

Received October 25, 2019, accepted November 8, 2019, date of publication November 14, 2019, date of current version December 2, 2019.

Digital Object Identifier 10.1109/ACCESS.2019.2953499

# A Survey on Digital Twin: Definitions, Characteristics, Applications, and Design Implications

**BARBARA RITA BARRICELLI<sup>ID1</sup>, (Member, IEEE), ELENA CASIRAGHI<sup>ID2</sup>, (Member, IEEE), AND DANIELA FOGLI<sup>ID1</sup>**

<sup>1</sup>Department of Information Engineering, Università degli Studi di Brescia, 25123 Brescia, Italy

<sup>2</sup>Department of Computer Science, Università degli Studi di Milano, 20133 Milano, Italy

Corresponding author: Barbara Rita Barricelli (barbara.barricelli@unibs.it)

**ABSTRACT** When, in 1956, Artificial Intelligence (AI) was officially declared a research field, no one would have ever predicted the huge influence and impact its description, prediction, and prescription capabilities were going to have on our daily lives. In parallel to continuous advances in AI, the past decade has seen the spread of broadband and ubiquitous connectivity, (embedded) sensors collecting descriptive high dimensional data, and improvements in big data processing techniques and cloud computing. The joint usage of such technologies has led to the creation of digital twins, artificial intelligent virtual replicas of physical systems. Digital Twin (DT) technology is nowadays being developed and commercialized to optimize several manufacturing and aviation processes, while in the healthcare and medicine fields this technology is still at its early development stage. This paper presents the results of a study focused on the analysis of the state-of-the-art definitions of DT, the investigation of the main characteristics that a DT should possess, and the exploration of the domains in which DT applications are currently being developed. The design implications derived from the study are then presented: they focus on socio-technical design aspects and DT lifecycle. Open issues and challenges that require to be addressed in the future are finally discussed.

**INDEX TERMS** Artificial intelligence, digital twin, human-computer interaction, Internet of Things, machine learning, sensor systems.

## I. INTRODUCTION

In 1956, John McCarthy organized a summer workshop, entitled the “Dartmouth Summer Research Project on Artificial Intelligence”, which is now considered by many [1], [2] the seminal event where Artificial Intelligence (AI) was officially declared a research field. At the workshop, researchers from several disciplines met to clarify, define ideas and establish a research program concerning “thinking machines”. They chose the name “Artificial Intelligence” for its broad sense, to avoid restricting the interests of this field to subjects such as cybernetics, automata theory and complex information processing.

Today, AI “concerns the theory and development of computerized systems able to imitate and simulate human intelligence and behavior” (Merriam-Webster

The associate editor coordinating the review of this manuscript and approving it for publication was Waleed Alsabhan<sup>ID</sup>.

Dictionary), essentially “being human-like rather than becoming human” [3], and “performing tasks normally requiring human intelligence, such as visual perception, speech recognition, decision-making, and translation between languages” (English Oxford Living Dictionary).

Since 1956, AI researches have succeeded in developing intelligent systems allowing machines doing not only all of the physical work, but also the reasoning, the predicting and the subsequent decision-making. Rather than trying to achieve a perfect replica of the human mind, AI systems exploit processes emulating human reasoning as a guide to provide both aiding tools and better services.

For this reason, and thanks to the continuous advances in the computational power, in Big Data processing, and in the machine learning (ML) and pattern recognition (PR) fields, AI applications are becoming a fundamental part of our everyday life, providing surprising benefits in several fields. Examples are researches in the medical fields, where

AI algorithms are developed with the aim of discovering novel biological relations [4] and treatments. Similarly, AI algorithms modeling biological structures and human reasoning are integrated either to develop Computer Aided Diagnosis Systems, aiding clinicians during their everyday diagnostics procedures [5], or to study organs' functioning and reaction to pharmacological treatments [6]–[8], eventually uncovering the hidden patterns and information encoded by the data, by reducing the data dimensionality to remove redundant information [9].

In the past twenty years, the advent of the Internet of Things (IoT) [10], [11] is changing the way data are exchanged among different sources. Indeed, the diffusion of technologies such as (embedded) sensors and actuators connected through the Internet, allows a continuous exchange of Big Data. This term refers to data Volume (having high dimensionality and requiring the storage of large amounts of data), Variety (data with heterogeneous nature, belonging to different sources), Velocity (the speed of production and acquisition, opposed to long processing time), and Value (the significance of the information carried by data) [12]–[14]. Luckily, scientific advances in data fusion techniques, high-dimensional data processing [9], big data analytics and cloud computing allow to store and elaborate Big Data to obtain important knowledge and improve the performance of physical systems.

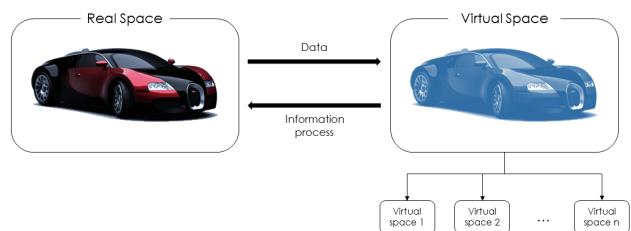
More specifically, the integration of AI models (of physical objects) and Big Data Analytics for processing IoT data [15]–[17] motivates one of the latest, and probably one of the most important advancement in the field of technology, that is, the Digital Twin (DT). DT models are gaining more and more interest for their potentials and strong impact in application fields, such as manufacturing, aerospace, healthcare, and medicine.

Despite successful DT technologies are now being investigated in the scientific field and are massively spreading in the corporate and business environments, literature works have never described in detail the characteristics of a generic DT. Indeed, each state-of-the-art paper concentrates on the development of few components of DTs.

In this work, we searched for answers to three specific research questions, related to the state-of-the-art definitions of Digital Twin technology, the main characteristics that a DT should possess, and the domains in which Digital Twin applications are currently being developed. After the presentation of the research background (Section II) and the methodology used for the study (Section III), three sections present the answer to each of the research questions (Section IV, V, and VI). In Section VII, we discuss some design implications that emerged from our analysis, while Section VIII presents the open issues and main challenges that still exist in this field of research.

## II. RESEARCH BACKGROUND

Since 1970, NASA creates mirrored systems to monitor unreachable physical spaces (e.g. spacecrafts in mission), and



**FIGURE 1.** Model of a digital twin. This picture is the result of an adaptation of Grieves' model [20].

eventually find out solutions to problems. The first and probably the most famous example, is a simulated environment developed during the Apollo 13 mission [18]. When, two days after the launch, one of the oxygen tanks exploded, the NASA flight control team in Houston found a solution by simulating and then analyzing such condition on a physical model (a mirrored system) of the spacecraft Apollo 13 and its components. Thanks to the simulated environment, engineers modeled and tested possible solutions and successfully found a way out, which was an improvised air purifier. From earth, engineers instructed the astronauts how to build it with materials available in the spacecraft. At the same time, astronauts on earth ran simulations at Houston and Kennedy Space Center to test procedures for getting the crew of Apollo 13 back to earth alive.

This example shows the potential of virtual and simulated models, nowadays considered the precursors of DTs, in bridging physical and virtual spaces; however, such models are not considered proper DTs, due to the lack of a seamless connection and real-time data exchange allowing the continuous, or at least periodic, “twinning” of the digital to the physical.

The DT concept has been informally introduced in 2002 by Michael Grieves, during his presentation about product life-cycle management (PLM) with the title “Conceptual Ideal for PLM”. Grieves' DT model, later formalized in his white paper [19] and in [20], was composed by three primary elements (see Fig. 1): 1) a real space containing a physical object; 2) a virtual space containing a virtual object; 3) the link for data flow from real space to virtual space (and virtual sub-spaces), and for information flow from virtual space (and sub-spaces) to real space. This last element is the enabler of data exchange, thus allowing the convergence and synchronization of the virtual and physical systems.

After just one year, the work of Framling *et al.* [21] proposed “an agent-based architecture where each product item has a corresponding virtual counterpart or agent associated with it”. Exploiting the seamless connection provided by the spread of Internet technologies, the envisioned agents (the product DTs, or at least their ancestors) should guarantee the synchronization with their physical counterpart, providing also services for them. The authors' proposal is based on the consideration that an effective PLM system should always have access to a faithful view of the product status and information, from when it is planned and

manufactured, through its time of use, and until the time of disposal. At the beginning of the millennium, the practice was to convey all this information by paper documents accompanying the product; however, this was not an effective practice, because product information usually changes during product lifecycle, so that huge amount of data (and papers) were needed to describe the product in its different phases. As a result, synchronization between product data and the products themselves was always missing. Obviously, the proposed virtual-physical coupling needs a way to uniquely identify the physical product, in order to allow a one-to-one (bijective) connection between the DT and its physical twin.

