconstruction algorithm, and image reconstruction method) [109].

- **Reports**: In the context of medical imaging, reports refer to narrative documents generated by radiologists summarizing their findings based on the analysis of the medical images. These reports are often used by referring physicians for treatment planning.

Medical imaging data has a wide range of applications in ML within the healthcare industry [110]. Some key applications include:

- **Disease Diagnosis and Classification**: ML algorithms can analyze medical imaging data to assist in the diagnosis and classification of various diseases and conditions, such as cancer, neurological disorders, cardiovascular diseases, and musculoskeletal disorders [111]–[116].
- **Computer-Aided Detection (CAD)**: CAD systems use ML algorithms to assist radiologists and clinicians in detecting abnormalities in medical images, such as tumors, lesions, fractures, and other anomalies. These systems can help improve diagnostic accuracy and efficiency [117], [118].
- **Medical Image Segmentation**: Segmentation involves partitioning an image into multiple segments to identify and analyze specific regions of interest, such as organs, tissues, or abnormalities. ML algorithms can be trained to perform image segmentation tasks, which are valuable for tasks such as tumor delineation, organ segmentation, and identifying abnormalities within tissues or organs [119]–[121].
- **Image-Based Biomarker Discovery**: ML algorithms can analyze medical imaging data to identify imaging biomarkers associated with specific diseases or treatment responses. These biomarkers can be valuable for predicting disease prognosis, assessing treatment efficacy, and guiding personalized medicine approaches [122], [123].
- **Treatment Planning and Monitoring**: Medical imaging data can be used to develop personalized treatment plans for patients based on their unique anatomical characteristics and disease progression. ML models can analyze imaging data to predict treatment outcomes, monitor disease progression over time, and optimize treatment strategies for individual patients [124].
- **Image Reconstruction and Enhancement**: ML techniques, such as deep learning-based image reconstruction and enhancement algorithms, can improve the quality of medical images acquired from various imaging modalities (e.g., Magnetic Resonance Imaging (MRI), Computed Tomography (CT), ultrasound). These techniques can help reduce imaging artifacts, enhance image resolution, and improve overall image quality for better interpretation by healthcare professionals [125]–[127].
- **Image Registration and Fusion**: Image registration and fusion techniques align and combine multiple medical images from different modalities or time points to provide comprehensive information for diagnosis and treatment planning. ML algorithms can be used to perform automatic image registration and fusion tasks, enabling more accurate visualization and analysis of complex medical data.

- **Drug Discovery and Development:** Medical imaging data can also be used in drug discovery and development processes. ML models can analyze imaging data to evaluate the effects of experimental drugs or therapies on disease progression, identify potential drug targets, and optimize drug delivery methods [128].

C. Genomic Data

Genomic data pertains to information concerning the organization and operation of the genome within an organism [129], [130]. Genomic data harnessed in healthcare ML pertains to the comprehensive information extracted from an individual's genome, encompassing the entirety of their DNA and genetic composition [131]–[137]. This invaluable dataset plays a pivotal role in healthcare applications, offering profound insights into genetic predispositions, treatment responses, and overall health [138]. Key components of Genomic data in medical use cases can be summarized as follows:

- **Genome Sequences:** The genome sequence represents the complete set of genetic material (DNA) present in an organism, including all of its genes and non-coding regions. It consists of a sequence of nucleotides (A, T, C, and G) that encode genetic information.
- **Genes:** Genes are specific sequences of DNA that encode instructions for the synthesis of proteins, which are essential for various biological processes in the body. Genomic data includes information about the location, structure, and function of genes within the genome.
- **Single Nucleotide Polymorphisms (SNPs):** SNPs are variations in a single nucleotide base at a specific position in the genome that occur with relatively high frequency within a population. These variations can influence traits, susceptibility to diseases, and drug responses. Genomic data includes information about SNPs and their association with phenotypic traits and diseases [139].
- **Copy Number Variations (CNVs):** CNVs are genomic alterations that involve changes in the number of copies of specific DNA segments, ranging in size from kilobases to megabases. CNVs can affect gene dosage and expression levels, leading to phenotypic variations and disease susceptibility. Genomic data includes information about CNVs and their association with various diseases and traits [140].
- **Gene Expression Profiles:** Gene expression refers to the process by which genetic information is used to synthesize proteins. Genomic data includes information about gene expression profiles, which can provide insights into the activity levels of different genes in specific tissues or under different conditions. Gene expression data is often generated using technologies such as microarrays or RNA Sequencing (RNA-Seq) [141].
- **Epigenetic Modifications:** Epigenetic modifications are heritable changes in gene expression that do not involve alterations in the DNA sequence itself. These modifications, such as DNA methylation and histone modifications, can influence gene activity and phenotype without changing the underlying DNA sequence. Genomic data includes information about epigenetic modifications and their role in regulating gene expression and disease susceptibility [142].
- **Genetic Variation Databases:** Genetic variation databases compile and organize genomic data from various sources, including population studies, disease databases, and clinical datasets. These databases provide comprehensive repositories of genetic variants, annotations, and associated phenotypic information, facilitating research on genetic variation and its implications for human health [143].

These components of genomic data are essential for understanding the genetic basis of diseases, identifying genetic risk factors, and developing personalized approaches to healthcare and medicine. Genomic data analysis plays a crucial role in advancing our understanding of genetics, genomics, and their implications for human health and disease. Utilization of genomic data in healthcare ML can be described as follows:

- **Disease prediction and Risk Stratification:** ML algorithms scrutinize genomic data to discern patterns and variations linked to specific diseases. This analytical approach allows for the assessment of the risk associated with certain health conditions [144]–[148].
- **Personalized Medicine:** genomic data forms the basis for the development of personalized treatment plans [149], [150]. ML models, through predictive analytics, anticipate individual responses to different medications, facilitating tailored and optimized treatment strategies [132], [134], [136], [148], [151], [152].
- **Drug Discovery and Computational genomics:** By leveraging ML, researchers can analyze genomic data to expedite drug discovery and development processes. This entails identifying potential drug targets and comprehending the genetic underpinnings of diseases, ultimately leading to more targeted and efficacious therapeutic solutions [153]–[156].
- **Genomic Counseling:** ML algorithms play a crucial role in delivering personalized genetic counseling by deciphering complex genomic data. This assists healthcare professionals in effectively communicating intricate genetic details, including health risks and familial implications [157], [158].
- **Early Detection and Diagnostics:** The integration of genomic data and ML algorithms facilitates the early detection and diagnosis of diseases. These algorithms can discern subtle genetic variations indicative of specific conditions, enabling timely intervention and enhanced prognostic outcomes [159]–[162].
- **Research and Population Health Informatics:** Aggregated and anonymized genomic data, subjected to ML methodologies, advances our understanding of the genetic foundations of diseases at a population level. This knowledge informs public health initiatives, epidemiological studies, and the identification of genetic factors influencing disease prevalence [163], [164].
- **Genomic Sequencing and Computational Analysis:** ML serves a crucial role in the interpretation of extensive

genomic datasets generated through advanced sequencing technologies. These algorithms play a pivotal role in identifying genetic mutations, variations, and other pertinent information impacting individual health [165]–[167].

D. Biometric Data

Biometric data in the medical context refers to unique physical or behavioral characteristics that can be used for identifying and monitoring individuals. This data is increasingly important in healthcare for patient identification, access control to medical records, personalized treatments, and monitoring of health conditions. The components of biometric data in medical data can include, but are not limited to:

- **Physiological Biometrics:** Consists of data types such as fingerprints data, facial recognition data, iris recognition data, Ear recognition data, retina scans, DNA, Smell recognition, and hand geometry data [168].
- **Behavioral Biometrics:** Consists of data types as follows: voice recognition data, gait analysis data, and typing dynamics data [168].
- **Health-Related Biometrics:** Consists of data types such as heart rate, blood pressure, blood Oxygen levels, Electrocardiogram (ECG) patterns [169], and brain wave patterns (i.e. Electroencephalogram (EEG) patterns) [170].
- **Emerging Technologies:** There are some recently emerging technologies for extracting biometric data such as:
 - 1) *Microbial Biometrics:* Analyzing the unique microbiome of an individual.
 - 2) *Olfactory Biometrics:* Unique body odors can potentially be used for the identification and detection of diseases.

Biometric data integrated into healthcare ML encompasses quantifiable physiological or behavioral attributes [168], [171], [172] unique to individuals. This data serves the purpose of accurate identification [173]–[176], secure access [177]–[179], and health assessment [180], [181] within healthcare settings. The primary application of biometric data in healthcare ML can be succinctly outlined as follows:

- **Biometric Identification and Access Control:** Biometric data, encompassing features like fingerprints or facial characteristics, is pivotal for precise identification and access control in healthcare environments. Implementation of biometric authentication ensures heightened security measures, governing access to sensitive areas, EHRs, and medical devices. ML algorithms play a crucial role in processing and analyzing these biometric patterns to enable swift and accurate verification [182], [183].
- **Patient Identification and Record Matching:** employing biometric identifiers such as fingerprints or iris scans ensures precise linkage of patients to their health records, minimizing the risk of identification errors [184]–[187]. ML algorithms enhance the accuracy of patient matching, mitigating potential medical errors and elevating the overall quality of patient care [188]–[190].
- **Biometric Monitoring for Health Assessment:** Continuous monitoring of biometric data—like heart rate, blood pressure, or ECG signals—via wearable devices

or sensors facilitates real-time health assessment [180]. ML algorithms analyze dynamic biometric data, enabling early detection of anomalies or health issues. This capability supports timely intervention and personalized healthcare management [191], [192].

- **Behavioral Biometrics for Mental Health Monitoring:** Behavioral biometrics, encompassing patterns like typing or voice modulation, contribute to mental health assessment and behavioral changes detection [193]–[196]. ML models discern patterns indicative of mental health conditions, aiding healthcare providers in delivering targeted interventions and support [197].
- **Biometric Data in Clinical Trials:** Biometric data usage in clinical trials spans participant identification, monitoring, and data integrity assurance [198]. ML assists in the efficient management and analysis of biometric data during clinical trials, informing researchers and ensuring study outcomes' validity [199], [200].
- **Voice and Speech Analysis for Diagnostics:** Voice pattern analysis serves diagnostic purposes, detecting potential markers for various medical conditions [201], [202]. ML algorithms process voice and speech data to identify indications of conditions such as Parkinson's disease [203]–[205] or respiratory disorders [206], [207], contributing to diagnostic capabilities.
- **Facial Recognition for Patient Monitoring:** Facial recognition technology is employed for patient well-being monitoring and distress detection [208]. ML algorithms analyze facial expressions, offering insights into patient comfort levels and potentially enhancing the quality of care in healthcare settings [209].

E. Sensor Data

Sensor data in medical contexts refers to the information collected from various devices and sensors used to monitor health, detect changes in patient conditions, and assist in diagnoses. These sensors can be wearable, implantable, or environmental, and they continuously collect data related to physiological parameters, activity levels, and environmental conditions. The components of sensor data in medical data can include:

- **Wearable Sensors:** These data are extracted from wearable devices such as heart rate monitors, activity trackers, blood pressure monitors, blood glucose monitors, and Oxygen saturation sensors (pulse Oximeters).
- **Implantable Sensors:** These data are extracted from cardiac monitors, glucose monitors, and intraocular pressure sensors.
- **Environmental sensors:** consists of the data gathered from air quality monitors that measure pollutants and allergens in the environment, which can affect respiratory conditions like asthma, and temperature and humidity sensors.
- **Specialized Medical Sensors:** Consist the data gathered from ECG sensors, EEG sensors, Electromyography (EMG) sensors, gait sensors, and sleep monitors.
- **Smart Health Homes:** These data are extracted from fall detectors (sensors that detect falls, especially important

for elderly patients), and bed sensors that monitor sleep patterns, bed occupancy, and vital signs during sleep.

Sensor data used in healthcare ML refers to information collected by various sensors, which can include wearable devices, medical equipment, and other monitoring tools [210], [211]. This data provides real-time insights into an individual's health and activities. Healthcare ML algorithms analyze sensor data to make predictions, identify patterns, and offer personalized insights. The utilization of sensor data in healthcare ML is detailed as follows:

- **Vital Signs Monitoring:** sensors capture vital signs such as heart rate, blood pressure, respiratory rate, and temperature [212], [213]. ML algorithms analyze continuous vital sign data to detect anomalies, predict health deteriorations, and offer early warnings to healthcare professionals [214]–[216].
- **Wearable Devices for Activity Tracking:** Wearable sensors, including accelerometers and gyroscopes, monitor physical activities and movement patterns [217]–[219]. ML models analyze this data to assess overall physical health, detect abnormalities, and provide personalized insights for fitness and rehabilitation plans [220], [221].
- **Blood Glucose and Continuous Glucose Monitoring (CGM):** Sensors continuously measure blood glucose levels [222], offering a comprehensive glycemic profile. ML algorithms analyze Continuous Glucose Monitoring (CGM) data to predict glucose level trends, recommend insulin dosages, and enhance diabetes management [223].
- **Electrocardiogram (ECG) Monitoring:** ECG sensors capture cardiac electrical activity. ML interprets ECG data to identify cardiac abnormalities, predict cardiovascular risk, and recommend early interventions [224]–[227].
- **Sleep Monitoring:** Wearable devices and bed-based sensors track sleep patterns, including duration and quality. ML algorithms analyze sleep data to identify disorders, provide insights into sleep hygiene, and recommend personalized interventions for improved sleep health [228], [229].
- **Environmental Sensors:** sensors measure environmental factors like air quality, temperature, and humidity. ML correlates environmental data with health outcomes, aiding in identifying triggers for respiratory conditions, allergies, or other health issues [230].
- **Medication Adherence Monitoring:** Smart pill bottles and medication dispensers with sensors track adherence. ML algorithms analyze adherence patterns, send reminders to patients, and provide healthcare providers with insights into patient compliance [231], [232].
- **Fall Detection and Activity Recognition:** Motion sensors detect falls and recognize different activities. ML models use this data for fall risk assessment, predicting accidents, and adapting care plans for individuals with mobility challenges [233], [234].
- **Biometric Sensors for Stress and Emotion Monitoring:** Biometric sensors, measuring skin conductance or heart rate variability, assess stress levels and emotional states.

