Models in Medicine: the Digital Twin for Health

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Resumen

Este artículo explora el papel de los modelos en la medicina con un enfoque en la evolución y aplicación de modelos matemáticos y computacionales, en particular los Gemelos Digitales (GDs). Los modelos en la ciencia sirven como herramientas esenciales para representar sistemas y fenómenos complejos, lo que permite a los investigadores predecir resultados y desarrollar estrategias efectivas. Históricamente, los modelos han sido fundamentales para los avances en varios campos médicos, desde la farmacocinética hasta la propagación de enfermedades y la respuesta tumoral a ciertos tratamientos. En la medicina moderna, los modelos predictivos, incluidos los GDs, ofrecen un potencial transformador al mejorar los resultados de los pacientes a través de la medicina personalizada, optimizar la gestión sanitaria y avanzar en la investigación biomédica. Los Gemelos Digitales, que son réplicas digitales detalladas de entidades físicas, están emergiendo como herramientas críticas en el ámbito de la salud, capaces de simular desde órganos individuales hasta sistemas hospitalarios completos. A pesar de su promesa, la implementación de los GDs enfrenta desafíos como la privacidad de los datos, la integración de información y la precisión de los modelos. Superar estos obstáculos requiere colaboración entre proveedores de salud, investigadores y desarrolladores tecnológicos. A medida que este campo avanza, se espera que estos modelos cambien significativamente el futuro de la ciencia médica.

Palabras clave: representación, predicción, matemático, in silico, ingeniería biomédica.

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Abstract

This paper explores the role of models in medicine with a focus on the evolution and application of mathematical and computational models, particularly Digital Twins (DTs). Models in science serve as essential tools for representing complex systems and phenomena, enabling researchers to predict outcomes and develop effective strategies. Historically, models have been integral to advancements in various medical fields, from pharmacokinetics to disease spread and tumor response to certain treatments. In modern medicine, predictive models, including DTs, offer transformative potential by improving patient outcomes through personalized medicine, optimizing healthcare management, and enhancing biomedical research. Digital Twins, which are detailed digital replicas of physical entities, are emerging as critical tools in healthcare, capable of simulating everything from individual organs to entire hospital systems. Despite their promise, the implementation of DTs faces challenges such as data privacy, integration, and model accuracy. Overcoming these obstacles requires collaboration among healthcare providers, researchers, and technology developers. As the field advances, these models are poised to significantly reshape the future of medical science.

Keywords: representation, prediction, mathematical, in silico, biomedical engineering.

1. Introduction

The use of models in science, particularly in medicine, has revolutionized the way researchers and practitioners understand complex phenomena. From the early days of ancient medical theories such as the balance of humors to the sophisticated mathematical and computational models employed in contemporary biomedical research, models have served as indispensable tools for representing, analyzing, and predicting various aspects of the physical world. In recent years, advancements in data science, artificial intelligence (AI), and computational power have paved the way for a transformative concept in healthcare: the Digital Twin (DT). Originally developed for engineering and space missions, the digital twin has rapidly gained prominence in medicine, promising to reshape patient care, drug development, and medical research through personalized and dynamic digital replicas of real-world entities.

The potential of Digital Twins for Health (DT4H) lies in their ability to replicate not just single organs but entire physiological systems or even healthcare environments, allowing for real-time monitoring, predictive analysis, and tailored medical interventions. These advancements, however, also bring about profound methodological, epistemological, and ethical challenges that must be addressed to ensure the safe and effective integration of DTs into mainstream medical practice.

This work explores the historical and contemporary use of models in medical science, focusing on the emergence and application of Digital Twins. It delves into the philosophical and practical implications of modeling, the role of predictive algorithms, and the opportunities DT4H presents for improving patient outcomes while critically assessing the challenges that accompany this evolving field. Through this lens, the discussion highlights how the Digital Twin concept has the potential to redefine the future of healthcare, making personalized medicine and *in silico* trials viable components of modern medical practice.

