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Review article

Digital twins in healthcare IoT: A systematic review

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ABSTRACT

Digital twin technology initially marked its presence in production and engineering, subsequently revolutionizing the healthcare sector with its groundbreaking applications. These include the creation of virtual replicas of patients and medical devices, enabling the formulation of personalized treatment plans. The rise of microcomputing, miniaturized hardware, and advanced machine-to-machine communications has laid the foundation for the Internet-of-Medical Things (IoMT), significantly transforming patient care through remote monitoring and timely diagnostics. Amid these technological strides, this paper offers a systematic review of digital twin technology's integration within healthcare IoT, underlining its crucial role in promoting personalized medicine and tackling the pressing security challenges inherent in healthcare IoT systems. Focusing solely on the growing field of smart healthcare systems powered by IoT infrastructure, we explore the use of digital twins in digital patient modeling, the lifecycle of smart hospitals, surgical planning, medical devices, the pharmaceutical industry, and the IoMT cyber infrastructure, demonstrating their transformative potential in modern healthcare. Building on these findings, we outline key technical implications and emerging trends, highlight current challenges, and propose future research directions to advance healthcare IoT and its digital twin applications.

1. Introduction

The Internet of Things (IoT) has seamlessly integrated into the fabric of daily life, connecting an ever-expanding array of devices and systems — from smartphones and smart homes to intelligent building management systems and health-monitoring wearables [1]. This integration extends significantly into the healthcare sector, where IoT technologies have revolutionized the way health systems operate. By embedding sensors and devices within the healthcare framework, IoT has enabled a more streamlined workflow, accelerated access to medical records, and enhanced the accuracy and reliability of data collected from diverse sources [2]. IoT's capacity to facilitate seamless data sharing among healthcare providers has also been crucial in combating global health crises, such as pandemics. By providing real-time data integration and communication, IoT systems help in tracking disease spread, managing resources, and implementing targeted responses more efficiently. Additionally, the technology plays a pivotal role in improving patient care by enabling the continuous monitoring of health conditions through wearable devices that communicate directly with healthcare providers. This direct line of communication ensures that any significant changes in a patient's condition are promptly addressed, potentially saving lives by allowing for immediate medical intervention [3].

In order to provide proactive patient care, medical professionals and engineers are moving towards using the digital twin (DT) technology to increase patient quality of life. By fusing AI and ML functionalities with different IoT elements, *e.g.*, cloud apps, DTs can use real-time data to make accurate predictions about people's health outcomes [4]. In its simplest form, a digital twin is indeed just a virtual model of a physical object. However, this basic definition barely scratches the surface of what DT technology entails and the complex functionalities it encompasses. Unlike a straightforward 3D model, which is static and merely represents the physical appearance of an object, a DT is dynamic and interactive. It integrates real-time data continuously updated from its physical counterpart, allowing it to simulate behavior and process in a real-world context.

The true power of DT lies in its versatility and depth. For instance, in the healthcare sector, a DT could be used to model complex biological systems such as the human heart. This is not just a structural replica but a functional one that can mimic the actual working conditions of the heart under various scenarios. By applying predictive analytics and machine learning algorithms, the DT can forecast potential health issues before they occur by analyzing deviations from normal operation patterns. Moreover,

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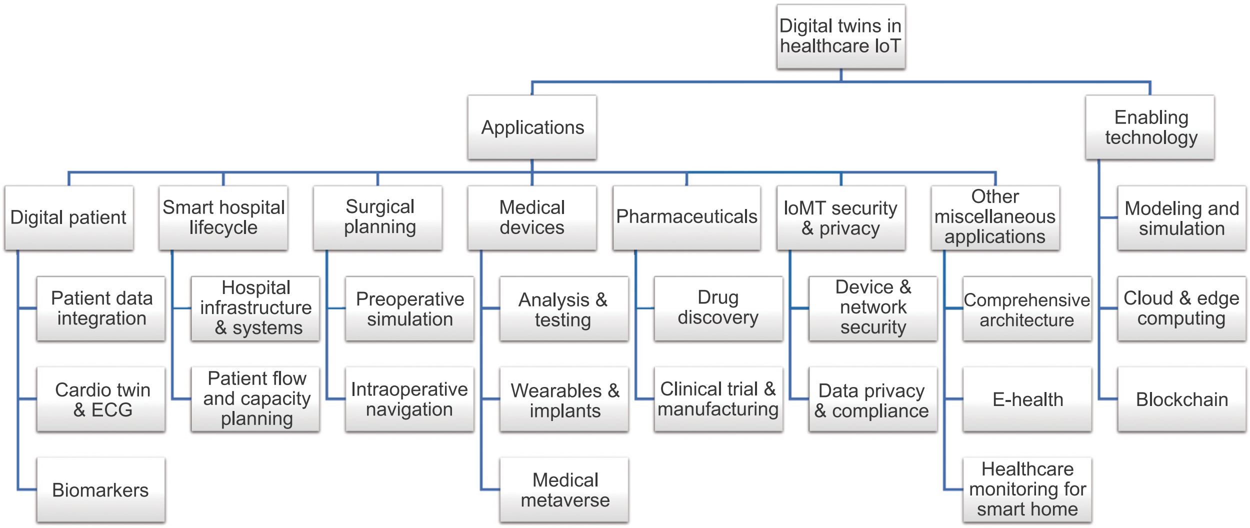

Fig. 1. A taxonomy of digital twins in smart healthcare domain.

a DT could represent broader systems such as a hospital's operations or even an entire population's health dynamics. These models can simulate public health responses and predict the outcomes of epidemics, helping in strategic planning and resource allocation. A DT is not only about visual representation but also about behavior and function. It is an evolving model that learns from multiple data streams, adapts to changes, and provides predictive insights. This capability makes DTs invaluable across various sectors, including manufacturing, automotive, and urban planning, where they contribute to enhanced efficiency, innovation, and decision-making.

Amid these technological advances, we present a comprehensive overview of the integration of DT technology within the healthcare IoT ecosystem, emphasizing its critical role in advancing personalized medicine and addressing the significant security challenges that are inherent in healthcare IoT systems. Concentrating exclusively on the field of smart healthcare systems with the IoT infrastructure, we explore the application of DTs in various facets of healthcare. Our investigation includes digital patient modeling, which utilizes DTs to create highly accurate and dynamic patient profiles that help in tailoring medical treatments more effectively. We also examine smart hospital lifecycle management, where DTs optimize hospital infrastructure and patient flow. Additionally, we discuss DT-based surgical applications, from preoperative and intraoperative planning to real-time surgical guidance.

Beyond clinical applications, we explore DT integration with medical devices, enhancing functionality, predictive maintenance, and safety. Additionally, we explore the impact of DTs in the pharmaceutical industry. Here, DTs are instrumental in streamlining drug development processes, from simulation of clinical trials to monitoring the manufacturing and distribution chains, thus ensuring higher efficiency and compliance with regulatory standards. Finally, we address security and privacy challenges in IoMT, an emerging yet critical area of research. By demonstrating these diverse applications, we highlight the transformative potential of digital twins in modern healthcare, showcasing how they can lead to more efficient, safe, and personalized medical services. This paper not only underscores the benefits but also discusses the technological and ethical challenges involved in integrating DTs into the healthcare sector, proposing pathways for future research and development. Fig. 1 shows a taxonomy of digital usage in the smart healthcare domain.

The remainder of the paper is organized as follows. Section 2 discusses the theoretical background, including various concepts of digital twins and market trends. Section 3 discusses the systematic review methodology. Section 4 discusses various applications of digital twin methods in healthcare IoT. Section 5 presents an overview of enabling technology. In Section 5, we discuss the current and emerging trends of DT usage and some technical implications. In Section 7, we discuss future directions and challenges. We conclude in Section 8.

2. Background and concepts

2.1. Digital twin concept

The concept of the digital twin was first introduced in 2003 [5] and has since captured the attention of numerous researchers [6, 7]. This concept has been explored and interpreted through various studies. Currently, one of the widely accepted definitions, which originates from NASA, describes a DT as "an integrated multiphysics, multiscale, probabilistic simulation of an as-built vehicle or system [8]. It leverages the best available physical models, sensor updates, fleet history, and more, to accurately reflect the life cycle of its real-world counterpart". Another perspective identifies DTs as virtual counterparts of physical systems, supporting decision-making by mirroring behaviors and integrating data from diverse sources to create accurate models [9]. These models are developed using technologies like simulation, machine learning, big data, and IoT, which collectively enhance operational optimization and support various decision-making processes

Some studies have used the terms "Medical Digital Twin" [10, 11] and "Health Digital Twin" [12,13] to represent simulation modeling focused on specific components of the healthcare sector. Another term "Human Digital Twin (HDT)" has been used by many studies that extend the DT technology beyond its applications in healthcare [14,15] to a wide range of engineering, industrial, and social domains [16–20]. An HDT is a dynamic digital representation of an individual human being, capturing in real-time the complex interactions of biological, psychological, and social factors.

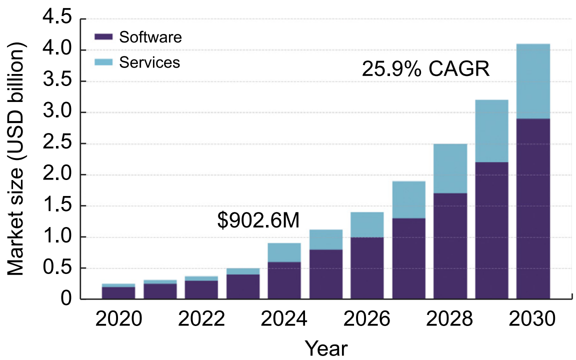

Fig. 2. Healthcare digital twins market size by component, 2020–2030.

2.2. Healthcare DTs market trends

The healthcare DT market is poised for significant growth, with an estimated market size of USD 902.59 million in 2024, projected to grow at a CAGR of 25.9% through 2030 [21]. DTs are revolutionizing the healthcare sector by providing real-time, integrated, and interactive approaches for data capture, simulation, and feedback, enabling improvements in efficiency, cost optimization, and future demand anticipation. The rising adoption of sensors, medical records, wearables, and mobile applications is driving this transformation, as these tools produce valuable data for simulating pharmaceuticals and medical equipment. Recent investments, such as Accenture's partnership with Virtonomy, highlight the push to accelerate innovation in life-saving medical devices using DT technology. Furthermore, funding initiatives, including over USD 6 million in grants from the U.S. National Science Foundation in collaboration with the NIH and FDA, underscore the growing momentum in DT research for healthcare and biomedical applications, promising a new era of personalized medicine and medical innovation. Fig. 2 illustrates the healthcare DT market size by component from 2020 to 2030.

Building on this momentum, the healthcare DT market is witnessing rapid growth across key segments. The providers segment leads with the largest market share at 36.2% in 2024 (see Fig. 3), as DTs are increasingly utilized in healthcare facilities to optimize staff management and detect resource shortages, such as bed availability, enabling more efficient decision-making and cost reduction [21]. For example, IBM's Process Mining software generates DTs to simulate hospital operations and identify potential challenges. Partnerships like the one between Strasys and Silico in December 2022 aim to deliver DTs for entire hospitals and healthcare systems, enhancing decision intelligence. Meanwhile, the pharma and biopharma segment is expected to grow at the fastest CAGR, driven by the demand for cost-effective drug development and personalized medicine. DTs are being used to simulate patient responses, optimize dosages, and develop targeted therapies, thereby accelerating the adoption of this technology across the industry.

2.3. Healthcare IoT

The concept of Healthcare IoT, or the Internet of Medical Things (IoMT), refers to the integration of connected devices in the medical and healthcare sectors to improve the efficiency and effectiveness of medical services. In simpler terms, this involves medical devices capable of sending data over a network autonomously, without the need for direct human-to-human or human-to-computer interaction [22]. Many studies explored and

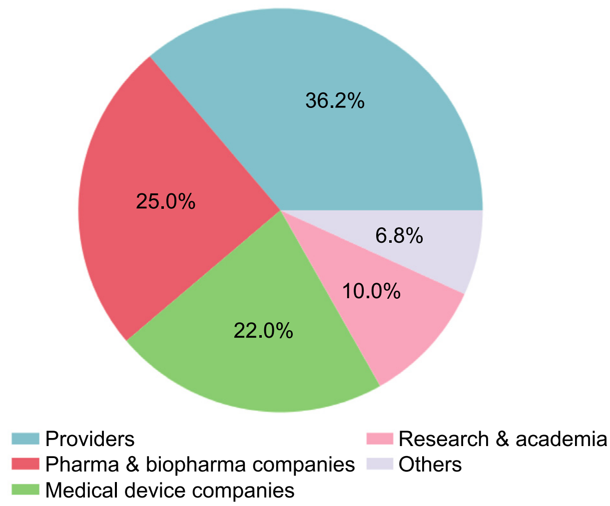

Fig. 3. Digital twins end-use market share in the healthcare industry.

initiated many aspects of IoT in healthcare in terms of architecture [23], implementation of an IoT based In-hospital healthcare [24], concepts [25], secure medical model [26,27], etc. Here are some key aspects and benefits of Healthcare IoT:

- Remote Monitoring: One of the most significant advantages of Healthcare IoT is the ability to monitor patients remotely. Devices can collect data on vital signs like heart rate, blood pressure, glucose levels, and more [28]. This data is sent to healthcare providers in real-time, enabling them to monitor patients' conditions without needing them to be physically present in a medical facility [29]. This is particularly beneficial for managing chronic conditions and elderly care.
- Data Collection and Analysis: IoT devices gather vast amounts of health data, which can be analyzed using AI and machine learning algorithms to provide insights into patient health trends, predict health episodes, and optimize treatment plans [30,31]. This data-driven approach can lead to more personalized and timely healthcare.
- Improved Patient Engagement and Compliance: Devices connected through the IoT can provide patients with regular updates and reminders about their health management tasks, such as taking medication, scheduling appointments, or exercising. This can help increase patient engagement with their health regimes and improve compliance with treatment plans.
- Enhanced Medical Device Management: IoT can also streamline the management of medical devices within healthcare facilities. For example, tracking devices can monitor the location and usage of medical equipment, helping to optimize resource allocation and reduce operational costs.
- Advanced Diagnostics and Treatment: IoT technologies enable the development of new diagnostic and treatment technologies. For instance, smart inhalers for asthma patients can track usage patterns and environmental triggers for asthma attacks, potentially leading to more effective management of the condition.
- Security and Privacy Concerns: Despite its benefits, Healthcare IoT raises significant security and privacy concerns, as medical data is highly sensitive and protecting it against cyber threats is crucial [32]. This requires robust encryption methods, secure data transmission protocols, and compliance with health data protection regulations.

