

Disclaimer : This is not the final version of the article. Changes may occur when the manuscript is published in its final format.

Biomaterials Connect

ISSN: 3105-0387

2026, Vol. 3, Cite as: doi:[10.x/journal.x.x.x](https://doi.org/10.x/journal.x.x.x)



Review Article

Digital Twin Applications in Biomaterials Science: Toward Predictive Design and Personalized Healthcare

Amudhavalli Victor*, Rakshita Hari, Habeeba Rihana

¹Department of Pharmaceutical Chemistry, School of Pharmacy, Sathyabama Institute of Science and Technology, Jeppiar Nagar, Chennai- 600 119, Tamilnadu, India.

Abstract:

The term Digital Twin (DT) is widely used in the industry to create digital replicas of real-world systems or objects. The active, two-way connection between the digital entity and physical counterpart permits for real time updates. DT is the strategic integration of digital technology into all areas of a business or organization. It isn't just about upgrading software; it's a fundamental change in how a business operates and delivers value to its customers.

Digital Twin technology is emerging as a transformative paradigm in biomaterials science, bridging the gap between computational modeling and real-world clinical application. This paper explores the integration of DTs to move beyond traditional "one size fits-all" approaches toward predictive design and personalized healthcare.

It is able to forecast disturbances associated with the operation of the physical object. With the potential to transform patient diagnosis and treatment, the apparent uses of DTs in healthcare and medicine are very alluring opportunities. However, it is challenging to accomplish the intended purposes due to issues like biological heterogeneity, ethical considerations, and technical barriers. Some challenges might be lessened by developments in the meta verse, embodied AI agents, and multi-modal deep learning techniques. Here, we go over the fundamental ideas behind DTs, the prerequisites for applying them in medicine, and their present and future applications in healthcare. In order to promote research in this area, we also offer our viewpoint on five characteristics of a healthcare DT system. This review highlights how advancing DT maturity will enable a shift from reactive medical interventions to proactive, data-driven material engineering, ultimately enhancing patient outcomes and accelerating the translation of lab scale innovations to the clinic.

Keywords

digital twins; personalized medicine; precise diagnosis; clinical optimization; biological heterogeneity; physical modeling

Introduction

Expectations for healthcare services are rising as a result of people's increased attention on healthy living and general well-being due to rapid economic and societal development and rising living standards. To address the need for earlier, quicker, more precise, and individualized disease diagnosis and treatment, medical professionals are actively investigating novel technologies and approaches. Digital twin technology is a cutting-edge strategy with revolutionary possibilities in the medical field. [1-3].

The term “digital twin” describes the process of creating virtual copies that are mapped to actual systems or entities through methods including data integration, sensor updates, and physical modeling. Based on their operational data and current status, the models are updated on a regular basis. Digital twins, as opposed to static simulations, represent the physical counterpart's current operational states. Digital twins facilitate proactive interventions, system optimization, and well-informed decision-making by modelling and forecasting the state, performance, and possible consequences of a physical system in a virtual setting. They can also increase service life. [4-6] Digital twin technology has become widely used as a result of the ongoing advancements in information technology, progressively expanding into a number of industries, including manufacturing, urban planning, and healthcare [Figure 1].

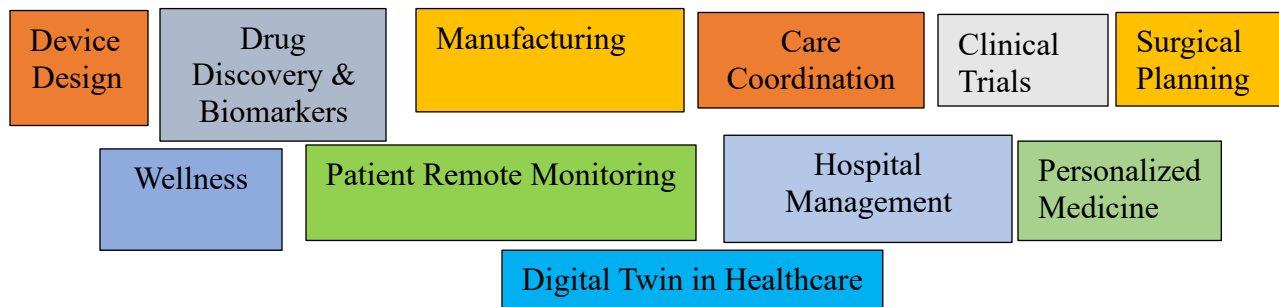


Figure.1 Prevalent Healthcare applications of digital twin

Digital twin technology provides a deeper understanding of body dynamics in the healthcare industry. Healthcare professionals can produce accurate virtual representations of organs, system, and even whole people by using digital twins. These models can be used to predict how a patient will react to treatment, stimulate the course of a disease, and assess the results of medical interventions before they are administered to a real patient. As a result, care routes are optimized, individualized treatment plans are created, and better decisions are made.

By enabling proactive health interventions and ongoing monitoring based on real time data from the virtual model, digital twins also help to improve patient management.