2. Models in Science

The concept of models in science is rooted in model theory, which examines the interpretation of any language—formal or natural—through set-theoretic structures. Modeling a phenomenon essentially involves constructing a formal theory to describe and explain it (Hodges 2023). According to Moulines, the model-based approach in the philosophy of science gained prominence around the 1970s. This approach emphasizes models rather than propositions as the fundamental units of scientific understanding, underscoring the importance of detailed reconstructions of scientific theories.

Scientific models are designed to represent specific parts or aspects of the world, referred to as the model's target system. These models can take various forms, including physical objects, fictional objects, abstract entities, set-theoretic structures, descriptions, and equations (Frigg 2024). Despite the multiple meanings associated with the concept of models, Cassini (2016) argues that they are fundamentally idealized representations of a phenomenon or domain. While the notion of representation is still evolving, modeling remains a central activity in modern science as cognitive vehicles.

In contemporary scientific research, models often replace the direct study of reality due to practical and economic considerations. By examining a model, researchers can uncover features and derive insights about the system it represents, enabling what is termed "surrogative reasoning."Swoyer (1991, p. 449) explains that this process involves generating hypotheses about phenomena based on a model. Redmond (2022, p. 11) expands on this concept, suggesting that surrogation should be viewed as a logical relationship wherein conclusions drawn from the model are applicable to the target system. In essence, surrogate reasoning allows inferences made within the model to be considered valid for the system it represents.

3. Models in Medical History

The concept of representation and surrogate reasoning in medicine dates back to ancient times. The theory of humors, practiced by Hippocrates and Galen, serves as an early example. This theory posited that the human body—the target system—was composed of four balanced humors—the model: black bile, yellow bile, blood, and phlegmeach influenced by environmental factors such as seasons, climate, diet, and geography. Illness was thought to result from an imbalance among these humors, and treatments aimed to restore balance through dietary adjustments, purges, enemas, herbal medications, or surgical procedures such as bloodletting (Lamas 2016, p. 82).

Although the humor theory fits the presented definition of modeling, it differs from modern modeling concepts as discussed here, particularly because the focus of this work is on modeling phenomena into formal languages, specifically mathematical and computational methods.

The modern use of models in medical science began in the 20th century, driven by technological advancements. These models employ mathematical algorithms to predict outcomes in biomedicine. For example, the Pharmacokinetic/Pharmacodynamic (PK/PD) models aid in understanding drug interactions within the body, helping determine appropriate dosages (Michaelis & Menten 1913, p. 333).

Another prominent example is the SIR Model (Susceptible-Infected-Recovered), which uses differential equations to simulate disease transmission dynamics (Kermack & McKendrick 1927, p. 115). The Hodgkin-Huxley Model (1952) describes how action potentials in neurons are initiated and propagated, using mathematical equations to represent ion channel activity in nerve cells, providing insights into neurological diseases and potential treatments (Hodgkin & Huxley 1952, p. 117).

In cancer medicine, the Tumor Growth Inhibition (TGI) Model, used since 2004, predicts how a tumor will grow or shrink in response to different treatments. This model helps oncologists determine the most effective therapy by simulating the tumor's response over time (Simeoni et al. 2004, p. 1094).

Additionally, non-mathematical models, such as high-fidelity patient simulators like SimMan, are used to replicate real-life scenarios like cardiac arrest or respiratory failure (Alinier et al. 2006, p. 359). Also, anatomical models like The Visible Human Project, a digital model of the human body providing detailed cross-sectional views of anatomical structures, are widely used in medical education.

Lastly, it is worth mentioning projects that aim to incorporate physiological features into these computational imaging databases, like the Virtual Physiological Human Initiative, with a holistic approach to medicine where the body is treated as one single, however complex, multiorgan system rather than as a collection of individual organs. This is the base of the notion of the Digital Twin (Paul 2023, pp. 8-15).