Given the will to increase knowledge about the concept of mirrored system and a desire to reduce costs and resources, NASA started investigating and developing DTs for its space assets. Precisely, ten years after Grieves' definition, NASA researchers, in their roadmap [22], which is now considered by aerospace researchers [23], [24] as the seminal work about DTs, suggested that DT would improve performance in the field of aviation. In this context, the authors defined the DT as "an integrated multi-physics, multi-scale, probabilistic simulation of a vehicle or system that uses the best available physical models, sensor updates, fleet history, etc., to mirror the life of its flying twin. The digital twin is ultra-realistic and may consider one or more important and interdependent vehicle systems, including propulsion/energy storage, avionics, life support, vehicle structure, thermal management/TPS, etc.".

In the same years, Tuegel *et al.* [24]–[26] proposed a conceptual model of how the DT can be used as a virtual sensor for predicting the life of aircraft structure and assuring its structural integrity. All the aforementioned research works brought to the definition of the Airframe Digital Twin (ADT) [25], [26], a computational model of individual aircrafts (tail-number specific). This model had the potential to improve the way U.S. Air Force aircrafts were managed over their entire lifecycle by creating individualized structural management plans. The ADT could provide configuration control for each aircraft in the inventory, and, thanks to computational simulations, could serve as a virtual health sensor and could provide a forecast of future maintenance needs for an individual aircraft.

In 2013, the U.S. Air Force [27] explicitly mentioned and interchangeably used the Digital Thread and the Digital Twin concepts, highlighting that they have a historical memory and the ability of exploiting previous and current knowledge to gain state awareness and system prognosis, thus providing the "agility and tailorability needed for rapid development and deployment". However, in other research works, the Digital Thread concept has been distinguished from the DT concept; e.g., in [28] it is claimed that digital thread refers to the "communication framework that allows a connected data flow and integrated view of the asset's data throughout its lifecycle across traditionally siloed functional perspectives".

As explained in [29], the digital thread is the communication framework that digitally links all the product data

(i.e., model data, product structure data, metadata, effec-tual data, and process definition data including supporting equipment and tools) to allow each user to access a single, consistent definition of the product and its modifications during its whole lifecycle. For a manufacturer, it provides a single reference point for design, engineering, and manufacturing.

Essentially, the digital thread allows linking and integrating all aspects of a system and models from various disciplines through common inputs and data flows, in an always-available, up-to-date single electronic representation that every decision maker involved in the process can access, thus speeding up design time, and enabling trades across traditionally isolated disciplines [30]. The digital thread concept raises the bar for delivering "the right information to the right place at the right time" [28].

Since its first declaration by the U.S. Air Force [27], the digital thread and DT concepts are gaining much interest beyond the aerospace and defense industry; being an essential part of the digital thread, and allowing the integration of digital manufacturing and cyber-physical systems, they are key point of Industry 4.0 [31]–[33] and Smart Manufacturing [34].

However, as they were defined, the digital thread only ensured the connection of heterogeneous elements; it did not have the DT's potentials of monitoring, maintaining, and optimizing the physical system. For this reason, and after including connection capabilities into the DT model, the latest has replaced the digital thread and is now considered, e.g. by "Siemens Theorists and Dreamers" [35], [36], as the next Generation Digital Thread.

At the state of the art, there are several papers reviewing the DT field. Our study differs from those works in different ways. First of all, our study was not focused on searching among papers framed in specific fields of applications, whilst many reviews on DTs present deep analyses focusing exclusively on the manufacturing domain [16], [37]–[40]. Our study considers different application domains and describes all of them in detail.

As to the study methodology, we did a systematic literature review and searched for papers without setting a specific time frame; on the contrary, other works that present systematic reviews have the searches performed with specific time frames (e.g., from 2001 to 2006 [41], from 2014 [37], from 2005 to 2016 [38]).

Furthermore, our study also considers sociotechnical design implications, and specifically focuses on the interaction of domain experts, designers and all stakeholders with the machines (either physical or virtual). To our knowledge, this aspect, which is crucial for a successful DT development, has never been identified and described by any state-of-the-art works.

Finally, it is important to point out that this study stems from, and is focused on, an interest in Digital Twin as a concept linked to AI. Despite this fact, we are fully aware of the influence that different other disciplines play

in DT development and that the same concept could be studied from other points of view (not AI-centered).

### III. METHODOLOGY

At the beginning of our study, we identified three specific research questions that led our entire research work:

- 1) RQ1: What are the definitions of Digital Twin that have been published in literature?
- 2) **RQ2: What are the main characteristics that should be present in a Digital Twin?**
- 3) RQ3: What are the domains in which Digital Twin applications have been developed and described in scientific literature?

We defined two different strings of words to be searched on Google Scholar: “digital twin artificial intelligence” and “digital twin model”. We chose Google Scholar to avoid bias in favor of any specific scientific publisher, as suggested by [42]. We did not specify a time range. The search was performed in July 2019, so the upper date range limit coincides with this date.

From the results, we excluded duplicates, extensions of previous published works, and papers not written in English, while we included all documents presenting DT applications (e.g., technical reports, white papers, online articles). We then performed snowballing on the set of found papers: we used the reference list of every paper for identifying possible new papers to include in the study. Again, we applied the same exclusion/inclusion criteria listed before. We stopped once no new papers were found and we had the definitive start set of 75 papers, concerning DT technology, which has been used for the study.

### IV. DIGITAL TWIN DEFINITIONS

To respond to RQ1, in this section we present the results of the analysis of the papers included in the study that present a definition of DT or other concepts (i.e. digital thread and product avatar) that are used to express the same meaning.

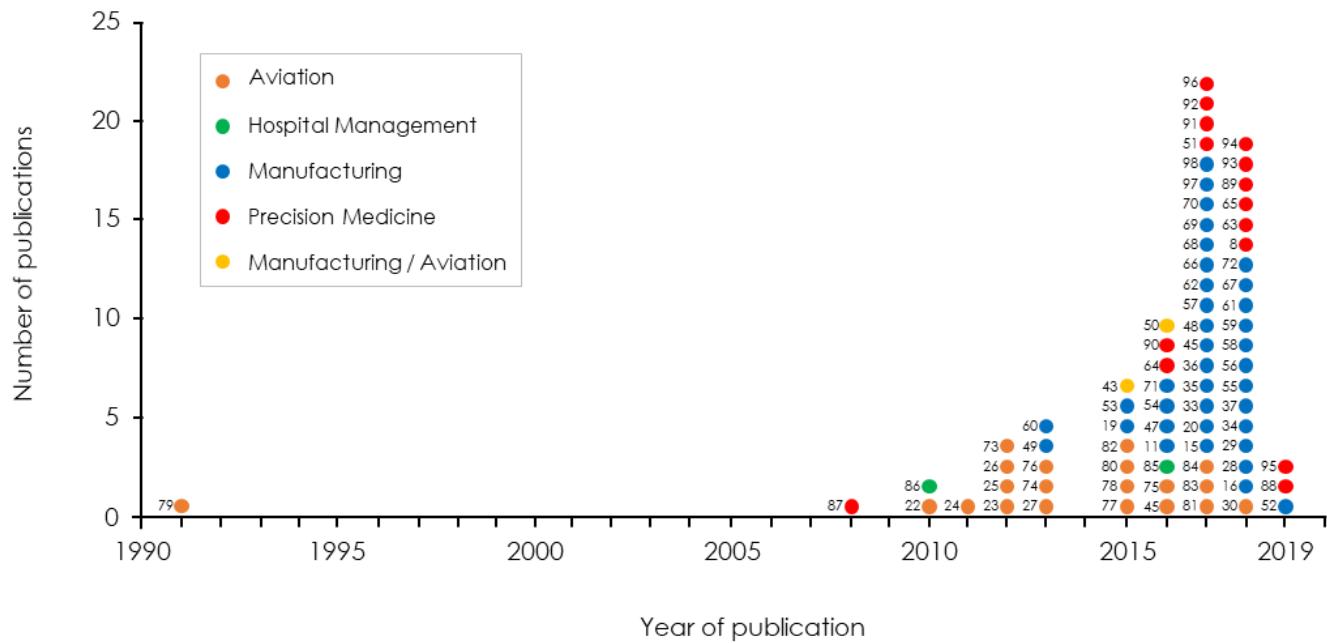
DTs can be defined as (physical and/or virtual) machines or computer-based models that are simulating, emulating, mirroring, or “twinning” the life of a physical entity, which may be an object, a process, a human, or a human-related feature. Each DT is linked to its physical twin through a unique key [43], [44], identifying the physical twin, and therefore allowing to establish a bijective relationship between the DT and its twin. **A DT is more than a simple model or simulation** [19], [37], [45], [46]. A DT is a living, intelligent and evolving model, being the virtual counterpart of a physical entity or process. It follows the lifecycle of its physical twin to monitor, control, and optimize its processes and functions. It continuously predicts future statuses (e.g., defects, damages, failures), and allows simulating and testing novel configurations, in order to preventively apply maintenance operations. More specifically, **the twinning process is allowed by the continuous interaction, communication, and synchronization (closed-loop optimization) between the DT, its physical twin and the external, surrounding environment.**

