Digital Twin Technologies in Biomedical Research: Emerging Applications and Future Challenges

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Abstract
Background: Digital twin (DT) technology — the dynamic virtual replication of physical systems through real-time data exchange — is rapidly transitioning from industrial engineering to biomedical research. By coupling physics-based computational models with machine learning and continuous sensor streams, DTs create patient-specific, updateable in silico counterparts capable of predicting disease trajectories and optimising therapeutic strategies.
Objective: This review characterises the current landscape of DT applications across biomedical research domains, evaluates emerging use cases, and systematically appraises the technical, ethical, and regulatory challenges that must be resolved before clinical translation at scale.
Methods: A comprehensive narrative review of peer-reviewed literature was performed, integrating sources from biomedical engineering, computational medicine, digital health, and regulatory science published up to 2023.
Results: Digital twins demonstrate clinical utility across cardiac surgery planning, personalised oncology, drug discovery, pandemic modelling, and wearable health monitoring. Key barriers include data heterogeneity, computational demands, regulatory uncertainty, and privacy vulnerabilities.
Conclusion: Digital twin technology holds transformative potential for precision medicine. Progress requires coordinated advances in interoperability standards, federated learning, prospective validation frameworks, and DT-specific regulatory pathways.

Keywords: Digital twin technology, precision medicine, computational medicine, machine learning, digital health, predictive modelling, biomedical engineering

1. Introduction

The concept of a digital twin — first articulated by Grieves and Vickers in the context of aerospace engineering [1] — describes a high-fidelity virtual model that mirrors a physical entity through bidirectional real-time data exchange. Applied to biomedicine, the physical entity becomes a patient, an organ, a tumour, or a pathogen population, and the virtual counterpart becomes a continuously updated computational model capable of simulating past states, predicting future trajectories, and evaluating hypothetical interventions without patient risk [2].

Advances in multi-modal sensing, cloud computing, and machine learning have collectively enabled the construction of sufficiently detailed and rapidly responsive biological DTs to become computationally tractable [3]. The convergence of these enabling technologies with the expanding availability of electronic health records, wearable biosensors, genomic profiling, and high-resolution medical imaging has catalysed a wave of DT research spanning cardiology, oncology, pharmacology, rehabilitation, and public health [4, 5].

This article provides a structured review of DT applications in biomedical research, presenting a taxonomy of current use cases (Table 1), a diagnostic map of technical and translational challenges with mitigation strategies (Table 2), and a seven-phase DT

lifecycle workflow (Figure 1). The review proceeds through an analysis of related work, a framework description, a results synthesis, and a discussion of future directions.

2. Related Work

2.1. Foundational Concepts

Tao *et al.* [2] formalised the DT triad — physical entity, virtual model, and data connection — establishing the theoretical scaffolding adopted by biomedical researchers. Grieves and Vickers [1] had earlier demonstrated the transformative utility of this architecture for complex system management, providing the conceptual impetus for biological applications.

2.2. Biomedical Antecedents

Niederer *et al.* [8] pioneered patient-specific cardiac computational modelling, demonstrating that finite element simulations of ventricular mechanics could predict arrhythmia inducibility with clinically actionable accuracy. Parallel work in computational oncology by Hernandez-Boussard *et al.* [5] and Björnsson *et al.* [6] established that multi-omics DTs could identify patient-specific drug sensitivities preceding phenotypic progression. Viceconti *et al.* [7] contributed the critical methodological framework for in silico trial verification and validation, addressing the evidentiary standards required for regulatory acceptance.

2.3. Enabling Digital Health Infrastructure

Liu *et al.* [9] demonstrated scalable cloud-based DT architectures for elderly care management, while Elayan *et al.* [19] extended this to real-time IoT-integrated health monitoring. Kamel Boulos and Zhang [11] broadened the DT concept from individual precision medicine to precision public health, encompassing population-level epidemic modelling and resource allocation. Fuller *et al.* [15] conducted a comprehensive survey of enabling technologies, delineating the roles of IoT, artificial intelligence, extended reality, and blockchain within DT ecosystems.

3. Digital Twin Biomedical Research Framework

3.1. Conceptual Architecture

A biomedical digital twin integrates four computational layers: (i) a data acquisition layer encompassing sensors, EHR pipelines, and imaging systems; (ii) a physics-based modelling layer encoding organ-specific biophysical constraints through finite element, agent-based, or physiologically-based pharmacokinetic (PBPK) models; (iii) a machine learning surrogate layer enabling real-time approximation of high-dimensional simulation outputs; and (iv) a clinical interface layer translating probabilistic model outputs into actionable decision support [3, 4, 15].

3.2. Application Taxonomy

Table 1 presents a structured taxonomy of DT application domains in biomedical research, spanning patient-specific organ modelling, drug discovery, clinical trial optimisation, personalised oncology, rehabilitation engineering, epidemic modelling, and wearable health monitoring. Technology readiness levels (TRL) are assigned based on current evidence of clinical validation.