Overall, Healthcare IoT holds the potential to revolutionize healthcare by making it more proactive, patient-centered, and efficient. However, it also necessitates careful consideration of privacy, security, and technical integration aspects to fully leverage its capabilities.

2.4. Related surveys and reviews

The scholarly interest in the integration of DTs within the smart healthcare sector has been extensively documented through various surveys and review papers. The majority of this research concentrates on replicating human organs, aiming to advance personalized medicine and improve treatment outcomes, while others focus on the application of hospital operations and medical devices. However, despite the broad scope of research into DTs in the healthcare sector, there appears to be a gap in the literature regarding IoT-driven systems. Specifically, there are no existing reviews or survey papers that exclusively focus on the integration of IoT with DTs in healthcare settings. Table 1 here summarizes the existing literature reviews.

Table 1
Summary of related surveys and reviews on DTs in healthcare.

Reference	Focus
Katsoulakis et al. [33]	Current applications, consortium research centers reviews, and emerging research opportunities.
Sun et al. [34]	Application examples of DT in many fields of medicine.
Elkefi et al. [35]	Application for improving healthcare management and discusses associated challenges.
Coorey et al. [13]	Challenges and applications of DT for cardiovascular disease.
Erol et al. [36]	Ongoing and planned DT studies in healthcare, highlighting future developments.
Okegbile et al. [15]	Architectural framework, design requirements, and applications of HDT with future directions.
Chen et al. [37]	Networking architecture and key technologies for HDT in personalized healthcare applications.
Haleem et al. [32]	Various features, services, and tools of DT for healthcare.
Bjelland et al. [38]	Concepts for arthroscopic knee surgery using patient-specific information and methods for soft tissue simulation.
Narigina et al. [39]	Highlighting development, methodologies, trends, challenges, and potential to improve patient care and healthcare innovation.
Xames et al. [40]	Using the PRISMA approach, identified research trends, gaps, and realization challenges.

3. Methodology

3.1. Search criteria

To ensure a comprehensive and unbiased survey of the literature, we conducted a systematic review following established guidelines for transparent reporting. The review protocol defined clear objectives and criteria before searching, in line with best practices. We identified relevant publications through database searches in multiple scholarly repositories, including, Google Scholar, IEEE Xplore, ACM Digital Library, and Scopus. A broad set of keywords was used to capture the domain, combining terms for DTs with those for healthcare and IoT (*e.g.*, "digital twin", "healthcare", "IoT", "smart health", "patient model", "medical device"). We also included synonyms and closely related phrases (such as "virtual patient", "cyber–physical system in healthcare", "medical digital twin") to ensure coverage of all relevant studies.

3.2. Inclusion criteria and study selection

In this systematic review, we included both original research studies and relevant survey/review articles to capture a comprehensive view of the field. The inclusion and exclusion criteria were defined a priori as follows:

Inclusion:
- Studies presenting or evaluating DT applications, implementations, or frameworks in a healthcare IoT context (e.g., patient monitoring, medical device DTs, hospital IoT systems).
- Original research articles reporting empirical findings, prototypes, or simulations related to healthcare DTs, and survey/review papers that specifically overview DT technology in healthcare IoT. (Including such survey papers provides valuable context and synthesis of the literature)
- Publications in peer-reviewed journals or conferences, written in English.

Exclusion:
- Studies not directly related to healthcare or medicine (*e.g.*, DT applications in manufacturing or smart cities with no healthcare focus), or not involving IoT aspects (*e.g.*, purely conceptual DT models without connectivity context).
- Theses, dissertations, book chapters, editorials, and non-peer-reviewed articles (grey literature) were excluded to ensure quality and consistency.
- Articles for which full-text was not available or those not meeting the inclusion criteria upon full-text review (*e.g.*, works that only mention "digital twin" briefly without substantive contribution to the topic) were also excluded.

In total, our searches initially identified 210 records. After removing irrelevant or duplicate topics, 120 unique articles remained. From this, 40 articles were excluded for not meeting the criteria (common reasons included lack of a true DT implementation, not being in a healthcare context, or insufficient IoT relevance). This final set comprises 80 articles with — 69 primary research articles on DT in healthcare IoT and additionally 11 survey (review) papers that examine the state-of-the-art in this domain. Including both original studies and survey papers allowed us to not only analyze individual innovations but also incorporate broader insights from prior literature reviews.

4. Applications in smart healthcare

4.1. Digital patient

The advancement of IoT infrastructure within the healthcare sector has significantly enhanced the use of DTs, especially in intelligent human body monitoring and the maintenance of medical devices. While the broader medical field increasingly adopts this technology to create virtual representations of the human body *i.e.*, "human digital twin (HDT)" or "digital patients", our discussion will specifically focus on those aspects of digital patient activities that are integrated with IoT components. This targeted exploration helps to understand how IoT connectivity can optimize health monitoring and device maintenance, thereby improving patient care and operational efficiency in healthcare settings. Fig. 4 shows the conceptual overview of a DT of a heart model as an illustrative example.

Patient data integration
Vats et al. [14] developed an IoT-based framework using HDT technology and machine learning to predict cardiovascular disease early, utilizing data from wearable sensors and a comprehensive dataset of 70,000 patient records. This approach achieved

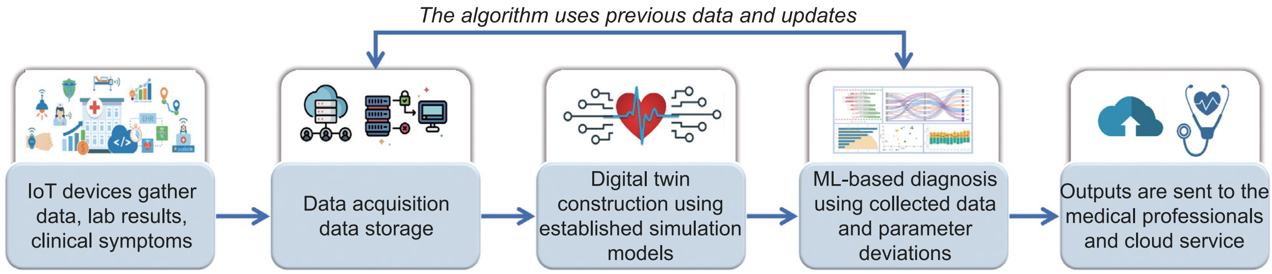

Fig. 4. Overview of a digital twin process of a patient organ: illustrative example for heart model.

an impressive prediction accuracy of 88.91% with XG Boost, enhancing the integration of patients and doctors and improving healthcare operations and services. Mourtzis et al. [41] proposed a conceptual framework that leverages information and communication technologies (ICT), augmented reality (AR), and artificial intelligence (AI) to enhance the visualization, data acquisition, and analysis of MRI scans for cancer diagnosis and prediction. The paper also discusses the preliminary development of this framework and explores potential future advancements in light of the challenges encountered.

Cardio twin and ECG

The majority of DT studies focusing on human organs have concentrated on the cardiology domain. Utilizing real-time ECG data, DTs of the heart allow for dynamic simulations and analysis, enhancing the accuracy of cardiac health assessments and the prediction of potential disorders. Comprehensive reviews (*e.g.*, [13,42] offer an extensive outlook on initiatives aimed at overcoming existing challenges and fully harnessing the potential of DTs to address cardiovascular disease. Elayan et al. [1] proposed and implemented an intelligent, context-aware healthcare system using a DT framework, enhancing digital healthcare by integrating real-time data for dynamic patient monitoring and operation improvement. The system includes an ML-based electrocardiogram (ECG) classifier that accurately diagnoses heart conditions, demonstrating how DT, combined with advanced neural network algorithms, can revolutionize continuous health monitoring and disease detection. Martinez et al. [43] introduced a Cardio Twin architecture, an edge-based system for ischemic heart disease detection using a convolutional neural network (CNN) that classifies conditions from electrocardiograms with 85.77% accuracy. Trained on data from 200 individuals, it highlights the feasibility of DT in demanding healthcare applications.

Biomarkers

Biomarkers are critical for creating personalized health profiles and predictive models. DTs using biomarker data can simulate disease progression and response to treatment at an individual level. Susilo et al. [44] developed a novel workflow to create DTs for each patient, forming a virtual population that represented variability in biological, pharmacological, and tumor-related parameters from the phase I trial, which predicted that increased mosunetuzumab exposure increases the proportion of patients with significant tumor reduction. They also identified that patients with indolent non-Hodgkin's lymphoma (NHL) showed increased sensitivity to treatment, with model simulations suggesting that intratumor expansion of pre-existing T-cells, serving as a biomarker, underlies the antitumor activity of mosunetuzumab. Li et al. [45] developed a scalable framework to model dynamic changes in DTs on cellulome- and genome-wide scales, which prioritizes upstream regulator (UR) genes for biomarker and drug discovery. Their approach, tested on single-cell and bulk-profiling data from seasonal allergic rhinitis (SAR) and other inflammatory diseases, successfully ranked URs based on predicted effects on downstream target cells, demonstrating a tractable method for UR prioritization.

4.2. Smart hospital lifecycle

The increasing complexity of hospital operations necessitates advanced digital solutions that enhance clinical decision-making, optimize resource allocation, and improve patient care. Traditional hospital management relies on fragmented data sources and isolated digital tools, limiting the ability to coordinate real-time responses and predictive analytics [46]. DTs address this by creating virtual replicas of hospital environments and integrating real-time data from IoT devices and medical records. While DTs have been widely used in manufacturing, their healthcare applications remain limited to isolated processes like surgical planning and equipment monitoring [47]. As hospitals adopt AI-driven, predictive models, DTs offer a pathway to smarter, more efficient healthcare systems. Fig. 5 shows an overview of DT for the smart hospital lifecycle.

Hospital infrastructure and systems

The overall hospital infrastructure is pivotal in ensuring efficient and patient-centered care within smart healthcare environments. By integrating advanced IoT devices, DT technology, and interconnected systems, modern hospitals are transforming their infrastructure to enable seamless patient pathways, real-time monitoring, and personalized treatment strategies. HospiT'Win [48] is a framework that uses IoT, body sensor networks (BSN), modeling, simulation, and AI to create a DT – a virtual replica of a hospital – to monitor patient pathways, predict outcomes, and improve care delivery. By synchronizing real-time patient data with the DT, it helps healthcare providers anticipate unexpected events, minimize their impact, and ensure timely, high-quality care. Karakra et al. [49] developed a DT model of hospital services using discrete event simulation (DES) integrated with healthcare information systems and IoT devices. This model enables real-time assessment of service efficiency and evaluates changes in healthcare delivery systems without disrupting hospital operations. For smart hospitals, Han et al. [50] proposed a conceptual DT framework to integrate real-time data from multiple sources, addressing both clinical and non-clinical operational needs. The pilot platform tested in a Shanghai municipal hospital demonstrated the potential to enhance digitization, automation, and intelligent control of hospital operations. Another interesting work by Aluvalu et al. [51] proposed a model for Emergency Room Service (ERS) using DTs, IoT devices, and sensors to fast-track patient treatment, reduce the length of stay, and assess risk factors by leveraging digital health records and biometric authentication. The model incorporates face recognition, cloud-based data access, and communication systems to notify families and experts, achieving an 80% success rate for an intelligent expert system to handle anonymous patients effectively.

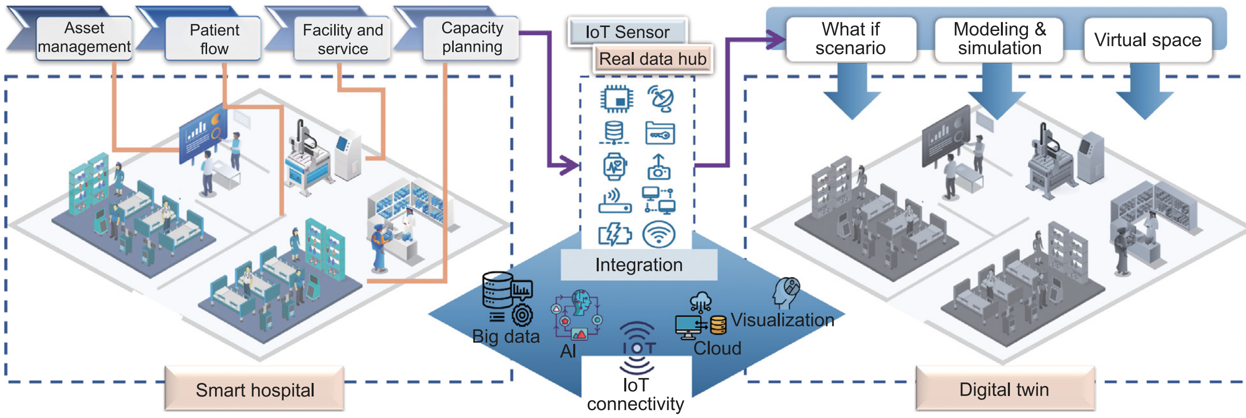

Fig. 5. Overview of a digital twin for smart hospital lifecycle.

Patient flow and capacity planning

Gorelova et al. [52] conducted simulations of patient flow in two assisted reproduction clinics using discrete event simulation techniques to evaluate the impact of smart health monitoring systems (SHMSs). By analyzing multiple scenarios, they identified bottlenecks, optimized staff allocation, and proposed the most efficient SHMS implementation. Their findings demonstrated reduced workloads for receptionists, ultrasound and blood collection areas, and physicians, improving overall clinic efficiency. Another recent work et al. [53] introduced a novel framework for dynamic task offloading in healthcare that integrates DT and social health determinants to enhance patient care and system performance. They demonstrate notable efficiency gains, such as a 20% latency reduction and over 50% power savings, when scaling to 30 MEC nodes, thus bridging significant research gaps and advancing healthcare technology integration.

4.3. Surgical planning

DTs in surgical planning involve using virtual models of patient anatomy to plan and simulate surgeries, enhancing precision and outcomes. This application impacts the operational and clinical aspects of hospital management.