ML analyzes biometric signals to provide insights into mental health, stress management, and emotional well-being [235]–[237].

F. Patient-Generated Data

Patient-Generated Data (PGD) within the realm of healthcare ML pertains to health-related information actively contributed by patients [238]. This data, distinct from traditional clinical records, is directly sourced from patients through various means, including wearables, mobile apps, and patient-reported outcomes. The incorporation of patient-generated data in healthcare ML fosters a patient-centric and data-driven healthcare approach, enabling personalized interventions, early detection of health issues, and improved communication between patients and healthcare providers [239]. However, it is imperative to prioritize the privacy and security of patient-generated data and uphold ethical considerations throughout the development and implementation of ML models in healthcare settings. Apart from the data gathered by sensors as mentioned in the previous subsection (i.e. Section II-E), the utilization of patient-generated data in healthcare ML is extended as follows:

- **Mobile Health Apps and Surveys:** Patients leverage mobile apps to input health-related information, participate in surveys, and provide feedback on their health status [240]–[242]. ML algorithms process patient-reported data to derive insights into treatment effectiveness, medication adherence, and overall patient satisfaction, thereby informing personalized care plans [243], [244].
- **Social Media and Online Communities:** Patients share health-related information, experiences, and concerns on social media platforms and online forums [245]. ML algorithms conduct analyses on social media data for health-related trends, sentiment, and public health monitoring, contributing valuable insights for population health research and understanding patient perspectives [246], [247].
- **Genomic and Genetic Data Sharing:** Patients voluntarily contribute genetic information through platforms facilitating data sharing for research purposes. ML analyzes aggregated genomic data to identify genetic factors associated with diseases, fostering advancements in precision medicine and contributing to genetic research [248].
- **Telehealth and Virtual Visits:** Patients engage in virtual consultations, offering health-related updates and information during telehealth visits. ML algorithms analyze patient-generated data from virtual visits to support clinical decision-making, monitor treatment progress, and enhance the overall quality of virtual healthcare interactions [249], [250].

G. Clinical Trial Data

Clinical trial data in the context of medical research refers to the information collected during the conduct of clinical trials. Clinical trials are systematic investigations designed to evaluate the safety, efficacy, and/or effectiveness of new drugs, medical devices, procedures, or interventions in human

subjects. These trials follow a carefully designed protocol or plan and are conducted to generate data that can be used to inform medical decision-making, regulatory approvals, and advancements in medical knowledge [251]. Integration of clinical trial data into ML models enables the development of predictive algorithms, risk assessment tools, and decision support systems in healthcare. This approach contributes to evidence-based medicine, supports personalized treatment strategies, and enhances the overall efficiency of clinical research and practice [116], [224], [252], [253]. Key components of clinical trial data can be summarized as follows:

- **Demographic Information:** This information consists of details about the study participants, including age, gender, race, ethnicity, and other relevant demographic characteristics. Demographic data can be incorporated into ML models to assess how different demographic groups respond to interventions. It helps in developing personalized treatment plans based on age, gender, and other demographic factors.
- **Informed Consent:** Normally contains documentation confirming that participants have been informed about the trial, its risks, and benefits, and have voluntarily agreed to participate. ML models can incorporate consent-related information to ensure that only data from participants who have provided informed consent are included in the analysis [254]. This is crucial for maintaining ethical standards and regulatory compliance [255].
- **Medical History:** Information about participants' pre-existing medical conditions, relevant medical history, and details about any concurrent medications. Medical history data can be utilized to identify pre-existing conditions or comorbidities that may impact treatment outcomes. ML models can predict how certain medical histories influence responses to interventions [47], [256].
- **Intervention Details:** Specifics about the investigational product or procedure being tested, including dosage, administration methods, and treatment protocols. ML algorithms can analyze intervention details to identify patterns associated with treatment success or failure [257]. This information is valuable for predicting the efficacy of similar interventions in future cases.
- **Clinical Assessments:** Physical examinations, laboratory tests and results, imaging studies, and other clinical measurements were conducted to assess participants' health status and response to the intervention. ML models can process clinical assessment data to identify trends, correlations, or anomalies that may be indicative of treatment responses or adverse events [258]. This assists in early detection and prediction of outcomes.
- **Adverse events:** Records of any adverse events or side effects experienced by participants during the trial, including their severity and relation to the intervention. ML algorithms can learn from historical adverse event data to predict the likelihood of adverse events for new interventions. This supports risk assessment and enables proactive management [259], [260].
- **Efficacy Endpoints:** Measurements and assessments

used to determine the effectiveness of the intervention, often focusing on outcomes such as improvements in disease markers or symptom relief. ML models can analyze efficacy endpoint data to develop predictive models for treatment success or failure. This facilitates the identification of key factors contributing to positive outcomes.

- **Follow-Up Data:** Information collected during follow-up visits, which may include data on long-term outcomes, treatment adherence, and any sustained effects of the intervention. Follow-up data is essential for longitudinal analyses. ML models can use this data to predict the long-term effects of interventions, allowing for the development of predictive models for sustained efficacy or potential relapses [261]–[263].
- **Protocol Deviations:** Documentation of any deviations from the original study protocol, including the reasons for these deviations. ML models can analyze protocol deviation data to identify how deviations impact study outcomes. This information can be used to adjust for deviations during analysis or predict their potential effects [264].
- **Statistical Analyses:** Methods and results of statistical analyses applied to the data, including primary and secondary endpoints, to draw conclusions about the efficacy and safety of the intervention. ML models can incorporate statistical analysis results to understand the significance of various factors on study outcomes. This facilitates the development of ML models that take into account the statistical nuances of the data [265].

H. Prescription and Medication Data

Prescription and medication data in medical records refer to information related to the medications prescribed to patients, including details about the prescribed drugs, dosage, frequency, and other relevant information. These data are crucial components of patient health records and play a significant role in managing and monitoring patient care. Prescription and medication data are important for ensuring patient safety, medication management, monitoring public health and treatment efficacy, research and analysis, regulatory compliance, and facilitating communication among healthcare providers. These data are integrated into EHRs to provide a comprehensive view of a patient's medication history, allowing healthcare professionals to make informed decisions about treatment plans and avoid potential drug interactions or adverse events. Additionally, aggregated and anonymized prescription and medication data are used in research to assess the effectiveness and safety of medications on a broader scale. Key components of prescription and medication data can be summarized as follows:

- **Patient Information:** These data consist of identification details of the patient, including name, date of birth, and other relevant demographic information. We already explained this kind of data and its use in ML.
- **Prescriber Information:** These data consist of records of details about the healthcare provider who prescribed the medication, including their name, credentials, and contact

information. Analyzing prescriber data can help identify patterns in prescribing behavior. ML models can be trained to recognize prescribing practices associated with positive patient outcomes, contributing to more informed decision-making [152].

- **Prescription Date:** contains records of the date on which the prescription was issued, indicating when the patient should start taking the medication. Temporal analysis of prescription dates can assist in predicting medication adherence and treatment outcomes. ML models may identify patterns related to the timing of prescription issuance and its impact on patient behavior [266].
- **Medication Name:** Contains the name of the prescribed medication, including the generic and brand names. ML models can categorize medications based on their therapeutic classes, aiding in the identification of commonalities and differences in treatment outcomes across different drug categories [267].
- **Dosage:** Consists of information about the prescribed amount or strength of the medication to be taken by the patient. Dosage and administration details are crucial for predicting medication adherence and potential adverse events. ML models can identify optimal dosage regimens and administration routes based on historical data [268], [269].
- **Frequency:** consists of instructions on how often the medication should be taken, such as daily, twice daily, or as needed.
- **Route of Administration:** The method by which the medication should be administered (e.g., orally, intravenously, topically).
- **Duration of Treatment:** Consists of the period for which the medication is prescribed, indicating the number of days or weeks the patient should take the medication. ML models can analyze the duration of treatment to predict long-term outcomes, including the likelihood of treatment success and the potential development of drug resistance [270], [271].
- **Instructions for Use:** Additional guidance on how to take the medication, such as whether it should be taken with food, at specific times of the day, or with other medications. Natural Language Processing (NLP) techniques can be applied to extract insights from free-text instructions, helping to identify specific nuances in how patients are instructed to take their medications [272], [273].
- **Refill Information:** Contains details regarding whether the prescription allows for refills and, if so, the number of authorized refills. Refill information is essential for predicting patient adherence and persistence with prescribed medications. ML models can identify factors influencing refill behavior and predict the likelihood of medication discontinuation [274], [275].
- **Allergies and contraindications:** contains records of information about any known allergies the patient has or contraindications that may affect the choice of medication. ML models can identify associations between patient allergies, contraindications, and adverse drug reactions. This information aids in predicting the safety and suitability

of specific medications for individual patients [276], [277].

- **Adverse Reactions:** contain documentation of any adverse reactions or side effects the patient experiences while taking the medication. Adverse reaction data can be analyzed to develop predictive models that identify patients at higher risk for experiencing specific side effects. This allows for proactive management and personalized interventions.
- **Medication Changes:** information about any changes made to the prescribed medication, including adjustments in dosage or switching to an alternative medication. ML models can analyze historical medication changes to predict the likelihood of treatment modifications in the future, assisting in the development of personalized treatment plans [248], [278].
- **Medication Discontinuation:** If applicable, the reason for discontinuing the medication and the date of discontinuation can be considered in this class of data. ML models can predict the factors contributing to medication discontinuation, helping healthcare providers identify patients at risk of stopping their medications and intervening to improve adherence [279].
- **Medication Administration Records (MAR):** contain records of actual medication administration, often documented in a healthcare setting, indicating when and by whom the medication was administered to the patient. Medication Administration Records (MAR) data can be used to train ML models for predicting medication administration patterns and identifying potential deviations from the prescribed regimen [280], [281].

I. Laboratory Data

Laboratory data in medical records refer to the results of tests and analyses conducted on patient samples in a laboratory setting. These tests are essential for diagnosing, monitoring, and managing various medical conditions. The types of laboratory data collected can vary depending on the patient's symptoms, medical history, and the healthcare provider's assessment. ML techniques, including supervised learning, unsupervised learning, and deep learning, can be employed depending on the nature of the data and the specific goals of the analysis. Common types of laboratory data are as follows:

- **Blood Tests:** Consists of a Complete Blood Count (CBC) that measures the number and types of blood cells, Blood Chemistry Panel (tests such as electrolytes, glucose, liver function tests, and kidney function tests), and Lipid Profile. In the context of ML, predictive models can be developed to identify patterns in CBC results associated with specific diseases, such as anemia or infections [282]–[284].
- **Urinalysis:** Examines the physical and chemical properties of urine to detect abnormalities. ML algorithms can process urinalysis data to detect patterns indicative of kidney disorders, urinary tract infections, or diabetes [285]–[287].

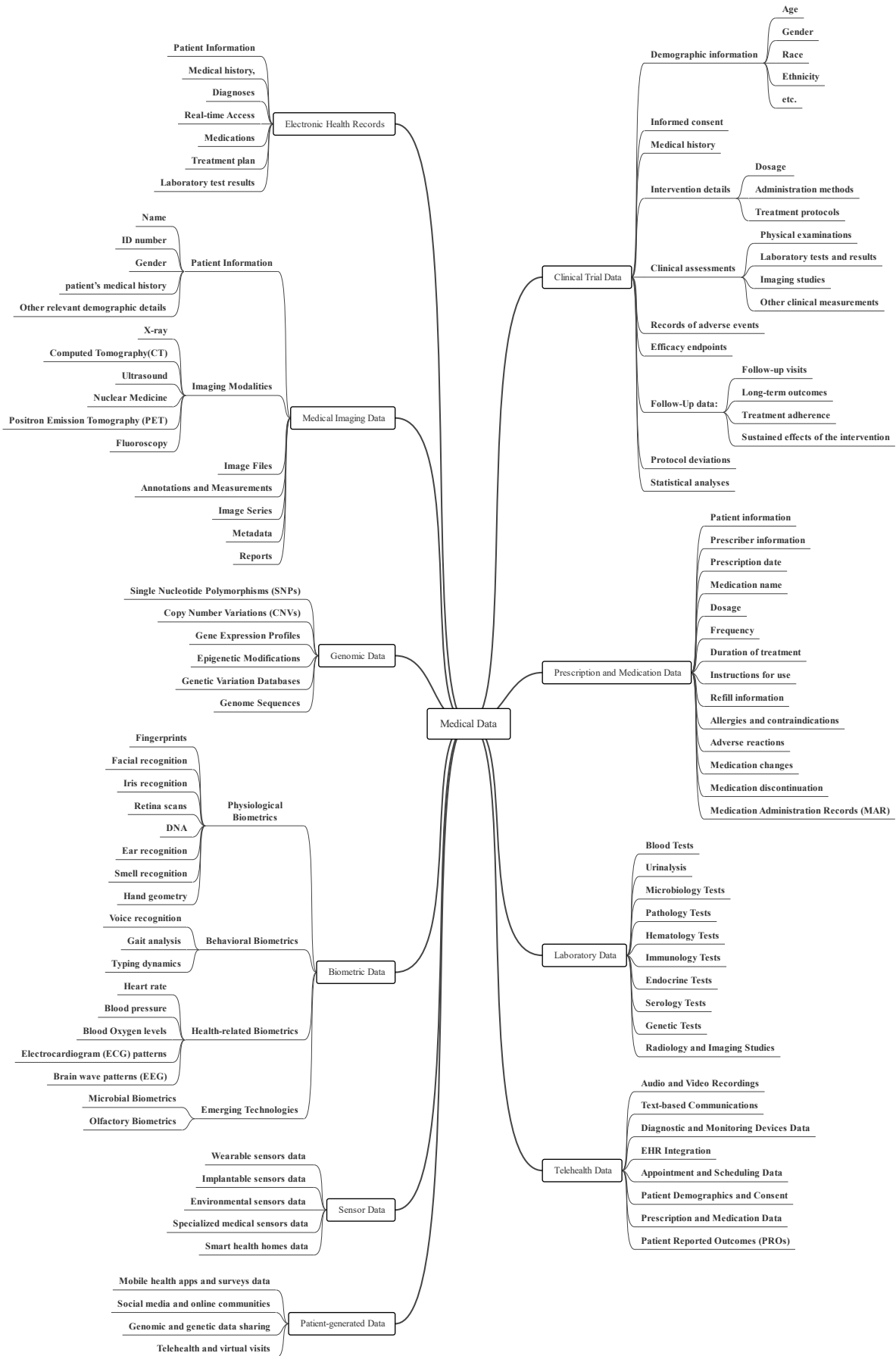


Fig. 1: Taxonomy of Medical Data Used for Machine Learning in Medical Applications