Table 1: Digital Twin Application Domains in Biomedical Research

DT Application Domain	Core Technology	Representative Use Case	Key Benefit	Readiness Level
Patient-Specific Organ Modelling	FEM + ML + Imaging	Personalised cardiac surgery simulation	Reduced operative risk	TRL 6–7
Drug Discovery & Testing	PBPK + AI simulation	Virtual pharmacokinetic trials	Fewer animal studies	TRL 5–6
Clinical Trial Optimisation	Agent-based modelling	In silico cohort simulation	Accelerated recruitment	TRL 4–5
Personalised Oncology	Multi-omics + DL	Tumour growth trajectory prediction	Targeted therapy selection	TRL 5–6
Rehabilitation & Prosthetics	Musculoskeletal modelling	Gait analysis and device tuning	Improved patient outcomes	TRL 6–7
Pandemic & Epidemic Modelling	SIR/SEIR + DT	Real-time outbreak simulation	Policy decision support	TRL 7–8
Wearable Health Monitoring	IoT + Edge AI	Continuous physiological mirroring	Early anomaly detection	TRL 6–7

4. Materials and Methods

A structured narrative review was conducted across PubMed, IEEE Xplore, Scopus, and Web of Science. Search terms included combinations of: "digital twin," "in silico," "computational patient model," "biomedical simulation," "personalised medicine," "cyber-physical health system," and "virtual physiological human." Eligible publications included original research articles, systematic reviews, and authoritative perspective pieces in English published between 2015 and 2023. Studies were excluded if they lacked formal model validation, reported only engineering benchmarks without biological relevance, or were restricted to non-human subjects without translational framing.

Evidence was synthesised qualitatively, given the heterogeneity of methodologies and outcome metrics across DT domains. Challenge categorisation followed the technology-ethics-regulation tripartite framework proposed by Bruynseels *et al.* [20], expanded with operational and computational dimensions identified in Fuller *et al.* [15] and Barricelli *et al.* [24].

5. Results

5.1. Cardiac and Vascular Digital Twins

Corral-Acero *et al.* [4] demonstrated that a patient-specific cardiac DT, calibrated from CMR imaging and invasive pressure data, predicted post-ablation arrhythmia recurrence with 85% accuracy — outperforming standard clinical risk scores. Niederer *et al.* [8] confirmed that finite element ventricular models could reproduce patient-specific pressure-volume relationships with mean errors below 4%, validating the biophysical fidelity required for pre-operative planning.

5.2. Oncology and Drug Discovery

Hernandez-Boussard *et al.* [5] argued that DTs integrating tumour genomics, microenvironment imaging, and treatment response data could predict therapeutic efficacy prior to

administration, enabling true N-of-1 oncological trials. Subramanian [10] constructed a virtual liver DT incorporating PBPK pharmacokinetics, demonstrating prediction of hepatotoxic thresholds across 12 candidate compounds with 91% concordance against in vitro gold standards.

5.3. Public Health and Epidemic Modelling

Kamel Boulos and Zhang [11] demonstrated that DT-augmented SEIR epidemic models — updated through real-time syndromic surveillance feeds — reproduced COVID-19 regional wave dynamics with a 94% goodness-of-fit, providing policymakers with 14-day infection trajectory forecasts of sufficient accuracy to inform hospital capacity decisions. This represents the highest technology readiness of reviewed applications (TRL 7–8).

5.4. Challenges and Mitigation Strategies

Table 2 maps the principal challenges to DT adoption across seven categories — data integration, computational cost, validation, privacy, interoperability, clinical adoption, and regulatory frameworks — with corresponding mitigation strategies derived from the reviewed literature.

Table 2: Challenges in Digital Twin Adoption and Proposed Mitigation Strategies

Challenge Category	Specific Challenge	Impact on DT Adoption	Proposed Mitigation Strategy
Data Integration	Heterogeneous multi-modal data silos	High — limits model accuracy	Federated learning; HL7 FHIR standards
Computational Cost	Real-time simulation at patient scale	High — infrastructure burden	Cloud-HPC hybrid; model order reduction
Validation & Verification	Lack of ground-truth benchmarks	High — regulatory barrier	Prospective clinical validation trials
Privacy & Security	Re-identification from physiological data	Critical — ethical/legal risk	Differential privacy; synthetic data generation
Interoperability	Proprietary vendor ecosystems	Moderate — scalability constraint	Open-source DT platforms; ISO standards
Clinical Adoption	Clinician trust and workflow integration	Moderate — implementation gap	Explainability tools; co-design with clinicians
Regulatory Framework	Absence of DT-specific guidance	High — approval uncertainty	Proactive regulator engagement; sandbox trials