4. Models in Modern Medicine

The complexities and dynamic nature of modern biomedicine require methodologies capable of processing the multiple factors involved in this field's phenomena. Mathematical and computational models, particularly predictive models, address this need. Predictive models involve the use of these methods to create models that can forecast future outcomes. The application of these techniques to the medical field is especially challenging since it deals with the dynamic nature of this discipline: the complexity of the human body of patients treated in modern healthcare settings. Moreover, developing and implementing effective predictive models requires a profound understanding of the data being used, along with adequate resources to properly support model development and implementation (Erdemir et al. 2020, p. 18).

Despite these challenges, predictive models have a wide range of applications in novel medical research. For example, recent studies analyzing anatomical structures via computer science have successfully used deep learning to detect vulnerable atherosclerotic plaque in preoperative patients (Toma 2023, p. 590). Similarly, computational modeling has established associations between tumor mutational burden and immunotherapy response across various cancer types (Cilla 2012, p. 59). Predictive algorithms have also been effective in identifying data patterns and forecasting surgical risks in adult spine surgery before the operation (Osorio 2016, p. 333).

Moreover, biological experiments based on computer simulation software are now referred to as “*in silico*”studies, a term derived from the silicon in computer chips, similar to the Latin terms “*in vitro*.ªnd “*in vivo*.”These novel applications of mathematical and computational models have significantly impacted the medical research field, not only in terms of their utility and potential but also in their ability to reshape the epistemological foundations of medicine.

These new modeling environments are ideal for developing predictive individualized healthcare solutions that can result in better patient outcomes, improved patient safety, and increased drug efficacy. This concept is central to the notion of *in silico* medicine.

In recent years, computational modeling and Artificial Intelligence (AI)/Machine Learning (ML) algorithms have already been widely used in disease modeling, target identification, *in silico* trial simulations, virtual or synthetic patients, virtual coaches, and personalized medicine. While these approaches form an essential part of creating virtual replicas of physical entities, they do not encompass the entire concept of the Digital Twin.

5. The Digital Twin

Digital Twins (DTs) are precise digital replicas of physical entities or systems, enabling real-time monitoring, simulation, and optimization. Originally employed by NASA during the Apollo missions in the 1960s to simulate and troubleshoot space systems remotely, DTs have since expanded into various fields, with healthcare emerging as a particularly promising area.

The actual term "digital twin" was coined in 2005 by Michael Grieves in product lifecycle management, and around 2010 NASA and John Vickers utilized the Digital Twin as a virtual model of a physical system. In the original description, a DT is characterized by three components: physical, virtual, and a connection where the virtual system is mapped to the physical system by exchanging information through a real-time data connection (Katsoulakis 2024).

The Digital Twin Consortium (2022) defined the DT as a virtual representation of real-world entities and processes synchronized at a specified frequency and fidelity. Their core characteristics are:

- DT systems transform business by accelerating holistic understanding, optimal decision-making, and effective action.
- DTs use real-time and historical data to represent the past and present and simulate predicted futures.
- DTs are motivated by outcomes, tailored to use cases, powered by integration, built on data, guided by domain knowledge, and

> implemented in Information Technology (IT)/Operational Technology (OT) systems.

The foundational elements of the definition are captured in the first sentence: the virtual representation, the real-world entities and processes it represents, and the mechanism by which the virtual and real-world entities are synchronized.

These definitions are consistent with the model notion explained above since they are representations of a targeted system, they can be used to make surrogate inferences, and they use mathematical and computational methods.

6. Digital Twins in Healthcare

In healthcare, DTs, known as Digital Twins for Health (DT4H), are transformative tools that can replicate anything from individual organs to entire hospital systems, enabling better diagnosis, treatment, and healthcare management. The development of DT4H is driven by advances in data science, AI, and the Internet of Things (IoT), which allow the creation of detailed, dynamic, and real-time models of biological systems.

Katsoulakis et al. (2024) envision that DTs should be individualized, interconnected, interactive, informative, and impactful (5Is). In the context of a patient-specific DT, the simulation, prediction, and analysis generated by the DT can be used to achieve better treatment outcomes with fewer adverse effects. Conversely, real-world data from the patient can be used to benchmark, validate, and improve the DT model.