- **Microbiology Tests:** Results of this test identify and determine the sensitivity of microorganisms to specific antibiotics or identify the type of bacteria present. ML can assist in the identification of microorganisms from culture data and predict antibiotic susceptibility, aiding in personalized treatment plans [288]–[291].
- **Pathology Tests:** These tests consist of tissue biopsy and Cytology where the former one examines tissue samples for abnormalities or diseases and the latter one examines cells for signs of disease, often used in cancer diagnosis. In the context of ML, image recognition models can be trained on pathology slides to assist pathologists in identifying abnormal tissue structures or cancerous cells [122], [292], [293].
- **Hematology Tests:** These tests can be classified as coagulation studies and Erythrocyte Sedimentation Rate (ESR). The first one assesses the blood clotting function while the second one measures inflammation in the body. In the context of ML, ML models can analyze coagulation studies to predict the risk of bleeding or clotting disorders [294]–[297].
- **Immunology Tests:** These tests consist of antibody tests that detect antibodies produced by the immune system and viral load that measures the amount of virus in the blood for certain infections. ML algorithms can identify patterns in antibody levels to diagnose autoimmune diseases or infectious conditions [298]–[300].
- **Endocrine Tests:** Assesses levels of hormones such as thyroid hormones, insulin, and others. ML models can analyze hormone levels to predict and monitor endocrine disorders such as thyroid dysfunction or diabetes [301], [302].
- **Serology Tests:** Analyze components in the liquid portion of blood (serum), including proteins, enzymes, and electrolytes. ML algorithms can be applied to serum test data to identify markers associated with specific diseases, aiding in early detection and monitoring [299], [303].
- **Genetic Tests:** Genetic tests involve the identification of specific genetic markers associated with particular conditions. These markers represent distinct genetic variations and play a crucial role in understanding and diagnosing various health conditions through genetic analysis. ML can be used to analyze genetic data for identifying disease risk, predicting treatment response, or diagnosing genetic disorders.
- **Radiology and Imaging Studies:** Although not conducted in a traditional laboratory, these tests are often considered part of the diagnostic process and contribute to the overall medical data. Image recognition and segmentation models can be trained on radiology images to assist in the diagnosis of conditions like tumors, fractures, or abnormalities.

J. Telehealth Data

Telehealth [304] data in medical records refers to the information collected during remote healthcare interactions between patients and healthcare providers. Telehealth data

play a crucial role in modern healthcare, especially during times when remote interactions are necessary [305]. Telehealth involves the use of technology, such as video calls, phone calls, and online platforms, to deliver healthcare services remotely. The data generated during telehealth encounters contribute to the overall patient record and can include various types of information. Here are some key components of telehealth data:

- **Audio and Video Recordings:** Recordings of virtual consultations between healthcare providers and patients can be stored for documentation, review, and quality assurance purposes. ML applications may analyze these recordings to extract useful information, such as sentiment analysis or clinical insights. Speech recognition algorithms can transcribe audio recordings, enabling the analysis of verbal communication between healthcare providers and patients [249]. Facial recognition and sentiment analysis can be applied to video recordings to assess patient emotions and engagement during telehealth consultations [306].
- **Text-Based Communications:** Consists of chat logs, text messages, or emails exchanged between patients and healthcare providers. These communications can contain important information about symptoms, treatment plans, and patient queries. NLP models can extract and categorize information from text-based communications [307]. This includes identifying symptoms, treatment discussions, and patient concerns. Sentiment analysis can help gauge patient satisfaction and emotional well-being.
- **Diagnostic and Monitoring Devices Data:** Includes all types of data from medical devices used by patients at home, such as remote monitoring devices for blood pressure, glucose meters, or wearable fitness trackers. These data enable continuous monitoring of patients' health remotely. ML models can analyze trends and patterns in this data to provide insights into the patient's condition. Time series analysis and predictive modeling can be applied to data from remote monitoring devices to detect trends and anomalies in vital signs. For example, ML algorithms can predict exacerbations of chronic conditions based on changes in physiological parameters [308].
- **EHR Integration:** Integration of telehealth data into EHRs or Electronic Medical Records (EMRs) facilitates a comprehensive view of the patient's health history, including both in-person and remote interactions, for healthcare providers. Integrating telehealth data into EHRs allows for a comprehensive patient profile. ML models can analyze the combined data to identify correlations between in-person and virtual interactions, improving diagnostic accuracy and treatment planning.
- **Appointment and Scheduling Data:** Contains information related to telehealth appointments, including scheduling details, appointment duration, and attendance, and can support efficient management of healthcare services. Analysis of scheduling data can optimize appointment availability and improve patient access to care. As well, predictive analytics can optimize appointment scheduling by analyzing historical data to identify peak appointment

times and anticipate patient demand. This can improve resource allocation and patient access to telehealth services.

- **Patient Demographics and Consent:** contains information about the patient, including demographic details and consent for telehealth services and ensures compliance with privacy regulations, and provides context for personalized care. ML applications may analyze demographic data for population health management. Moreover, ML models can analyze patient demographic data to identify population health trends, target interventions, and personalize healthcare services. Consent data can be used to ensure compliance with privacy regulations and customize communication preferences.
- **Prescription and Medication Data:** Contains information related to prescriptions, medication management, and adherence and Supports virtual prescription refills and medication management. Predictive modeling can be applied to medication adherence data to identify patterns and factors influencing adherence. This information can inform personalized interventions to improve patient compliance. ML can also analyze prescription data to identify medication-related risks and interactions [309].
- **Patient Reported Outcomes (PROs):** Contains patient-reported data on symptoms, well-being, and treatment effectiveness and provides valuable insights into the patient's subjective experience. ML can help analyze PROs to predict treatment responses or identify trends in symptoms. Text mining and sentiment analysis can be applied to PROs to extract valuable insights into patient experiences and treatment effectiveness. Predictive modeling can correlate PROs with clinical outcomes to inform treatment decisions [310].

III. ARTIFICIAL INTELLIGENCE

AI is revolutionizing healthcare, impacting diagnosis, treatment, and patient care. This section explores the evolution of AI in healthcare, from its historical roots to cutting-edge developments, showcasing its potential across various healthcare domains. We will further delve into FL as a key technology for the future. FL's collaborative approach enables privacy-preserving data analysis, making it a powerful tool for healthcare research and delivery. We will discuss its applications, case studies, current challenges, and future directions.

A. Evolution of AI in Healthcare

The journey of AI in healthcare began in the late 1950s and early 1960s with foundational work in AI and its potential applications [311]. Early systems, such as ELIZA (1966) [312] and MYCIN (1974) [313], demonstrated AI's capabilities in mimicking human conversation and decision-making in medical diagnostics, respectively. These systems laid the groundwork for future AI applications in healthcare. By delving into the key milestones marking the evolution of AI in healthcare, we can categorize it into distinct periods:

- **1990s to Early 2000s:** The advancement of ML algorithms, particularly in neural networks [314], led to

increased interest in AI's applications in healthcare. The development of algorithms for pattern recognition in medical imaging [315] and the emergence of EHRs [316] provided vast data sources for AI analysis.

- **Mid-2000s to 2010s:** This period saw significant advancements in deep learning, dramatically improving the performance of AI in image recognition [317] and natural language processing [318]. The launch of IBM's Watson in 2011 marked a significant milestone [319], showcasing AI's ability to analyze and interpret medical literature and patient data.
- **Recent Developments:** The last decade has witnessed exponential growth in AI applications in healthcare [320]. The advent of big data analytics [321], cloud computing [322] and improved algorithms have enabled more sophisticated and accurate AI tools [323]. These developments have facilitated breakthroughs in precision medicine, predictive analytics, and patient care management.

B. Potential of AI in Healthcare

AI is transforming healthcare across a wide spectrum, from disease diagnosis to patient care management. Here are some key areas where AI is making significant contributions:

- **Disease Diagnosis and Imaging:** AI has revolutionized medical imaging by providing tools for more accurate and faster diagnosis [324]. Deep learning models, trained on large datasets of X-rays [325], MRIs [326], and CT scans [327], can identify patterns undetectable to the human eye. AI aids in early detection of diseases like cancer, cardiovascular abnormalities, and neurological disorders.
- **Drug Development and Personalized Medicine:** AI algorithms have streamlined the drug development process by predicting molecular behavior [328] and identifying potential drug candidates [329]. In personalized medicine, AI analyzes patient data, including genetic information, to tailor treatments to individual patients, improving efficacy and reducing side effects [330].
- **Predictive Analytics in Patient Care:** AI's predictive analytics are crucial to preventive medicine. By analyzing EHRs [331], AI can predict patient risks for diseases [332], hospital readmission [333], and other adverse events, enabling proactive care and intervention [334].
- **Robotics and Surgical Assistance:** Robotics integrated with AI has improved surgical precision and outcomes [335]. AI-driven robots assist surgeons in complex procedures, reducing human error and patient recovery time. AI also plays a role in training surgeons through virtual reality simulations [336].
- **Patient Engagement and Telemedicine:** AI-powered chatbots and virtual health assistants provide 24/7 support and health monitoring [337], enhancing patient engagement and adherence to treatment plans. In telemedicine, AI tools assist in remote diagnosis and consultation [338], making healthcare more accessible.
- **Healthcare Administration and Management:** AI streamlines administrative tasks in healthcare, such as



Fig. 2: Exploring the Convergence of Artificial Intelligence with Healthcare: Trends, Applications, and Future Perspectives.

scheduling, billing, and claims processing [339]. It also optimizes hospital operations, resource allocation, and patient flow, improving overall efficiency and reducing costs [340].

- **Global Health and Epidemic Response:** AI has been pivotal in global health, particularly in tracking and predicting the spread of infectious diseases [341]. During the COVID-19 pandemic, AI models were instrumental in analyzing virus transmission [342], vaccine development [343], and managing healthcare resources.

C. Fundamentals of Machine Learning

ML, a pivotal branch of AI, is fundamentally reshaping our approach to problem-solving across various domains [344], including healthcare [345]. At its core, ML involves the development and application of algorithms that enable computers to learn from and make decisions or predictions based on data. This capacity for self-improvement and adaptation without explicit programming is what sets ML apart.

The cornerstone of ML is data. Algorithms learn from data patterns, and the quality and quantity of this data significantly influence their performance as explained in the previous section. ML algorithms are sets of rules or instructions given to computers to help them learn from data. These algorithms can be broadly categorized into supervised learning [335], [346]–[351], unsupervised learning [352]–[359], semi-supervised [360]–[365] and reinforcement

learning [366]–[373].

C.1. Supervised Learning

Supervised learning, a dominant branch of ML, plays a crucial role in healthcare by leveraging labeled datasets to train models that can make predictions or categorize data [346]. This approach is especially powerful in scenarios where the relationship between input data and the output is known and can be modeled [335].

- **Labeled Data:** In supervised learning, the training data is labeled, meaning that the outcome of each data point is known. This label guides the algorithm in learning the relationship between the input features and the output.
- **Classification and Regression:** The two primary tasks in supervised learning are classification (predicting discrete outcomes) and regression (predicting continuous outcomes). Classification might involve diagnosing whether a patient has a specific disease, while regression could involve predicting a patient's recovery time. We will explore these concepts in greater depth in the classification and regression subsection, providing more detailed insights and applications.
- **Model Training and Validation:** The process involves training the model on a portion of the data and then validating its accuracy on a separate, unseen dataset. This helps in ensuring that the model generalizes well to new data.

Supervised learning has a big impact in healthcare with

use in applications such as disease diagnostics, treatment personalization, and patient management.