Preoperative simulation

Bjelland et al. [38] conducted a systematic review using the PRISMA protocol to summarize and analyze the literature on designing an arthroscopic DT with patient-specific information and methods for interactive surgical soft tissue simulation. They proposed a novel macro-level conceptual system that integrates patient-specific images, diagnostic data, intraoperative sensor data, and surgical practice inputs, aiming to enhance surgical skills training, and preoperative planning, and create a database of virtual surgeries. Kleinbeck et al. [54] developed a neural rendering-based method to create immersive DTs of complex medical environments from casual video capture, enabling spatial planning of surgical scenarios in virtual reality. Their evaluation showed that this approach significantly increased perceived utility and presence, with higher exploratory behavior, indicating its potential for effective spatial planning without requiring expert knowledge or specialized hardware. Tai et al. [55] created a DT-enabled IoMT system for telemedical simulation, integrating mixed reality (MR), 5G cloud computing, and a generative adversarial network (GAN) to achieve remote lung cancer implementation. Their system demonstrated high accuracy in lung cancer and pulmonary embolism prediction and enhanced remote surgical implementation by projecting real-time operating room perspectives to the surgeon, significantly improving clinical data processing and deep learning analytics for DT-based surgical procedures.

Intraoperative navigation

The work of Tai et al. [55] mentioned above is also relevant here as it helps in real-time surgical implementation by projecting live operating room perspectives to the surgeon. In the case of remote surgery, Laaki et al. [56] developed a novel DT prototype to analyze communication requirements, focusing on low latency, high security, and reliability, using a robotic arm and HTC Vive VR system connected over a 4G mobile network. Despite limitations in VR capabilities and robot feedback, their research provided insights into communication establishment and cybersecurity technologies necessary for DT architecture development, highlighting the need for cross-disciplinary development and integration challenges in realizing Industry 4.0 concepts. A virtual TAVR planning process was performed by Obaid et al. [57], using patient-specific 3D models created from ECG-gated CT images with HeartNavigator III software. This simulation enabled the selection of a safe implant strategy and guided precise deployment, avoiding interactions between the aortic prosthesis and the Starr-Edwards mitral cage. More recently, Shu et al. [58] developed Twin-S, a DT framework specifically for skull base surgeries, which combines high-precision optical tracking and real-time simulation to integrate into image-guided interventions. Their evaluation showed that Twin-S accurately mirrors real-world drilling with an average error of 1.39 mm, enhancing situational awareness for surgeons by providing augmented surgical views. Intraoperative activity can also extend into the postoperative phase, where data and observations collected during the operation are analyzed to inform recovery strategies, assess surgical outcomes, and guide future clinical decisions, as illustrated in Fig. 6.

4.4. Medical devices

DTs in healthcare IoT represent a paradigm shift in the management of medical devices, leveraging real-time data to enhance patient outcomes and device performance. DTs expedite continuous monitoring of devices, such as wearables and implantables, facilitating early detection of anomalies and reducing downtime using predictive maintenance. Despite these advancements, challenges such as data security, model accuracy, and interoperability persist, necessitating further research. As IoT technology continues to evolve, DTs are poised to redefine the landscape of medical device management and personalized care.

Anaysis and testing

EnvDT et al. [59] is a model-based approach designed to simulate the environmental factors of medical device DTs under uncertainty, improving the reliability of healthcare IoT application

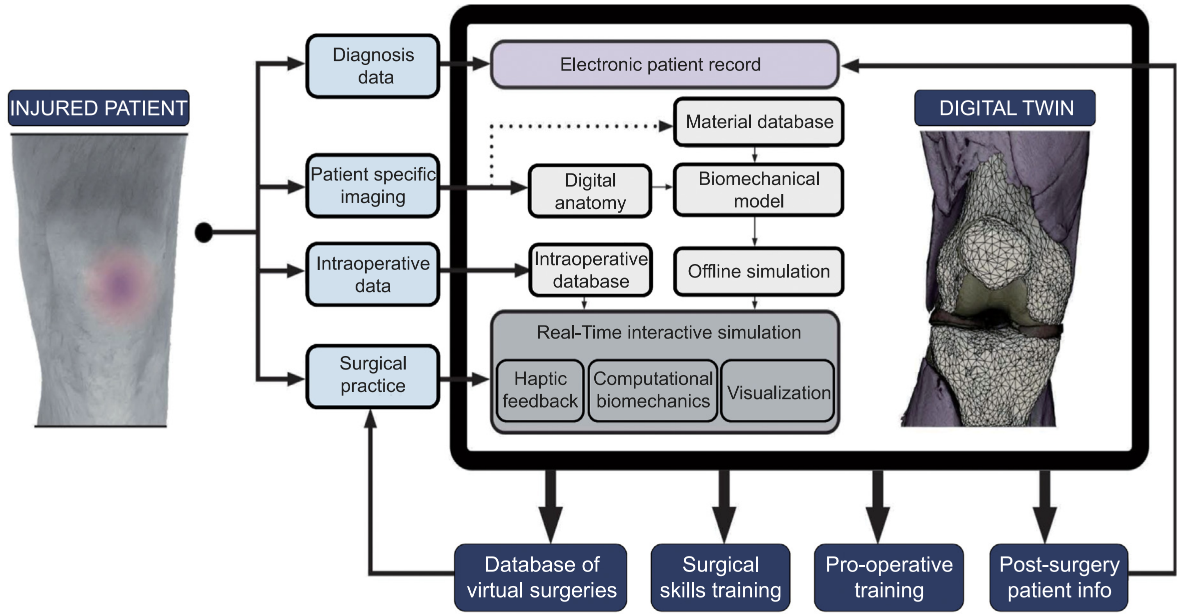

Fig. 6. Digital twin framework for arthroscopic knee surgery: training, planning, and postoperative analysis [38].

testing. It achieves approximately 61% coverage of environment models and generates diverse uncertain scenarios with a near-maximum diversity value of 0.62, ensuring more comprehensive and realistic DT-based testing. Ahmed et al. [60] highlighted how DTs can help healthcare organizations optimize medical processes, enhance patient experiences, and reduce operational costs. By continuously monitoring medical devices like X-ray and CT scan machines, DTs can mitigate system failures, ensuring reliable data collection and analysis, which is especially crucial during high-demand situations like the COVID-19 pandemic. Bersani et al. [61] explored the potential of DTs in medical systems by addressing challenges related to human behavior uncertainty and sensitive data protection. As a proof of concept, they apply their DT framework to a mechanical ventilator for COVID-19 patient care, aiming to enhance reliability, trustworthiness, and security in next-generation lung ventilators.

In the case of endoscopic medical devices, Kalozoumis et al. [62] developed a DT of the gastrointestinal tract (GIT) to provide a cost-effective and safer alternative to in vivo animal studies and clinical trials. By reconstructing intestinal geometry from medical images and creating a multiphysics model, they enable the study of device-tissue interactions, aiding in the evaluation and optimization of advanced endoscopic technologies. Another study [63] developed a DT-based simulator within a hardware-in-the-loop framework to support a clinical study on a connected medical device for lymphedema prevention in breast cancer patients after axillary lymph node dissection (ALND). By using statistical calibration and sensitivity analysis, they established measurement protocols that enabled mobile devices to detect significant signal changes, allowing early intervention and timely alerts to therapists.

Wearables and implants

Wearable medical devices monitor health in real-time as individuals go about their daily lives, either worn on the body or attached to clothing [64]. Implantable medical devices, which replace or support biological structures, remain a key research area due to their healthcare potential [65]. Integrating these devices with DT technology enables dynamic virtual models that replicate patient conditions, optimize device performance, and enhance predictive analytics for better medical outcomes.

Chen et al. [66] used DT technology to improve healthcare monitoring in smart homes by enabling real-time visualization, anomaly prediction, and intelligent control. By combining high-fidelity DT models with wearable ECG devices and WiFi-based sensing, they develop smart algorithms for fall detection and atrial fibrillation screening, showing strong potential for more accurate and reliable healthcare monitoring. A recent work [67] proposed a DT-enabled smart system that integrates DT technology with wearable medical devices to enhance personalization in design, manufacturing, and healthcare monitoring. Through case studies on rehabilitation training, wheelchair use, and fall detection, the system demonstrates high accuracy in data tracking and customization, highlighting its potential for large-scale applications in personalized medicine. Another work [68] achieved remarkable outcomes by developing an intelligent wearable system that integrates motion and emotion recognition using multiple sensors and a novel human action recognition network (TB-SFENet), achieving 97.04% accuracy on the UCI-HAR dataset. To bridge the gap between the physical and virtual worlds, DT technology was used to create a 3D visualization platform that enables real-time interaction of activity, emotion, location, and monitoring data. Additionally, the study introduced the TGAM electroencephalogram emotion classification (TEEC) dataset with 120,000 data points, further enhancing the system's potential for applications in intelligent healthcare and virtual reality.

Yang et al. [69] proposed a decision support framework that utilizes DT technology and expert system methodologies to personalize therapy for Implantable Medical Devices (IMDs) based on real-time physiological data. By integrating a dynamic DT, reinforcement learning, and specialized algorithms, they demonstrate improved therapy customization, surpassing traditional methods in both effectiveness and patient safety, as validated through a case study on Implantable Cardioverter Defibrillators (ICDs).

Medical metaverse

The term "metaverse" was first introduced in Neal Stephenson's 1992 science fiction novel Snow Crash. It is a blend of "meta" and "verse" — a shortened form of the universe. The integration of IoT with the medical metaverse presents innovative platforms for healthcare education and clinical training.

Through the convergence of IoT-generated data streams and extended reality (XR) technologies — merging both virtual reality (VR) and augmented reality (AR), healthcare practitioners can now participate in high-fidelity clinical simulations. Ghaempanah et al. [70] developed an application that involves IoT-assisted patient simulators that provide instantaneous biometric feedback during virtual surgical procedures, helping medical trainees to develop and refine their technical skills. It also facilitates medical training, where surgeons can practice complex procedures in hyper-realistic virtual environments before performing them on real patients. This sophisticated approach to medical simulation improved the acquisition of procedural competencies and clinical readiness through experiential learning methodologies.

MeDeT [71] is a meta-learning-based approach designed to generate and adapt DTs of medical devices, addressing the challenges of integrating evolving devices in healthcare IoT testing. Evaluated in collaboration with Oslo City's health department, MeDeT achieves over 96% fidelity, adapts to new device versions in approximately one minute, and efficiently operates 1,000 DTs concurrently, providing a scalable and cost-effective alternative to physical device testing.

4.5. Pharmaceuticals

While the pharmaceutical industry may seem less directly connected to smart IoT technologies and DT integration, it involves several critical areas where DTs can have a significant impact. In this paper, we explore their role in drug discovery, clinical trials, and biomanufacturing, highlighting their potential to enhance efficiency, accuracy, and innovation in these domains.

Drug discovery

DTs combined with IoT technologies, have emerged as transformative tools in drug discovery and vaccine development. Physical systems like DTs leverage real-time data to simulate biological and chemical interactions to optimize therapeutic processes in various health issues. DTs can revolutionize drug discovery by simulating the human response to different compounds, predicting efficacy and side effects before actual clinical trials. Drug discovery has traditionally relied on labor-intensive, cost-prohibitive methods. Recent advancements in digital technologies, including DTs and IoT, are changing this landscape. DTs offer dynamic and real-time simulations of biological systems, helping researchers to study drug interactions, predict outcomes, and refine therapeutic strategies. Moreover, IoT devices enhance this capability by providing continuous, real-world data streams, making DTs highly robust and adaptive. IoT devices, such as biosensors, wearable health monitors, and lab equipment, feed these simulations with real-time data, bridging the gap between in silico models and in vivo conditions. Alexandre et al. [72] illustrated the transformative potential of DTs in personalized medicine, highlighting their role in patient monitoring, risk assessment, clinical trials, and drug development. While DTs enable precise health insights and tailored treatments, they also raise ethical concerns regarding data privacy, consent, and potential biases in healthcare. Balancing innovation with ethical responsibility, they emphasize the need for robust regulations to ensure the responsible and effective integration of DTs in patient care.

Medical DTs are also transforming precision oncology by combining individual patient data with population-level insights and healthcare IoT. These models continuously monitor new data and physician decisions, allowing real-time treatment adjustments. Zhang et al. [73] portrayed that continuous feedback is particularly valuable for cancer treatment by predicting drug resistance, suggesting alternative treatments based on tumor genetics, and personalizing chemotherapy while minimizing side effects. Wu et al. [74] has shown promising results in triple-negative breast cancer treatment prediction and metastatic disease detection through radiology report analysis, which is an emerging study on cancer research. Immunology research is vital in healthcare because it helps us understand how the immune system defends against diseases, leading to breakthroughs in vaccines, autoimmune treatments, and infectious disease control. Scientists are trying to develop effective vaccines that protect against deadly pathogens like COVID-19, influenza, and tuberculosis. DTs in immunology utilize computational models and real-time data to enhance the development and manufacturing of vaccines. By integrating molecular dynamics simulations, structural biology insights, and machine learning techniques, these virtual models can predict antibody-antigen interactions, stability, and production feasibility. Recent advancements [75] have shown promising results in designing antibodies for emerging diseases and complex therapeutic targets, reducing costs and development time while enhancing therapeutic effectiveness.

Clinical trials and manufacturing

Clinical trial research is essential in healthcare because it ensures the safety, efficacy, and effectiveness of new medical treatments, drugs, and medical devices before they reach patients [76]. These trials provide scientific evidence to determine whether a new intervention works better than existing treatments or has fewer side effects. One of the most promising applications of DTs in clinical trials is the development of virtual control groups, which reduce the need for placebo arms while maintaining statistical robustness [77]. Sel et al. [78] proposed an approach that enhances patient recruitment and retention while speeding up trial completion. Additionally, this research supports adaptive trial designs, where real-time patient data dynamically modifies study parameters. Recently, regulatory agencies, such as the FDA and EMA, have explored DT-based trial validation frameworks in healthcare that will be expected to redefine precision medicine and accelerate the development of life-saving treatments. TWIN-GPT [79] is a large language model-based approach for creating personalized DTs that establish cross-dataset associations of medical information, enabling more accurate clinical trial outcome predictions even with limited data. Through comprehensive experiments, we demonstrate that TWIN-GPT outperforms previous methods in prediction accuracy and generates high-fidelity trial data, showcasing its potential to enhance virtual clinical trials and advance healthcare research.