In the medical field the physical object can be used to the patient under study in their actual life, taking into account all environmental, lifestyle, physiological, and molecular data over time. As a result, the virtual entity is a digital duplicate of the patient or perhaps a virtual environmental that contains numerous digital patients.

Because these digital copies share traits with the patient, data gathered from the patient can be used to forecast and stimulate biological processes or disease states. To enable constant updating of the parameters that represent the physical entity's state, the physical and virtual entities interact through a physical-to-virtual connection.

A medical DT is essentially a virtual environment in which clinical and medical judgements can be tested prior to being implemented in a real patient.

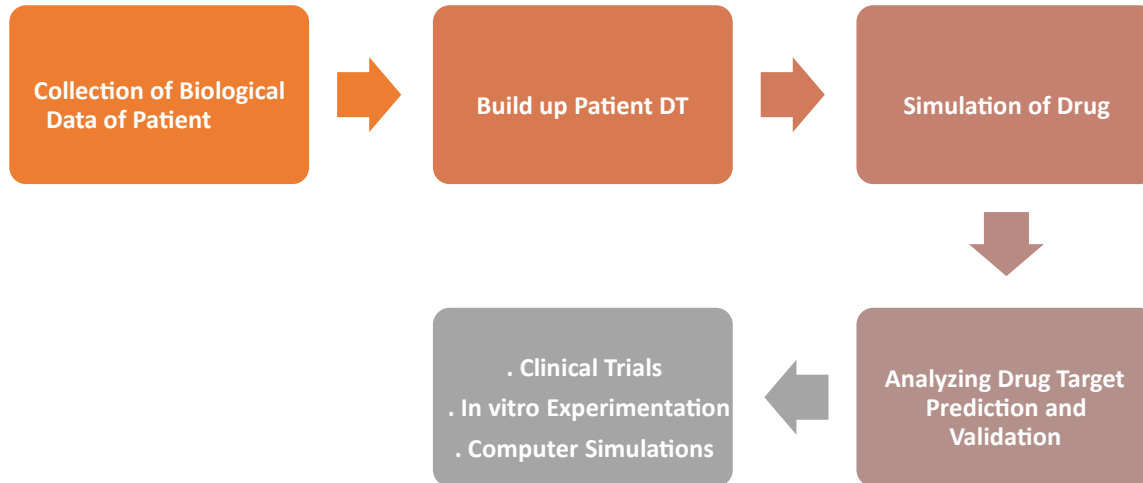


Figure. 2 Digital twin in Drug discovery through clinical trials

This makes personalized therapy a fascinating possibility by allowing the dynamic modelling of biochemical pathways, cells, tissues, diseases, and eventually the entire human body in real time.

By treating the human population as an individual, DTs present special opportunity to give more individualized and effective treatments and preventions. It will be necessary to integrate a variety of data, including clinical data, real time physiological changes, and an individual's omics, in order to develop a DT in medicine [Figure 2]. For instance, DTs may make it possible to provide a customized, on demand risk profile for chronic illnesses, make lifestyle recommendations to reduce these risks, issue alerts for preventative diagnostic tests, and provide warnings about imminent health hazards. It will also be feasible to predict the effectiveness and likely side effects of a certain medication and assess how each patient will react to it. Thus, DTs, are a faithful application of individualized medication. [7-15].

Digital twin technology uses machine learning algorithms and patient data analysis to enable predictive analytics and preventive interventions. Digital twins are able to identify high risk individuals, forecast the course of diseases, and suggest preventative actions.

This Proactive approach improves patient safety, long term outcomes, and resource allocation in healthcare systems [16]. Therefore, digital twin technology may have the potential to completely transform healthcare systems through the use of real time data integration, advanced analytics, and virtual simulations.

Predictive analytics, training simulation, clinical operations, and patient care can all be enhanced by it. The primary focus of this analysis was on how digital twins in healthcare systems can improve patient outcomes, operational efficiency, and overall healthcare quality.

In recent years, engineer's academics have become more interested in the idea of a digital twin. The differences between digital twins and other related ideas are starting to disappear as the fields commercial and academic study progress. Initially, the scope of the digital twin encompassed both physical and virtual products, along with the connections between them [17].

Rapid developments in big data analysis, sensor technology, communication technology, the internet of Things (IoT), [Internet of Things (IoT) is the network of physical objects—"things"— that are embedded with sensors, software, and other technologies for the purpose of connecting and exchanging data with other devices and systems over the internet.] and simulation technology have led to an evolution of this idea [18]. Significant research on digital twins has been spurred by this growth.

Applications in fields like health and well-being were introduced when the term "digital twin" was later reinterpreted as a digital counterpart of a living or nonliving physical entity [19]. A digital twin is a dynamic notion that represents a virtual representation of human organs, tissues, cells, or microenvironments that continuously adjusts to changes in real-time data and forecasts related future events [20]. But thanks to new technology, a digital twin is more than just a digital model connected to its real-world counterpart. Through a closed-loop interaction between the digital twin and its surroundings, it becomes a sentient, intelligent, and evolving model that can continuously forecast future states, including defects, damages, and failures, and optimize processes.