- **Disease Diagnosis and Prognosis:** Perhaps the most significant application of supervised learning in healthcare is in disease diagnosis [347]. ML models are trained on clinical data, including patient symptoms, lab results, and medical imaging, to identify diseases. For instance, ML models trained on imaging data can detect abnormalities such as tumors in radiographic images with high accuracy [348].
- **Personalized Treatment Plans:** Supervised learning algorithms analyze patient data to predict how individual patients might respond to different treatments. This personalized approach is particularly effective in oncology [349], where treatment plans are tailored based on the genetic makeup of a patient's tumor.
- **Risk Assessment:** Models trained on historical patient data can assess the risk of developing certain conditions, like diabetes or heart disease, based on a patient's lifestyle, genetics, and other factors [350].
- **Readmission Prediction:** Supervised learning can predict a patient's likelihood of readmission to a hospital. This is vital for improving patient care and reducing healthcare costs [351].

ML offers invaluable tools through its capabilities in classification and regression tasks, as previously mentioned. These foundational types of supervised learning tasks play a crucial role across a wide spectrum of applications, ranging from diagnosing diseases to forecasting patient outcomes. Below, we provide specific examples of both classification and regression tasks, highlighting their profound impact on improving healthcare delivery and enhancing patient care. Classification in the realm of ML entails categorizing data into predetermined classes or categories. In healthcare, this capability is crucial for:

- **Disease Diagnosis:** ML models are trained to classify patient data into disease categories. An example includes the use of Convolutional Neural Networks (CNNs) for classifying dermatological images into benign or malignant skin lesions [374].
- **Heart Disease Prediction:** Algorithms can analyze patient data such as age, blood pressure, cholesterol levels along with other clinical parameters to classify individuals into risk categories for heart disease. This classification aids in early intervention and preventive care [375].
- **Patient Triage in Emergency Rooms:** ML models can classify patients based on the severity of their condition. By analyzing symptoms, vital signs, and medical history, algorithms can assist in determining the urgency of each case, optimizing patient flow and resource allocation in emergency departments [376].

Regression tasks in ML deal with predicting continuous outcomes. In healthcare, regression models are applied to:

- **Predicting Patient Outcomes:** ML models can predict quantitative outcomes, such as the length of hospital stay, recovery time after surgery, or progression of a disease. For example, regression models might be used to predict blood sugar levels in diabetic patients based on their diet,

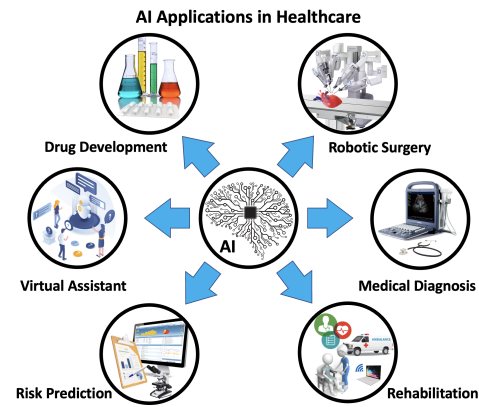


Fig. 3: Schematic Diagram Showing Six Application Scenarios of Artificial Intelligence in Healthcare.

medication, and physical activity [377].

- **Dosage Prediction:** In pharmacotherapy, regression algorithms can predict the optimal drug dosage for individual patients [378]. This application is particularly important in treatments like chemotherapy, where the dosage needs to be carefully balanced to be effective yet not overly toxic [379].
- **Disease Progression Modeling:** Regression models are used to understand and predict the progression of chronic diseases such as Alzheimer's, Parkinson's, or multiple sclerosis. By analyzing patient data over time, these models can forecast the rate of disease progression, aiding in treatment planning and patient counseling [46].
- **Survival Analysis:** In oncology, regression models are crucial for predicting patient survival times post-diagnosis or treatment [380]. These predictions, based on patient characteristics and treatment variables, are vital for treatment planning and patient management.

C.2. Unsupervised Learning

Unsupervised learning, a fundamental category of ML, involves analyzing and grouping unlabeled data based on similarities and differences, without any predefined labels [352]. Two critical techniques in unsupervised learning are clustering [353]–[355] and dimensionality reduction [356]–[359], each playing a vital role in healthcare, particularly in genomics and medical imaging.

Clustering is the process of grouping a set of objects in such a way that objects in the same group (or cluster) are more similar to each other than to those in other groups. Its applications in healthcare are significant:

- **Genomic Data Analysis:** In genomics, clustering helps in categorizing genes with similar expression patterns, which can be crucial for understanding gene functions, identifying disease markers, and revealing biological pathways. For instance, clustering can be used to identify groups of genes that are co-expressed in certain diseases, such as cancer and autoimmune disorders. This capability aids in discovering potential therapeutic targets by revealing genes that work in concert across these conditions, enhancing our understanding of disease mechanisms and treatment strategies [353].

- **Patient Stratification:** Clustering algorithms can segment patients into groups based on similarities in their medical records or genetic information [354]. This stratification aids in identifying subtypes of diseases with distinct clinical outcomes or responses to treatments, facilitating personalized medicine approaches.
- **Medical Imaging:** In medical imaging, clustering is used for image segmentation, which is the process of partitioning a digital image into multiple segments (sets of pixels). This technique plays a crucial role in identifying regions of interest, such as tumors in MRI or CT scans, and helps in the accurate diagnosis and treatment planning [355].
Dimensionality reduction is the process of reducing the number of random variables under consideration, by obtaining a set of principal variables. It's particularly important in dealing with high-dimensional data, as is often the case in healthcare:
- **Genomic Data Analysis:** Genomic data is inherently high-dimensional, with thousands of genes contributing to complex traits. Dimensionality reduction techniques like Principal Component Analysis (PCA) [356] and t-distributed Stochastic Neighbor Embedding (t-SNE) [357] are used to reduce the complexity of genomic data. This simplification helps in visualizing data, identifying genetic markers, and understanding the genetic architecture of diseases.
- **Medical Imaging:** High-resolution medical images contain a vast amount of data, making their analysis computationally intensive. Dimensionality reduction techniques can be applied to reduce the number of features in these images while retaining essential information [358]. This reduction is crucial for efficient storage, processing, and analysis of medical images, and facilitates the development of more efficient diagnostic algorithms [359].

C.3. Semi-Supervised Learning

Semi-supervised learning, a fundamental category of ML, occupies a unique position in healthcare by leveraging both labeled and unlabeled data to improve model performance [360], [361]. In scenarios where obtaining labeled data is expensive or time-consuming, semi-supervised learning offers a cost-effective solution by utilizing the abundance of unlabeled data available in healthcare settings.

- **Utilizing Unlabeled Data:** In semi-supervised learning, algorithms exploit the vast amounts of unlabeled data commonly present in healthcare databases [362]. This unlabeled data, although lacking explicit annotations, often contains valuable information that can complement the labeled data, enhancing the model's understanding of complex medical phenomena.
- **Combining Labeled and Unlabeled Data:** By incorporating both labeled and unlabeled data during model training, semi-supervised learning algorithms can learn more robust representations of the underlying data distribution [363]. This holistic approach improves the model's generalization capabilities, leading to more accurate predictions and classifications.

- **Semi-Supervised Techniques:** Various techniques are employed in semi-supervised learning, including self-training, co-training, and semi-supervised support vector machines. These methods iteratively refine the model's predictions using the labeled data while leveraging the unlabeled data to enhance its overall performance [363].

In healthcare, semi-supervised learning finds applications in diverse areas such as medical image analysis, clinical diagnosis, and patient monitoring.

- **Medical Image Analysis:** Semi-supervised learning algorithms can analyze large volumes of unlabeled medical images to identify subtle patterns or anomalies that may not be apparent to human observers. By combining this unsupervised analysis with labeled data, these algorithms can improve the accuracy of tasks such as tumor detection, organ segmentation, and disease classification [365].
- **Clinical Diagnosis:** In clinical settings, semi-supervised learning can assist healthcare professionals in diagnosing diseases or predicting patient outcomes by leveraging both labeled patient data and unlabeled population health data [364]. This integrated approach enhances the model's diagnostic accuracy and reliability, leading to more informed clinical decisions and improved patient care.
- **Patient Monitoring:** Semi-supervised learning techniques can also be employed for continuous patient monitoring, where large streams of unlabeled patient data, such as electronic health records and physiological signals, are analyzed to detect deviations from normal health patterns [381]. By incorporating this unlabeled data into predictive models, healthcare providers can proactively identify and intervene in adverse health events, minimizing patient risks and improving health outcomes.

Overall, semi-supervised learning offers a powerful framework for leveraging the wealth of unlabeled data in healthcare to enhance the performance of ML models, ultimately advancing medical research, diagnosis, and treatment strategies [382], [383].

C.4. Reinforcement Learning

Reinforcement Learning (RL) is a type of ML that is particularly suited for situations where an agent must make a sequence of decisions to achieve a goal [366]. Within RL, there are several approaches to learning optimal policies, two of which are:

- **Dynamic Programming:** This approach to RL involves breaking down a decision-making problem into simpler sub-problems and solving them recursively. It is particularly effective in environments with a perfect model, where all states and transitions are known beforehand.
- **Monte Carlo Methods:** These methods rely on repeated random sampling to approximate the optimal policy. They are model-free approaches, which means they do not require complete knowledge of the environment and are particularly useful for problems with stochastic dynamics and rewards.

In the context of healthcare, RL offers innovative ways to approach complex, dynamic decision-making problems [367]. It operates on the principle of reward and penalty, learning

optimal actions through trial and error to maximize cumulative rewards.

Some of the key concepts of reinforcement learning can be summarized as follows:

- **Agent and Environment:** In RL, an 'agent' (e.g., a healthcare model) interacts with its 'environment' (e.g., patient data or medical scenarios). The agent makes decisions or actions, and the environment provides feedback in the form of rewards or penalties.
- **Policy:** A policy is a strategy used by the agent to determine the next action based on the current state of the environment. In healthcare, this might involve choosing a treatment plan based on a patient's current health status.
- **Reward Signal:** The agent's actions are guided by a reward signal. Positive rewards encourage the agent to continue making similar decisions, while negative rewards signal the agent to adjust its approach.
- **Value Function:** This function estimates the expected cumulative reward of taking a certain action in a given state, helping the agent predict long-term outcomes.
- **Exploration vs. Exploitation:** RL involves balancing exploration (trying new actions) with exploitation (using known actions that yield high rewards). In healthcare, this might mean balancing between tried-and-tested treatments and experimental therapies.

Reinforcement learning can also be very useful in healthcare, with applications such as treatment optimization, clinical trial design, robotic surgery, and healthcare management.

- **Treatment Optimization:** RL can optimize treatment strategies, adjusting them over time based on patient response [368]. For chronic diseases like diabetes, RL models can suggest insulin dosages, dietary recommendations, and exercise plans that adapt to changing health indicators.
- **Clinical Trial Design:** In designing clinical trials, RL can help in determining the most effective trial structures, treatment regimens, and patient selection criteria, enhancing the efficiency and success rates of trials [369].
- **Robotic Surgery and Rehabilitation:** RL is used in training robotic systems for surgery and rehabilitation, allowing them to adapt to patient-specific conditions and improve over time based on feedback from surgical outcomes or patient recovery rates [370].
- **Personalized Medicine:** RL models can analyze patient data over time to predict the most effective treatment plans, considering the unique health trajectory and response patterns of each patient [371], [372].
- **Healthcare Resource Management:** RL algorithms can assist in managing healthcare resources, such as hospital bed allocation, staff scheduling, and equipment usage, by learning optimal allocation strategies based on demand patterns and resource availability [373].

C.5. Case Studies of Machine Learning in Healthcare

ML has made significant inroads into the healthcare sector, offering groundbreaking applications that are transforming patient care, diagnostics, treatment planning, and disease management. Below are some notable real-world examples of ML

applications in healthcare, highlighting both their successes and the challenges they face.

- **Diagnostic Imaging and Radiology:** ML algorithms, particularly deep learning models, have achieved remarkable success in interpreting medical images. For instance, Google Health developed an ML model for breast cancer screening that outperformed human radiologists in detecting cancer in mammograms [384]. However, challenges remain in integrating these systems into clinical workflows, dealing with diverse data quality, and ensuring consistent performance across different populations and equipment.
- **Drug Discovery and Development:** ML has accelerated the drug discovery process, reducing costs and time. Atomwise uses AI to predict which molecules could lead to effective drugs, and in 2020, they used their platform to identify promising compounds for treating COVID-19 [328]. Nevertheless, the primary challenge lies in validating AI-discovered drugs in clinical trials, a process that is time-consuming and requires substantial investment.
- **Predictive Analytics in Patient Care:** ML models are increasingly used for predictive analytics in patient care. An example is the use of ML by a team at Johns Hopkins University, to predict sepsis in hospitalized patients, enabling early intervention [334]. However, the challenge here involves ensuring data privacy, overcoming data silos in healthcare settings, and dealing with the potential biases in the data used to train these models.
- **Personalized Medicine:** In personalized medicine, ML aids in tailoring treatments to individual patients' genetic profiles. A team in Earle A. Chiles Research Institute uses ML to analyze genetic data from cancer patients to identify the most effective treatment plans [385]. Challenges include managing the vast amounts of genetic data, ensuring accurate interpretations of this data, and integrating these insights into routine clinical practice.
- **Mental Health Applications:** ML models are used for monitoring and diagnosing mental health conditions. For example, apps like Ginger.io use ML algorithms to analyze user interaction and provide personalized mental health support [386]. Challenges include addressing privacy concerns, ensuring the sensitivity and specificity of the algorithms in diverse populations, and integrating these tools with traditional mental health services.

