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Seminar Paper

Digital Twins in Biomedicine

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Contents

1 Abstract

Digital twins, virtual representations of physical entities, have gained significance in diverse industries, including healthcare. They are created using complex mathematical and computational models aimed at recreating physical entities such as organisms, engines etc. Their applications span from biomedicine, to industrial uses, to mechanical engineering. In this paper, focused on their biomedical uses, we will define their three core elements, explain their historical evolution, and finally highlight their potential uses in personalized medicine, drug development, surgical planning, and virology. Finally, we will discuss some of the future challenges in their development.

2 Introduction

Digital twins (DT) are virtual representations of physical objects, created with the use of mathematical and computational models. They are highly versatile and have become important across a range of diverse industries, spanning from manufacturing and healthcare to aerospace, urban planning, automotive and energy sectors. Their ability to optimize processes and to enhance decision making has increased their significance over the past decade [1]. The benefits of using digital twins in the healthcare sector are huge and in this report, we will mainly be focusing on their usage in biomedicine.

This paper explores the three core elements of a digital twin and traces their historical evolution. It delves into their versatile applications across diverse fields, such as personalized medicine, drug development and surgical planning, revealing how in the future they might help and improve the process of scientific research.

3 Three Element Composition of a Digital Twin

To understand how the concept of a DT works, we must take a deeper look at the subsections that compose it. The first thing needed, is a data feed that continuously reports the current state and tracks all the changes in the original biological entity, machine, or component in almost real-time.[2] This way the DT is always up to date, as it is provided with a continuous stream of information about the entity's behavior and characteristics.

A DT also includes a virtual model/representation of the physical entity. It mirrors its functionalities and characteristics, based on the collected data obtained from the data-feed. It is a very important part of the structure, as it is used to simulate and predict the real entity's behavior. This approach allows the physical entity to be subjected to further testing, analyzing potential changes, and understanding how it might behave under different conditions. [2]

The last, but nonetheless important, element is the comparator which compares two sets of data. One set consists of the obtained data from the tests on the virtual representation. The set is compared to the initially predicted outcome of the actual entity. The initially predicted outcome of the actual entity is derived through algorithms, based on the known behavior and characteristics of the physical system. The comparator basically examines how closely the observed and the predicted outcomes are, which validates the accuracy of the DT.[2]

4 History of Digital Twins

Dr. Michael Grieves from the University of Michigan initially introduced the concept of a DT in 2002, originally termed the "Conceptual Ideal for Product Lifecycle Management (PLM)." Its main focus was on the linkage of real space and virtual space.[1 Quote] In 2010 the term "digital twins" was introduced by

NASA for the first time, as they used it to embody the technological process of replicating and connecting physical objects with their digital counterparts.[3] One of the first, but often cited as the most significant studies for modern understanding on DTs was published in 2011 [3]. In the subsequent years, it was followed by a vast number of papers surrounding this topic, like a study by M. Grieves and J. Vickers [4], which introduced new key concepts surrounding a DT.

It then found its usage in manufacturing [2], were engineers created a digital replica of an aircraft engine, carefully constructed to mirror its exact design parameters and performance characteristics. The digital copy works just like the actual engine. Moreover, real engines have sensors that constantly gather different data as they run. The comparison of real-time data from the sensor-filled engines with the digital model's expectations, helps to closely monitor any changes in the engine's functioning. Any disparity detected between the projected and actual values, signals potential issues within an engine, so it can be pulled out of service [2].

5 Use Cases

DT have proven to be incredibly versatile in biomedicine. These virtual replicas of biological systems offer a wide range of uses.

5.1 Personalized Medicine

Personalized medicine involves customizing healthcare decisions and medical treatments to individual patients. A study by the US Food and Drug Administration (FDA) revealed, that medication-based treatments for common diseases have been ineffective for 38-75% of patients [5]. This issue shows how tricky common diseases can be, especially if we consider that everybody's genetic composition is different, which implies that medical treatments might work for some patients but not for others. In cancer therapy for example, it has shown that patients receiving targeted therapies, have a much higher survival rate than patients receiving generic treatments.[6] This is where the use of DTs offers a distinct solution for the problem. The general idea is to create digital replicas of patients to simulate and predict responses to treatments, drugs, or therapies. The Swedish Digital Twin Consortium (SDTC) is already working on a project which utilizes this concept as a foundation in its application. The approach to develop this, is to first construct unlimited copies of network models of all molecular, phenotypic and environmental factors relevant to disease mechanisms in individual patients and 2) computationally treat those twins with thousands of drugs in order to identify the best drug or combination of drugs to 3) treat the patient accordingly [7].