In general, the technologies required for digital twins fall into two categories: one incorporates data and knowledge from several scales into a mechanical model, and the other uses a data-driven statistical model [21,22]. The numerical model computes structural performance, while the analytical model aids structural analysis. Real-time structural insights are extracted from sensor data by an artificial intelligence (AI) model that has been trained using numerical data and samples. AI or Artificial Intelligence refers to the simulation of human intelligence by machines, especially computer systems. It involves the creation of algorithms that allow computers to perform tasks that typically require human cognition, such as learning, reasoning, and problem-solving.

Giant companies have adopted digital twins to boost production and identify issues since they are drastically altering several industries. The healthcare industry is also embracing this revolutionary technology. In this regard, patients can be treated by digital twins as virtualized, stand-alone resources that can be used in a variety of healthcare situations [23, 24]. This possibility has a great deal of promise for enhancing hospital and individual patient care and diagnosis.

A digital twin as used in healthcare, is a computerized model of a real-world item or process, such as a patient, their body, or a hospital setting. The development of core technologies like the Internet of Things and artificial intelligence (AI), along with the availability of an increasing range of precise and easily accessible data types (from behavioral and biometric data to emotional, cognitive, and psychological insights), have sparked increased interest and investigation in the study and potential applications of digital twins in the healthcare industry [25]. Digital twin technology has the potential to significantly enhance patient care through the use of real-time data integration, advanced analytics, and tailored insights.

Electronic health records (EHRs), wearable technology, medical devices, and genetic data are just a few of the sources of patient data that these tools can help healthcare providers collect and analyze [26]. Digital twins provide a comprehensive picture of the patient by combining and evaluating this data, enabling medical practitioners to create individualized treatment regimens [17,20,27]. Improved treatment outcomes and patient satisfaction are the results of this strategy, which takes into account the unique characteristics of each patient, medical history, genetic factors, and real time physiological data to customize therapies and drugs to the patient's needs [28-30].

Digital twins could assist medical personnel in making accurate and quick diagnosis [31]. Digital twins can help with differential diagnosis and the identification of patterns that conventional diagnostic methods alone might miss by simulating different diagnostic scenarios through the analysis of patient data and symptoms [26,32]. This leads to more effective and focused treatments by increasing diagnostic accuracy, decreasing errors, and facilitating earlier intervention. Continuous patient monitoring is made possible by the combination of digital twins with real time data from wearable technology, remote monitoring systems, and Internet of Things devices [33]. Digital twins can identify early indicators of decline or abnormalities by continuously monitoring vital signs, physiological parameters, and other health-related data. This makes it possible for medical professionals to take preemptive measures, avoid difficulties, and enhance treatment regimens. Patient with chronic illness benefit most from real-time monitoring by digital twins, which allows for remote patient management and lessens the need for frequent hospital visits [26,34,35]

Patients can take an active role in their own care with the help of digital twins [36]. Patients can take a more active role in their own health management by having access to their digital twin data, which includes treatment plans, lifestyle changes, and self-management techniques are the results of this enhanced engagement [37]. Additionally, digital twins can help patients and healthcare professionals communicate and work together, which encourages shared decision-making and patient-centered care [38].

To predict the course of a disease and the results of treatment, these technologies can make use of machine learning algorithms and predictive analytics [28]. Digital twins can detect high-risk individuals, forecast possible issues, and suggest preventive steps by examining patient data and historical trends. In the end, this proactive approach to care improves patient safety and long-term results by enabling healthcare providers to prevent adverse events, optimize treatment plans based on anticipated patient responses, and intervene early [39].

Digital twins can facilitate seamless continuity of care by securely sharing patient data across various healthcare settings and providers [35]. By guaranteeing that all participating medical providers have access to the most current and thorough patient data, this promotes coordinated treatment, minimizes test duplication, and lowers medical errors. Digital twins may help healthcare teams collaborate and communicate more effectively, which would improve patient care overall [38, 40].

Digital twin technology for identification of health hazards

Digital twin technology has enormous promise for predictive analytics and preventative healthcare interventions because of its capacity to combine real time data with sophisticated analytics. Digital twins can anticipate the course of diseases, identify possible health hazards, and facilitate preemptive therapies

by utilizing patient data, machine learning algorithms, and predictive modeling [17]. S. Talu discussed the significance of Texture analysis methods for the characterization of biological and medical images [41]. A holistic view of an individual's health can be fostered by integrating and evaluating a wide range of patient data, such as a medical history, lifestyle factors, genetic information, and real-time physiological data [34].

Digital twins can pattern correlations and anomalies in the data by using machine learning algorithms and advanced analytics. This could make it possible for medical practitioners to identify health risks early on, such as the emergence of chronic illnesses, drug side effects, or possible complications.