In the specialized field of biomanufacturing, DT innovation is transforming multiple aspects of production, including process development, validation protocols, and operational management. The application of DTs in biomanufacturing creates an intricate, mathematically driven model that captures every aspect of the production process. This comprehensive simulation spans the entire manufacturing journey, beginning with raw material inputs and continuing through to the final product output. Herwig et al. [80] highlighted that DTs have expanded beyond biomolecule production into chemical synthesis. This system's sophistication lies in its ability to continuously integrate both historical process data and real-time information, monitoring and analyzing crucial parameters such as temperature fluctuations, pH levels, and nutrient concentration variations for drugs.

4.6. IoMT security and privacy

The rapid adoption of the IoMT has significantly improved healthcare delivery by enabling real-time monitoring, remote diagnostics, and personalized treatments [81]. However, the increasing interconnectivity of medical devices introduces substantial cybersecurity risks, including data breaches, unauthorized

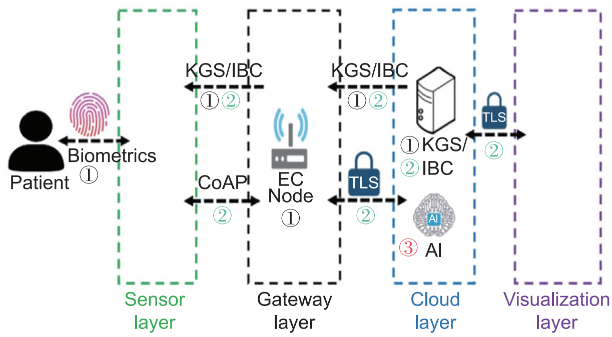

Fig. 7. A proposed IoMT secure system architecture [83].

access, and system vulnerabilities that could compromise patient safety. For instance, a security breach in data collected by a smartwatch or fitness tracker could expose sensitive personal details such as a user's health metrics, daily activities, and demographic information [82]. Securing IoMT ecosystems requires robust measures across data collection, transmission, and storage, especially as DT technology becomes more integrated into healthcare, further emphasizing the need for resilient cybersecurity frameworks. In an IoMT environment, DT solutions demand robust security across all layers – sensor, gateway, cloud, and visualization – to safeguard patient data and ensure system integrity, as depicted in Fig. 7. The figure illustrates how IoMT sensors interface with edge computing nodes and secure protocols, forming a critical foundation for real-time data exchange and effective healthcare monitoring.

Device and network security

Zachos et al. [84] presented an innovative hybrid anomaly-based Intrusion Detection System (AIDS) designed to address security vulnerabilities in IoMT networks. Additionally, they developed a functional IoT/IoMT security testbed, enabling the assessment of AIDS against various cyber threats and providing a valuable tool for researchers working on IoT security solutions. DT-IoMT [85] is a DT reference model designed to integrate the human body and medical devices within IoMT, enabling real-time health monitoring and secure, autonomous diagnostics. This paper presents a conceptual architecture that incorporates smart sensors, advanced communication protocols, and biomedical signal monitoring while addressing security challenges, making it a foundation for future implementations in chronic disease management and smart hospitals.

In the case of cyber resilience, a study [86] proposed a new deep learning scheme to automatically detect vulnerabilities in healthcare DTs by capturing bi-directional context relationships among risky code keywords. Through extensive experiments on IoT-related software, the approach outperforms state-of-the-art methods, addressing the complexity and scale of emerging 6G healthcare DT applications. Jimenez et al. [87] explored the implementation of Wireless Body Area Networks (WBAN) in healthcare, highlighting performance and security challenges, especially concerning wearable or implanted devices. They also provide definitions of Medical Cyber-Physical Systems (MCPSs) and DTs, discussing how these technologies, alongside IoT and cloud computing, can improve patient care. Sharma et al. [88] proposed a novel approach that merges elliptic curve cryptography (ECC) with blockchain technology to secure IoT-based healthcare DTs, while employing a genetic algorithm-optimized random forest (GAO-RF) to enhance feature selection. They demonstrated robust performance, achieving an F1-score of 97.3% and an accuracy of 98.4%, thereby instilling trust in the healthcare system by effectively safeguarding patient data.

Data privacy and regulatory compliance

Ensuring robust data protection and regulatory adherence is critical for maintaining trust in digital healthcare systems. By incorporating strong privacy measures and compliance frameworks, healthcare providers can safeguard patient information while supporting innovative solutions like DTs. Lutze et al. [89] presented a novel approach for managing AI-driven eHealth systems using DTs, categorized into personal, group, and system-level twins. This framework enables compliance with EU-GDPR by allowing the unlearning of personal data, enhances system transparency to ensure unbiased conclusions, and incorporates self-monitoring mechanisms to reassess prior diagnoses based on newly acquired knowledge. Akash et al. [90] proposed a mathematical data model to systematically collect and organize patient information, ensuring privacy and security. Building on this model, they introduced a healthcare DT system underpinned by blockchain, explaining its components and protocol flows. Finally, they evaluated its feasibility by comparing it with other relevant approaches. PSim-DTH [91] is an efficient and privacy-preserving scheme that employs a partition-based tree (PB-tree) and matrix encryption to securely handle healthcare data on a DT cloud platform. By enabling similarity queries without revealing personal information, it supports continuous patient health monitoring while safeguarding sensitive details. The scheme's evaluation demonstrates its strong data protection capabilities and high query efficiency.

Another work [92] proposes a DT-enabled Asynchronous SplitFed Learning (DT-ASFL) framework for e-healthcare classification, utilizing model splitting and feature-only data transmission to handle heterogeneous IIoT resources and privacy constraints. By employing DT for real-time device monitoring and asynchronous updates, the approach enhances communication efficiency and accommodates resource-constrained devices, thus improving performance over existing methods. Tang et al. [93] explored a blockchain-based framework to enhance the security and privacy of healthcare DT data (HDTD) sharing, addressing concerns related to data accessibility and integrity. By implementing an access control scheme with cloud storage and attribute encryption, they enable secure interactions between users. Additionally, they develop an HDTD missing value prediction algorithm to mitigate data loss and ensure real-time data reliability, demonstrating improved security and reduced interaction delays compared to existing methods.

4.7. Other miscellaneous applications

In addition to the literature reviews presented in the previous sections, several other significant studies deserve attention but were not explicitly categorized within those sections. These works focus on key areas such as comprehensive system architecture, advancements in e-health, and innovative approaches to healthcare monitoring for smart home systems.

Comprehensive architecture

Several studies have proposed comprehensive architectures for health-related DTs across various domains, aiming to address multiple challenges concurrently. Some examples [1], [56, 85] have already been highlighted in the personalized sections. Benedictis et al. [94] reviewed the current literature on DT in healthcare, categorized its applications into four main domains, and proposed a reference DT architecture. They then introduce CanTwin – a real-life canteen service DT developed by Hitachi – for social distancing, queue inspection, and occupancy monitoring, demonstrating the practical utility of DT in virus containment. Iqbal et al. [95] explored the potential of DTs in healthcare by addressing key challenges related to their design, components, and operational requirements. By proposing an implementation architecture and presenting a proof-of-concept prototype, they demonstrate how DTs can enhance healthcare services while highlighting open challenges and future research directions.

Pellegrino et al. [96] conducted a meta-review using the PRISMA methodology to analyze 20 selected reviews from 1,075 studies, identifying key functional, technological, and operational aspects of DTs in healthcare. Based on this analysis, they develop a conceptual framework that clarifies the hierarchical relationships among these aspects, facilitating the effective design, evaluation, and implementation of DTs in digital health. Alqahtani et al. [97] proposed a secure framework that integrates DT technology, IoT-edge computing, and blockchain to monitor adults' physical activity while ensuring the privacy of health data. By leveraging deep learning-assisted CNN and LSTM models for real-time vulnerability assessment, their approach outperforms state-of-the-art techniques in prediction accuracy and reliability.

E-health

Since the DT concept has now expanded to include both living and inanimate entities, its potential for use in eHealth and wellness applications has significantly grown [98,99]. CloudDTH [100] is a novel cloud-based healthcare framework designed for real-time monitoring, diagnosing, and predicting health conditions using wearable medical devices. It bridges physical and virtual healthcare spaces through a DT model, offering enhanced personal health management and real-time supervision, especially for elderly patients. Garg et al. [101] proposed a system integrating DTs and CPS to gather and analyze real-time patient data via wearable health instruments, maintaining parallel physical and virtual databases for diagnosis and monitoring. They further secure e-health cloud data using a two-phase iris biometric authentication method based on an EfficientNet CNN, effectively differentiating genuine from spoofed samples. Another work [102] expanded on the DT concept for health and medical software by incorporating regulatory standards, unique device identification (UDI) systems, and full lifecycle management across personal, group, and system-level twins. They also explore the strengths and weaknesses of using DTs in software design and development, emphasizing the benefits of agile approaches over traditional V-model methods. Furthermore, DT-ASFL [92], which we discussed before, improves IIoT healthcare learning by enabling asynchronous updates and partial training, allowing low-resource devices to contribute without sacrificing performance.

Healthcare monitoring for smart home

DT is increasingly being explored for healthcare monitoring in smart homes, enabling real-time visualization, anomaly detection, and intelligent control. By integrating DT with wearable sensors and AI-driven analytics, researchers aim to enhance remote patient monitoring, predict health risks, and improve personalized care, ultimately fostering a smarter and more responsive home healthcare environment [103]. Akram et al. [104] introduced the AI-Generated Optimal Decision (AIGOD) algorithm and the Deep Diffusion Soft Actor-Critic (DDSAC) framework to enhance the integration of HDTs with AI-Generated Content (AIGC) in IoMT-based smart homes. Their AI-generated content-as-a-service (AIGCaaS) architecture, optimized for IoMT environments, demonstrated superior performance, with DDSAC achieving a 20% improvement in task completion rates and a 15% increase in overall utility, highlighting its potential for personalized and proactive healthcare interventions. Another interesting work [105] proposed a DT-based model for home-device (HD) control, integrating IoT, virtual simulation, and remote intelligent control to establish a human cyber–physical system (HCPS). By utilizing a game theory approach for modeling IoT-based smart devices and enhancing sensing networks, they improve virtual reality synchronization, positional accuracy, and quality control in HDDT development.

Rivera et al. [106] investigated how DT may transform healthcare by facilitating ongoing monitoring and enhancing communication between patients, caregivers, and systems. Through virtual health tracking and therapy evaluation, they hope to improve precision medicine by combining DT with data-driven techniques like machine learning. Their research presents a reference model that uses DT, autonomic computing, and self-adaptive systems to create intelligent, adaptable healthcare solutions that facilitate treatment customization and decision-making. Another work [107] proposed a context-aware framework that uses DT to monitor indoor air quality and human activity, integrating IoT, 6G networks, edge computing, and AI-driven analytics. By developing an architecture with sensors, gateways, and a DT object on the Azure cloud, they enhance healthcare monitoring through real-time data processing and predictive insights. Their contributions include linking 6G sensing with IoT techniques and achieving high-accuracy human activity recognition using deep learning models. Furthermore, there are studies [91,100] that used the cloud-based healthcare monitoring system discussed previously.

4.8. Summary of DT applications in healthcare IoT

To synthesize the findings across the diverse application domains discussed in Section 4.1 to 4.7, Table 2 presents a consolidated summary of representative studies on DTs in healthcare IoT. This table captures the core methodologies or algorithms employed, evaluation metrics used, targeted application domains, and the specific strengths and limitations of each approach. It provides a comparative view that allows readers to quickly identify trends, assess the effectiveness of various DT implementations, and recognize gaps or limitations that persist across the literature. By organizing these studies in a structured format, this summary also serves as a bridge between the detailed narrative analysis and the forthcoming discussion on enabling technologies.

From the summary, one can observe that DT applications in healthcare IoT are multifaceted. Some works focus on smart hospital management, using twins to improve operational efficiency or environmental safety. Others center on patient-specific modeling for personalized care (such as the diabetes and cardiac twins), leveraging real patient data streams to tailor healthcare decisions. Yet others target medical devices and infrastructure, ensuring that the underlying IoT-enabled systems (from wearable sensors to large imaging devices) are reliable, secure, and optimized. Evaluation metrics across studies vary according to these goals — ranging from technical performance indicators (latency, detection accuracy, simulation error) to clinical/proxy outcomes (like predicted health metrics or workflow improvements). Each approach brings certain strengths: for instance, data-driven twins with machine learning excel at real-time prediction, while physics-based twins offer interpretability and physiological insight. However, limitations are also evident. Common challenges noted in Table 2 include limited clinical validation (many are prototypical demonstrations or simulations), scalability issues (handling the volume and velocity of IoT data in real hospital settings), and interoperability and privacy concerns (integrating diverse IoT devices and ensuring patient data security). These observations set the stage for a deeper discussion on open research questions and the future directions needed to advance DT technology in healthcare.

Table 2
Summary of Representative Studies on Digital Twins in Healthcare IoT.