Advanced imaging, boosted by artificial intelligence, helps create detailed models. In cancer, it means understanding the unique features of a tumor without invasive procedures. These virtual models bring us closer to personalized

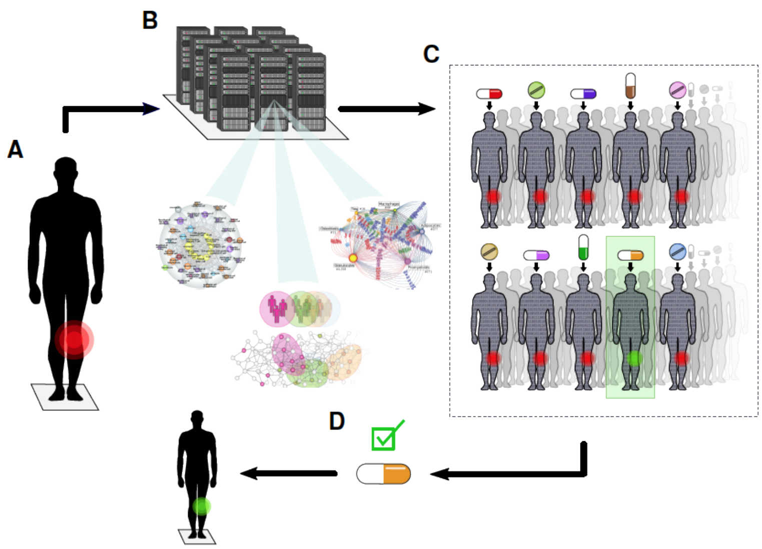

Figure 1: Representation of DTs in personalized medicine. A) th e patient has a disease in one part of the body. B) Based on computational Models many DTs are created. C) Every single DT is tested with a different drug. The drug with the best effect is given to the patient.[8]

medicine, where treatments are precisely tailored to each patient. In the future this will lead to a true patient-centered strategy, where for every patient there will be the perfect match of the right medicine, for the right disease at the right dosage for the right patient [6].

5.2 Drug Development and Research

Over the past decades pharmaceutical companies have researched, developed and tested drugs on animals. The ongoing debate of the ethical concerns and scientific reliability of this practice continues to fuel discussions worldwide. It is known that besides the immorality, this practice has also some more downsides like inaccuracy in predicting human response, high costs, limited applicability to human health, etc. Therefore, it is probable that future testing will transition towards utilizing DTs, where no living biological organism will be harmed, and the accuracy of the testing results is going to be much higher.

To understand why DTs can help us in the research of drugs, it is important to understand the term "target identification". Target identification is the process of pinpointing a crucial molecule, called target. In pharmaceutical science, it aims to identify the specific target that a medication effectively interacts with. This understanding is crucial for developing effective drugs.[9] The main advantage DTs will give us over the use of animals, is the ability to understand how a drug interacts with specific receptors in the body. Observing this interaction allows the creation of multiple drugs that work similarly by replicating it. By doing so, these newly developed drugs can produce the same beneficial effects in treating a particular condition or disease, maximizing efficacy while minimizing the toxicity of the drug.[10]

5.3 Surgical Planning and Training

DTs are also finding their way into surgery. By replicating a patient's surgical site, i.e., the part of a human's body were surgery is going to be performed, it allows surgeons to use the model for planning the surgery beforehand, even in multidisciplinary groups. It is important to note, that they may be used as a decision support tool [11]. This offers a big advantage for surgery success, as the procedure can be practiced as often as desired in the simulator. As an example, specific actions in dubious proceedings can be studied beforehand, resulting in the best possible outcome for the patient.[11] This new method could raise