Effective mitigation or management of these hazards is made possible by early detection, which permits prompt interventions and preventive measures [42]. Using patient information and past patterns, digital twins can model the course of a disease [20]. Digital twins can create predictive models to predict the course of a disease by examining patterns, treatment results, and patient characteristics. Healthcare professionals can use this knowledge to predict possible side effects, modify treatment regimens, and enhance treatments to halt or reduce the progression of disease. By taking into account the unique characteristics of each patient, including their genetic makeup, lifestyle, and response histories, digital twins enable individualized disease modelling, which produces more precise forecasts and specialized treatments [43]. Digital twins can help with risk stratification by classifying patients into different risk groups based on their health information and prediction models [44].

Healthcare professionals can more effectively allocate resources, concentrate on preventive treatments, and put focused initiatives into action by identifying high-risk individuals. Digital twins offer valuable information on which patients are most likely to benefit from particular interventions, lifestyle changes, early screenings or preventive measures. This focused strategy lowers expenses, improves patient outcomes, and better allocates healthcare resources [45]. By instantly warning medical professionals of possible health hazards, digital twins might facilitate proactive treatments and preventive care [46]. Digital twins can discover early warning indicators, detect changes from normal health parameters, and initiate timely interventions by continuously monitoring patient data. Digital twin based preventive care involves lifestyle changes, medication adherence support, screening reminders, and individualized health recommendations [44].

Disease prevalence patterns by using predictive analytics on this data. With the use of digital twins, medical professionals can create population-level preventive measures and targeted interventions, including community-based interventions, immunization campaigns and public health campaigns. Preventing illness start, enhancing health outcomes, and lessening the overall strain on the healthcare system are the goals of the population health strategy [47,48].

DT in clinical bottlenecks and its optimization

There is a lot of promise for improving clinical operations in healthcare systems with digital twin technologies. Digital twins allow healthcare providers to better allocate resources, analyze and optimize workflows, and increase operational efficiency by building virtual versions of physical systems and incorporating real-time data [31]. Digital twins give healthcare providers a comprehensive view of the clinical workflow, allowing them to evaluate and improve procedures. Digital twins give healthcare providers a comprehensive view of the clinical workflow, allowing them to evaluate and improve procedures. Digital twins identify bottlenecks, inefficiencies, and places for development by integrating

data from many sources, such as administrative systems, medical devices and electronic health records [27].

Healthcare practitioners can improve clinical operations overall efficiency by streamlining workflows and eliminating unnecessary tasks thanks to this analysis.

By examining patient data, past trends, and current information, digital twins help healthcare systems optimize resource allocation by providing insights into patient volumes, demand patterns, and resource use [49]. This makes it possible for healthcare professionals to efficiently distribute personnel, tools, and facilities, guaranteeing maximum use and cutting down on wait times. Additionally, digital twins help with capacity planning, which enables healthcare institutions to foresee future needs and make well informed choices about expansions and resource investments. Digital twins may help with operational decision-making through machine learning algorithms and predictive analytics. In order to predict future operating scenarios, they examine data from multiple sources, including patient flow, staffing levels, and equipment usage [16].

In order to maximize resource usage and enhance patient care, this empowers healthcare practitioners to take proactive measures including postponing procedures, optimizing bed allocation, and modifying staffing schedules [16].

Digital twins can quickly detect departures from expected norms and trigger alerts by tracking key performance indicators, patient flow, and operational data [50, 51].

This reduces interruptions and guarantees seamless operations by enabling healthcare professionals to quickly handle problems like equipment failures, staffing shortages, or patient bottlenecks.

In clinical operations, digital twins can increase patient safety and assist with quality improvement projects [52]. Digital twins assist in pinpointing areas for improvement by examining data on bad occurrences, near misses, and process variations. Digital twins can be used by healthcare providers to standardize procedures, apply evidence-based practices, and keep an eye on protocol compliance. This improves patient safety throughout clinical operations, lowers error, and cultivates a culture of continuous improvement.

Digital twins create a shared virtual platform that facilitates communication and collaboration between different departments and healthcare professionals. This technology improves communication procedures, enables collaboration on patient care plans, and allows real-time data sharing [49, 53].

Digital twins facilitate real-time data exchange, teamwork on patient care plans, and efficient communication by offering a shared virtual platform. In the end, this results in more effective clinical operations and better patient outcomes by strengthening interdisciplinary teamwork, decreasing delays, and improving care coordination. Clinical processes can be continuously monitored and improved iteratively with the help of digital twins. Digital twins offer insights into operational performance over time through ongoing data collection and analysis. Based on real-time feedback, healthcare providers can evaluate the effects of process modifications, spot trends, and iteratively improve operations. Healthcare businesses can eliminate inefficiencies, adjust to changing needs, and continuously enhance clinical operations with this iterative improvement method.

Digital twin technology and its sophisticated simulations

In healthcare industry, digital twin technology can present beneficial training and simulation opportunities [54]. Digital twins give healthcare workers a safe and realistic setting in which to practice difficult operations, develop their abilities, and make better decisions by building virtual versions of actual systems that are combined with real time data and sophisticated simulations.

The role of digital twins in healthcare training and simulation is examined in this section [55].