D. Federated Learning

Within the field of ML, data security and privacy are paramount concerns. Traditional ML approaches often require centralized data storage, which can raise privacy issues and limit participation due to data ownership restrictions. FL emerges as a groundbreaking solution, offering a decentralized paradigm for collaborative ML [387]. In FL, multiple entities, such as healthcare institutions or research centers, collaborate to train a model without sharing their raw data. Each entity trains a local model on its own data and shares only model updates, such as gradients or parameters, with a central server. This collaborative approach allows for

distributed learning while preserving data privacy and security.

D.1. Federated Learning Types

FL encompasses various implementations tailored to diverse scenarios and constraints. In the following, we delve deeper into the three prominent types of FL implementations: horizontal FL, vertical FL, and federated transfer learning. Each type addresses specific challenges and offers unique advantages in FL environments.

- **Horizontal Federated Learning (HFL):** HFL involves training models across multiple devices or clients that possess similar data distributions but are unable to share raw data due to privacy or regulatory concerns. In this approach, each client trains a local model using its data and shares only model updates, such as gradients or model parameters, with a central server [388]. The server aggregates these updates to refine a global model, which is then redistributed to clients for further refinement. This iterative process continues until convergence is achieved. Horizontal federated learning is particularly suitable for scenarios where data is distributed across devices or clients with similar characteristics, such as mobile phones in a collaborative learning setting, edge devices in Internet of Things (IoT) networks [389] or EEG data for electroencephalography [390]. Challenges in horizontal federated learning often revolve around privacy-preserving techniques, communication efficiency, and model aggregation strategies to ensure convergence and accuracy while preserving data privacy and security [391].

- **Vertical Federated Learning (VFL):** Vertical federated learning addresses scenarios where data is distributed across multiple parties with complementary features but cannot be directly shared due to privacy or proprietary concerns. Unlike horizontal federated learning, which focuses on data with similar distributions, vertical federated learning operates on data with different but complementary features [392].

In vertical federated learning, each party holds a subset of features relevant to the learning task, and the goal is to collaboratively train a model without sharing raw data. Secure Multi-Party Computation (SMPC) and homomorphic encryption techniques are commonly employed to enable computations on encrypted data while preserving privacy [393]. These techniques allow parties to jointly compute model updates or predictions without revealing sensitive information about their data.

Vertical federated learning finds applications in scenarios such as healthcare, where different institutions may hold complementary patient data (e.g., medical records, lab results) that are crucial for training accurate models while preserving patient privacy and data ownership [394].

- **Federated Transfer Learning (FTL):** Federated transfer learning extends traditional transfer learning to federated settings, where models are trained across multiple decentralized datasets to leverage knowledge from related tasks or domains [395]. Unlike traditional transfer learning, where a pre-trained model is fine-tuned on a target dataset, federated

transfer learning involves aggregating knowledge from multiple decentralized datasets to improve model performance. In federated transfer learning, a base model is initialized either with a pre-trained model or from scratch, and model updates from decentralized clients are aggregated to refine the base model. This approach allows for leveraging knowledge from diverse data sources while accommodating variations in data distributions and characteristics across clients [396].

Federated transfer learning is beneficial in scenarios where labeled data is scarce or unevenly distributed across clients such as electrocardiogram signal analysis [397], enabling collaborative model training while leveraging knowledge from related tasks or domains to improve model performance.

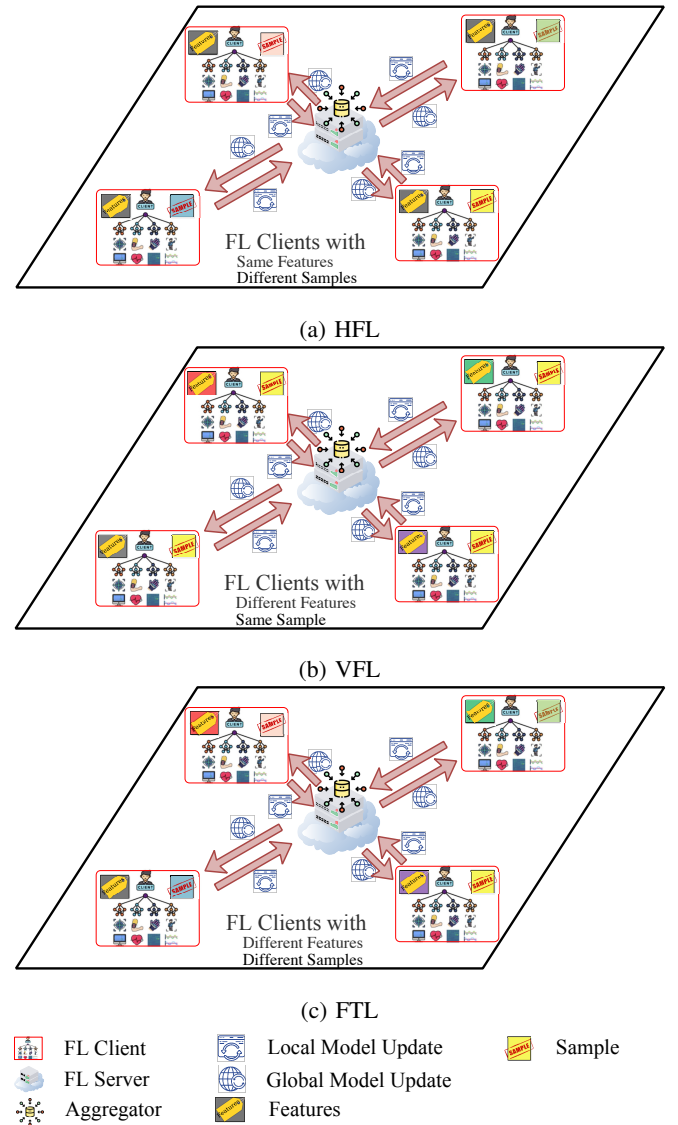


Fig. 4: Types of Federated Learning

D.2. Case Studies of Federated Learning in Healthcare

FL holds promise in healthcare by facilitating the collaborative development of robust ML models across various

institutions, such as hospitals and research centers, while safeguarding patient data privacy [12], [398]. This approach entails training ML models on local datasets, with only model updates shared, rather than raw data, to a central server for aggregation, thus mitigating privacy concerns and reducing data transfer costs [399]. FL in healthcare offers several advantages over traditional centralized learning, including enhanced privacy and the utilization of diverse datasets without necessitating centralization. Below, we delve into real-world examples of FL applications in the healthcare sector:

- **Multi-Institutional Collaboration for Disease Diagnosis:** One of the most significant successes of FL in healthcare is observed in collaborative projects for disease diagnosis. For example, a consortium of international medical centers used FL to develop models for predicting patient outcomes in critical care. By leveraging data from diverse populations while maintaining data privacy, these models achieved high accuracy in predicting outcomes such as mortality and length of hospital stay. One successful implementation is seen in the Rhino Health consortium collaboration, which involves prestigious institutions and experts from around the world. Participants in this collaboration include Massachusetts General Hospital (U.S.), University of Cambridge School of Medicine (UK), Lahey Hospital and Medical Center (U.S.), Assuta Medical Centers (Israel), Dasa S.A. (Brazil), National Taiwan University (Taiwan), and Seoul National University Hospital (South Korea). These collaborations underscore the global effort to harness the power of FL in enhancing medical research and healthcare delivery while upholding data privacy and security.
- **Enhancing Drug Discovery and Development:** FL has been used in pharmaceutical research to create predictive models for drug response and toxicity. A notable instance is a project where multiple pharmaceutical companies shared algorithmic models, not data, to predict the success of drug compounds, expediting the drug discovery process while maintaining the confidentiality of proprietary data [400].
- **Collaborative Research:** In oncology, FL enables institutions to collaborate on cancer research without sharing sensitive patient data. A notable example is the collaboration facilitated by Intel and Penn Medicine, utilizing FL to identify brain tumors [401]. These case studies demonstrate how FL enables institutions to collaborate in advancing medical research while maintaining the confidentiality of their data.

D.3. Challenges of Federated Learning in Healthcare

FL presents a groundbreaking opportunity in healthcare, facilitating the collaborative development of potent ML models while safeguarding patient data privacy and minimizing data transfer costs. However, realizing the full potential of FL requires overcoming significant challenges. Below, we delineate these challenges to underscore the complexities FL encounters in healthcare:

- **Data Heterogeneity and Model Generalizability:** One of the primary challenges in FL is the heterogeneity of medical data across different institutions having data in various for-

ats and from diverse populations. This variability can lead to challenges in model convergence and performance, as models must be generalizable to diverse patient populations and data types.

- **Technical and Computational Limitations:** Implementing FL requires significant computational resources and technical expertise, which may not be uniformly available across all participating institutions. Balancing these computational disparities is a challenge that needs to be addressed for the successful implementation of FL.
- **Regulatory and Ethical Compliance:** FL must navigate complex regulatory and ethical landscapes. This includes ensuring compliance with healthcare regulations such as Health Insurance Portability and Accountability Act (HIPAA) in the US, and the General Data Protection Regulation (GDPR) in Europe, which govern patient data privacy and security. Ethical considerations include ensuring that patient consent is obtained for the use of their data in such models and that the benefits of such research are equitably distributed. Addressing these considerations requires clear data governance policies and ethical frameworks for FL deployment in healthcare.
- **Scalability and Real-Time Learning:** While FL allows for collaborative model building, scaling these models to accommodate real-time learning and large datasets poses technical challenges. Efficiently managing and updating models with new data in real time remains a hurdle.
- **Future Prospects:** Looking forward, the integration of FL with emerging technologies such as IoT devices and real-time health monitoring systems holds great potential. This could enable the continuous improvement of ML models with real-time data from diverse and distributed sources, leading to more dynamic and responsive healthcare solutions. Additionally, advancements in edge computing could further enhance the efficiency and scalability of FL in healthcare.
- **Possible Solutions:** Addressing these challenges can be achieved through several approaches: firstly, by establishing standardized data formats across participating entities, ensuring consistency and compatibility in the data used for FL. Secondly, by implementing comprehensive data preprocessing pipelines, which enhance the quality and usability of the data before it is fed into the learning models. Additionally, designing FL algorithms that are adept at handling diverse data types and can operate effectively across varying computational resources is crucial.

E. Current Trends and Future Directions in FL for Healthcare

The landscape of FL in healthcare is rapidly evolving, driven by technological advancements and the growing need for collaborative and privacy-preserving data analysis. This section outlines the current trends shaping FL in healthcare and forecasts its future trajectory.

E.1. Current Trends in FL for Healthcare

The prevailing trends shaping FL in healthcare reflect a dynamic evolution towards enhanced analytics, privacy, collaboration, and ethical considerations. These trends include:

- **Integration with Advanced Analytics and AI:** FL is increasingly being integrated with sophisticated AI techniques, such as deep learning, to enhance its analytical capabilities [402], [403]. This integration allows for more complex and accurate models, capable of addressing intricate healthcare challenges like personalized medicine and predictive analytics [12].
- **Emphasis on Data Privacy and Security:** In the wake of heightened concerns about data privacy, FL is gaining traction as a preferred method for collaborative healthcare research [404]. Its inherent design, which allows for model training without sharing raw data, aligns well with stringent data privacy regulations like those of HIPAA and GDPR.
- **Cross-Institutional Collaborations:** There is a growing trend of cross-institutional collaborations facilitated by FL as is explained above. These collaborations can unite hospitals, research centers, and academic institutions, enabling them to pool their knowledge and data resources for collective model improvement while maintaining data sovereignty.
- **Ethical and Fair AI Development:** As FL continues to evolve, there will be an increased focus on ethical AI development. This includes ensuring that FL models are fair, unbiased, and representative of all patient demographics, thereby addressing concerns around algorithmic bias [405]–[407].

E.2. Future Directions in FL for Healthcare

FL in healthcare stands on the brink of significant expansion, propelled by emerging technological advancements and evolving healthcare landscapes. This forthcoming evolution encompasses:

- **Expansion into Global Health Initiatives:** FL has the potential to significantly impact global health research, particularly in areas with stringent privacy laws or limited data-sharing capabilities. It could facilitate the analysis of global health trends and the development of models that are representative of diverse populations [12].
- **Automated and Dynamic Model Updating:** The future of FL in healthcare might see more automated and dynamic updating of models [408]. This would enable healthcare systems to respond quickly to new data or changing health trends, making FL models more adaptive and responsive.
- **Use in Remote and Real-Time Monitoring:** With the proliferation of wearable devices and IoT in healthcare, FL is poised to play a significant role in real-time patient monitoring and remote healthcare, providing personalized insights and treatments based on data collected from diverse patient populations [409].
- **Edge Computing Integration:** Integrating FL with edge computing could decentralize the computational workload, allowing for faster and more efficient model training and updates, especially in real-time applications [406], [410], [411].
- **Integration with Blockchain for Enhanced Security:** The integration of FL with blockchain technology is a promising development, which forms the central theme of this tutorial. This combination not only bolsters

data security but also adds a layer of transparency and traceability to the FL process, ensuring immutable record-keeping and verifiable model updates in FL networks [412].

In summary, FL in healthcare is at a dynamic juncture, with its trajectory poised to reshape healthcare research and delivery. Its alignment with current needs for privacy, collaboration, and advanced analytics, coupled with its adaptability for future technological trends, positions FL as a key player in the future landscape of healthcare technology. The ongoing advancements in FL are not just technological but also pave the way for more equitable, secure, and efficient use of healthcare data globally.

IV. BLOCKCHAIN

BC technology has undergone a remarkable evolution since its inception in 2009 with the creation of Bitcoin by an individual or group using the pseudonym Satoshi Nakamoto [413]. The primary purpose of Bitcoin was to establish a decentralized digital currency, and the innovation that made this possible was the blockchain—a distributed ledger that records transactions across a network of computers securely and transparently.