Descriptive data are continuously exchanged and updated thanks to the (nowadays-affordable) real-time data uploading and big data storage capabilities. Thanks to real-time updates from its physical twin and from digital twins in the surrounding environment, the digital twin is always aware of what is happening in the physical world. By applying data fusion algorithms followed by Big Data analytics and AI descriptive algorithms, it evolves together with its physical twin thanks to a modular and highly parameterized architecture, which allows a fast reconfiguration. The DT is then constantly synchronized to its physical twin and changes with it, and the change reflects, and is governed by, the properties of the physical object being mirrored. **Beside this comprehensive emulation, being equipped with AI, the DT is able to uncover information including system description, hidden patterns, and unknown correlations. The ability of recording, controlling, and monitoring the conditions and changes of the physical system allows to apply AI predictive and prescriptive techniques for forecasting failures, testing the outcome of possible solutions, and activating self-healing mechanisms. This brings to the so-called predictive maintenance approach, where failures are predicted, and fixes and/or modifications can be simulated in order to avoid errors or find the best solutions.** This real-time system modification leads to dramatic improvements, e.g., in the manufacturing field as well as in medical-system engineering, since the prediction capability allows planning repairs or maintenance, thus preventing disruptions and potentially costly breakdowns. The DT allows all users and stakeholders to access and monitor the physical twin status, no matter where they are physically located. This brings to improved and faster cooperation.

A DT may be part of a Cyber-Physical System [47], [48], which can be described as a set of physical entities (e.g. devices, objects, equipment, humans) that interact with a virtual cyberspace through a communication network. Each physical entity has its cyber part as its digital representation, culminating in the DT.

In literature, the DT concept is viewed as similar to that of “Product Avatar” (PA), which is the digital counterpart, or a set of digital counterparts, of an “Intelligent” or “Smart Products”, where “intelligent products are physical items, which may be transported, processed or used and which comprise the ability to act in an intelligent manner” [49]. Specifically, PAs have been developed to let any user or stakeholder access the attributes and services of the Smart Product during its whole lifecycle [43], [49], [50]. **The differences between DTs and PAs is that they derived from two different research lines** [43], **have different capabilities, and are therefore used for different purposes.** In particular, as explained in Section VI.A, while the DT has the intelligence for triggering actions on its physical twin, the intelligence of the PA is limited to making it a perfect virtual replica of the physical twin.

To sum up, data fusion, AI applications and big data analytics harnessing IoT sensors allow communication and intelligent interaction between a generic physical system



**TABLE 2.** Classification of literature per application domain.

Application Domain	References
Manufacturing	
- <i>With definition</i>	[11], [15], [16], [19], [20], [28], [29], [33], [34], [43], [46], [47], [48], [49], [52], [53], [54], [55], [56], [57], [58], [59], [60], [61], [62], [66], [67]
- <i>Without definition</i>	[35], [36], [37], [50], [68], [69], [70], [71], [72], [97], [98]
Aviation	
- <i>With definition</i>	[22], [24], [27], [30], [43], [45]
- <i>Without definition</i>	[23], [25], [26], [50], [73], [74], [75], [76], [77], [78], [79], [80], [81], [82], [83], [84]
Hospital Management	
- <i>With definition</i>	--
- <i>Without definition</i>	[85], [86]
Precision Medicine	
- <i>With definition</i>	[51], [63], [64], [65]
- <i>Without definition</i>	[8], [87], [88], [89], [90], [91], [92], [93], [94], [95], [96]

This table classifies the literature analyzed for this study according to the application domain. Two references ([43] and [50]) present works that belong to two domains (Manufacturing and Aviation), therefore they appear twice in this table.

Analogously, we classify in Table 2 the references according to the application domain they are framed in and we point out if the references provide or not a definition for the concept they present (Digital Twin, Digital Thread, or Product Avatar).

As reported in Table 1, 31 papers out of 75 provide a definition of Digital Twin concept. Due to repetition of the same definition in more than one paper, there are 29 different definitions that can be grouped according to key points (see Table 3). 11 out of 34 papers use the key points “virtual”, “mirror”, and “replica” to define the Digital Twin concept, and 8 of them are linked to works in the manufacturing application domain.

## V. DIGITAL TWIN CHARACTERISTICS

This section focuses on RQ2. By analyzing the selected papers, we have been able to identify the main characteristics that DTs are supposed to possess. Both the physical and the digital twins must be equipped with networking devices to guarantee a *seamless connection and a continuous data exchange* either through direct physical communications or through indirect cloud-based connections.

Thanks to the *seamless connection*, the DT continuously receives *dynamic (eventually sensed) physical twin data*, which describe the physical twin status and change with time

**TABLE 3.** Digital twin definitions.

Key points	Definitions	References
Integrated system	Integrated multi-physics, multiscale, and probabilistic simulation composed of physical product, virtual product, data, services and connections between them.	[16], [57], [58]
	An ultra-realistic integrated multi-physics, multiscale, probabilistic simulation of a system.	[22]
	A big collection of digital artifacts that has a structure, all elements are connected and there exists meta-information as well as semantics.	[53]
	Comprehensive physical and functional description of a component, product or system together with all available operational data.	[55]
	A systematic approach consisting of sensing, storage, synchronization, synthesis and service.	[60]
Clone, counterpart	Computerized clones of physical assets.	[15]
	The virtual and computerized counterpart of a physical system.	[46]
	Functional system formed by the cooperation of physical production lines with a digital copy.	[33]
Ties, links	Connections of data and information that ties the virtual and the real product together.	[19]
	New mechanisms to manage IoT devices and IoT systems-of-systems.	[11]
	Technology that links the real and the digital worlds.	[65]
Description, construct, information	Comprehensive physical and functional description of a component, product or system.	[45]
	A digital information construct about a physical system.	[24]
	The notion where the data of each stage of a product lifecycle is transformed into information.	[62]
Simulation, test, prediction	A safe environment in which you can test the impact of potential change on the performance of a system.	[51]
	Reengineering computational model of structural life prediction and management.	[20]
	A simulation based on expert knowledge and real data collected from the existing system.	[54]
	Virtual models for physical objects to simulate their behaviors.	[56]

**TABLE 3.** (Continued.) Digital twin definitions.

Virtual, mirror, replica	A virtual representation of the system.	[27]
	Digital mirror of the physical world.	[61]
	Digital model that dynamically reflects the status of an artifact.	[63]
	Detailed virtual model of ourselves. <sup>a</sup>	[64]
	Virtual representation of a real product.	[47]
	A digital copy of a physical system.	[66]
	Virtual model of a physical asset.	[67]
	A replication of real physical production system.	[59]
	Cyber copy of a physical system.	[48]
	A dynamic digital representation of a physical system.	[52]
	A virtual model of physical object.	[34]

The definitions reported in this table are the result of the authors' elaboration and are not to be intended as precise quotations from the original sources.

<sup>a</sup> This definition refers to Human Digital Twins.

along its lifecycle, and *dynamic environment data* describing the surrounding environment status. Moreover, it continuously sends back to its physical twin, to the domain experts, and to other DTs in the environment, predictions and prescriptions for system maintenance and for function optimizations.

There are mainly three types of *communication processes* that need to be designed:

- 1) Between the physical and the virtual twin.
- 2) Between the DT and different DTs in the surrounding environment.
- 3) Between the DT and domain experts, which interact and operate on the DT, through usable and accessible interfaces.