Surgeons and other medical professionals can practice and improve their surgical abilities in a simulated setting by using digital twins [56]. Surgeons can test various techniques, obtain practical experience, and hone their skills without endangering actual patients by using digital twins to simulate various scenarios and replicate surgical procedures. Hand-eye coordination, surgical skills, and decision-making abilities are all improved by this immersive training, which eventually improves patient outcomes and safety.

Digital twins can give medical experts a platform to model different medical treatments [17]. Digital twins can mimic procedures and help medical professionals practice and improve their methods, whether they are invasive or non-invasive. This includes catheter insertions, Ultrasound guided treatments, and more. By providing a realistic virtual environment, digital twins help healthcare professionals gain confidence, enhance their procedural skills, and ensure patient safety during actual surgeries.

Thus, these materials may be particularly useful for training healthcare professionals on emergency response situations [57] by simulating significant occurrences, such as cardiac arrests, trauma scenarios, or mass causality catastrophes, digital twins allow healthcare professionals to practice their response skills, teamwork and decision-making under high-stress situations. In real-world emergency situations, they will be more capable of handling crises, improving teamwork, and optimizing patients' outcomes thanks to this training.

Medical personnel can develop and hone clinical decision-making abilities by using digital twins to help simulate complex clinical circumstances. By merging patient data, medical history, and real time monitoring information, digital twins provide medical professionals with real-world examples to study, diagnose, and develop treatment plans. With the aid of these interactive simulations, which provides a worthwhile educational experience, healthcare professionals can enhance their diagnostic reasoning, consider several treatment choices, and make well-informed judgements in a risk-free environment.

Physical Entity	Mechanism Endpoint
Lung	Runs simulations of blood and Foresee ventilation necessities oxygen flow

Heart	Simulates the structure and physiologic function of the heart	Customization and optimization of cardiac strategies
Heart	Simulates the structure and physiologic function of the heart	Cardiac resynchronization
Heart	simulated TAVR implantations with different aortic prosthesis	Surgical planning
Spine	Predict Vertebral Fracture after treatment side effects	Optimal radiation plan to minimize Stereotactic Body Radiotherapy
Alzheimer's disease	Predicting the individual outcome of neurological diseases ultimately	DT of controls of clinical trial and in clinical interventions
Breast lesions	Image based virtual patients comparing digital mammography better at detecting breast lesions to tomosynthesis	Determine which imaging tool is better
Oropharyngeal cancer	Optimal treatment selection	Determine optimal treatment plan for oropharyngeal cancer
Type 2 Diabetes	Disease reversal in type 2 diabetes	Randomized control trial examining twin precision treatment vs. standard of care
Mental health		Wellness

Pharma Lab		Optimize drug manufacturing
Biomanufacturing	Adjust input conditions Key and Critical Process Parameters	Predictive biomanufacturing
Drug Discovery		Drug Discovery
Hospitals		Earlier response times for critical patients, supply chain organization, plan

Table.1. Classes of Digital Twin in healthcare (Reproduced from [58])

Digital twins offer a common virtual platform for interprofessional cooperation and communication, facilitating effective collaboration amongst healthcare professionals from many disciplines [59]. With digital twins, healthcare professionals may effectively coordinate patient care, communicate and engage in interdisciplinary teamwork.

This enhances patient outcomes, fosters teamwork, and broadens awareness of each professional's role by ensuring comprehensive and coordinated care.

Healthcare professionals may find a platform for continuous professional development through the use of digital twins [Table.1]. Self-paced learning and ongoing training promote lifetime learning, enhance professional growth, and ensure that healthcare professionals are prepared to deliver high quality treatment.

Digital twins can also be a helpful tool for healthcare innovation and research [58, 60]. Researchers can use digital twins for hypothesis testing, experimentation, and data analysis.

These technologies enable researchers to simulate different patient demographics, treatment modalities, and sickness situations to generate insights that could drive evidence-based practices and innovation in healthcare.

Conclusion

In conclusion, digital twin technology holds great promise for enhancing patient care and revolutionizing healthcare systems. BY combining real-time data, advanced analytics, and virtual simulations, digital twins offer personalized treatment plans, predictive analytics, improved clinical operations, and immersive

training opportunities. Medical professionals may monitor patients in real time, make accurate diagnoses, and take preemptive action to avoid unfavorable outcomes thanks to digital twins.

Additionally, it encourages cooperative decision-making between patients and healthcare professionals and empowers people to actively engage in their own care.

Furthermore, digital twins increase operational efficiency, enhance resource allocation, and streamline operations in healthcare systems. The healthcare industry stands to gain much from the use of digital twin technology, which could result in notable advancements in patient outcomes, safety, and innovation. Problems with data privacy, interoperability, data quality, ethics, resource intensity, workflow integration, validation, education, scalability, and cultural shifts must be addressed, however, if it is to be successfully deployed.

List of Abbreviations

DT digital twin

AI artificial intelligence

IoT internet of Things

Author Contributions

AV: Conceptualization, methodology, visualization, supervision; RH: conducted validation, formal analysis; HR: Investigation, resources, data curation, writing—original draft preparation, writing—review and editing. All authors have read and approved the published version of the manuscript.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Funding No external funding was received for the compilation of this article.