In the following years, the potential applications of blockchain technology expanded beyond cryptocurrency. Vitalik Buterin introduced Ethereum [414] in 2015, introducing the concept of smart contracts—self-executing contracts with the terms of the agreement directly written into code. This development opened up a broader spectrum of Decentralized Applications (DApps) and laid the foundation for blockchain's role in facilitating not only Peer-to-Peer (P2P) transactions but also complex programmable interactions.

The years that followed witnessed a surge in blockchain projects and platforms, each aiming to address specific challenges across various industries. The technology gained recognition for its potential to enhance transparency, security, and efficiency. Consortia and collaborations emerged, with enterprises exploring how blockchain could optimize supply chains [415]–[419], streamline financial transactions, and enhance data integrity.

To the best of our knowledge in January 2024, blockchain continues to evolve, with ongoing efforts to address scalability issues, energy consumption concerns, and regulatory considerations. From its humble beginnings as the underlying technology for Bitcoin, blockchain has grown into a versatile tool with the potential to reshape how industries manage and verify data. The technology's journey reflects an ongoing quest for innovative solutions to long-standing challenges in the digital realm.

In this section, we provide a concise overview of fundamental concepts, features, structure, and taxonomy within the realm of blockchain technology.

A. Blockchain Technology: An Overview

BC technology is a decentralized and distributed ledger system designed to facilitate secure and transparent transactions without the need for a central authority. At its core,

a blockchain consists of a chain of blocks, each containing a list of transactions. These blocks are linked together in a chronological and immutable manner, forming a continuous chain. One of the key features of blockchain is its decentralization, meaning that the ledger is maintained by a network of nodes rather than a single central entity. This distributed nature enhances security, reduces the risk of fraud, and ensures transparency in the transaction process.

BC technology possesses several distinctive features that contribute to its popularity and versatility across various industries. We summarize the features of blockchain technology as follows:

- **Decentralization:** blockchain operates on a P2P network. This fact eliminates the need for a central authority or intermediary. Decentralization enhances security, reduces the risk of a single point of failure, and promotes trust among mutually untrusted participants [420].
- **Immutability:** Immutability is the capability of a blockchain ledger to remain unchanged. Once a block is added to the blockchain, it becomes virtually impossible to alter or delete the information within it. Immutability ensures the integrity of the transaction history and builds trust in the accuracy of recorded data.
- **Transparency:** means the entire transaction history is visible to all participants in the network. Transparency fosters trust and accountability as participants can independently verify transactions and the state of the blockchain.
- **Security:** blockchain employs cryptographic techniques to secure transactions and control access to the network. Consensus mechanisms, such as Proof of Work (PoW) or Proof of Stake (PoS), enhance security by preventing unauthorized changes to the blockchain [421]–[423].
- **Distributed Ledger:** The ledger is distributed among the nodes over the network and each node in the network holds a copy of the blockchain. This distribution ensures redundancy, resilience, and a shared source of trust among the participants.
- **Consensus Mechanisms:** Consensus is a mechanism that gives the ability to the network to agree upon the validity of transactions (and blocks) and the order in which they can be added to the blockchain.
- **Anonymity and Privacy:** While all the transactions in the blockchain network are transparent, participants will remain pseudonymous due to the use of public/private key pairs.
- **Efficiency and Speed:** BC reduces the need for intermediaries and manual processes, leading to faster and more efficient transactions. In some cases, however, the speed of transactions may depend on the specific consensus mechanism employed. For instance, PoW blockchains, like Bitcoin, tend to be slower (i.e. with less throughput) compared to traditional payment systems like Visa and Mastercard. The primary reason for this is the inefficiency of the underlying consensus mechanisms and the way transactions are processed [424].
- **Interoperability:** BC interoperability refers to the ca-

capacity of various blockchain networks to interact seamlessly, facilitating the exchange of messages, data, and tokens among them. [425]–[429]. Standards and protocols are evolving to enable such a communication and data exchange between disparate blockchain platforms. The Inter-Blockchain Communication (IBC) protocol [430] is designed to facilitate this interoperability by providing a standardized way for independent blockchains to transfer and communicate with each other.

- **Ability to Support Smart Contracts:** Smart contracts are self-executing contracts with the terms directly written into code. These contracts automate and enforce predefined rules and agreements, reducing the need for intermediaries and streamlining processes [431], [432].

B. Consensus in Blockchain

Consensus in the context of blockchain refers to the mechanism by which a distributed network of nodes agrees on the state of the system or the validity of transactions [433]–[435]. Since blockchain operates in a decentralized and trustless environment, consensus is crucial to ensure that all participants have a consistent view of the blockchain's history and current state. The consensus mechanism is responsible for preventing double-spending (where the same digital asset is spent more than once) and maintaining the integrity of the blockchain. Different blockchain networks employ various consensus algorithms, each with its own set of rules and processes. The most prominent and currently existing consensus protocols are as follows:

B.1. Proof of Work

This is the original consensus algorithm used by Bitcoin [413] and many more cryptocurrencies. In PoW, participants (miners) solve complex mathematical puzzles to validate transactions and create new blocks. The first miner to solve the puzzle gets the right to add a new block to the blockchain. PoW is resource-intensive and requires a significant amount of computational power [436]. BCs that rely on PoW are more prone to forks. A fork in blockchain technology refers to a split in the blockchain's transaction history, resulting in two or more separate paths. This can occur for various reasons, such as changes in the protocol rules, disagreements among participants, or software upgrades [437].

B.2. Proof of Stake

In PoS [438], validators (i.e. block proposer participants) are chosen to create new blocks based on the amount of cryptocurrency they hold and are willing to "stake" as collateral. This eliminates the need for energy-intensive mining and aims to provide a more energy-efficient alternative to PoW. Participants are chosen to create new blocks and validate transactions based on the amount of cryptocurrency they hold and are willing to stake as collateral. Examples include Ethereum's [439] transition to Ethereum 2.0, Cardano [440], and Algorand [441]. Delegated Proof of Stake (DPoS) is an improvement over traditional PoS in terms of scalability and efficiency [442].

B.3. Byzantine Fault Tolerance

Byzantine Fault Tolerance (BFT) consensus algorithms are a class of protocols designed to achieve consensus in distributed systems, even in the presence of faulty or malicious nodes. In a Byzantine Fault Tolerant-based consensus (BFT-based consensus) algorithm, a network of nodes collaborates to agree on the state of the system or the validity of transactions. The term "Byzantine Fault" originates from the Byzantine Generals' Problem [443], a theoretical scenario where a group of generals must come to a unanimous agreement on a coordinated action, despite the possibility of some generals being traitors and sending conflicting messages. Practical Byzantine Fault Tolerance (pBFT) is the most prominent variant of BFT-based consensus protocols [444]. This algorithm is designed to tolerate up to one-third of the total number of nodes being faulty or malicious. This means that as long as no more than one-third of the nodes in the network exhibit Byzantine behavior (i.e., they may fail arbitrarily or behave maliciously), pBFT can still reach consensus and continue to operate correctly. Some variants of BFT (e.g. pBFT and Improved Byzantine Fault Tolerance (IBFT)) are supported by Hyperledger Fabric [445].

B.4. Proof of Capacity

Proof of Capacity (PoC) is a consensus mechanism used in blockchain networks as an alternative to PoW and PoS. In PoC, the ability to mine or validate transactions is determined by the amount of storage space (capacity) a participant allocates rather than computational power or stake in the network's native cryptocurrency. Participants, also known as miners or validators, allocate a certain amount of their available storage space to participate in the consensus process, often precomputing and dedicating this storage space solely for mining purposes. They generate plots, which are essentially pre-computed sets of data representing potential solutions to cryptographic puzzles, and store these plots in the allocated storage space. When a new block needs to be added to the blockchain, miners search their precomputed plots for solutions to a cryptographic puzzle, and the miner who finds a valid solution first is eligible to add the new block to the blockchain and is rewarded accordingly. To verify the validity of a block generated through PoC, other nodes in the network check that the solution provided by the miner corresponds to the pre-computed data in their plots, ensuring consensus. PoC offers advantages such as energy efficiency, decentralization, and fair reward distribution, as it consumes less electricity, allows for a more decentralized network without the need for expensive specialized hardware, and distributes block rewards more evenly among participants based on the amount of storage space allocated. However, challenges include the initial investment of time and resources required for generating plots and allocating storage space, as well as the significant storage space requirements, which may limit participation for some individuals or entities with limited resources. Overall, PoC presents an alternative approach to achieving consensus in blockchain networks, emphasizing energy efficiency, decentralization, and fair reward distribution. A more energy-efficient variant of PoC

called Proof of Space and Time (PoST) is being used by Chia [446].

B.5. Direct Acyclic Graph Tangle

Direct Acyclic Graph Tangle (DAG) consensus protocols are a class of distributed consensus algorithms that use a data structure called a directed acyclic graph to achieve agreement on the order of transactions or events in a decentralized network. Unlike traditional blockchain-based consensus protocols where transactions are organized into linear blocks, DAG-based protocols organize transactions in a more flexible graph structure [447].

One of the most well-known implementations of DAG consensus is the Tangle [448], which is used in the IOTA cryptocurrency network [449]. In the Tangle, each transaction directly references and approves two previous transactions, forming a directed acyclic graph structure. The most prominent blockchains that run on proof of capacity include Signum, Chia, and SpaceMint.

B.6. Proof of Burn

Proof of Burn (PoB) is a consensus mechanism utilized in which the participants, also known as burners, demonstrate their commitment to the network by sending cryptocurrency tokens to a verifiably unspendable address, termed the "burn address," effectively destroying or burning the tokens [450]. This process is integral to PoB, as it signifies participants' investment in the network. Following the token burning, participants provide evidence, or proof of the burned tokens, typically recorded transparently and verifiably on the blockchain. This proof serves to validate the burn event and participants' commitment to the network. In some PoB systems, participants demonstrating proof of burn may be eligible for rewards or incentives, which can include newly minted tokens, voting rights, or other benefits within the blockchain ecosystem. PoB offers several key advantages, including the allocation of resources by participants as a form of investment or commitment, leading to a fairer distribution of tokens and resistance against Sybil attacks [451] due to the deterrent effect of burning tokens. However, PoB also presents challenges such as potential token scarcity resulting from the reduction in the overall token supply, as well as economic considerations for participants regarding the permanent loss of token value. Overall, Proof of Burn represents an innovative consensus mechanism that emphasizes commitment and resource allocation, offering advantages such as fair distribution and Sybil resistance, albeit accompanied by challenges related to token scarcity and economic implications.

B.7. Hybrid Consensus Protocols

Hybrid consensus models in blockchain combine elements of multiple traditional consensus mechanisms to leverage their respective strengths and mitigate their weaknesses. These models aim to achieve a balance between decentralization, security, scalability, and energy efficiency [452]. Here are some examples of hybrid consensus models in blockchain:

B.8. Proof of Stake and Proof of Work Hybrid

Some blockchain networks combine PoS and PoW mechanisms to achieve consensus (e.g. TwinsCoin [453]). For example, a PoW component may be used for initial block creation, while PoS is utilized for subsequent block validation or as a way to elect validators. This hybrid approach aims to maintain security through PoW while improving scalability and energy efficiency with PoS.

B.9. Proof of Authority and Proof of Work Hybrid

In this hybrid model, a network may utilize PoW for initial block creation and Proof of Authority (PoA) for block validation. PoW ensures the initial distribution of tokens and secures the network against Sybil attacks, while PoA provides fast finality and scalability by relying on known and trusted validators.

B.10. Delegated Proof of Stake and Proof of Authority Hybrid

DPoS allows token holders to vote for a limited number of delegates who are responsible for block validation. In a hybrid approach, DPoS can be combined with PoA, where the initial set of validators is determined through PoA, and then token holders can vote for additional delegates using DPoS. This hybrid model aims to achieve both decentralization and scalability.

B.11. Proof of Work and Byzantine Fault Tolerance Hybrid

This hybrid model combines the energy-intensive PoW with a BFT-based consensus algorithm such as pBFT or Tendermint [454]. PoW is used for block creation, while BFT consensus ensures finality and Byzantine fault tolerance. This approach aims to achieve both security and efficiency in blockchain networks [455].

B.12. Hybrid Voting Systems

Some blockchain networks combine different voting mechanisms, such as direct voting by token holders and voting by elected delegates. This hybrid voting system aims to balance the influence of token holders with the expertise and accountability of elected representatives.

C. Blockchain Data Structure

In blockchain technology, the data structure plays a pivotal role in ensuring the integrity, security, and immutability of the distributed ledger. At its core, a blockchain is composed of a series of blocks, each containing a bundle of transactions. These blocks are cryptographically linked together sequentially, forming a continuous chain. The data structure of a block typically includes several key components: a header, a list of transactions, and a cryptographic hash. The header contains metadata such as the block's unique identifier (block hash), a timestamp, and a reference to the previous block's hash, thus establishing the chronological order of blocks. The list of transactions records the details of all transactions included in the block, such as sender and receiver addresses, transaction amounts, and cryptographic signatures for verification. Additionally, each block is assigned a cryptographic hash,

computed based on its contents using a hashing algorithm like SHA-256. This hash serves as a unique identifier for the block and is crucial for maintaining the integrity of the blockchain. Any alteration to the data within a block would result in a change in its hash, thereby breaking the chain's continuity and signaling tampering. This inherent immutability and tamper-resistance of the data structure in blockchain ensure that once recorded, transactions cannot be altered or deleted without consensus from the network participants, establishing a reliable and transparent system for recording and verifying transactions [456].