All the exchanged data must be stored in a *data storage* system, accessible by the digital twin. Together with *dynamic data*, the data storage contains *historical static data*, which reflect the physical twin memory and record historical information provided by human expertise or by past actions, and *descriptive static data*, which describe important characteristics of the physical twin that must not change over time (e.g. its requirements and constraints, in the case of a product or device [44]).

Moreover, since the DT continuously receives data from different sources, it must exploit *proper ontologies* for data comprehension and formalization. Ontologies are a well-established approach for leveraging data and information sources with semantics, thus providing a shared, machine-understandable vocabulary for information exchange among dispersed agents (e.g. humans and different machines) interacting and communicating in an heterogeneous distributed intelligent system [46], [99]–[103].

The DT must be able to treat high-dimensional data, and must therefore be equipped with effective *high-dimensional data-(de)coding and analysis techniques*, as well as *data fusion algorithms* for integrating the multiple data sources and produce more consistent, accurate, and useful information than that provided by any individual data source.

DT technology encompasses a continuously improving AI, which refers to supervised/unsupervised learning algorithms, whose predictive capability is refined as they process the continuously received sensed data from the physical twin and the surrounding environment. This virtual (cognitive) brain applies descriptive, predictive, and prescriptive algorithms thus allowing to perform a set of tasks as an intelligent product.

Among AI algorithms, *feature selection and feature extraction tasks* reduce the data dimensionality while keeping the most informative data. This allows extracting and storing only the useful information ("right data"), thus reducing the cost for storage and the computational processing costs [66].

Feature extraction and selection is important for dealing with big data. Extracting the salient value and information associated with the continuously acquired and exchanged big data is important to enable effective real-time cyber-physical synchronization and the so called "closed-loop optimization" [44], [56]. Closed-loop optimization refers to the continuous exchange of data between the cyber and physical worlds in order to continuously optimize the physical side. The DT is a virtual model of the physical object with the potential of understanding changes in the status of the physical entity through sensing data, to analyze, predict, estimate and optimize changes. The physical entity should respond to the changes according to the optimized scheme received from the DT [53], should continuously send real-time data describing novel statuses, and then be ready to respond to novel optimizing "commands" received from the DT. Through such cyber-physical closed-loop optimization, DT technology could enable the performance improvement of the whole manufacturing process [44].

The DT characterizes, understands, clusters, and classifies the input data from the physical twin and/or the surrounding IoT environment, thanks to *pattern recognition, unsupervised/supervised learning, and statistical applications* [66]. This allows to detect changes and identify important patterns and trends by analyzing data.

The DT has *self-adaptation and self-parametrization capabilities*, which allow to resemble the physical twin during its whole lifecycle [67], [97]. This task might be easily and quickly accomplished, by developing a highly modular and parameterized DT. Modularity guarantees that changes in one module do not affect other modules. Parameterization guarantees an easy modification of DT status. Evolutionary algorithms [104], or stochastic optimization [59] may be used for choosing the parameter settings producing the best fit between the DT and its twin.

The DT exploits *predictive analytics* [105], [106] to predict future statuses and important changes (such as failures) in the product lifecycle.

The DT uses the result of descriptive and predictive techniques as input of *prescriptive analytics* [107] to make decisions relevant to its own destiny, by computationally determining a set of high-value alternative actions or decisions given a complex set of objectives, requirements, and constraints (described by the historical and static data). It eventually applies (*stochastic*) optimization algorithms to achieve the best outcome, while addressing uncertainty in the data [59].

Beyond applying predictive and prescriptive algorithms, the DT codes the computed prescriptions and optimization schema by exploiting proper *ontologies and high-dimensional data-coding techniques*. This allows sending feedback to both the physical twin and to other DTs in the whole environment. On the other side, end users may exploit interaction interfaces to access the computed information and to view the DT status.

Finally, the DT provides *modeling and simulation applications* for representing, in a realistic and natural way, both the current status of the physical twin, and different “what-if” scenarios.

## VI. DIGITAL TWIN APPLICATION CASES

This section is aimed at responding to RQ3. From our analysis, several application cases of Digital Twin emerge, and they are mainly grouped in three domains: *manufacturing* (which also includes *model-based system engineering, MBSE*), *aviation*, and *healthcare*.

### A. MANUFACTURING

Several works in the manufacturing field exploit the DT to optimize all aspects of the product manufacturing process and process lifecycle. Among them, the work of Rosen *et al.* [53] highlights that the usage of DTs may allow to develop a computerized system supervising each step of manufacturing through a modular approach. Precisely, the authors propose a modular Smart Manufacturing approach [108], where autonomous modules execute high-level tasks without human control, deciding among a set of alternative actions, and responding to failures or unexpected events without affecting the work of other modules (thus avoiding changes and re-configurations at the supervisory level). To this end, the modules must have access to very realistic information describing the current state of the process and of the products. This can be obtained by using faithful virtual replica of the physical entities, i.e. a DT. In the depicted scenario, DTs also allow a continuous communication between the system and the physical asset. Though highlighting its potential in the field of manufacturing, the work of Rosen *et al.* [53] seems referring to the DT as a realistic model or simulation with the ability of continuously communicating with its physical twin, which is a too simplistic way for describing it. DTs must not be confused with simulations or with the avatars produced

by virtual/augmented reality applications [49]. As already introduced in Section IV, what makes a simulated model or (Product) Avatar a DT is the artificial intelligence and the continuous (or at least periodic) real-time data exchange between the physical model and its virtual counterpart. Moreover, the DT must be developed by integrating the knowledge provided by human experts and by real (historical) data collected by present and past systems [54]. Such data are required not only to describe the physical twin’s behavior but also to derive solutions relevant for the real system [45], [55]. Essentially, DTs are particular simulations, specifically designed for their intended purpose, which evolve along with the real system, during its whole life cycle.

Similar to the work of Rosen *et al.* [53], Qi and Tao [56] presented the benefits of a Data Driven Smart manufacturing (BDD-SM) approach exploiting DTs. BDD-SM exploits sensors and the IoT to produce and transport big data. These data can be processed through AI applications and big data analytics executed on the cloud, to monitor the processes, identify failures, and find the optimal solution. On the other side, DT technology enables manufacturers to manage the real-time and two-way mappings between physical object and digital representation, bringing to an “intelligent, predictive, prescriptive” approach where targeted monitoring, optimization, and self-healing actions are taken.

Though the DT model is generally viewed as a three-dimensional structure where physical entities and their virtual models communicate through proper connections, Tao and Zhang [57], Tao *et al.* [58], while describing their concept of DT shop floor, gave more importance to the intelligent applications (called services) embedded into the virtual parts, and to the fused data belonging to different sources. Precisely, beside the physical space (PS), the virtual space (VS) twinning the PS, and the connection between them, the two elements introduced by the authors are the Service System (SS) and the Digital Twin Data (DTD), which are processed by SS. The SS is an integrated software platform for management, control, and optimization, which contains all the functions (sub-services) for providing solutions to specific requests from PS and VS. DTD is the repository of current and historical data comprising fused data converging information from the PS, VS, and external environment. Playing a central role in the integration of data flows gathered in a heterogeneous environment, it provides comprehensive and consistent information.

A similar structure has been envisioned in [59], where the DT model comprises five enabling components: PS, VS, sensors, integration technologies, and analytics. Sensors allow bidirectional real-time communication between PS and VS using integration technologies, which include communication interface and security. Exchanged data are processed through analytics techniques that compute prescriptions on the basis of simulation results.

Several state-of-the-art works in the field of manufacturing bring to light the fact that a continuous interaction, convergence, and self-adaptation of the DT are of great importance

for guaranteeing a full synchronization between the DT and its physical twin, which is necessary to obtain consistent monitoring, optimizations, predictive maintenance processes, and so on [56]. At the state-of-the-art, the synchronization need has indeed been highlighted and studied by several authors. Precisely, Uhlemann *et al.* [68], Uhlemann [69], while working on the realization of a Cyber Physical Production System, identified real time multi-modal data acquisition, and subsequent simulation-based data processing, as important factors allowing cyber-physical synchronization. Indeed, multi-modal data acquisition enables a coupling of the production system with its digital equivalent as a basis for minimizing the delay between the time of data acquisition and the creation of the DT.