Acknowledgments

Authors would like to thank Sathyabama Institute of Science and Technology, Jeppiar Nagar, for the technical and scientific support rendered throughout the completion of the work.

AI-declaration

We acknowledge the use of writing tools (<https://quillbot.com/>) to refine the academic language and accuracy of our own work and entered the prompts Improve the academic tone and accuracy of language, including grammatical structures, punctuation and vocabulary.

Reference

1. A., Wu, Z., Wu, E., Wu, M., Snyder, M.P., Zou, J., and Wu, J.C. Leveraging physiology and artificial intelligence to deliver advancements in health care. *Physiol. Rev.* 2023; 103: 2423–2450. <https://doi.org/10.1152/physrev.00033.2022>

2. Lavanya Sharma, Pradeep Kumar Garg. Digital Twins and Simulation Technology: Concepts and Applications, 1st Edition, 2025, Chapman and Hall/CRC, DOI <https://doi.org/10.1201/9781003582489>
3. Ringeval, M., Etindele Sosso, F. A., Cousineau, M., & Paré, G. Advancing health care with digital twins: Meta-review of applications and implementation challenges. *Journal of Medical Internet Research*, 2025; 27: e69544. <https://doi.org/10.2196/69544>
4. Rajpurkar, P., Chen, E., Banerjee, O., and Topol, E.J. AI in health and medicine. *Nat. Med.* 2022; 28:31–38. <https://doi.org/10.1038/s41591021-01614-0>.
5. Grieves, M., and Vickers, J. Digital twin: Mitigating unpredictable, undesirable emergent behavior in complex systems. In *Transdisciplinary perspectives on complex systems* (Springer), 2017; 85–113.
6. Rhee, H., Miner, S., Sterling, M., Halterman, J.S., and Fairbanks, E. The development of an automated device for asthma monitoring for adolescents: methodologic approach and User acceptability. *JMI RMhealth Uhealth*. 2014;2,e27. <https://doi.org/10.2196/mhealth.3118>
7. Emmert-Streib, F., and Yli-Harja, O. What Is a Digital Twin? Experimental Design for a Data-Centric Machine Learning Perspective in Health. *Int. J. Mol. Sci.* 2022; 23: 13149. <https://doi.org/10.3390/ijms232113149>
8. Topol, E.J. High-performance medicine: the convergence of human and artificial intelligence. *Nat. Med.* 2019; 25: 44–56. <https://doi.org/10.1038/s41591-018-0300-7>
9. San, O. The digital twin revolution. *Nat. Comput. Sci.* 2021; 1: 307–308. <https://doi.org/10.1038/s43588-021-00077-0>.
10. Potter, D., Brothers, R., Kolacevski, A, Koskimaki, J.E., McNutt, A. Miller, R.S., Nagda, J., Nair, A., Rubinstein, W.S., Stewart, A.K., et al. Development of Cancer L in Q, a Health Information Learning Platform from Multiple Electronic Health Record Systems to Support Improved Quality of Care. *JCO Clin. Cancer Inform.* 2020; 4: 929–937. <https://doi.org/10.1200/CCI.20.00064>.
11. Coorey, G., Figtree, G.A., Fletcher, D.F., and Redfern, J. The health digital twin: advancing precision cardiovascular medicine. *Nat. Rev. Cardiol.* 2021; 18: 803–804. <https://doi.org/10.1038/s41569-021-00630-4>
12. Tortora, M., Pacchiano, F., Ferracioli, S. F., Criscuolo, S., Gagliardo, C., Jaber, K., Angelicchio, M., Briganti, F., Caranci, F., Tortora, F., & Negro, A. Medical digital twin: A review on technical principles and clinical applications. *Journal of Clinical Medicine*, 2025; 14(2): 324. <https://doi.org/10.3390/jcm14020324>
13. Walsh, J.R., Smith, A.M., Pouliot, Y., Li-Bland, D., Loukianov, A., and Fisher, C.K.; Consortium, f.t.M.S.O.A. Generating Digital Twins with Multiple Sclerosis Using Probabilistic Neural Networks. Preprint at arXiv. 2020. <https://doi.org/10.48550/arXiv.2002.02779>.

14. Fisher, C.K., Smith, A.M., Walsh, J.R., and Coalition Against Major, Machine learning for comprehensive forecasting of Alzheimer’s Disease progression. *Sci. Rep.* 2019; 9: 13622. <https://doi.org/10.1038/s41598-019-49656-2>
15. Masison, J., Beezley, J., Mei, Y., Ribeiro, H., Knapp, A.C., Sordo Vieira,L., Adhikari, B., Scindia, Y., Grauer, M., Helba, B., et al. A modular computational framework for medical digital twins. *Proc. Natl. Acad. Sci. USA* 2021; 118: e2024287118. <https://doi.org/10.1073/pnas.2024287118>.
16. van Dinter R, Tekinerdogan B, Catal C. Predictive maintenance using digital twins: a systematic literature review. *Inf Softw Technol.* 2022; 151:107008. doi: 10.1016/j.infsof.2022.107008
17. Sun T, He X, Li Z. Digital twin in healthcare: recent updates and challenges. *Digit Health.* 2023; 9:20552076221149652. doi: 10.1177/20552076221149651
18. Li L, Lei B, Mao C. Digital twin in smart manufacturing. *J Ind Inf Integr.* 2022; 26:100289.