D. Blockchain Network and Architecture

The network architecture in blockchain is a distributed and decentralized system that enables the secure and transparent exchange of data and value across a network of interconnected nodes. At its core, blockchain operates as a P2P network where each participant, or node, maintains a copy of the entire blockchain ledger. This distributed architecture ensures that there is no single point of failure, as the data is replicated and synchronized across multiple nodes. Nodes communicate with each other through a consensus mechanism that we already explained. Depending on the consensus algorithm employed, nodes may take on different roles, such as miners in PoW or validators in PoS systems. Transactions are broadcasted to the network and validated by consensus, typically requiring confirmation from a majority of nodes before being added to the blockchain. This network architecture provides several benefits, including resilience against censorship and tampering, increased transparency and accountability, and enhanced security through cryptographic techniques. Additionally, the decentralized nature of blockchain networks promotes trust among participants by eliminating the need for intermediaries and central authorities, thereby fostering a more inclusive and democratic ecosystem for conducting transactions and exchanging value [457].

BC technology typically consists of several layers, each serving a specific purpose in the functioning and security of the blockchain network. The most common layers include:

- 1) *Network Layer*: The network layer serves as the foundation of the blockchain system, facilitating communication between nodes (individual computers) in the network. It is responsible for transmitting data, such as transactions and blocks, across the network using protocols like TCP/IP, HTTP, and P2P protocols.
- 2) *Data Layer*: The data layer stores the actual blockchain data, including blocks, transactions, smart contracts, and other relevant information. It includes data structures, databases, and storage mechanisms optimized for storing and retrieving blockchain data in a secure and efficient manner.
- 3) *Consensus Layer*: The consensus layer ensures that all nodes in the network agree on the validity of transactions and the order in which they are added to the blockchain. Different blockchain networks employ various consensus mechanisms, such as PoW, PoS, DPoS, and Practical pBFT, to achieve agreement among participants.

- 4) *Smart Contract Layer*: Smart contracts are self-executing contracts with terms directly written into code. This layer enables the creation and execution of programmable contracts, powering various DApps. Smart contract platforms like Ethereum provide the infrastructure for developers to build applications ranging from Decentralized Finance (DeFi) to supply chain management.
- 5) *Incentive Layer*: The incentive layer provides mechanisms to incentivize participants, such as miners or validators, to contribute resources and maintain the security and integrity of the blockchain network. Incentives typically include block rewards and transaction fees, which compensate participants for their contributions. Examples include Bitcoin's block rewards and Ethereum's gas fees.
- 6) *Application Layer*: This layer encompasses the user-facing applications and interfaces that interact with the blockchain network. It includes DApps, wallets, smart contracts, and other software built on top of the blockchain protocol.

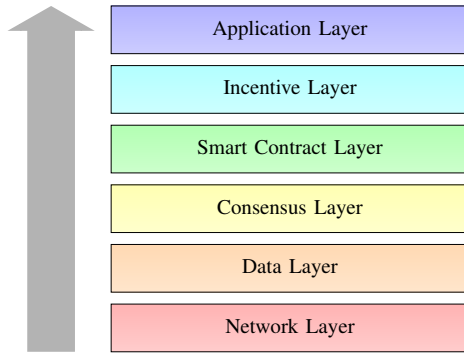


Fig. 5: Blockchain Layers

E. Inter-Blockchain Communication (IBC) Protocol

Interoperability is one of the most important features of the next-generation blockchain networks and refers to the ability of different blockchain platforms to communicate, share data, and transact with each other seamlessly. It enables interoperability between disparate blockchain networks, allowing them to interact and exchange information or assets without the need for intermediaries or centralized exchanges. Interoperability is essential for realizing the full potential of blockchain technology by facilitating cross-chain transactions, asset transfers, and data sharing between different blockchain ecosystems [430].

The IBC protocol is a set of standards and protocols designed to enable communication and interoperability between independent blockchain networks. IBC facilitates the secure and trustless transfer of assets and data across different blockchains, allowing them to interact and transact with each other directly. The protocol defines a standardized messaging format and a set of rules for validating and verifying transactions between participating blockchains. By implementing the IBC protocol, blockchain networks can establish inter-

connectivity, enabling cross-chain transactions, decentralized exchanges, and interoperable DApps [427], [458], [459].

IBC is one of the pillars of the Internet of Blockchains (IoB) [460], [461]. The concept of IoB refers to a vision where blockchain networks are interconnected in a similar way to how the Internet connects various computer networks globally. IoB aims to create a decentralized and interoperable network of blockchains, where different blockchain platforms can seamlessly communicate and transact with each other, just as different devices and systems are connected over the internet. The IoB enables a decentralized and open ecosystem where data, assets, and services can flow freely between different blockchains, unlocking new possibilities for innovation and collaboration. Examples of interoperability solutions and projects in the blockchain space include:

- 1) *Cosmos*: Cosmos is a decentralized network of interconnected blockchains that utilize the IBC protocol to enable communication and interoperability between different blockchain platforms [462]. Cosmos Hub serves as the primary hub for connecting various blockchains within the Cosmos ecosystem, allowing them to transfer assets and data securely and efficiently.
- 2) *Polkadot*: Polkadot is a multi-chain blockchain platform that enables interoperability between different parachains (parallel blockchains) within its network. Polkadot's relay chain facilitates communication and interoperability between parachains, allowing them to share data and assets and interact with each other seamlessly [463].
- 3) *Wanchain*: Wanchain is a cross-chain blockchain platform that focuses on interoperability and connecting different blockchain networks. Wanchain's interoperability protocol enables the secure and decentralized exchange of assets between different blockchains, including Bitcoin, Ethereum, and others [464].

F. Blockchain Taxonomy

At a high level, blockchain networks are classified into three main categories: private, public, and consortium blockchains. We briefly explain each of them as follows.

F.1. Private Blockchain

A private blockchain is a permissioned blockchain network where access and participation are restricted to authorized entities only. These entities typically have known identities and are granted permission to join the network by a central authority or administrator. Private blockchains are often used by enterprises and organizations to build internal blockchain solutions for specific use cases such as supply chain management, document verification, or intercompany transactions. They offer enhanced privacy, control, and scalability compared to public blockchains [465]–[468]. For instance, Hyperledger Fabric is a private blockchain framework developed by the Linux Foundation's Hyperledger project [445], [469]. It is designed for enterprise use cases and enables organizations to create permissioned blockchain networks with customizable features and governance models.

F.2. Public Blockchain

A public blockchain is a permissionless blockchain network that is open to anyone to join, participate, and transact without requiring permission or identification. Public blockchains are decentralized networks where transactions are transparent, immutable, and verifiable by anyone. They offer high levels of transparency, censorship resistance, and security but may sacrifice scalability and privacy due to their open nature [470]–[473]. Public blockchains are often used for cryptocurrencies, DApps, and tokenized assets. For instance, Bitcoin is the first and most well-known public blockchain, created by an anonymous entity or group of individuals using the pseudonym Satoshi Nakamoto. It operates as a decentralized peer-to-peer network for sending and receiving the Bitcoin cryptocurrency.

F.3. Consortium Blockchain

A consortium blockchain is a semi-decentralized blockchain network governed by a consortium or group of organizations rather than a single centralized entity. Consortium blockchains are permissioned networks where the consensus process and governance are shared among a predefined set of participants. Consortium blockchains are commonly used in industries or sectors where multiple organizations collaborate on shared processes or infrastructure while still maintaining some level of control and privacy [474]–[477]. They offer a balance between the decentralization of public blockchains and the control of private blockchains. For instance, R3 Corda is a consortium blockchain platform developed by the enterprise blockchain consortium R3. Corda is designed for use cases that require privacy, scalability, and interoperability in multiple organizations in sectors such as finance, healthcare, and supply chain.

V. INTEGRATION OF FEDERATED LEARNING WITH BLOCKCHAIN

Integrating blockchain technology with FL has emerged as a novel approach to address inherent data privacy, security, and trust challenges within distributed ML systems [478]–[480]. FL, characterized by training ML models across decentralized devices without centrally aggregating raw data, offers significant advantages in preserving user privacy and data confidentiality. In other words, in federated ML, the exchange occurs at the parameters level instead of transmitting raw data. This approach mitigates the risk associated with centralized computing architectures, which are susceptible to targeted attacks and potential denial of service due to their single-point-of-failure vulnerability. A detailed discussion on FL is presented in Section III-D, including its different types (horizontal, vertical, federated transfer learning), applications (particularly in healthcare), and potential future directions (integration with advanced analytics, cross-institutional collaborations), highlighting FL’s pivotal role in reshaping healthcare technology.

However, concerns persist regarding the integrity of FL systems, particularly regarding data tampering or manipulation by malicious or compromised nodes. BC, renowned for

its immutable and transparent ledger capabilities, presents a compelling solution to these challenges. By leveraging blockchain’s decentralized consensus mechanisms and cryptographic primitives, FL systems can ensure data integrity, traceability, and transparency throughout the ML model training process [481]–[483]. Moreover, blockchain’s smart contract functionality enables the establishment of auditable and self-executing agreements among participants, further enhancing the trustworthiness of FL collaborations [478]. This integration not only addresses privacy and security concerns but also fosters a more collaborative and inclusive environment for distributed ML research and applications. As such, the motivation behind the integration of blockchain and FL lies in the pursuit of enhancing data privacy, security, and trust in decentralized ML ecosystems, ultimately advancing the adoption and efficacy of FL methodologies in various domains such as healthcare [412], [483], [484].

BC technology holds immense potential to significantly enhance the security, transparency, and trustworthiness of FL systems. By addressing key challenges like verifying local model updates, aggregating the global model, and incentivizing participants, blockchain can pave the way for a more secure and collaborative future in AI development. In the following, we explore how blockchain technology can significantly enhance these aspects of FL.

- **Verifying Local Model Updates:** BC offers an immutable and tamper-proof record of transactions, acting as a secure ledger for local model updates from participants. These updates can be recorded as transactions, ensuring their validity and preventing any unauthorized modifications. Additionally, smart contracts can be employed to define specific rules for model updates, functioning as verification mechanisms. These smart contracts can even execute algorithms to validate the integrity and accuracy of the updates [485].
- **Global Model Aggregation:** BC empowers FL with decentralized consensus mechanisms, such as PoW or PoS. These algorithms enable participants to collectively agree on the process of aggregating the global model. Furthermore, the entire aggregation process can be transparently recorded on the blockchain. This transparency allows participants to verify the fairness and accuracy of the final model [486].
- **Incentivizing Participants:** One of the key strengths of blockchain lies in its ability to create tokenized incentives. These tokens or cryptocurrencies can be used to reward participants who contribute data or computational resources to the FL process [487]. Smart contracts further enhance this system by automating the distribution of incentives based on predefined criteria. For instance, the quality of contributions or the amount of computational resources provided by a participant could determine the reward [488]. Importantly, the entire distribution process remains transparently recorded on the blockchain, ensuring accountability and fairness [489].

By leveraging the unique strengths of blockchain technology, FL systems can achieve a new level of security, trans-

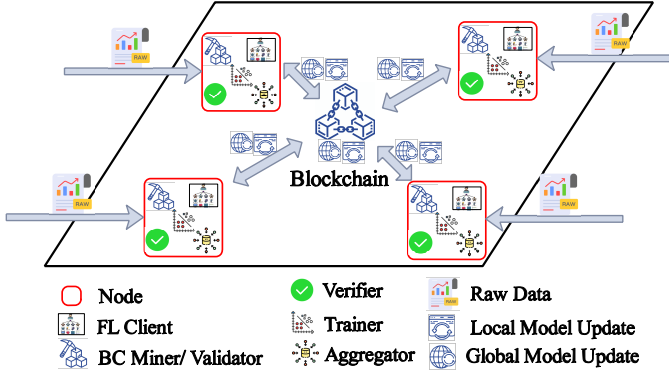


Fig. 6: Fully Coupled Architecture

parency, and trust, ultimately fostering a more collaborative and efficient environment for AI development.

A. Integration Architecture

Several research efforts have identified distinct architectures for integrating blockchain and FL. This paper proposes a similar framework to [490] with slight variations in terminology. Based on the level of interaction between blockchain and FL entities, we categorize these architectures as fully coupled, semi-coupled, and loosely coupled.

A.1. Fully Coupled Architecture

In the fully coupled architecture, blockchain nodes (i.e. miners or validators), perform dual roles as FL clients. Within this architecture, FL clients engage in computing local model updates as well as validating these updates as blockchain nodes. Notably, blockchain nodes not only partake in training local models but also participate as the global model aggregator. The aggregator, which may be a selected node, a designated leader, or a collection of nodes based on the predefined protocol, is responsible for gathering local model updates. Every node in this model has the opportunity to function as a blockchain validator, a local model trainer, and a global aggregator concurrently. Consequently, both local model updates and global model updates are contained within the blockchain. Importantly, the absence of a necessity to transmit the global model to a central server mitigates the risk of a single point of failure within this architecture. A schematic of this architecture is depicted in Figure 6.