In the context of manufacturing optimization, Lee *et al.* [60] described their vision regarding a Cyber Physical System governing a specific manufacturing company by managing and optimizing all the machinery and equipment processes through the inter-connection among DTs. In this context, they described a DT (of a machine and/or equipment) as a “coupled model that operates in the cloud platform and simulates the health condition with an integrated knowledge from both data driven analytical algorithms as well as other available physical knowledge. The DT model can also be described as a 5S systematic approach consisting of Sensing, Storage, Synchronization, Synthesis and Service”. In this context, the authors concentrated on the potentiality of a DT to process historical data acquired from the early design, system information, and physical knowledge, to “construct a digital image” (simulation model) of the machine that continuously records and tracks machine conditions during later utilization stages, thus enabling machines and systems with self-aware capabilities.

A recent work in the field of MBSE is described in [61], where authors suggested the usage of DT models for factory design and brought to evidence the potentials provided by a modular parameterized architecture of the DT model. Factory design concerns the design of the factory concept, the design of the optimal layout and equipment configuration, the design of the logistic unit control strategy, and the whole integration of all the equipment in the production line, to finally build the physical factory. An optimal design allows speeding up the production, while simultaneously cutting the production costs. Its complexity requires frequent changes from its initial version to its final version, and this is particularly true when considering traditional factories, which are increasingly transforming into smart factories, thus requiring a simultaneous factory redesign. Exploiting the DT to virtually simulate the designed factory system, the designers' decisions are tested, eventually optimized (by analyzing the current state, considering also historical data) and then validated. Modularity and parameterization of the DT model allow to implement generic functions that can be tuned (by changing the parameters values) to solve similar problems. A modular approach facilitates multi-person collaboration in the development of the factory. Moreover,

changes in the factory design are quickly implemented since they require the change of only a small number of modules. Following this implementation idea, the DT starts living when the factory concept is created in the designers' brain, and it continuously reflects and evolves with the evolving factory design, until its last stage, when the DT fully resembles the factory to be practically built. When the factory is being used, a modular design also allows a fast and easy automatic reconfiguration of small modules in case of necessary changes in the production line [70].

Another work [71] presenting a Web application to develop a digital factory (DF), which is the DT of a factory, similarly exploits a modular structure where ontologies play a key role in the representation of the capability model of the factory. The DF provides a virtual representation of a manufacturing facility, in terms of installed machinery, material handling equipment, and layout. Thanks to such DT, both manufacturers can monitor their (physical and virtual) factory, and external customers have an easier access to the factory. Through exploring and querying the capability model of DFs, companies can develop a deeper and more precise understanding of the technological capabilities of prospective suppliers, thus making more informed decisions when building supply chains. Thanks to a modular architecture, the DF is easily modified to reflect the changing physical factory and the reconfiguration happens in real-time. The work reported in [33] highlighted the optimization advantages provided by DTs of factories.

Since modularity allows a real-time reconfiguration and self-adaptation, the work of Abramovici *et al.* [62] presents a conceptual approach to the reconfiguration of Smart Products. The presented method monitors, controls, and reconfigures the physical object by directly working on its DT. Recalling the intelligent Tesla cars, the efficacy of the approach is prototypically demonstrated by considering a model environment for smart cars, which are temporarily reconfigured during their use phase.

## B. AVIATION

While DT technology in manufacturing is appreciated both for allowing predictive maintenance [57] and for its capability of optimizing and speeding production [72], in the aviation field the DT is mainly used as a mean for predictive maintenance – e.g. to detect dangerous changes in the structural aircraft and then triggering self-healing mechanisms – decision support, optimization, and diagnostics. Examples are state of the art works for assessing the prediction confidence of a DT model; by defining a quality measure to be used as a decision-making metric for autonomous model fidelity selection, the DT model that best represents the interactions of the multi-physics, fluid-thermal-structural coupling applicable to hypersonic flow conditions of aircraft can be chosen [73]. In the work of Yang *et al.* [74], authors described an aircraft DT exploiting an automatic image tracking method to obtain insights about the crack tip deformation and crack growth behavior of aluminum alloy and steel.

The acquired information allows the DT model to predict sub-cycle fatigue crack growth mechanisms of aircraft materials during the whole aircraft lifecycle, thus allowing to reduce the cost and time for both development and maintenance [75]. Majumdar *et al.* [76] developed a DT modeling the way multi-physical environments (such as electrical field) cause microstructural changes in structural composites and hence may affect structural performance. Bielefeldt *et al.* [77] proposed a DT detecting fatigue cracks by using a finite element model of an aircraft wing containing shape memory alloy particles embedded in key regions of the aircraft structure. Particularly, authors modeled an aircraft wing subjected to loading experienced during flight, and then simulated the response of the localized particles in the key regions to detect structural dangerous changes. To provide diagnostic and prognostic capabilities to the DT of an aircraft, the work proposed in [78] used the Finite Element Alternating Method (FEAM) for computing Stress Intensity Factor [79], and an improved Moving Least Squares (MLS) law for computing fatigue crack growth rates [80]; **in this way, high-performance fatigue mechanics were used to detect and predict damaged aircraft structures.** In [81] authors discussed a DT exploiting a modified dynamic Bayesian network structure to control the state of aircraft wings. Based on a similar idea, the work reported in [82] combined developments in modeling of fatigue-damage, isogeometric analysis of thin-shell structures [109], and structural health monitoring [110], to develop a computational steering framework for fatigue-damage prediction in full-scale laminated composite structures, and successfully tested it on wind-turbine blades. To perform real-time prediction of damage, some state-of-the-art aircraft DTs analyze the responses of a guided wave [83]. As the guided wave interacts with damage, the signal attenuates in some directions and reflects in others. This results in a difference in signal magnitude, as well as phase shifts between signal responses for damaged and undamaged structures. During damage detection and evaluation, accurate estimation of damage size, location, and orientation is computed by evaluating the cumulative signal responses at various pre-selected sensor locations using a genetic algorithm [111]. The work of Zakrajsek and Mall [84] introduced a DT model (DTw) of a specific aircraft tire at touchdown. The proposed DTw was built from high fidelity testing data with the aim of improving the tire-touchdown wear prediction to avoid tire flat spots and mishaps, which might cause high program costs, and increase the logistical and environmental footprint of the aircraft. Since flat tires are mainly caused by non-ideal touchdowns (generating spin-up) during landings, the developed DTw guides the various landing parameters, e.g., touchdown speed, sink rate, yaw angle, and tire conditions (either new or worn), by considering the probability of failure (POF) for varying distributions of such parameters. The described DTw is notable since it concerns the DT of a product component (the tire of the aircraft) in a specific moment of its lifecycle (the touchdown). This example brings to light that the DT of a whole product

usually comprises, or interacts with, several and not necessarily simpler DTs of the product components.

The aforementioned DTs are examples of AI machines that should not be considered as independent and autonomous computational models [54]; as mentioned in Section VII, human expertise, supervision and intervention are some of the key factors for their successful development and usage. Each DT should be continuously supervised, to eventually run simulations and plan intervention actions on the physical system, but also to be modified and improved.

### C. HEALTHCARE

In the healthcare context, DTs have been firstly used for predictive maintenance of medical devices and for their performance optimization (in terms of examination speed and energy consumption). Other applications of the DT technology regard the optimization of hospital lifecycle. Examples of DTs applied to hospital management optimization are those developed by GE Healthcare. This large enterprise has long been focusing its predictive analytics platform and AI applications to the transformation of large and various patient data into actionable intelligence.

The final aim is to help hospitals and government associations in the management and coordination of patient care initiatives from a social and population perspective. As an example, leveraging medical AI applications, GE Healthcare developed a “Capacity Command Center” [85] that applies simulations and analytics for better decision-making in the Johns Hopkins Hospital in Baltimore. By building a DT of patient pathways, the hospital predicts patient activity and plans capacity according to demand, thus significantly improving patient service, safety, experience, and volume.

Similarly, Siemens Healthineers has developed a DT for optimizing the Mater Private Hospitals (MPH) in Dublin [86], which was suffering from growing patient demand, increasing clinical complexity, ageing infrastructure, lack of space, increase of waiting times, interruptions, delays, and rapid advances in medical technology, which were evidencing the need to implement additional equipment. To overcome these challenges, MPH and Siemens Healthineers redesigned the radiology department by developing an AI computer model of the radiology department and its operations. The result was a medical DT enabling digital process optimization by usage of workflow simulations and testing of different new operational scenarios and layouts. The faithful and realistic 3D animations provided by the DT, as well as the produced descriptive and quantitative reports, allows predicting the operational scenarios and instantly evaluating alternative options to find the right solution to transform care delivery.