Study (Year)	Method/Algorithm	Evaluation Metrics	Application Domain	Limitations
Elayan et al. (2021) [1]	Intelligent context-aware DT with ML-based ECG classifier	ECG classification accuracy, real-time context detection	Patient monitoring, dynamic healthcare improvement	Complex architecture; privacy and security considerations
Karaka et al. (2019) [48]	IoT and AI-based DT for hospital patient pathways	Prediction accuracy for patient outcomes, real-time monitoring effectiveness	Hospital management and operational efficiency	Integration complexity; scalability for large hospitals untested
Laaki et al. (2019) [56]	DT prototype with robotic arm and VR via 4G mobile network	Network latency, reliability, cybersecurity robustness	Surgical planning, remote robotic surgery	Limited VR feedback; early-stage prototype limitations
Chen et al. (2023) [66]	Smart home healthcare DT combining wearable ECG and WiFi sensing	Anomaly detection accuracy, effectiveness in fall detection	Home healthcare monitoring, elderly care	Requires reliable IoT connectivity; scalability not fully validated
Zhang et al. (2022) [73]	DT for cancer treatment personalization using genetic data	Prediction accuracy for drug resistance; effectiveness of personalized chemotherapy	Pharmaceuticals, personalized cancer treatment	Relies heavily on genetic data quality; complexity in clinical validation
Zachos et al. (2023) [84]	Hybrid anomaly-based IDS for IoMT security	Intrusion detection accuracy; security testbed effectiveness	IoMT security, cybersecurity for medical IoT networks	Integration complexity; indirect impact on direct patient outcomes
Garg et al. (2022) [101]	DT and CPS-integrated e-health system with iris biometric authentication	Authentication accuracy (EfficientNet CNN); effectiveness in spoof detection	E-health cloud data	High computational cost; biometric system complexity
Benedictis et al. (2022) [94]	Real-life "CanTwin" DT implementation for social distancing, queue inspection, and occupancy monitoring	Practical effectiveness in occupancy and social distancing monitoring	Comprehensive architecture on virus containment, healthcare facility management	Primarily focuses on specific scenarios; broader clinical integration and scalability not thoroughly evaluated

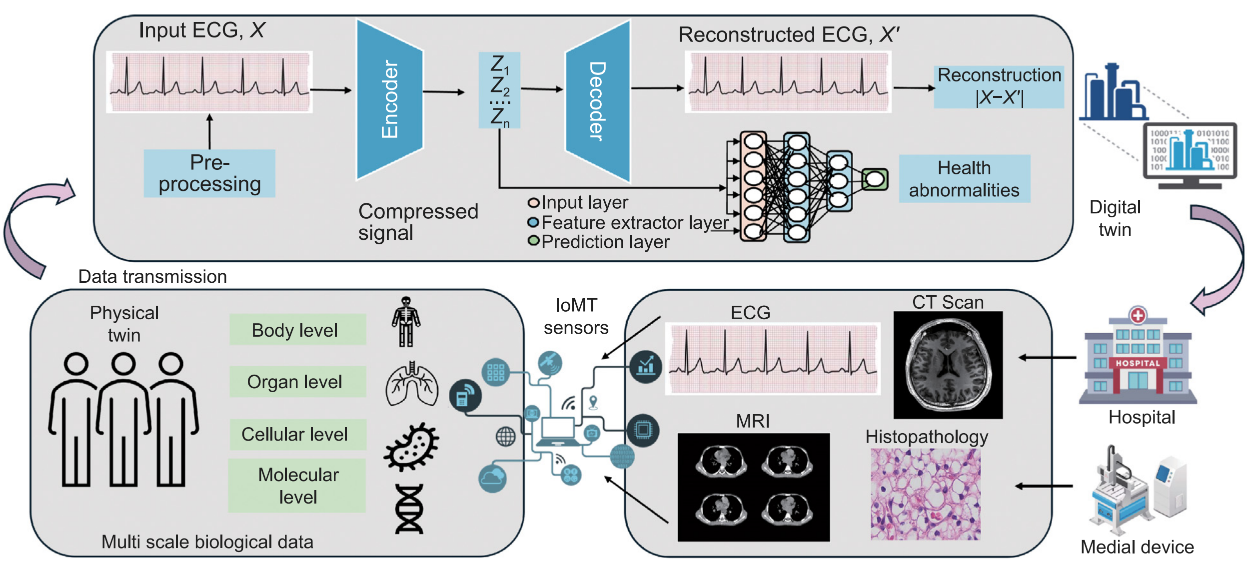

Fig. 8. An overview of Gen AI-based digital twins in healthcare with a focus on ECG data as an illustrative example.

5. Healthcare DT enabling technologies

5.1. Modeling and simulation

A simulation model remains static unless the designer manually adds new components. In contrast, a DT initially appears similar to a simulation model but acquires dynamic properties by integrating real-time data, enabling it to adapt and evolve over time [108]. This real-time data feeds into sophisticated AI-driven predictive models, enabling disease trajectory forecasting and treatment optimization. Elayan et al. [1] implemented a model that successfully predicted a particular heart condition with high accuracy in different algorithms. The findings showed that integrating DT with the healthcare IoT field would improve healthcare technologies by bringing patients and healthcare professionals together in a robust, cost-effective, and scalable health ecosystem.

Data-driven approaches, *i.e.*, machine learning algorithms, deep learning models, and advanced AI techniques – including Generative AI (Gen AI), artificial intelligence-generated content (AIGC), and Large Language Models (LLMs) – are increasingly being leveraged to prototype and develop high-impact DTs across various sectors within healthcare. As Gen AI continues to advance and shape the future, Fig. 8 provides a high-level overview of its integration with DTs in healthcare. Applications of various approaches include but are not limited to — validation using gradient boosting regressor [109], LLM-based DT [79], GAN based DT [55], long-term memory (LSTM) model for predictive analysis [1,110], improved Random Forest for clinical big data analytics [111], support vector machine (SVM) for stroke diagnosis [112], customized CNN [86], mobile AIGC-driven HDT [113], Gen AI with 3D modeling [114] etc. Furthermore, several impactful studies [115,116] have explored model-based approaches and system-level DTs, demonstrating their effectiveness in enhancing simulation accuracy and predictive capabilities. Given the diverse methodologies and emerging trends discussed above, a concise summary and comparative analysis of how these DT modeling paradigms specifically impact healthcare IoT scenarios are provided in Table 3, which outlines their respective effectiveness, key benefits, and associated challenges, facilitating a clearer understanding of their applicability.

5.2. Cloud and edge computing

The computational architecture supporting DTs integrates both cloud and edge computing paradigms to deliver essential processing power, real-time analytics, and seamless data synchronization. Cloud computing plays a crucial role by offering vast storage capacity, facilitating AI model training, and enabling large-scale data analysis, which is particularly valuable for long-term patient monitoring, electronic health records (EHR) management, and predictive diagnostics in hospitals. Meanwhile, edge computing ensures immediate data processing at the source, reducing latency and enabling real-time decision-making for critical applications such as intensive care unit (ICU) monitoring, remote patient monitoring, and computer-assisted surgical procedures [117]. By using IoT-enabled edge computing, hospitals can process patient data locally, reducing dependence on cloud networks and ensuring rapid response times, which is essential for emergency care and high-risk patient management. This synergy between cloud and edge computing enhances the efficiency of DT-based healthcare systems by optimizing resource allocation, improving data security, and ensuring compliance with regulatory standards such as HIPAA and GDPR. Alsuba et al. [110] proposed an intelligent athlete healthcare framework using IoT-edge computing to monitor real-time health data and assess probabilistic health state susceptibility during intense training. By integrating a Bayesian classification model and a multi-scale LSTM model for predictive analysis, they demonstrate superior performance over existing techniques in terms of classification efficiency, predictive accuracy, and system stability.

5.3. Blockchain technology

To ensure service sustainability, a trustworthy and shareable ledger, commonly known as the blockchain, is maintained for certain DT systems [118]. Blockchain compiles dispersed, secure, and verifiable records of data collected from multiple sources, linking them in a single chain of interconnected blocks [119,120]. It plays a vital role in DT healthcare frameworks by enabling secure, immutable, and distributed data exchange while addressing key requirements such as data security, privacy protection, and regulatory compliance [121]. Some applications are focused on data privacy, as we discussed in . Key studies have explored the use of blockchain for various applications, including privacy and security [90,93], integration with ECC [88], irregular event analysis [122], and public auditing schemes [123], among others.

6. Discussion

According to this review, DT research in healthcare systems is experiencing rapid global growth, focusing on three primary objectives: current trends, healthcare innovation, and applications. However, the field faces two key challenges: an unclear definition of essential DT characteristics of data management and a limited exploration of IoT modeling techniques for healthcare applications. Recent trends indicate that most DT studies focus on problem formulation and conceptualization, with a substantial portion dedicated to enhancing patient care without considering real-world applications. Despite this initial approach being both fundamental and relevant, we argue that expanding DT applications of healthcare systems and understanding provider decision-making processes could significantly enhance care quality and system resilience.

6.1. Current trends

Since it was proposed in 2002 by Professor Grieves, DT has expanded its healthcare research [124], covering various sources, indicating multidisciplinary interest and applications. We have analyzed the recent trends in significant research publications that focus on DTs in healthcare IoT over the past few years. Fig. 9 The pie chart presents the distribution of research papers on DT research in healthcare from 2012 to 2024 across various academic journals and conference proceedings. The largest share of publications appears in IEEE Access, which accounts for 17.4% of the total research output in this field, followed closely by Sensors at 14.9%. Several Lecture Notes series, including those in electrical engineering, networks and systems, computer science, and civil engineering, collectively represent a substantial portion of the published work, indicating their significance in disseminating DT research. Additionally, other important publication venues include Scientific Reports, Applied Sciences, Journal of Physics: Conference Series, and Mechanical Systems and Signal Processing, each contributing between 6% and 8% of the total papers. The distribution of these publications highlights the interdisciplinary nature of DT research in healthcare, spanning fields such as engineering, computer science, and applied sciences in healthcare. This visualization provides valuable insights for researchers looking to identify relevant journals and conferences for publishing their work, as well as for tracking trends in the field over time.

We also conducted a year-by-year search for articles using the keyword "digital twin in healthcare" while including health-related studies. This approach aimed to capture the overall growth of DT technology in the literature, in terms of the healthcare domain. Fig. 10 illustrates the number of documents published over time from 2012 to 2023, showing a significant upward trend in recent years. From 2012 to around 2017, the number of documents remained consistently low, with minimal fluctuations. However, starting in 2018, there was a gradual increase, followed by a sharp exponential rise from 2019 onward. The publication count peaked around 2022–2023, indicating a surge in research activity. This pattern suggests growing interest and advancements in the subject area, with an accelerating rate of publications in recent years.

Table 3
Comparison of Modeling and Simulation Paradigms for DTs in Healthcare IoT.

Approach	Contributions	Effectiveness	Limitations
Data-driven Models	Real-time predictive analytics, personalized patient monitoring, anomaly detection	Highly effective in data-rich environments; excels at personalized health monitoring and rapid anomaly detection	Requires substantial amounts of high-quality data; privacy and ethical challenges; limited interpretability (*"black-box"*)
Physics-based Models	Provides mechanistic insights, scenario simulation, supports *"what-if"* analysis	Effective in scenarios requiring physiological fidelity and causality (*e.g.*, surgical planning, device testing)	Computationally intensive; demands extensive patient-specific data for model calibration; challenging real-time deployment
Hybrid Models	Combines data-driven accuracy and physics-based interpretability; suitable for complex, multi-modal systems	Highly effective in balancing predictive power and interpretability; adaptable and scalable for complex healthcare scenarios	Complex implementation; integration challenges; difficult model validation and debugging due to multiple interacting components

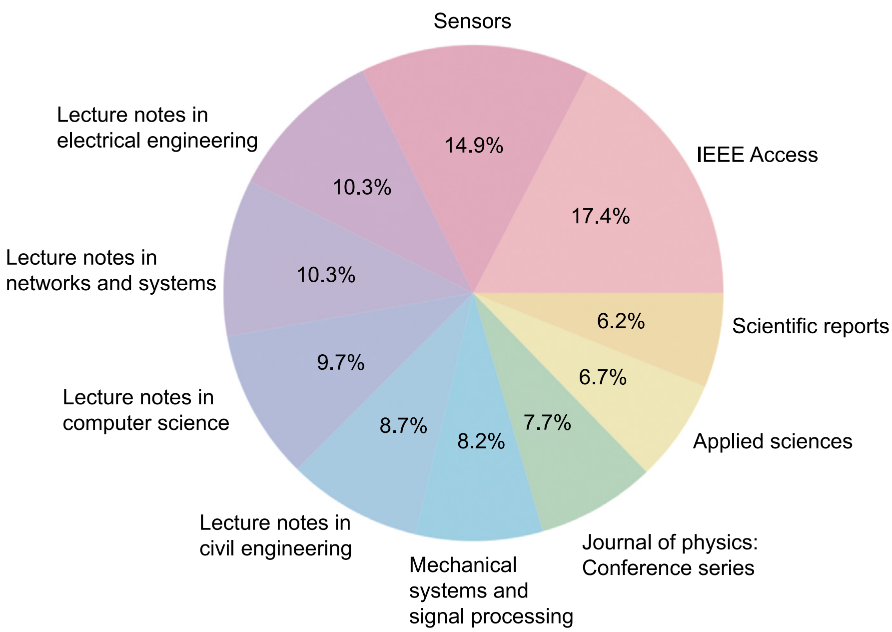

Fig. 9. Major domains in digital twin research in healthcare from 2012 to 2024.

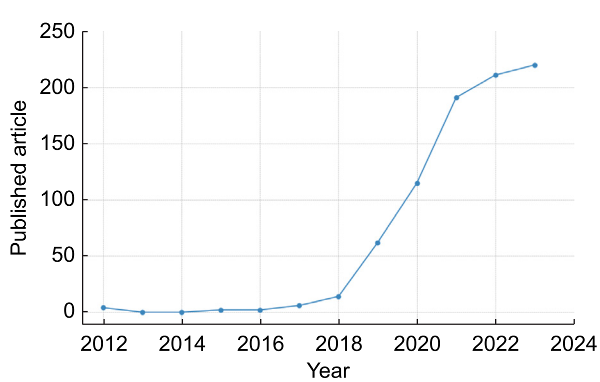

Fig. 10. Digital twin research trends in healthcare from 2012 to 2024.

6.2. Emerging trends

Recent developments reveal novel applications and underexplored domains for DTs in healthcare IoT that extend beyond the scope of prior surveys. One notable domain is mental health, where DT technology remains largely untapped. The use of DTs in mental health is *"yet to be explored"*, indicating a clear research gap. While most healthcare DT efforts focus on patient-level or device-level twins, DTs can also model entire clinical workflows and healthcare facilities. For example, a DT of a hospital or clinic can optimize patient flow, predict ICU bed occupancy, and manage resource allocation in real-time. A recent review noted that using DTs to manage healthcare systems is an *"emerging topic"* supported by limited literature so far [35]. Nevertheless, early implementations demonstrate potential: hospital-level twins are being used to simulate emergency department workflows and identify bottlenecks, with significant promise for improving operational efficiency. The COVID-19 pandemic catalyzed interest in such system-level twins, as they could help model and respond to surges in patient volume and resource needs. This trend underscores a broader vision of population-level or public health DTs, where entire patient populations or health systems are replicated virtually to test policies and pandemic responses in a risk-free environment.