A.2. Semi-Coupled Architecture

In the semi-coupled architecture, blockchain and FL clients inhabit separate networks, although FL clients retain the capability to interact with the blockchain and manipulate the distributed ledger. FL clients gather data from diverse sources, train local models, and subsequently upload local model updates to the blockchain. BC nodes (i.e. miners or validators) are tasked to validate the uploaded local model updates that will be used for training the global model. Upon the preparation of the global model, blockchain nodes will store it within the blockchain. Participant rewards are allocated based on a predefined incentive mechanism. This

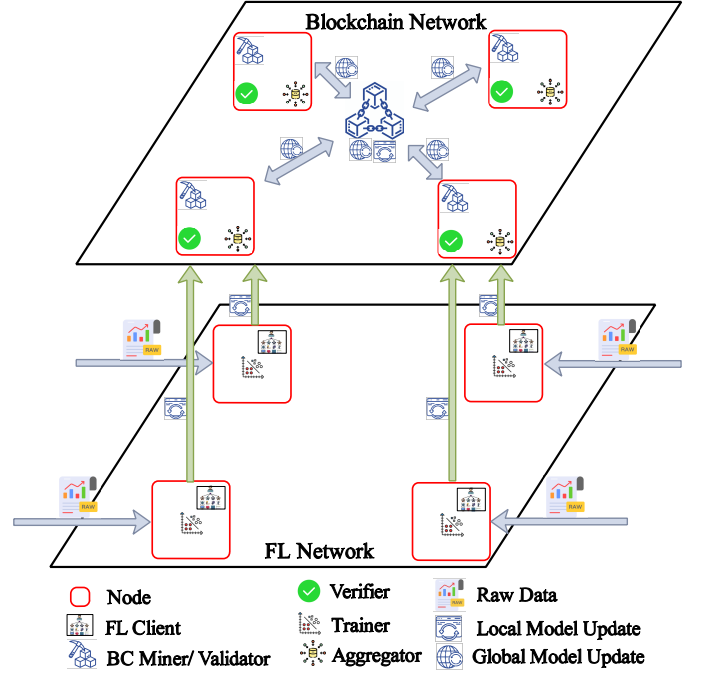


Fig. 7: Semi-Coupled Architecture

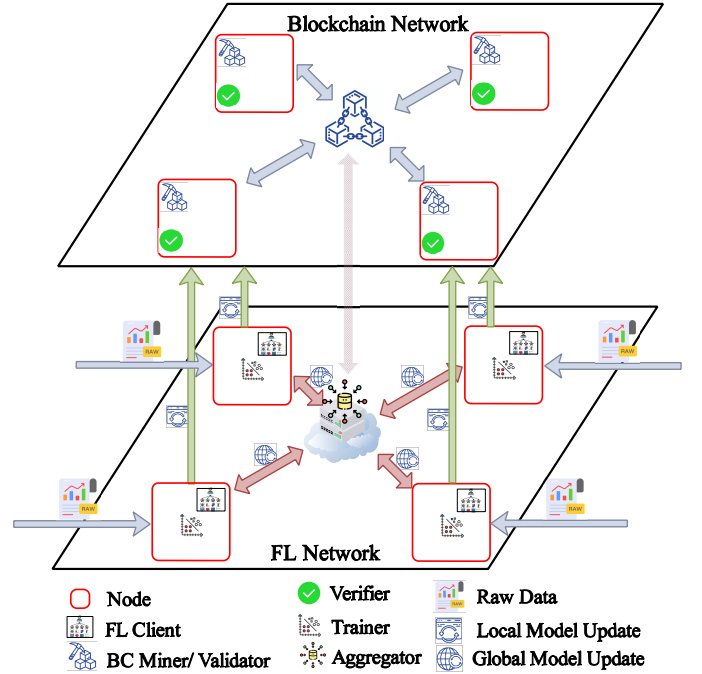


Fig. 8: Loosely Coupled architecture

architecture also circumvents the potential for a single point of failure. A schematic of this architecture is depicted in Figure 7.

A.3. Loosely Coupled Architecture

In the loosely coupled architecture, blockchain nodes and FL clients are in two distinct networks. This architecture introduces reputation as a criterion for measuring the reliability of the clients. In this architecture, the primary function of the blockchain is to furnish a coordination mechanism for clients, manage their reputation, authentication, validation of local

model updates, and incentives management (i.e. contributions are managed to ascertain reputation and incentivize participation). While the blockchain validates local model updates, it refrains from storing them. In contrast, it stores the data related to the reputation of the participants. The responsibility of the FL clients is to train local models and upload the updates to the blockchain for validation. After validations, these updates will be sent to an aggregator, which can be a distinct server or a cloud space. A schematic of this architecture is depicted in Figure 8.

VI. RELATED WORKS

In this section, we comprehensively explore existing research endeavors focusing on integrating BCFL frameworks within healthcare contexts. Initially, we delve into the corpus of literature dedicated to elucidating the practical applications, methodologies, and outcomes of utilizing blockchain technology in conjunction with FL for healthcare use cases. In addition, we aim to provide a taxonomy and categorize the existing works based on the insights garnered throughout this paper. To achieve this, we classify the works according to their integration architecture (i.e., fully coupled, semi-coupled, and loosely coupled), blockchain platform, FL type, and data type. Furthermore, we highlight their primary contributions as well as their limitations. In the sequel, we will examine existing surveys and reviews focusing on blockchain-assisted FL in healthcare. This will give us insights into the overall research landscape and help identify any gaps or areas for further exploration.

A. Literature review

Liang et al. [491] propose a software architecture integrating FL and blockchain to mitigate bias and fairness issues in healthcare predictive modeling while safeguarding patient privacy. Om et al. [492] introduce a mechanism to reward organizations participating in the FL process, ensuring privacy-preserving model transfer using loosely coupled integration with the Ethereum blockchain. Moulahi et al. [493] integrate FL and blockchain to develop a trusted system for predicting diabetes risk while ensuring data privacy and model integrity.

Ali et al. [494] focus on integrating blockchain with FL for secure and decentralized analysis of EMRs in precision medicine. Chang et al. [495] propose an integration of adaptive differential privacy and gradient verification-based consensus protocols in a fully coupled architecture for healthcare analytics. Lian et al. [496] present a blockchain-based personalized FL system for ensuring security and privacy in the IoMT.

Farooq et al. [497] develop an automated system for analyzing patients' live data within a fully coupled architecture, while Zhang et al. [498] propose a blockchain-enabled FL framework for healthcare data privacy protection. Aich et al. [483] introduce a blockchain-assisted FL framework for personal data preservation, and Passerat et al. [499] propose a novel architecture for FL integrated with blockchain within healthcare systems. A taxonomy of the existing research studies, along with additional relevant works, has been compiled in Table II.

B. Existing Surveys

To the best of our knowledge, comprehensive surveys or reviews focusing on the integration of blockchain and FL for healthcare use cases are scarce. While individual studies have explored the potential of each technology independently within healthcare settings, there is a notable lack of resources delving into the synergistic benefits and challenges of combining blockchain's immutable ledger capabilities with FL's decentralized model training approach.

Noteworthy initial explorations, such as those conducted by Myrzashova et al. (2023) [412] and Nguyen et al. (2021) [510], offer valuable insights but often lack a broader perspective. Myrzashova et al. [412], for instance, analyze the advantages and disadvantages of BC-FL integration in healthcare, but they overlook the importance of a data type taxonomy. Understanding the diverse medical data types (e.g., genomics, imaging) used in healthcare ML is crucial as different data may have varying security and privacy requirements. Similarly, Nguyen et al. [510] introduce a new conceptual architecture that integrates blockchain and AI for combating the COVID-19 pandemic. While offering valuable insights into addressing specific challenges posed by the pandemic, its scope is limited to COVID-19 and related data, lacking a broader analysis of the integration's potential for various healthcare use cases beyond this specific context.

In contrast to these existing works, this tutorial offers a more comprehensive perspective. We present a taxonomy of medical data used for ML, providing a foundational understanding of the diverse data types relevant to this integration. Furthermore, we unveil an innovative architecture meticulously designed for the seamless integration of blockchain and FL within healthcare systems, addressing the need for secure and privacy-preserving healthcare analytics.

VII. CONCLUSION

This paper explored the transformative potential of integrating blockchain technology and FL for secure and privacy-preserving healthcare analytics. We highlighted how this synergy leverages the strengths of both blockchain's immutable ledger and ensures data integrity and transparency, while FL facilitates collaborative model development without compromising patient privacy. The three proposed architectural models (fully coupled, semi-coupled, and loosely coupled) offer flexibility in tailoring FL to specific healthcare requirements, balancing decentralization, scalability, and reliability.

We explored how FL empowers various healthcare applications, including disease prediction, medical image analysis, patient monitoring, and drug discovery. By enabling model training on local devices at healthcare institutions, FL eliminates the need for centralized data storage, addressing privacy concerns associated with traditional ML approaches.

While FL offers privacy benefits, it introduces vulnerabilities. BC's tamper-proof nature and smart contracts address these challenges by ensuring data integrity and mitigating malicious activities. This tutorial provided a foundational understanding of medical data, FL, and their integration for healthcare applications.

TABLE II: Related works on Blockchain-assisted Federated Learning in Healthcare

Ref.	Main Contribution	Architecture	BC platform	FL type	Data type	Limitations
[491]	Software architecture integrating FL and blockchain to tackle bias and fairness issues in healthcare predictive modeling while safeguarding patient privacy	Semi-coupled	Rahasak	Unknown	Unknown	Reliance on simulated validations rather than experimental implementations
[492]	Introduces a mechanism to reward organizations participating in the FL process, ensuring privacy-preserving model transfer between users and organizations using BC	Loosely coupled	Ethereum	HFL	Medical Imaging Data (Covid-19 CT)	Not explicitly stated
[493]	Integrating FL and BC technology to develop a trusted system for predicting diabetes risk while ensuring data privacy and model integrity	Semi-coupled	Ethereum	HFL	Sensor Data (IoT)	Not explicitly stated
[494]	Integration of BC with FL to enable secure and decentralized analysis of EMRs in precision medicine	Loosely coupled	Ethereum, Hyperledger Fabric (simulation)	HFL	EMR	Reliance on simulated validations rather than experimental implementations
[495]	Integration of adaptive differential privacy and gradient verification-based consensus protocols	Fully coupled.	Ethereum	HFL/VFL	Internet of Medical Things (IoMT) Sensor Data	scalability challenges, increased complexity, potential computational overhead, and the need for further validation across diverse medical conditions and datasets
[496]	BC-based personalized FL system to address security and privacy concerns in the IoMT	Fully coupled	Unknown (Consortium PoS BC)	VFL	IoMT Sensor Data (Fashion-MNIST)	Reliance on simulated validations rather than experimental implementations
[497]	Developing an automated system for analyzing patients' live data	Fully coupled	Ethereum	HFL	IoMT Sensor Data	Limited empirical validation or real-world testing of the proposed framework
[498]	Propose a BCFL framework for healthcare data privacy protection	Fully coupled	Unknown (conceptual)	HFL	EHR (MNIST)	Theoretical model only, not supported via experimental implementations
[483]	Proposes a BC-assisted FL framework for personal data preserving	Loosely coupled	Unknown (conceptual)	-	No data	Reliance on conceptual assumptions without real-world application
[499]	Propose a novel architecture for FL integrated with blockchain within healthcare system	Loosely Coupled	Ethereum	-	No data	Not explicitly stated
[500]	Proposes a BCFL framework for COVID-19 applications to classify IoHT data	Loosely coupled	Ethereum	FL type	Sensor Data (IoMT)	Not explicitly stated
[501]	Integrating BC technology with FL to enhance privacy preservation and scalability in healthcare data management	Fully coupled	Unknown	Unknown	Sensor Data (IoT)	Theoretical model only, not supported via experimental implementations
[24]	Propose a new BC-enabled Fed-based Generative Adversarial Networks (GANs) framework for secure COVID-19 data analytics	Semi-coupled	Unknown (conceptual)	HLF	Medical Imaging Data (Covid-19 CT)	BC model is conceptual and real-world implementation was not reported
[502]	proposes A framework of BC-empowered FL in healthcare-based Cyber-Physical Systems (CPS)	Fully coupled	Ethereum	HFL	EHR (MNIST HAM10000)	Not explicitly stated
[503]	Proposes a novel solution for revolutionizing healthcare systems by considering concepts like distributivity, self-learnability, and autonomy.	-	Unknown (conceptual)	Unknown	No Data	Only introduces a theoretical framework without an empirical validation
[504]	blockchain empowered method to detect patterns of COVID-19 from the lung CT scans	Fully coupled	Unknown	HFL	Medical Imaging Data (Covid-19 CT)	The paper does not extensively discuss the generalization capabilities of the proposed model to handle variations in COVID-19 manifestations across different patients.
[505]	A concise review of BCFL in healthcare, concepts and taxonomy	-	Unknown	Unknown	Unknown	article is very brief and does not cover all concepts
[506]	Propose a FL-based BC-Enabled Task Scheduling (FL-BETS) framework with different dynamic heuristics for healthcare applications	Loosely coupled	Unknown	Unknown	Sensor Data (IoMT)	Dynamic and run-time unknown attacks are against IoMT were not considered in this work
[507]	Introduces FedMedChain as a BCFL framework for medical data privacy-preserving	Loosely coupled	Unknown	Unknown	Sensor Data (Unknown)	Not explicitly stated
[508]	Introduces a privacy protection framework for medical data using BC and FL for secure and auditable data sharing among medical institutions using a secure aggregation scheme based on homomorphic encryption.	Loosely coupled	Ethereum	HFL	EHR (MNIST different datasets)	Not explicitly stated
[509]	Proposes a BCFL architecture to enable accountability in FL systems.	Loosely coupled	Ethereum	HFL	Medical Imaging Data (Covid-19 CT)	Lack of real-world deployment analysis

Looking forward, continued research, collaboration, and innovation across the research community hold immense promise to unlock the full potential of FL. This collaborative effort will pave the way for a more secure, transparent, and inclusive healthcare ecosystem, ultimately leading to improved patient outcomes.

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