In the medical and clinical fields, the interest in DT technology is often due to the aim of building a human DT. A human DT could show what is happening inside the linked physical twin’s body, making it easier to predict the occurrence of an illness by analyzing the real twin’s personal history and the current context such as location, time, and

activity [63]. This would allow a radical paradigm shift in the way treatments are delivered in medicine, which is a shift from the “one-size-fits-all” treatments to tailor-made treatments, based on the individual “physical asset”, which is defined by all the structural, physical, biological, and historical characteristics of the individual. The branch of healthcare promoting individualized treatments in healthcare is generally referred to as “precision medicine” [112] (more generally referred to as “personalized medicine”), an emerging approach for disease treatment and prevention encompassing the use of new diagnostics and therapeutics, targeted to the needs of a patient based on their own genetic, biomarker, phenotypic, physical or psychosocial characteristics [113]. Essentially, patients are treated as individuals, rather than according to some “norm” or “Standard of Care” (delivering the right treatments, at the right time, to the right person) [114], [115].

The precursor of the human DT is the Virtual Physiological Human (VPH) [64], a concept first discussed in the late nineties, almost 20 years ago. It is a detailed computer model developed to “enable collaborative investigations of the human body as a single complex system”. By customizing a VPH to any patient, researchers and clinicians would have a platform to test any treatment protocol. A VPH may act as a “Virtual Human Laboratory”, facilitating for instance in-silico clinical trials or testing [116].

The great deal of research effort [87] devoted to the development of VPHs has brought to the development of computational models such as the “AnyBody Modeling System” (see <https://www.anybodytech.com>), which allows to simulate the human body working in concert with its environment. With the AnyBody model users can run advanced simulations to calculate: 1) individual muscle forces; 2) joint contact-forces and moments; 3) metabolism; 4) elastic energy in tendons; and 5) antagonistic muscle action.

A physiological model virtualized by a DT would allow physicians to make in silico predictions of how the real organ might behave in any given situation. The automated analysis provided by CAD systems would allow evaluating the effectiveness of tailored treatments, paving the way to the expansion of precision medicine. Particularly significant in this field are the continuous advances in the medical AI applications, simulations, and virtual reality, together with the spread of Picture Archiving and Communication Systems (PACS) [117], which provide economical storage and convenient access and exchange of medical examinations (mainly images) from multiple modalities (source machine types). Today, some DTs of organs (e.g. heart) or parts of human body (e.g. airway system) have already been developed. Note that, they differ greatly from the industrial approach; the main reason for this difference lies in the fact that humans are not equipped with embedded sensors, and medical data describing their status can be extracted only from medical examinations. Therefore, the seamless connection between a human and his DT cannot be guaranteed.

From the study presented in this paper it emerges that some organs’ DTs have already been used in the clinical practice as a valid aid for experts, while some others are still under validation.

The Living Heart [88] developed by the French software company Dassault Systèmes has been released in 2015 (May) and is currently available for research. It has been the first DT of organs that takes all aspects of the functionality of the organ (including blood flow, mechanics and electrical impulses) into account. The software requires input of a 2D scan, which is translated into a faithful 3D model of the organ. Thanks to the heart model, physicians can run hypothetical scenarios (e.g., adding a pacemaker or reversing the heart’s chambers) to predict the patient outcome and make decisions.

Another DT of heart, developed by Siemens Healthineers [89], is currently used for testing and research purposes by Cardiologists of the Heidelberg University Hospital (HUh) in Germany. To develop such a DT model, Siemens Healthineers has exploited the data collected in a vast database containing more than 250 million of annotated images, reports, and operational data. The AI-based DT model was trained to weave together data about the electrical properties, the physical properties, and the structure of a heart into a 3D image. To test the technology, cardiologists at the HUh created 100 digital heart twins of patients being treated for heart failure in a six-year trial, and compared the actual outcome (ground truth) with the predictions made by the computer after the analysis of the DT status. Preliminary results seemed promising but the conclusions after the experimental tests are not yet available.

Another example of organ DT is that of the human airway system, which has been developed by researchers at Oklahoma State University’s Computational Biofluidics and Biomechanics Laboratory (CBBL) [90]–[94]. Considering that patients receiving aerosol-delivered chemotherapeutic drugs have a lot to lose when tumor-targeting treatments “hit” healthy tissue, researchers at CBBL exploited the ANSYS computational fluid dynamics simulations to study the precision-delivery of an inhaler, which delivers cancer-destroying drugs to tumor-only locations in the lungs. They found that, though the drug is distributed evenly throughout the volume of the aerosol, upon reaching the lungs, the drug reaches its target with less than 25% of accuracy [91], [92]. The remaining drug falls on healthy tissue; beside the drug loss, this might also cause side effects and damage of healthy lung tissue. To solve this problem, authors firstly developed a prototype of human DT [93] virtualizing a standing 47 years old digital male with the high-resolution human respiratory system covering the entire conducting and respiratory zones, lung lobes, and body shell. This “individualized digital twin”, referred to as the “virtual human V1.0”, enabled ANSYS computational fluid dynamics simulations, and the subject-specific body shell also enabled the subject-specific health risk assessment for in-silico occupational exposure studies, including simulations of real-time ventilation, skin

absorption, and lung deposition. Moreover, it allowed the replacement of lung airways and body shells; this opened the way to its structural modifications (e.g., to make it either standing or seating, male or female, adults or kids, with or without lung diseases).

Leveraging their virtual human V1.0, experts at the CBBL created the virtual human V2.0, a human DT that could be made patient-specific by performing a CT/MRI scan of the patient and importing the geometry of the lungs into the shell of the digital twin. Exploiting the developed V2.0 DT, CBBL researchers then created a large group of human DTs (virtual population group - VPG), consisting in a set of detailed, high-resolution anatomical models. The VPG allowed analyzing variations in the general population or within specific subpopulation groups, increasing the statistical robustness of numerical studies. Precisely, authors could simulate several different scenarios of the aerosol particles' movement by varying parameters such as the diameters of the particles, inhalation flow rates and the initial locations of the medication within the aerosol. These simulations allowed to show that the design of a patient-specific targeted drug delivery method, which restricts the active drug's particle size and region within the aerosol (versus distributing them evenly throughout the spray), would allow to increase the local deposition efficiency of drugs to 90% [91].

The last example of commercialized organs' DT is the one developed by France-based startup Sim&Cure, which is virtualizing a patient-based aneurysm and surrounding blood vessels (see <https://sim-and-cure.com/>). Aneurysms are blood vessel bulges caused by a weakening in an arterial wall. They can be found in 2% percent of the population. A small, but terrifying, fraction of these aneurysms can then result in clots, stroke and death. Brain surgery is typically the last resort to repair aneurysms. Endovascular repair, however, is a less-invasive option that is associated with a lower risk. It uses a catheter-guided implant (a device with a certain size) to shore up damaged arteries and relieve the pressure on the aneurysm caused by irregular blood flow. However, choosing the device with an optimal size might be difficult even for experienced surgeons. The DT developed by Sim&Cure, which got the regulatory approval, has been developed to help surgeons select an optimal implant to form-fit both the cross-section and length of the aneurysm, thus optimizing aneurysm repair. Precisely, after the patient is prepared for surgery, a DT (represented by a 3D model) of the aneurysm and the surrounding blood vessels is created by processing a 3D rotational angiography image. The personalized DT allows surgeons to run simulations and helps surgeons gain a keen understanding of the interactive relationship between the implant and the aneurysm. In less than five minutes, numerous implants can be assessed to optimize the procedure. Preliminary trials have shown to provide promising results [95], [96], provided that there is good quality of 3D-Angiography base data [96], though further evaluation is required to clarify the impact of device-dimension modifications on outcome.

## VII. DESIGN IMPLICATIONS

In this section, we provide an overview of design implications we derived from this study. In particular, we first illustrate the need of a sociotechnical and collaborative approach to the design process, and then we outline two different lifecycles that describe a DT's life, from its design to its dismissal.

### A. SOCIOTECHNICAL AND COLLABORATIVE DESIGN

The variety, complexity and the increasing scale of DT design projects require all end users (also called "domain experts" because they are specialized in specific application domains different from Computer Science) to act in concert and collaborate in teams, by applying the respective knowledge to extend or modify the system. This allows satisfying needs and requirements that cannot be anticipated at design time. The need of finding new strategies to support such collaboration therefore becomes an open issue. The challenge is to bridge the communication gaps among stakeholders with diverse cultural and professional backgrounds. It is necessary to develop open-ended software environments that can be evolved and tailored in opportunistic ways to tackle the co-evolution of users and systems [119].