As discussed earlier in Section 5.1, the integration of advanced AI techniques – particularly generative AI (e.g., GANs, LLMs, AIGC) and federated learning – has already begun to transform the development of DTs in healthcare. These technologies enable high-fidelity virtual modeling, privacy-preserving distributed training, and synthetic data generation, especially valuable in data-scarce or privacy-sensitive clinical environments. A recent survey [125] emphasizes that *"generative AI may be a promising solution"* for improving digital human twins by augmenting digital models with realistic data while accurately reflecting real-time physical states. Looking forward, sustained progress in GenAI and federated architectures will be crucial for scaling adoption, enhancing model generalizability, and maintaining ethical compliance. Future research should prioritize validation, transparency, and regulatory alignment for these AI-enhanced DTs.

6.3. Architecture and infrastructure implications

As outlined in Section 5.2, a *layered edge–cloud architecture* is now the de facto design pattern for healthcare DTs. In short, time-critical analytics (*e.g.*, real-time vital-sign monitoring) run on local edge servers to minimize latency and keep sensitive data on-site, while computationally heavy tasks – such as high-fidelity organ simulation or cross-patient model retraining – are offloaded to secure cloud resources. Discussion here therefore, focuses on the deployment implications that arise from this pattern.

- **Interoperability:** Successful scaling hinges on adopting open healthcare data standards and middleware that can translate heterogeneous IoMT data streams into those formats. Standards-compliant middleware future-proofs the platform: new sensors or EMR systems can be integrated without re-engineering the twin.
- **Security & Privacy:** Because twins aggregate high-value clinical data, end-to-end protection is mandatory. Recommended safeguards include transport-layer encryption, role-based access control, and tamper-evident ledgers (*e.g.*, blockchain) for model-update provenance [84]. For multi-institutional learning, *federated analytics* or secure multi-party computation can keep raw data local while still improving a global twin.
- **Network Readiness:** Emerging 5G/6G links offer the ultra-low latency and bandwidth required for continuous, bidirectional streaming between devices, edge nodes, and cloud datacentres—an essential enabler for closed-loop twins.
- **Take-away:** A practical healthcare DT stack must therefore combine (i) edge servers for on-premises real-time analytics, (ii) standards-based middleware for data normalization, and (iii) security-by-design at every layer. These architectural pillars transform the abstract concept of DTs into a deployable, scalable clinical technology.

6.4. Healthcare data standards

The successful implementation of DTs in healthcare IoT hinges on the adoption of established data standards – namely HL7, FHIR, and the OMOP Common Data Model – to ensure seamless data exchange and consistent representation of patient information [126]. These standards enable a secure, interoperable environment where real-time updates from multiple healthcare systems can be compiled into accurate digital replicas. Dolin et al. [127] introduced HL7 as an international set of standards designed to streamline healthcare information exchange, creating a structured framework for efficiently sharing, integrating, and retrieving electronic health data. Building on HL7 principles, the Fast Healthcare Interoperability Resources (FHIR) standard modernizes data transactions by incorporating web technologies, thereby facilitating the continuous flow of real-time clinical information into digital models. This capability is vital for applications that rely on current patient data from diverse providers and systems.

Equally important, Makadia et al. [128] developed the OMOP Common Data Model, offering a unified structure for storing and querying healthcare data. By converting heterogeneous data sources into a consistent format, DT platforms can more effectively process and analyze large-scale patient information, ultimately yielding deeper insights into health patterns and outcomes. In this way, HL7, FHIR, and OMOP CDM collectively form the foundational layer that enables DTs in healthcare IoT — ensuring data integrity, interoperability, and real-time responsiveness.

7. Future directions and challenges

Although this discussion does not serve as a comprehensive methodological review of DT technologies, it is important to acknowledge and highlight several well-documented challenges that continue to hinder advancements in this field. Many implementations remain pilot projects or lab demonstrations, and there is a significant journey ahead to achieve widespread clinical adoption. In fact, a recent review found that about 98% of purported healthcare DTs are still in preclinical phases, underscoring that most work has not yet translated into routine clinical practice [129]. In this section, we outline the key open research questions and persistent technical and clinical challenges that must be addressed. We also provide recommendations for researchers and practitioners aimed at propelling this field forward.

7.1. Open research questions and gaps

How to achieve high-fidelity, validated digital twins? One fundamental open question is how to ensure that a DT accurately reflects the complex reality of a patient or system over time. Rigorous validation against clinical outcomes is often lacking. Researchers are asking what level of modeling detail is truly necessary for a twin to be *trustworthy* in decision-making, and how to validate these models prospectively in clinical trials or real-world deployments.

What are the generalizable frameworks or benchmarks? As the field grows, there is a need to move from bespoke solutions to general frameworks. An open question is whether a *common reference architecture* (or set of design patterns) for healthcare IoT twins can be defined, to avoid each project reinventing the wheel. Similarly, the lack of benchmarks and shared datasets makes it hard to compare approaches.

How to enable two-way interaction and control? Many current DT implementations are largely one-way (streaming data from the patient/device to the twin). Only a minority (around 11% in one analysis) support full *bi-directional* data flow or closed-loop control [129]. It is still an open research problem to develop twins that not only passively reflect the physical system but actively intervene (*e.g.*, sending control signals to IoT devices or real-time decisions in a feedback loop).

What are the long-term impacts and emergent behaviors? As DT systems become more complex (incorporating AI, simulating physiology, etc.), unforeseen behaviors might emerge. Researchers are curious about the long-term performance: *Will a twin remain accurate as a patient's condition evolves? How do we update models to avoid drift?* Also, if multiple DTs interact, what are the system-level effects? [130].

Addressing these open questions will likely require interdisciplinary efforts, combining insights from computer science, biomedical engineering, and even fields like complex systems theory and human factors. Each question points to a gap in knowledge that future research must fill to move DTs from promising prototypes to reliable tools in healthcare IoT.

7.2. Challenges

From an engineering standpoint, implementing DTs in the healthcare IoT context presents several technical challenges:

- Data management and quality: Healthcare IoT devices generate enormous amounts of data, often continuously. Ensuring data quality, consistency, and completeness is non-trivial — sensors can fail or drift, and biomedical data can be noisy. Techniques for real-time data filtering, anomaly detection, and handling missing data are critical. Scalable database solutions and edge computing for preprocessing are active areas of development to address this challenge.
- Interoperability and standardization: The current ecosystem of medical IoT devices is highly fragmented. Devices from different manufacturers use different data formats and communication protocols. A DT that aggregates data from, say, a wearable heart monitor, an implantable device, and a smart bed in a hospital must interface with all seamlessly. Lack of standard data models and APIs in healthcare IoT hampers integration. Efforts like open data standards need to be extended to cover the type of real-time streaming data used in DTs.
- Model accuracy vs. complexity trade-off: Technically, there is a tension between the fidelity of a DT and the complexity of its computations. High-fidelity physics-based models can be very accurate but computationally intensive, whereas simpler data-driven models run faster but might miss important nuances. One approach is multi-level modeling: a coarse, fast model for routine use and a finer, detailed model invoked when needed, but orchestrating such hybrid models adds complexity.

On the clinical side, there are significant challenges in translating DT innovations into practice:

- Clinical validation and evidence generation: Perhaps the most pressing issue is the lack of substantial clinical validation for most DT solutions to date. Healthcare, being a highly evidence-driven field, requires robust studies to prove that a DT actually improves patient outcomes or operational efficiency. Without stronger evidence, clinicians may be hesitant to trust and adopt these systems.
- Integration into clinical workflow: Even if a DT tool is proven effective, integrating it seamlessly into existing clinical workflows is non-trivial. Challenges include designing user interfaces that clinicians find intuitive and useful, determining how and when the twin's outputs should be presented to the care team, and ensuring the twin does not generate excessive false alarms or irrelevant information. Achieving the right level of automation is also a challenge, *e.g.*, should the twin automatically change a ventilator setting or just recommend it to a physician?
- Interdisciplinary communication: The development and deployment of DTs require tight collaboration between technical teams (engineers, data scientists) and clinical teams (doctors, nurses, biomedical experts). There is a cultural and language gap to bridge — clinicians need to trust the twin's model and outputs, while technologists need a deep understanding of clinical realities. Fostering interdisciplinary teams and perhaps training "*clinical data scientists*" will help mitigate this gap.

In summary, while the technical development is critical, clinical adoption will depend on trust, evidence, and ease of use. Overcoming these challenges requires not just technological innovation, but also workflow design, medical research, and clear demonstrations of value in patient care.

7.3. Recommendations for advancing the field

To overcome the above challenges and knowledge gaps, we propose several future directions and recommendations for researchers, clinicians, and other stakeholders working on DTs in healthcare IoT:

Focus on interdisciplinary collaboration

The development of effective healthcare DTs should involve a tight collaboration loop between technologists and healthcare practitioners. We recommend forming interdisciplinary teams that include software/AI engineers, clinicians, biomedical scientists, security experts, and even patients. Such teams can ensure that the solutions address real clinical needs, are technically sound, and ethically grounded. Regular workshops or joint "*clinician-in-the-loop*" design sessions can help align the twin's functionality with frontline medical workflows.

Develop open platforms and standards

To accelerate progress, the community would benefit from open reference architectures and shared tools. We encourage the creation of open-source platforms for DT development specific to healthcare, where common services are provided. This would let researchers focus on novel modeling aspects without rebuilding infrastructure. In parallel, engaging with standards organizations to push for interoperability standards will reduce integration friction. A concerted effort towards standardizing how IoT data feeds into DT models and how results are output will make it easier to adopt these systems across different hospitals and device ecosystems.

Strengthen validation and publish negative results

Academic and industry researchers should prioritize rigorous validation studies and openly share results. This includes not only publishing success stories but also *negative or inconclusive findings*, which are equally informative. For instance, if a certain approach to modeling failed to improve outcomes, reporting it can save others time and guide the field away from blind alleys. We recommend establishing *benchmark datasets and challenge competitions* (as in AI fields) for tasks like predicting patient deterioration can drive progress. Collaborating with clinical units on pilot studies will help build the needed evidence base and accelerate learning from real-world results.

Invest in scalability, security, and robustness research

As identified, technical robustness is a major challenge. Funding and research efforts should be devoted not only to novel applications but also to the "*boring*" but crucial aspects of scalability and security. This means developing algorithms that can handle big data with constrained resources (perhaps using edge computing for initial data crunching) and exploring advanced security measures. For example, incorporating blockchain or distributed ledger techniques for tamper-proof logging of twin data transactions or using differential privacy methods to allow data analysis with mathematical privacy guarantees. We also recommend stress-testing DT systems under worst-case scenarios (network down, data corrupted, etc.) to ensure failsafes are in place. These engineering investments might not be as glamorous as new AI models, but they are vital for deployment in the safety-critical healthcare arena.

Engaging all stakeholders and educating end-users

Finally, we recommend that hospital administrators and policymakers be informed of DTs' potential to improve outcomes and reduce costs, using case studies or ROI simulations to gain support. Clinicians and staff need training to understand and interpret DT outputs through programs or CME modules. Patient education is equally important — introducing the concept via brochures or consent discussions can help build trust and avoid confusion when DTs are used in care. Informed stakeholders and users enable more effective adoption and impact.

8. Conclusion

DT technology is rapidly transforming the healthcare landscape, offering unprecedented opportunities for personalized medicine, efficient hospital management, and enhanced patient care. By integrating real-time data with IoT infrastructure, DTs enable dynamic patient modeling, predictive diagnostics, and optimized medical device performance. Additionally, their role in the pharmaceutical industry, from clinical trial simulations to supply chain monitoring, highlights their broader impact on healthcare innovation. Amid these technological advancements, this paper has provided a systematic review of DT integration within the healthcare IoT ecosystem, emphasizing its critical role in enabling personalized medicine and addressing pressing security challenges. We have explored the applications of DTs in digital patient modeling, smart hospital lifecycle management, medical device optimization, and pharmaceutical advancements, demonstrating their transformative potential in modern healthcare.

Despite these advancements, several challenges remain, including data security, interoperability, and the ethical implications of patient data usage. Addressing these concerns is crucial for ensuring the widespread adoption and reliability of DTs in healthcare. Moving forward, continued research and development in AI-driven analytics, secure data-sharing mechanisms, and regulatory frameworks will be essential to unlocking the full potential of DTs in smart healthcare systems. By overcoming these barriers, DTs can pave the way for a more efficient, proactive, and patient-centered healthcare ecosystem.

CRediT authorship contribution statement

Md Rafiul Kabir: Writing – original draft, Supervision, Methodology, Funding acquisition, Conceptualization, Writing – review & editing, Visualization, Project administration, Investigation, Data curation. **Fairuz Shadmani Shishir:** Writing – original draft, Investigation, Conceptualization, Visualization, Data curation. **Sumaiya Shomaji:** Writing – review & editing, Supervision, Validation, Funding acquisition. **Sandip Ray:** Writing – review & editing, Project administration, Supervision, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] H. Elayan, M. Aloqaily, M. Guizani, Digital twin for intelligent context-aware IoT healthcare systems, IEEE Internet Things J. 8 (23) (2021) 16749–16757, http://dx.doi.org/10.1109/JIOT.2021.3051158.

[2] A.A. Hussain, O. Bouachir, F. Al-Turjman, M. Aloqaily, Notice of retraction: AI techniques for COVID-19, IEEE Access 8 (2020) 128776–128795.

[3] P. Kumar, P. Singh, M. Diwakar, D. Garg, Healthcare industry assessment: analyzing risks, security, and reliability, 2024.

[4] A. Fuller, Z. Fan, C. Day, C. Barlow, Digital twin: Enabling technologies, challenges and open research, IEEE Access 8 (2020) 108952–108971.

[5] M. Grieves, J. Vickers, Digital twin: Mitigating unpredictable, undesirable emergent behavior in complex systems, in: Transdisciplinary Perspectives on Complex Systems, Springer, 2017, pp. 85–113.

[6] E. Glaessgen, D. Stargel, The digital twin paradigm for future NASA and US air force vehicles, in: 53rd AIAA/ASME/ASCE/AHS/ASC Structures, Structural Dynamics and Materials Conference 20th AIAA/ASME/AHS Adaptive Structures Conference 14th AIAA, 2012, p. 1818.

[7] W. Kritzinger, M. Karner, G. Traar, J. Henjes, W. Sihn, Digital twin in manufacturing: A categorical literature review and classification, Ifac-Pap. 51 (11) (2018) 1016–1022.

[8] H.Y. Jeon, C. Justin, D.N. Mavris, Improving prediction capability of quadcopter through digital twin, in: AIAA Scitech 2019 Forum, 2019, p. 1365.