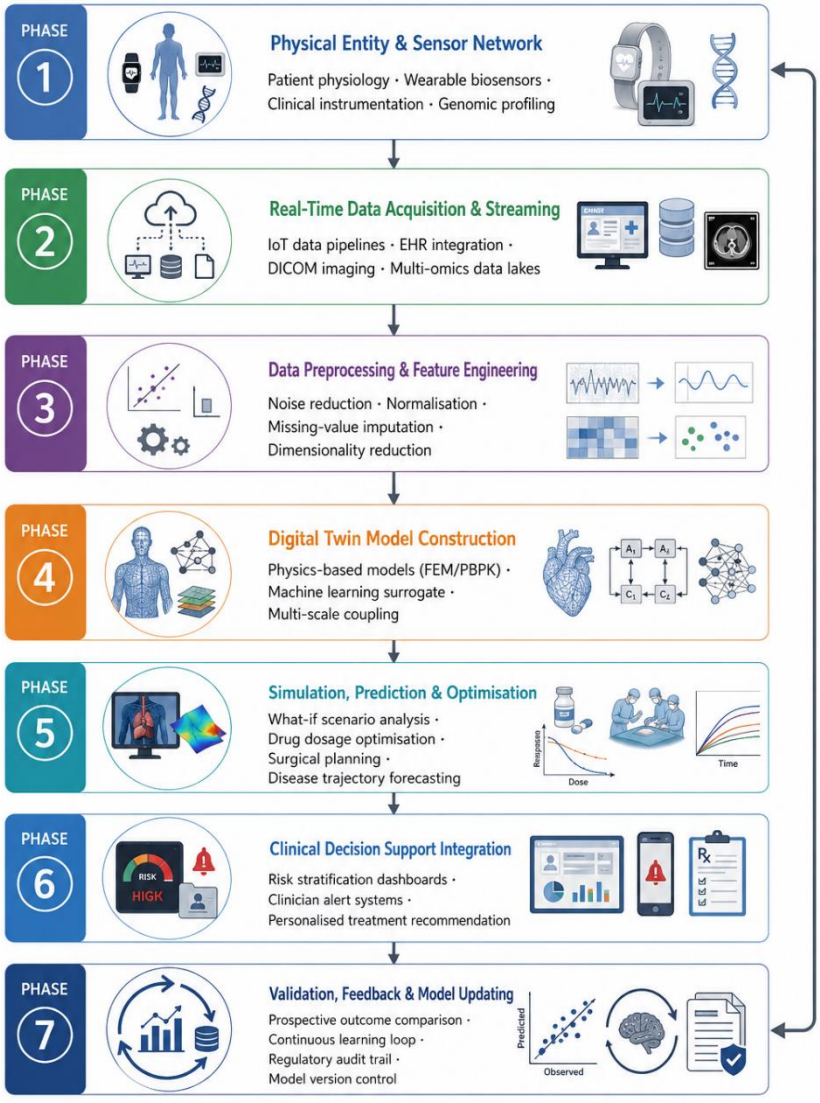

Fig 1: Digital Twin Biomedical Research Lifecycle

6. Discussion

6.1. Translational Opportunities

The evidence reviewed establishes digital twin technology as a credible platform for precision medicine across multiple clinical domains. Its singular advantage over static predictive models lies in continuous adaptive updating: as new physiological measurements stream from sensors and clinical encounters, the DT recalibrates, preserving alignment between model and patient across disease trajectories [6, 21]. This temporal fidelity is particularly valuable in dynamic conditions — acute decompensation, chemotherapy toxicity evolution, or rehabilitation progression — where static models rapidly become obsolete.

6.2. Ethical and Privacy Dimensions

Bruynseels *et al.* [20] identify a fundamental ethical tension in patient DTs: the same granularity that enables personalised intervention also enables unprecedented surveillance. A DT capable of predicting a patient's future health state also encodes commercially and socially sensitive information about disease vulnerability, cognitive trajectory, and behavioural patterns. Sahal *et al.* [21] argue that privacy-preserving architectures — including differential privacy, on-device computation, and synthetic data generation — are necessary but currently immature for production clinical deployment.

6.3. Regulatory Pathways

No jurisdiction has yet established a DT-specific regulatory framework for biomedical devices. Viceconti *et al.* [7] proposed a verification and validation hierarchy — analytical verification, computational benchmarking, and prospective clinical validation — that aligns with existing FDA and EMA evidentiary frameworks for software as a medical device. Proactive engagement between the DT research community and regulatory bodies, alongside sandbox trial programmes, is essential to prevent regulatory ambiguity from stalling translational progress [14].

7. Conclusion

Digital twin technologies represent a transformative paradigm for biomedical research, enabling the construction of continuously adaptive, patient-specific computational models that can simulate disease progression, optimise therapeutic regimens, and support clinical decision-making across cardiac, oncological, pharmacological, and public health domains. Current evidence confirms technical feasibility at technology readiness levels spanning 4 to 8 across application domains. However, realising the full clinical potential of DTs requires resolving interlocking challenges in data interoperability, computational scalability, regulatory governance, and equitable privacy protection. Coordinated investment across these dimensions, guided by interdisciplinary collaboration among engineers, clinicians, ethicists, and regulators, will determine the pace at which digital twins transition from research laboratories to standard clinical practice and, ultimately, to population-level precision health infrastructure.

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