Collaborative design involving end users has emerged as a response to the needs felt by various organizations of adapting software to specific environments and users. When designing DTs, it has to be taken into account that during time the users and the environments will co-evolve [120].

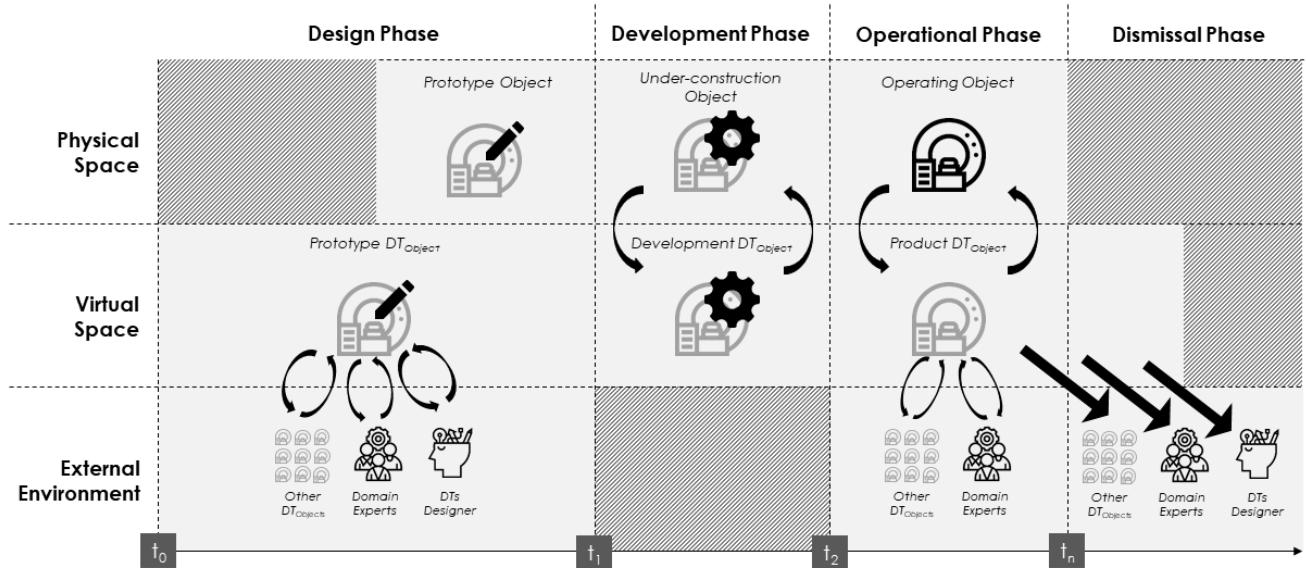
A sociotechnical design approach is needed to bridge the communication gaps raised during collaborative design activities [121]. Such approach can be framed into Human Work Interaction Design (HWID) [122], a lightweight version of Cognitive Work Analysis, addressing the concept of Work in Human-Computer Interaction.

To enable end users, even if domain experts, in modifying and extending features of DT systems, End-User Development (EUD) methods and tools can be implemented. As defined in [123], EUD is "the set of methods, techniques, tools, and socio-technical environments that allow end users to act as professionals in those ICT-related domains in which they are not professionals, by creating, modifying, extending and testing digital artifacts without requiring knowledge in traditional software engineering techniques".

EUD is well established both in literature and in practice when dealing with collaborative systems for domain experts, and is currently mostly used in the Internet of Things domain [124]–[128].

### B. LIFECYCLES

This study led us to describe two possible lifecycles for DTs, from their design to their dismissal. The former refers to a case where the object that has to be twinned still does not exist and, in this case, the design process simultaneously conceives both the object and its DT. The latter is about an object that already exists but has no DT in place; in this case, the design process focuses on the extension of the objects to make it connected.



**FIGURE 3.** The lifecycle of a computer tomography scanner and its DT, from their design to their dismissal. At first, during the Design Phase, the Prototype DT<sub>Object</sub> is designed, then the Prototype Object Design starts and the Prototype DT<sub>Object</sub> is eventually adapted according to technical requirements. The two prototypes are then used in the Development phase to obtain the operating Object and its Product DT<sub>Object</sub>. During the Operational phase, the Digital Twin is paired with the Object in a synergic and continuous interaction. The dismissal of the Object starts as first, followed by the dismissal of the DT<sub>Object</sub> in a second part of the Dismissal Phase.

Both lifecycles share the same timeline: a first Design phase, followed by a Development phase, an Operational phase, and finally a Dismissal phase. For describing these two lifecycles, we use a running example of a medical device (the object) – i.e. a computer tomography scanner.

The first lifecycle is shown in Fig. 3. In this first case, the DT starts living before the physical object as a Prototype (Prototype DT<sub>Object</sub>), which is then used by designers during the Design phase of the Prototype Object. During the initial part of the Design phase, the Prototype DT<sub>Object</sub> is used, as if it was the real prototype, to simulate, test, change, and eventually validate design choices, until the best solution is found. During this part of the design phase, designers exploit:

- 1) Historical data the Prototype DT<sub>Object</sub> acquires from any other already existing DTs linked to similar devices.
- 2) Static data (e.g., data describing the product requirements, customer preferences, bill of materials).
- 3) The results of simulations performed by the Prototype DT<sub>Object</sub>, the result of predictions computed by the Prototype DT<sub>Object</sub>, and its suggestions and optimization schema.

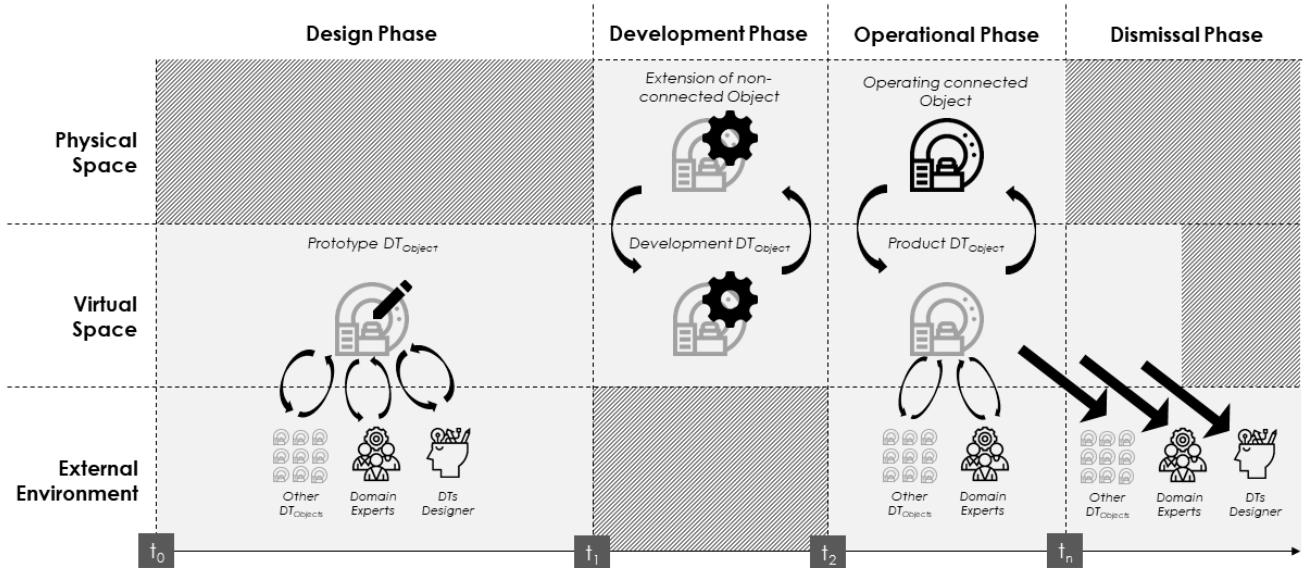
When the design of Prototype DT<sub>Object</sub> is completed, the process moves to the Design of the prototype Object, during which the Prototype DT<sub>Object</sub> is eventually modified to address technical constraints that may arise during the prototyping of the physical Object. During the Development Phase, the Prototype DT<sub>Object</sub> evolves becoming a Development DT<sub>Object</sub>, which must interact with the production machines to follow and optimize the assembly/construction

of the Object, i.e. its physical twin. When the Object is finally built, the Development DT<sub>Object</sub> starts being a Product DT<sub>Object</sub>, and this moves the process into the Operational phase. The Product DT<sub>Object</sub> fully resembles the Object: it has the AI acquired by the preceding stages of its life, and is therefore ready to follow and mirror the medical device (Object) while it is being used.