[9] M.R. Kabir, S. Ray, Virtual prototyping for modern internet-of-things applications: A survey, IEEE Access 11 (2023) 31384–31398.

[10] C. Groth, S. Porziani, M. Biancolini, E. Costa, S. Celi, K. Capellini, M. Rochette, V. Morgenthaler, The medical digital twin assisted by reduced order models and mesh morphing, in: International CAE Conference, vol. 10, 2018.

[11] Y. Chu, S. Li, J. Tang, H. Wu, The potential of the medical digital twin in diabetes management: a review, Front. Med. 10 (2023) 1178912.

[12] G. Coorey, G.A. Figtree, D.F. Fletcher, J. Redfern, The health digital twin: advancing precision cardiovascular medicine, Nat. Rev. Cardiol. 18 (12) (2021) 803–804.

[13] G. Coorey, G.A. Figtree, D.F. Fletcher, V.J. Snelson, S.T. Vernon, D. Winlaw, S.M. Grieve, A. McEwan, J.Y.H. Yang, P. Qian, et al., The health digital twin to tackle cardiovascular disease—a review of an emerging interdisciplinary field, NPJ Digit. Med. 5 (1) (2022) 126.

[14] T. Vats, S.K. Singh, S. Kumar, B.B. Gupta, S.S. Gill, V. Arya, W. Alhalabi, Explainable context-aware IoT framework using human digital twin for healthcare, Multimedia Tools Appl. (2023) 1–25.

[15] S.D. Okegbile, J. Cai, D. Niyato, C. Yi, Human digital twin for personalized healthcare: Vision, architecture and future directions, IEEE Netw. 37 (2) (2022) 262–269.

[16] B.R. Barricelli, E. Casiraghi, J. Gliozzo, A. Petrini, S. Valtolina, Human digital twin for fitness management, Ieee Access 8 (2020) 26637–26664.

[17] I. Graessler, A. Pöhler, Integration of a digital twin as human representation in a scheduling procedure of a cyber-physical production system, in: 2017 IEEE International Conference on Industrial Engineering and Engineering Management, IEEM, IEEE, 2017, pp. 289–293.

[18] A. Löcklin, T. Jung, N. Jazdi, T. Ruppert, M. Weyrich, Architecture of a human-digital twin as common interface for operator 4.0 applications, Procedia CIRP 104 (2021) 458–463.

[19] B. Wang, H. Zhou, G. Yang, X. Li, H. Yang, Human digital twin (HDT) driven human-cyber-physical systems: Key technologies and applications, Chin. J. Mech. Eng. 35 (1) (2022) 11.

[20] B. Wang, H. Zhou, X. Li, G. Yang, P. Zheng, C. Song, Y. Yuan, T. Wuest, H. Yang, L. Wang, Human digital twin in the context of industry 5.0, Robot. Comput.-Integr. Manuf. 85 (2024) 102626.

[21] Healthcare digital twins market size | industry report, 2030, 2024, (Accessed 1 January 2025). URL https://www.grandviewresearch.com/industry-analysis/healthcare-digital-twins-market-report.

[22] S. Vishnu, S.J. Ramson, R. Jegan, Internet of medical things (IoMT)-an overview, in: 2020 5th International Conference on Devices, Circuits and Systems, ICDCS, IEEE, 2020, pp. 101–104.

[23] L. Catarinucci, D. de Donno, L. Mainetti, L. Palano, L. Patrono, M.L. Stefanizzi, L. Tarricone, An IoT-aware architecture for smart healthcare systems, IEEE Internet Things J. 2 (6) (2015) 515–526, http://dx.doi.org/10.1109/JIOT.2015.2417684.

[24] R.K. Kodali, G. Swamy, B. Lakshmi, An implementation of IoT for healthcare, in: 2015 IEEE Recent Advances in Intelligent Computational Systems, RAICS, 2015, pp. 411–416, http://dx.doi.org/10.1109/RAICS.2015.7488451.

[25] B. Farahani, F. Firouzi, K. Chakrabarty, Healthcare iot, Intell. Internet Things: From Device To Fog Cloud (2020) 515–545.

[26] M. Elhoseny, G. Ramírez-González, O.M. Abu-Elnasr, S.A. Shawkat, N. Arunkumar, A. Farouk, Secure medical data transmission model for IoT-based healthcare systems, Ieee Access 6 (2018) 20596–20608.

[27] A. Ukil, S. Bandyoapdhyay, C. Puri, A. Pal, IoT healthcare analytics: The importance of anomaly detection, in: 2016 IEEE 30th International Conference on Advanced Information Networking and Applications, AINA, IEEE, 2016, pp. 994–997.

[28] A. Zahid, J.K. Poulsen, R. Sharma, S.C. Wingreen, A systematic review of emerging information technologies for sustainable data-centric health-care, Int. J. Med. Informatics 149 (2021) 104420.

[29] A. Khang, AI and IoT Technology and Applications for Smart Healthcare Systems, CRC Press, 2024.

[30] A.K. Tyagi, Richa, Digital twin technology: Opportunities and challenges for smart era's applications, in: Proceedings of the 2023 Fifteenth International Conference on Contemporary Computing, 2023, pp. 328–336.
[31] O. Khan, M. Parvez, P. Kumari, S. Parvez, S. Ahmad, The future of pharmacy: how AI is revolutionizing the industry, Intell. Pharm. 1 (1) (2023) 32–40.
[32] A. Haleem, M. Javaid, R.P. Singh, R. Suman, Exploring the revolution in healthcare systems through the applications of digital twin technology, Biomed. Technol. 4 (2023) 28–38.
[33] E. Katsoulakis, Q. Wang, H. Wu, L. Shahriyari, R. Fletcher, J. Liu, L. Achenie, H. Liu, P. Jackson, Y. Xiao, et al., Digital twins for health: a scoping review, Npj Digit. Med. 7 (1) (2024) 77.
[34] T. Sun, X. He, Z. Li, Digital twin in healthcare: Recent updates and challenges, Digit. Heal. 9 (2023) 20552076221149651.
[35] S. Elkefi, O. Asan, Digital twins for managing health care systems: rapid literature review, J. Med. Internet Res. 24 (8) (2022) e37641.
[36] T. Erol, A.F. Mendi, D. Doğan, The digital twin revolution in healthcare, in: 2020 4th International Symposium on Multidisciplinary Studies and Innovative Technologies, ISMSIT, IEEE, 2020, pp. 1–7.
[37] J. Chen, C. Yi, S.D. Okegbile, J. Cai, X. Shen, Networking architecture and key supporting technologies for human digital twin in personalized healthcare: A comprehensive survey, IEEE Commun. Surv. & Tutorials 26 (1) (2023) 706–746.
[38] Ø. Bjelland, B. Rasheed, H.G. Schaathun, M.D. Pedersen, M. Steinert, A.I. Hellevik, R.T. Bye, Toward a digital twin for arthroscopic knee surgery: a systematic review, IEEE Access 10 (2022) 45029–45052.
[39] M. Narigina, A. Romanovs, R. Bruzgiene, Digital twin technology in healthcare: A literature review, in: 2024 IEEE 11th Workshop on Advances in Information, Electronic and Electrical Engineering, AIEEE, IEEE, 2024, pp. 1–8.
[40] M.D. Xames, T.G. Topcu, A systematic literature review of digital twin research for healthcare systems: Research trends, gaps, and realization challenges, IEEE Access 12 (2024) 4099–4126.
[41] D. Mourtzis, J. Angelopoulos, N. Panopoulos, D. Kardamakis, A smart IoT platform for oncology patient diagnosis based on ai: Towards the human digital twin, Procedia CIRP 104 (2021) 1686–1691.
[42] I.N. Weerarathna, P. Kumar, P. Verma, D. Raymond, A. Luharia, G. Mishra, Leveraging digital twin technology to combat cardiovascular disease: A comprehensive review, in: 2024 2nd DMIHER International Conference on Artificial Intelligence in Healthcare, Education and Industry, IDICAIEI, IEEE, 2024, pp. 1–6.
[43] R. Martinez-Velazquez, R. Gamez, A. El Saddik, Cardio twin: A digital twin of the human heart running on the edge, in: 2019 IEEE International Symposium on Medical Measurements and Applications (MeMeA), IEEE, 2019, pp. 1–6.
[44] M.E. Susilo, C.-C. Li, K. Gadkar, G. Hernandez, L.-Y. Huw, J.Y. Jin, S. Yin, M.C. Wei, S. Ramanujan, I. Hosseini, Systems-based digital twins to help characterize clinical dose–response and propose predictive biomarkers in a phase I study of bispecific antibody, mosunetuzumab, in NHL, Clin. Transl. Sci. 16 (7) (2023) 1134–1148.
[45] X. Li, E.J. Lee, S. Lilja, J. Loscalzo, S. Schäfer, M. Smelik, M.R. Strobl, O. Sysoev, H. Wang, H. Zhang, et al., A dynamic single cell-based framework for digital twins to prioritize disease genes and drug targets, Genome Med. 14 (1) (2022) 48.
[46] Q. Lu, X. Xie, A.K. Parlikad, J.M. Schooling, Digital twin-enabled anomaly detection for built asset monitoring in operation and maintenance, Autom. Constr. 118 (2020) 103277.
[47] J.K.W. Wong, J. Ge, S.X. He, Digitisation in facilities management: A literature review and future research directions, Autom. Constr. 92 (2018) 312–326.
[48] A. Karakra, F. Fontanili, E. Lamine, J. Lamothe, HospiT'Win: a predictive simulation-based digital twin for patients pathways in hospital, in: 2019 IEEE EMBS International Conference on Biomedical & Health Informatics, BHI, IEEE, 2019, pp. 1–4.
[49] A. Karakra, F. Fontanili, E. Lamine, J. Lamothe, A. Taweel, Pervasive computing integrated discrete event simulation for a hospital digital twin, in: 2018 IEEE/ACS 15th International Conference on Computer Systems and Applications, AICCSA, IEEE, 2018, pp. 1–6.
[50] Y. Han, Y. Li, Y. Li, B. Yang, L. Cao, Digital twinning for smart hospital operations: Framework and proof of concept, Technol. Soc. 74 (2023) 102317.
[51] R. Aluvalu, S. Mudrakola, A. Kaladevi, M. Sandhya, C.R. Bhat, et al., The novel emergency hospital services for patients using digital twins, Microprocess. Microsyst. 98 (2023) 104794.
[52] A. Gorelova, S. Meliá, D. Gadzhimusieva, A discrete event simulation of patient flow in an assisted reproduction clinic with the integration of a smart health monitoring system, IEEE Access (2024).
[53] A.K. Jameil, H. Al-Raweshidy, Ai-enabled healthcare and enhanced computational resource management with digital twins into task offloading strategies, IEEE Access (2024).
[54] C. Kleinbeck, H. Zhang, B.D. Killeen, D. Roth, M. Unberath, Neural digital twins: reconstructing complex medical environments for spatial planning in virtual reality, Int. J. Comput. Assist. Radiol. Surg. (2024) 1–12.
[55] Y. Tai, L. Zhang, Q. Li, C. Zhu, V. Chang, J.J. Rodrigues, M. Guizani, Digital-twin-enabled IoMT system for surgical simulation using rAC-GAN, IEEE Internet Things J. 9 (21) (2022) 20918–20931.
[56] H. Laaki, Y. Miche, K. Tammi, Prototyping a digital twin for real time remote control over mobile networks: Application of remote surgery, Ieee Access 7 (2019) 20325–20336.
[57] D.R. Obaid, D. Smith, M. Gilbert, S. Ashraf, A. Chase, Computer simulated "Virtual TAVR" to guide TAVR in the presence of a previous starr-edwards mitral prosthesis, J. Cardiovasc. Comput. Tomogr. 13 (1) (2019) 38–40.
[58] H. Shu, R. Liang, Z. Li, A. Goodridge, X. Zhang, H. Ding, N. Nagururu, M. Sahu, F.X. Creighton, R.H. Taylor, et al., Twin-S: a digital twin for skull base surgery, Int. J. Comput. Assist. Radiol. Surg. 18 (6) (2023) 1077–1084.
[59] H. Sartaj, S. Ali, J. Marie Gjøby, Uncertainty-aware environment simulation of medical devices digital twins, Softw. Syst. Model. (2024) 1–27.
[60] I. Ahmed, M. Ahmad, G. Jeon, Integrating digital twins and deep learning for medical image analysis in the era of COVID-19, Virtual Real. Intell. Hardw. 4 (4) (2022) 292–305.
[61] M.M. Bersani, C. Braghin, A. Gargantini, R. Mirandola, E. Riccobene, P. Scandurra, Engineering of trust analysis-driven digital twins for a medical device, in: European Conference on Software Architecture, Springer, 2022, pp. 467–482.
[62] P.G. Kalozoumis, M. Marino, E.L. Carniel, D.K. Iakovidis, Towards the development of a digital twin for endoscopic medical device testing, in: Digital Twins for Digital Transformation: Innovation in Industry, Springer, 2022, pp. 113–145.
[63] L. Bethencourt, W. Dabachine, V. Dejouy, Z. Lalmiche, K. Neuberger, I. Ibnouhsein, S. Chereau, C. Mathelin, N. Savy, P. Saint Pierre, et al., Guiding measurement protocols of connected medical devices using digital twins: A statistical methodology applied to detecting and monitoring lymphedema, IEEE Access 9 (2021) 39444–39465.
[64] S.M. Iqbal, I. Mahgoub, E. Du, M.A. Leavitt, W. Asghar, Advances in healthcare wearable devices, NPJ Flex. Electron. 5 (1) (2021) 9.
[65] W. Khan, E. Muntimadugu, M. Jaffe, A.J. Domb, Implantable medical devices, Focal Control. Drug Deliv. (2014) 33–59.
[66] J. Chen, W. Wang, B. Fang, Y. Liu, K. Yu, V.C. Leung, X. Hu, Digital twin empowered wireless healthcare monitoring for smart home, IEEE J. Sel. Areas Commun. (2023).
[67] Z. Zhu, R.Y. Zhong, A digital twin enabled wearable device for customized healthcare, Digit. Twin 2 (2025) 17.
[68] F. Yu, C. Yu, Z. Tian, X. Liu, J. Cao, L. Liu, C. Du, M. Jiang, Intelligent wearable system with motion and emotion recognition based on digital twin technology, IEEE Internet Things J. (2024).
[69] H. Yang, Z. Jiang, Decision support for personalized therapy in implantable medical devices: A digital twin approach, Expert Syst. Appl. 243 (2024) 122883.
[70] F. Ghaempanah, B. Moasses Ghafari, D. Hesami, R. Hossein Zadeh, R. Noroozpoor, A. Moodi Ghalibaf, P. Hasanabadi, Metaverse and its impact on medical education and health care system: A narrative review, Heal. Sci. Rep. 7 (9) (2024) e70100.
[71] H. Sartaj, S. Ali, J.M. Gjøby, MeDeT: Medical device digital twins creation with few-shot meta-learning, ACM Trans. Softw. Eng. Methodol. (2024).
[72] A. Vallée, Envisioning the future of personalized medicine: Role and realities of digital twins, J. Med. Internet Res. 26 (2024) e50204.
[73] Q. Zhang, Y. Xu, S. Kang, J. Chen, Z. Yao, H. Wang, Q. Wu, Q. Zhao, Q. Zhang, R.-h. Xu, et al., A novel computational framework for integrating multidimensional data to enhance accuracy in predicting the prognosis of colorectal cancer, MedComm– Futur. Med. 1 (2) (2022) e27.
[74] C. Wu, A.M. Jarrett, Z. Zhou, N. Elshafeey, B.E. Adrada, R.P. Candelaria, R.M. Mohamed, M. Boge, L. Huo, J.B. White, et al., MRI-based digital models forecast patient-specific treatment responses to neoadjuvant chemotherapy in triple-negative breast cancer, Cancer Res. 82 (18) (2022) 3394–3404.
[75] T.C. Silva, M. Eppink, M. Ottens, Digital twin in high throughput chromatographic process development for monoclonal antibodies, J. Chromatogr. A 1717 (2024) 464672.
[76] S. Namasudra, IoT and ML for Information Management: A Smart Healthcare Perspective, Springer, 2024.
[77] J.H. Creemers, J. Textor, Leveraging mathematical models to improve the statistical robustness of cancer immunotherapy trials, Curr. Opin. Syst. Biology 40 (2025) 100540.
[78] K. Sel, A. Hawkins-Daarud, A. Chaudhuri, D. Osman, A. Bahai, D. Paydarfar, K. Willcox, C. Chung, R. Jafari, Survey and perspective on verification, validation, and uncertainty quantification of digital twins for precision medicine, Npj Digit. Med. 8 (1) (2025) 40.
[79] Y. Wang, T. Fu, Y. Xu, Z. Ma, H. Xu, B. Du, Y. Lu, H. Gao, J. Wu, J. Chen, TWIN-GPT: digital twins for clinical trials via large language model, ACM Trans. Multimed. Comput. Commun. Appl. (2024).