Wakefield (2022) defines DTs as exact replicas of physical entities designed to improve or provide feedback to their real-life counterparts, similar to surrogate reasoning in other scientific models. He highlights the value of DTs in healthcare, particularly within the domain of *in silico* medicine.

Continuous improvements in product design and engineering activities have made it possible to build personalized models for patients, which can be continuously adjusted based on tracked health and lifestyle parameters. This approach can lead to the development of a virtual patient with a detailed description of the individual's healthy state, not only based on previous records but also by comparing statistics to the population to more easily identify patterns.

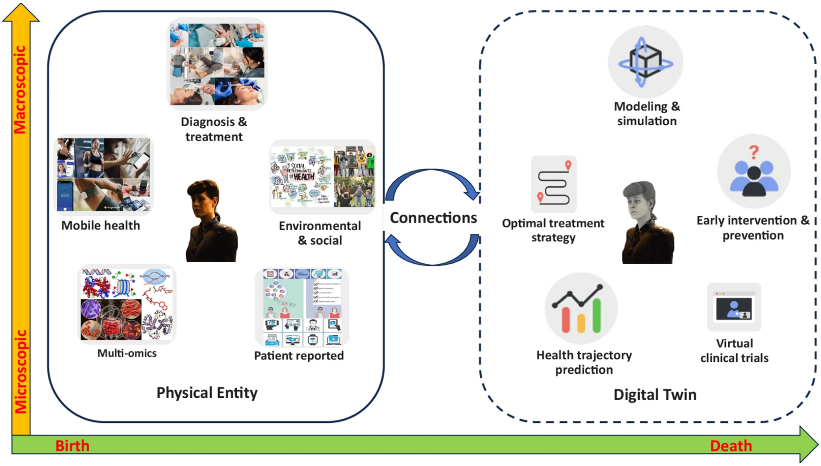

Figura 1: Digital Twin for health (DT4H) envisioned. This general scheme overviews the key factors that this model should comprehend. Both the physical entity and the Digital Twin have their intrinsic characteristics and are set in a specific scale and time (Katsoulakis 2024, p. 2).

The applications of DTs in medicine are diverse, ranging from representations of tissues, organs, organisms, patients, communities, and even healthcare systems. For example, DTs are used in hospital management and care coordination to create digital representations of healthcare data, hospital environments, operational staff, and lab results, optimizing resource utilization, improving workflow efficiency, and enhancing patient care.

In medical device design, DTs help customize devices such as those developed in the SIMULIA Living Heart project, which uses a DT of the human heart to study drug interactions and develop cardiac devices like pacemakers (Baillargeon 2014, p. 48).

In surgical planning, DTs allow surgeons to simulate procedures on virtual models before actual surgery (Sun 2022, p. 9), which is particularly useful in complex cardiac procedures, orthopedics, and cancer treatments. In drug discovery and biomarker identification, DTs accelerate the process by simulating biochemical reactions and predicting drug efficacy, reducing the time and cost involved in bringing new drugs to market (Rifaioglu 2019, p. 20).

DTs are also used to simulate clinical trials virtually, allowing researchers to test the efficacy of treatments on virtual patients. This approach can reduce the cost and time associated with traditional clinical trials and addresses the issues concerning the recruitment of patients in the trials, which is particularly useful in fields like oncology (Kolla 2021).

Furthermore, DTs enable personalized medicine, integrating clinical history and genomic profiling by simulating the effects of different therapies on individual patients, predicting responses to chemotherapy and other treatments (Katosulakis et al. 2020).

Also, DTs have been employed to monitor and promote general health and well-being. For example, they can track fitness data from wearable devices and provide personalized health recommendations to improve overall wellness (Sahal et al. 2022, p. 22).