doi: 10.1016/j.jii.2021.100289
19. El Saddik A. Digital twins: the convergence of multimedia technologies. *IEEE Multimed.*

2018; 25:87–92. doi: 10.1109/MMUL.2018.023121167
20. Sun T, He X, Song X, Shu L, Li Z. The digital twin in medicine: a key to the future of healthcare? *Front Med.* 2022; 9:907066. doi: 10.3389/fmed.2022.907066
21. Corral-Acero J, Margara F, Marciniak M, Rodero C, Loncaric F, Feng Y, et al. The “digital twin” to enable the vision of precision cardiology. *Eur Heart J.* 2020; 41:4556–64. doi: 10.1093/eurheartj/ehaa159
22. Peirlinck M, Costabal FS, Yao J, Guccione JM, Tripathy S, Wang Y, et al. Precision medicine in human heart modeling: perspectives, challenges, and opportunities. *Biomech Model Mechanobiol.* 2021; 20:803–31. doi: 10.1007/s10237-021-01421-z
23. Vallée, A. Digital twin for personalized medicine development. *Frontiers in Digital Health*, 2025; 7: 1583466. <https://doi.org/10.3389/fdgh.2025.1583466>
24. Vallée A. Digital twin for healthcare systems. *Front. Digit. Health*, 2023; 5:1253050. doi: 10.3389/fdgh.2023.1253050
25. Schwartz SM, Wildenhaus K, Bucher A, Byrd B. Digital twins and the emerging science of self: implications for digital health experience design and “small” data. *Front Comput Sci.* 2020; 2: <https://www.frontiersin.org/articles/10.3389/fcomp.2020.00031> (accessed 31 May2023). doi: 10.3389/fcomp.2020.00031
26. Voigt I, Inojosa H, Dillenseger A, Haase R, Akgün K, Ziemssen T. Digital twins for multiple sclerosis. *Front Immunol.* 2021; 12:669811. doi: 10.3389/fimmu.2021.669811

27. Haleem A, Javaid M, Pratap Singh R, Suman R. Exploring the revolution in healthcare systems through the applications of digital twin technology. *Biomed Technol.* 2023; 4:28–38. doi: 10.1016/j.bmt.2023.02.001
28. Johnson KB, Wei W, Weeraratne D, Frisse ME, Misulis K, Rhee K, et al. Precision medicine, AI, and the future of personalized health care. *Clin Transl Sci.* 2021; 14:86–93. doi: 10.1111/cts.12884
29. Goetz LH, Schork NJ. Personalized medicine: motivation, challenges and progress. *Fertil Steril.* 2018; 109:952–63.
30. Subbiah V. The next generation of evidence-based medicine. *Nat Med.* 2023; 29:49–58. doi: 10.1038/s41591-022-02160-z
31. Venkatesh KP, Raza MM, Kvedar JC. Health digital twins as tools for precision medicine: considerations for computation, implementation, and regulation. *Npj Digit Med.* 2022; 5:1–2.
32. Zhong D, Xia Z, Zhu Y, Duan J. Overview of predictive maintenance based on digital twin technology. *Heliyon.* 2023; 9:e14534. doi: 10.1016/j.heliyon.2023.e14534
33. Volkov I, Radchenko G, Tchernykh A. Digital twins, internet of things and Mobile medicine: a review of current platforms to support smart healthcare. *Program Comput Softw.* 2021; 47:578–90.
34. Drummond, D., & Gonsard, A. Definitions and characteristics of patient digital twins being developed for clinical use: Scoping review. *Journal of Medical Internet Research*, 2024; 26: e54321.
35. Elkefi S, Asan O. Digital twins for managing health care systems: rapid literature review. *J Med Internet Res.* 2022; 24:e37641. doi: 10.2196/37641
36. Syed-Abdul S, Li Y-C. Empowering patients and transforming healthcare in the post COVID-19 era: the role of digital and wearable technologies. *J Pers Med.* 2023; 13:722. doi: 10.3390/jpm13050722
37. Abernethy A, Adams L, Barrett M, Bechtel C, Brennan P, Butte A, et al. The promise of digital health: then, now, and the future. *NAM Perspect.* 2022. doi: 10.31478/202206e
38. Hassani H, Huang X, Mac Feely S. Impactful digital twin in the healthcare revolution. *Big Data Cogn Comput.* 2022; 6:83. doi: 10.3390/bdcc6030083
39. Allen A, Siefkas A, Pellegrini E, Burdick H, Barnes G, Calvert J, et al. A digital twins machine learning model for forecasting disease progression in stroke patients. *Appl Sci.* 2021; 11:5576. doi: 10.3390/app11125576
40. Pang TY, Pelaez Restrepo JD, Cheng C-T, Yasin A, Lim H, Miletic M. Developing a digital twin and digital thread framework for an ‘industry 4.0’ shipyard. *Appl Sci.* 2021; 11:1097. doi: 10.3390/app11031097
41. Ş. Tjalu, Texture analysis methods for the characterization of biological and medical images. *ELBA Bioflux*, 2012; 4(1): 8-12
42. Ginsburg O, Yip C-H, Brooks A, Cabanes A, Caleffi M, Dunstan YJ, et al. Breast cancer early detection: a phased approach to implementation. *Cancer.* 2020; 126:2379–93. doi: 10.1002/cncr.32887
43. Pascual H, Masip-Bruin X, Alonso A, Cerdá J. A Systematic Review on Human Modeling: Digging into Human Digital Twin Implementations. <https://doi.org/10.48550/arXiv.2302.03593>