[80] C. Herwig, R. Pörtner, J. Möller, Digital Twins: Tools and Concepts for Smart Biomanufacturing, Springer, 2021.
[81] N. Goel, R.K. Yadav, Internet of Things Enabled Machine Learning for Biomedical Applications, CRC Press, 2024.
[82] A.M.V.V. Sai, C. Wang, Z. Cai, Y. Li, Navigating the digital twin network landscape: A survey on architecture, applications, privacy and security, High- Confid. Comput. 4 (4) (2024) 100269.
[83] A. Ghubaish, T. Salman, M. Zolanvari, D. Unal, A. Al-Ali, R. Jain, Recent advances in the internet-of-medical-things (IoMT) systems security, IEEE Internet Things J. 8 (11) (2020) 8707–8718.
[84] G. Zachos, G. Mantas, I. Essop, K. Porfyrakis, J.M.C. Bastos, J. Rodriguez, An IoT/IoMT security testbed for anomaly-based intrusion detection systems, in: 2023 IFIP Networking Conference (IFIP Networking), IEEE, 2023, pp. 1–6.
[85] M.R. Kabir, S. Ray, DT-IoMT: A digital twin reference model for secure internet of medical things, in: 2024 IEEE Computer Society Annual Symposium on VLSI, ISVLSI, IEEE, 2024, pp. 433–438.
[86] J. Zhang, L. Li, G. Lin, D. Fang, Y. Tai, J. Huang, Cyber resilience in healthcare digital twin on lung cancer, IEEE Access 8 (2020) 201900–201913.
[87] J.I. Jimenez, H. Jahankhani, S. Kendzierskyj, Health care in the cyberspace: Medical cyber-physical system and digital twin challenges, Digit. Twin Technol. Smart Cities (2020) 79–92.
[88] V. Sharma, A. Kumar, K. Sharma, Digital twin: securing IoT networks using integrated ECC with blockchain for healthcare ecosystem, Knowl. Inf. Syst. (2024) 1–32.
[89] R. Lutze, Digital twins in ehealth–: Prospects and challenges focussing on information management, in: 2019 IEEE International Conference on Engineering, Technology and Innovation (ICE/ITMC), IEEE, 2019, pp. 1–9.
[90] S.S. Akash, M.S. Ferdous, A blockchain based system for healthcare digital twin, IEEE Access 10 (2022) 50523–50547.
[91] Y. Zheng, R. Lu, Y. Guan, S. Zhang, J. Shao, Towards private similarity query based healthcare monitoring over digital twin cloud platform, in: 2021 IEEE/ACM 29th International Symposium on Quality of Service, IWQOS, IEEE, 2021, pp. 1–10.
[92] V. Stephanie, I. Khalil, M. Atiquzzaman, Digital twin enabled asynchronous SplitFed learning in E-healthcare systems, IEEE J. Sel. Areas Commun. 41 (11) (2023) 3650–3661.
[93] Y. Tang, K. Wang, D. Niyato, J. Li, O.A. Dobre, T.Q. Duong, Secure data sharing and prediction with digital twin and blockchain in healthcare, IEEE Commun. Mag. (2025).
[94] A. De Benedictis, N. Mazzocca, A. Somma, C. Strigaro, Digital twins in healthcare: an architectural proposal and its application in a social distancing case study, IEEE J. Biomed. Heal. Informatics 27 (10) (2022) 5143–5154.
[95] M. Iqbal, S. Suhail, R. Matulevičius, R. Hussain, Towards healthcare digital twin architecture, in: International Conference on Business Informatics Research, Springer, 2023, pp. 45–60.
[96] G. Pellegrino, M. Gervasi, M. Angelelli, A conceptual framework for digital twin in healthcare: Evidence from a systematic meta-review, Inf. Syst. (2024).
[97] A. Alqahtani, S. Alsubai, M. Bhatia, Digital-twin-assisted healthcare framework for adult, IEEE Internet Things J. 11 (8) (2023) 14963–14970.
[98] F. Laamarti, H.F. Badawi, Y. Ding, F. Arafsha, B. Hafidh, A. El Saddik, An ISO/IEEE 11073 standardized digital twin framework for health and well-being in smart cities, Ieee Access 8 (2020) 105950–105961.
[99] C. Suraci, V. De Angelis, G. Lofaro, M.L. Giudice, G. Marrara, F. Rinaldi, A. Russo, M.T. Bevacqua, G. Lax, N. Mammone, et al., The next generation of ehealth: A multidisciplinary survey, IEEE Access 10 (2022) 134623–134646.
[100] Y. Liu, L. Zhang, Y. Yang, L. Zhou, L. Ren, F. Wang, R. Liu, Z. Pang, M.J. Deen, A novel cloud-based framework for the elderly healthcare services using digital twin, IEEE Access 7 (2019) 49088–49101.
[101] H. Garg, B. Sharma, S. Shekhar, R. Agarwal, Spoofing detection system for e-health digital twin using EfficientNet convolution neural network, Multimedia Tools Appl. 81 (19) (2022) 26873–26888.
[102] R. Lutze, Digital twin based software design in ehealth-a new development approach for health/medical software products, in: 2020 IEEE International Conference on Engineering, Technology and Innovation (ICE/ITMC), IEEE, 2020, pp. 1–9.
[103] S.A. Mila, B.B.Y. Ravi, M.R. Kabir, S. Ray, MASC: Wearable design for infectious disease detection through machine learning, IEEE Access (2025).
[104] J. Akram, M. Aamir, R. Raut, A. Anaissi, R.H. Jhaveri, A. Akram, Ai-generated content-as-a-service in iomt-based smart homes: Personalizing patient care with human digital twins, IEEE Trans. Consum. Electron. (2024).
[105] M.U. Shoukat, L. Yan, J. Zhang, Y. Cheng, M.U. Raza, A. Niaz, Smart home for enhanced healthcare: exploring human machine interface oriented digital twin model, Multimedia Tools Appl. 83 (11) (2024) 31297–31315.
[106] L.F. Rivera, M. Jiménez, P. Angara, N.M. Villegas, G. Tamura, H.A. Müller, Towards continuous monitoring in personalized healthcare through digital twins, in: Proceedings of the 29th Annual International Conference on Computer Science and Software Engineering, 2019, pp. 329–335.
[107] R. Brahmi, N. Boujnah, R. Ejbali, Elaboration of innovative digital twin models for healthcare monitoring with 6g functionalities, IEEE Access 12 (2024).
[108] F. Tao, F. Sui, A. Liu, Q. Qi, M. Zhang, B. Song, Z. Guo, S.C.-Y. Lu, A.Y. Nee, Digital twin-driven product design framework, Int. J. Prod. Res. 57 (12) (2019) 3935–3953.
[109] M.A. Ahmad, V. Chickarmane, F.S.A. Pour, N. Shariari, T.D. Roy, Validation of a hospital digital twin with machine learning, in: 2023 IEEE 11th International Conference on Healthcare Informatics, ICHI, IEEE, 2023, pp. 465–469.
[110] S. Alsubai, M. Sha, A. Alqahtani, M. Bhatia, Hybrid IoT-edge-cloud computing-based athlete healthcare framework: Digital twin initiative, Mob. Networks Appl. (2023) 1–20.
[111] Z. Lv, J. Guo, H. Lv, Deep learning-empowered clinical big data analytics in healthcare digital twins, IEEE/ ACM Trans. Comput. Biology Bioinform. (2023).
[112] I. Hussain, M.A. Hossain, S.-J. Park, A healthcare digital twin for diagnosis of stroke, in: 2021 IEEE International Conference on Biomedical Engineering, Computer and Information Technology for Health, BECITHCON, IEEE, 2021, pp. 18–21.
[113] J. Chen, C. Yi, H. Du, D. Niyato, J. Kang, J. Cai, X. Shen, A revolution of personalized healthcare: Enabling human digital twin with mobile AIGC, IEEE Netw. (2024).
[114] S. Gebreab, A. Musamih, K. Salah, R. Jayaraman, D. Boscovic, Accelerating digital twin development with generative AI: A framework for 3D modeling and data integration, IEEE Access (2024).
[115] S. Khan, A. Alzaabi, Z. Iqbal, T. Ratnarajah, T. Arslan, A novel digital twin (DT) model based on WiFi CSI, signal processing and machine learning for patient respiration monitoring and decision-support, IEEE Access 11 (2023) 103554–103568.
[116] H. Sartaj, S. Ali, T. Yue, K. Moberg, Model-based digital twins of medicine dispensers for healthcare IoT applications, Softw.: Pr. Exp. 54 (6) (2024) 1172–1192.
[117] P. Amudhavalli, S. Urmela, G. Vishnupriya, N. Gopinath, R. Anandh, L.R. Buckingham, Investigating the revolution of healthcare application with intense comparisons and case study, Impact Algorithmic Technol. Heal. (2025) 421–445.
[118] C. Wang, Z. Cai, Y. Li, Sustainable blockchain-based digital twin management architecture for IoT devices, IEEE Internet Things J. 10 (8) (2022) 6535–6548.
[119] S. Suhail, R. Hussain, R. Jurdak, C.S. Hong, Trustworthy digital twins in the industrial internet of things with blockchain, IEEE Internet Comput. 26 (3) (2021) 58–67.
[120] S. Zhu, W. Li, H. Li, L. Tian, G. Luo, Z. Cai, Coin hopping attack in blockchain-based IoT, IEEE Internet Things J. 6 (3) (2018) 4614–4626.
[121] G.B. Raja, M.P. Devi, T. Sathya, A.S. Balakrishnan, Collaboration of blockchain-based digital twins in the healthcare industry: From idea to implementation, Blockchain- Based Digit. Twins: Res. Trends Challenges (2025) 223.
[122] A. Manocha, Y. Afaq, M. Bhatia, Digital twin-assisted blockchain-inspired irregular event analysis for eldercare, Knowl.-Based Syst. (2023).
[123] D. Kumari, P. Kumar, S. Prajapat, A blockchain assisted public auditing scheme for cloud-based digital twin healthcare services, Clust. Comput. (2024).
[124] B. Sheng, Z. Wang, Y. Qiao, S.Q. Xie, J. Tao, C. Duan, Detecting latent topics and trends of digital twins in healthcare: A structural topic model-based systematic review, Digit. Heal. 9 (2023) 20552076231203672.
[125] J. Chen, Y. Shi, C. Yi, H. Du, J. Kang, D. Niyato, Generative AI-driven human digital twin in IoT-healthcare: A comprehensive survey, IEEE Internet Things J. (2024).
[126] K.P. Venkatesh, M.M. Raza, J.C. Kvedar, Health digital twins as tools for precision medicine: Considerations for computation, implementation, and regulation, NPJ Digit. Med. 5 (1) (2022) 150.
[127] R.H. Dolin, L. Alschuler, C. Beebe, P.V. Biron, S.L. Boyer, D. Essin, E. Kimber, T. Lincoln, J.E. Mattison, The HL7 clinical document architecture, J. Am. Med. Informatics Assoc. 8 (6) (2001) 552–569.
[128] R. Makadia, P.B. Ryan, Transforming the premier perspective® hospital database into the observational medical outcomes partnership (omop) common data model, Egems 2 (1) (2014).
[129] D. Drummond, A. Gonsard, Definitions and characteristics of patient digital twins being developed for clinical use: Scoping review, J. Med. Internet Res. 26 (2024) e58504.
[130] M. De Domenico, L. Allegri, G. Caldarelli, V. d'Andrea, B. Di Camillo, L.M. Rocha, J. Rozum, R. Sbarbati, F. Zambelli, Challenges and opportunities for digital twins in precision medicine from a complex systems perspective, Npj Digit. Med. 8 (1) (2025) 37.