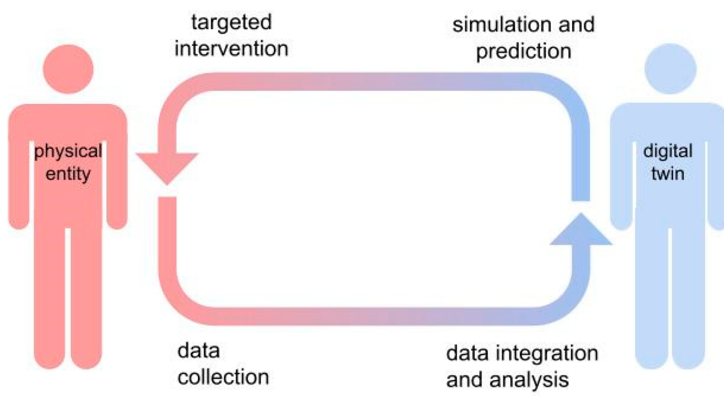

Figure 2: A digital twin gathers data and simulates interventions that can be applied to a real individual.[12]

some moral questions and doubts, whether it is reasonable and safe to rely on machines to treat such sensible matters. On this topic, we distinguish between two distinct types: Clinical decisions, which are decisions made by healthcare professionals in direct patient care, based on medical evidence, patient-specific factors, symptoms, test results, etc., and regulatory decisions, which involve the approval and oversight of authoritative bodies. As per now, computational data is deemed acceptable for inclusion in submissions to regulatory bodies.[13]

A concrete instance of this concept is already being used for cardiac procedures. A company called "Heartflow" is using a computed tomography (CT) scan of an individual's heart, along with computational fluid dynamics (CFD), to build a three-dimensional representation of the heart which simulates blood flowing through the arteries.[2]. A surgeon can then try different placements of veins, to assure that the blood flows well. Although the concept is similar to the one of a DT, it is not exactly the same, as this 3D model is more of a snapshot of a patient's heart, as the continuous data-feed depicting the evolving state of the entity is missing, and it therefore does not quite fall under the category of a DT[2]. But this example is a good illustration for the use of virtual replicas in surgical planning.

5.4 Digital Twins in Virology

With the emergence of the highly contagious respiratory virus SARS-CoV-2 (Covid-19) in 2019, all the focus of viral research was shifted towards it, as the main goal was to stop the pandemic which was putting the whole world on hold. The same was for the epidemiological computer models originally developed for other pandemics.[14] The idea was to use DTs for complex therapies, combining antivirals and multiple immune-stimulating and anti-inflammatory drugs, so that they could improve diagnosis, prognosis, and treatment. However, creating a DT that accurately mirrors the intricate nature of infection and immune responses, enabling precise individualized treatment guidance, remains beyond our current capabilities.

But how would it have looked like, building a DT to fight a viral infection and what are its main challenges? Building DTs for viral infections is like creating a computer copy of how our body fights a virus. There are lots of smaller models that show how different parts of our body work on different levels during an infection. On subcellular scale, which would be the smallest scale, we look at the gene expression in cells to understand how they react during infections. On a multicellular scale, special imaging helps us see how our body's defenses function in different areas. At the organ scale, computer simulations help understand how parts of our lungs react to pathogens. Here computational fluid dynamics (CFD) are used to simulate airflow in the lungs. On a systemic scale everything is put together and computer models are used to figure out how air moves in our lungs and how different body parts work together during an infection. However, putting all this information together to form a complete picture is still a big challenge. But it is evident how this might help fighting pandemics in the future.[14]

6 Conclusion

In summary, DTs have emerged as a promising frontier in biomedicine, offering versatile applications across personalized medicine, drug development, surgical planning and potential insights into infectious diseases. Looking ahead, the future of Digital Twins hinges on advancements in computational prowess and interdisciplinary collaborations.

But there are still some major challenges to overcome before they might become a viable technology. Among these we count data standardization, data management, data security and the difficulty of implementing such technologies or transforming legacy systems to accommodate them. Other challenges are updating old infrastructure, the handling of sensitive data and the lack of standardized modeling approaches. This is further complicated by the high development costs, the complexity of the technology and the difficulties of implementing it into other systems, such as proprietary software or older IT infrastructure.[15]

On the biological side, scientists are still struggling with a lack of ground truth of the underlying biological systems and processes which DTs are trying to model. In essence, while Digital Twins offer immense promise in revolutionizing healthcare, the journey towards unlocking their full potential necessitates a deeper understanding of the human body's intricacies. In addition, there are significant technological and economical hurdles to overcome, before DTs can become a viable alternative to biological systems. Addressing this challenge through continued research and technological advancements will drive DTs toward a future where healthcare becomes increasingly precise, personalized, and impactful.[16]

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