44. Coorey G, Figtree GA, Fletcher DF, Snelson VJ, Vernon ST, Winlaw D, et al. The health digital twin to tackle cardiovascular disease—a review of an emerging interdisciplinary field. *Npj Digit Med.* 2022; 5:1–12. doi: 10.1038/s41746-022-00640-7
45. Morande S. Enhancing psychosomatic health using artificial intelligence-based treatment protocol: a data science-driven approach. *Int J Inf Manag Data Insights.* 2022; 2:100124.
46. Sahal R, Alsamhi SH, Brown KN. Personal digital twin: a close Look into the present and a step towards the future of personalised healthcare industry. *Sensors.* 2022; 22:5918. doi: 10.3390/s22155918
47. Popa EO, van Hilten M, Oosterkamp E, Bogaardt M-J. The use of digital twins in healthcare: socio-ethical benefits and socio-ethical risks. *Life Sci Soc Policy.* 2021; 17:6. doi: 10.1186/s40504-021-00113-x
48. Calcaterra V, Pagani V, Zuccotti G. Digital twin: a future health challenge in prevention, early diagnosis and personalisation of medical care in paediatrics. *Int J Environ Res Public Health.* 2023; 20:2181. doi: 10.3390/ijerph20032181
49. Elayan H, Aloqaily M, Guizani M. Digital twin for intelligent context-aware IoT healthcare systems. *IEEE Internet Things J.* 2021; 8:16749–57. doi: 10.1109/JIOT.2021.3051158
50. Kaur MJ, Mishra VP, Maheshwari P. The convergence of digital twin, IoT, and machine learning: transforming data into action. In: Farsi M, Daneshkhah A, Hosseinian-Far A, Jahankhani H, editors. *Digital twin technologies and smart cities.* Cham: Springer International Publishing 2020; 3–17.
51. Canedo A. Industrial IoT lifecycle via digital twins. *Proceedings of the eleventh IEEE/ACM/IFIP international conference on hardware/software codesign and system synthesis.* New York, NY, USA: Association for Computing Machinery .2016; 1.
52. Bruynseels K, Santoni de Sio F, van den Hoven J. Digital twins in health care: ethical implications of an emerging engineering paradigm. *Front Genet.* 2018; 9:31. doi: 10.3389/fgene.2018.00031
53. Liu Y, Zhang L, Yang Y, Zhou L, Ren L, Wang F, et al. A novel cloud-based frame work for the elderly healthcare services using digital twin. *IEEE Access.* 2019; 7:49088–101. doi: 10.1109/ACCESS.2019.2909828
54. Erol T, Mendi AF, Doğan D. The digital twin revolution in healthcare. *2020 4th international symposium on multidisciplinary studies and innovative technologies (ISMSIT) 2020;* 1–7.
55. Alazab M, Khan LU, Koppu S, Ramu SP, Iyapparaja M, Boobalan P, et al. Digital twins for healthcare 4.0—recent advances, Architecture, and open challenges. *IEEE Consum Electron Mag.* 2022;1–8.
56. Moztarzadeh O, Jamshidi M, Sargolzaei S, Jamshidi A, Baghalipour N, Malekzadeh Moghani M, et al. Metaverse and healthcare: machine learning-enabled digital twins of cancer. *Bioengineering.* 2023; 10:455. doi: 10.3390/bioengineering10040455
57. Fan C, Zhang C, Yahja A, Mostafavi A. Disaster city digital twin: a vision for integrating artificial and human intelligence for disaster management. *Int J Inf Manag.* 2021; 56:102049. doi: 10.1016/j.ijinfomgt.2019.102049
58. Evangelia Katsoulakis, Qi Wang, Huanmei Wu, Digital Twins for health: a scoping review. *Npj digital medicine,* 2024; 7:77. <https://doi.org/10.1038/s41746-024-01073-0>
59. Iqbal JD, Krauthammer M, Biller-Andorno N. The use and ethics of digital twins in medicine. *J Law Med Ethics J Am Soc Law Med Ethics.* 2022; 50:583–96. doi: 10.1017/jme.2022.97
60. Semeraro C, Lezoche M, Panetto H, Dassisti M. Digital twin paradigm: asystematic literature review. *Comput Ind.* 2021;130:103469. doi: 10.1016/j.compind.2021.103469