Finally, the Virtual Physiological Human (VPH) initiative, through the DISCIPULUS project of the European Commission, over a decade of development, concluded in the Digital Twin roadmap. They envision an ideal of a patient's medical data, which enables the database of the VPH to be transformed into the avatar of a specific patient. Modeling studies of the avatar are guided by population-level data in the medical literature (DISCIPULUS Project 2012).

7. Discussion

The use of models in medical science has already proven to be useful and still remains a promising field. It not only encompasses a novel research methodology but also aligns with the modelistic era of scientific progress and has the potential to change the current paradigm of healthcare.

Notwithstanding, the development and application of the DTs arise challenges concerning its introduction into mainstream science. From a methodological and an epistemological perspective, we recognize some of the main challenges.

- **What kind of representation is involved in DTs?** As a new paradigm in modeling, it is philosophically unclear how conclusions can be drawn from mathematical models and how this information is extrapolated to the complex and dynamic nature of human physiology. The strength of the inference itself poses a logical challenge.

- **How secure is the information used by the DTs?** They rely heavily on vast amounts of personal health data to create accurate models. This raises concerns about patient privacy and the potential misuse of sensitive medical information. Securing this data from cyberattacks and unauthorized access is critical but challenging.

- **Can we rely on what DTs mean?** The accuracy of a DT depends on the quality and completeness of the data used to create it. Incomplete, outdated, or inaccurate data could lead to erroneous conclusions or predictions, potentially harming patients by suggesting incorrect treatments or interventions.

- **How ethical is the use of DTs?** The use of digital twins in healthcare raises ethical questions about consent, especially regarding how patient data is used and shared. Patients must be fully informed and give explicit consent for the use of their data in creating and maintaining digital twins. Additionally, concerns about equitable access arise as advanced digital health tools may not be available to all populations, potentially exacerbating health disparities.

- **How valid are DTs in clinical contexts?** The effectiveness and safety of using digital twins for medical decision-making must be thoroughly validated through clinical trials and evidence-based research. Without rigorous validation, the use of digital twins could introduce risks, particularly if used to replace or guide critical medical decisions.

Some of these challenges have just begun to be addressed, like the Ten Rules to create a credible practice of modeling and simulation in healthcare published by Erdermir et al. (2020): to define context clearly, to use contextually appropriate data, to evaluate within context, to list limitations explicitly, to use version control, to document appropriately, to disseminate broadly, to get independent reviews, to test competing implementations, and finally to conform to standards.

Can a new epistemological paradigm be born in medical research? Away from the solid and constant weight of medical tradition and work and in hand with the modern notion of medicine based on evidence? Only time and scientific scrutiny will tell whether this new paradigm of Medicine Based on Prediction could further develop.

8. Conclusion

The integration of models, particularly Digital Twins (DTs), into medical science represents a significant shift in the way healthcare is approached, researched, and practiced. Historically, models have been indispensable in simplifying and understanding complex systems, from the humoral theories of ancient medicine to the predictive algorithms of modern biomedicine. Digital Twins, however, push the boundaries of this tradition by offering dynamic, individualized simulations that have the potential to enhance decision-making, improve patient outcomes, and streamline drug discovery.

As DT4H continues to develop, it introduces not only groundbreaking opportunities but also critical challenges. From methodological concerns regarding the accuracy and representation of complex biological systems to ethical dilemmas around data security, privacy, and equitable access, the path forward is as complex as it is promising. For DTs to be successfully integrated into mainstream medicine, they must undergo rigorous validation, be supported by high-quality data, and be deployed with careful consideration of their broader social and ethical implications.

Despite these hurdles, the potential of Digital Twins to revolutionize healthcare is undeniable. Their ability to simulate patient-specific conditions, predict treatment responses, and optimize healthcare delivery could mark the beginning of a new era in medicine—one based not only on historical evidence but also on real-time prediction and personalization. The future of medical science may well rest on how effectively these models can bridge the gap between digital representation and clinical reality, shaping a new paradigm in healthcare that is more precise, individualized, and dynamic than ever before.

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