During its existence, the intelligence of the DT<sub>Object</sub> grows and self-adapts to the Object (in the case of the medical equipment, for example, it might start learning the most requested examinations, and the days when more or less examinations are performed).

When the Object stops being used (due to obsolescence or any other reason) it must be disassembled, and the Dismissal phase begins, first for the Object and then for the DT<sub>Object</sub>. The stored historical data of the Product DT<sub>Object</sub> are backed-up and made available to other DT<sub>Object</sub> as well as to domain experts; in this way, designers, or any other domain expert, will be able to use the collected information to optimize the production of future devices.

The second lifecycle is shown in Fig. 4. The difference between this lifecycle and the previous one (Fig. 3), is that the Object is already in place and in use, but it does not have a connected DT yet. In this case, the Design phase regards the development of a novel Prototype DT<sub>Object</sub> (which is tested, changed and finally validated), the Development phase regards the development of connections between the existing Object and the DT<sub>Object</sub> (which is called Development DT<sub>Object</sub> in this phase), while the Operational phase regards the operational life of the two twins, the Connected



**FIGURE 4.** This figure describes the lifecycle of an already existing computer tomography scanner that is however not yet connected to a DT. Being already existing, it is not depicted in the Design phase, but it appears directly in the Development one. On the other hand, during the design phase, the prototype DT<sub>Object</sub> is designed. During the development phase, the object is extended and connected to its DT<sub>Object</sub> and then they both start (twinned) their Operational phase. The dismissal, as in the previous lifecycle depicted in Fig. 3, sees the dismantling of the Operating Object and then the one of the product DT<sub>Object</sub>.

Object and Product DT<sub>Object</sub>, which live in concert until their dismantle in the Dismissal phase.

To sum up, during their lifecycle, the (physical and digital) twins base each step of their existence on a synergic and continuous interaction, which allow monitoring, predicting, and optimizing all their functionalities. The continuous interaction hides the differences among them, and they can act as a whole (“Synergy is the creation of a whole that is greater than the sum of its parts” [129]).

## VIII. OPEN ISSUES AND CHALLENGES

There are currently some important issues and challenges that need to be further studied and addressed, and are related to different aspects, all important for the future of the research in this field.

### A. ETHICAL ISSUES

Developers must address the ethical issues raised by the exchange of data describing/being produced by/being analyzed by multiple sources, such as the manufacturing company exploiting the developed DTs, its partners and customers, or by twinned hospitals, clinical experts and patients. **This requires developers and users to treat data according to privacy statements and legal limits that must still be set. This is especially true and critical with personal medical records.** Indeed, especially in healthcare and medicine, access to high-quality data with high cardinality and containing enough variation will be crucial to opportunely train effective AI models. **Such datasets could be formed as a mixture of publicly available data, data from clinical trials or from collaborations with hospitals, as well as some data from customers.** Proper regulations should guarantee that all of

these records are made anonymous and are only used with patients' consent.

### B. SECURITY AND PRIVACY

Due to the usage of the IoT and cloud computing, any DT environment must be developed with a particular attention to robustness with respect to hacking and viruses. **Hacking of private, confidential or valuable information could damage all the sources involved in the physical environment being twinned. Especially for DT technology in medicine and healthcare sectors, security and privacy should be deeply taken care of.**

### C. COST OF DEVELOPMENT

**Developing a DT environment requires to reconsider and reconfigure the underlying software platform, as well as the hardware of production machines and their cloud/physical interconnection.** This implies huge costs and might open the way to the spread of DT technologies only for large companies with the necessary capital and human resources.

Luckily, lot of research work is being pursued, experimental DTs have already been developed both in the manufacturing and in the medical field, and some of them have been already published or distributed as open repositories for research purposes. Without open repositories, the process of building DTs and the adoption of DTs may be restricted to an industrial oligopoly. The vast majority of companies cannot deploy an army of engineers to create custom digital twins for their exclusive experiments. On the contrary, the development of a common platform on the cloud and a modular organization would allow researchers and small companies to contribute as well, by developing particular modules that

others can buy. The number of unknown unknowns and the known unknowns in the process of developing DTs makes it imperative to create global infrastructures and organize groups to pursue the development of fundamental building blocks and new ideas through research [98].

#### D. EQUALLY DISTRIBUTED WEALTH

Development of distributed DT environments require all the involved parties to be furnished with seamless and ubiquitous connection, sensors and know-how. This feature is missing when Under Development Countries (UDC) are considered. The spread of DT technology in manufacturing could thus widen the gap between the rich and the poor, the urban and the rural. Considering also the case of DTs of human organs, doctors and researchers have to be taught how to use them correctly to foster their interest in using DT. Therefore, a common framework for specialized training and capacity building is significant and is needed to ensure the spread of medical DTs. The advantage would be a globalized improvement of healthcare.

#### E. GOVERNMENT REGULATIONS FOR MEDICAL DTS

Government needs to set regulations and rules establishing how predictive physiological and biological computational models can be validated and approved before any physician is willing to trust a diagnosis generated by a machine, or any patient is trusting the diagnostic evaluation of any expert analyzing a simulation on a virtual model. In other words, proper validation methodologies must be set to assess the credibility of computational models in biology and medicine [130]. Moreover, regulations should be set to define the extent of virtualization of the human being.

#### F. HWID AND EUD

DTs must be equipped with well-designed, usable and accessible interfaces, to let anyone (particularly non-informatic experts, but experts in specific domains) interact with DTs in a natural, effective, and efficient way.

Unfortunately, HWID and EUD are often neglected by computer scientists, who prefer to concentrate on the development and usage of DTs than on its design process and on the role of the end user. A Human Work Interaction Design approach, applied since the beginning of the DT ideation and creation, might help all the stakeholders understand the potentials of sociotechnical design.

#### G. TECHNICAL LIMITATIONS

Currently, there are many technical limitations that still represent open issues in the field. First of all, we need to make a distinction between a DT linked to an Object ( $DT_{Object}$ ) and a DT linked to a human being ( $DT_{Human}$ ). Both DTs share the same characteristics but differ in the way the twins (physical and digital) communicate. While  $DT_{Object}$  can exploit a real-time continuous connection with its twin, the  $DT_{Human}$  is connected with its physical twin through third devices (typically software applications or sensors) not necessarily

guaranteeing a seamless connection and a high throughput. As an example, consider those mobile apps that allow users to gather data about their health (e.g., glucose meters, prothrombin meters, weight, blood pressure). This is somehow a weakness, in that a stable, intelligent, ubiquitous, and continuous interaction between  $DT_{Human}$  and the human being may improve the knowledge of a generic DT, making it able to quickly react to unexpected changes [108]. Unluckily, at the present time this is currently not a viable option (not only for technical but also for ethical constraints). Other technical limitations that affect the way DT technology is developed and used, is about the need of having fast Internet connections that need to be also extremely reliable. This requirement is still hard to be met in many areas worldwide. Moreover, another critical issue is that the collection of large quantities of data makes it difficult to design effective interfaces for its visual representation and to enable an effective user interaction. Research on data visualization must be pursued to allow the spread of such visual information and an easy interaction between the end-user and the DT data.

#### IX. CONCLUSION

In the past twenty years continuous advances in AI, Big Data processing techniques, cloud computing, high dimensional data coding, sensor technologies, and IoT, have fostered DT technology, so that several DTs have already been developed and used in a variety of fields, including manufacturing, system engineering, robotics, healthcare and medicine. In this research work, we have described some of the most interesting DT descriptions and applications that have been published in scientific literature.

Our study has answered three research questions: What are the definitions of Digital Twin that have been published in literature so far? What are the main characteristics that should be implemented in a Digital Twin? What are the domains in which Digital Twin applications have been developed?

As far as the applications are concerned, note that, even though applications in the manufacturing, aviation and healthcare sectors emerged from our search in the scientific literature, we are aware that many other possible applications of DT could be viable. Our future research will therefore be focused on the investigation of novel application trends and developments of DT technology.

The contribution of this paper also consists in the illustration of the two possible lifecycles for DTs. The first lifecycle describes the life of a DT that starts living in the design phase of its physical twin, which is not existent yet; when the physical twin is built, the DT and its twin live together in seamless communication and interaction. The second scenario regards a DT that is created when the physical twin has already been operating for a while (e.g. in the case of a manufacturing device that becomes a connected device through Industry 4.0 solutions); in this case the DT must be connected to the physical twin, and the two continue their life in seamless interaction.

We finally discussed a set of open issues and main challenges that still affect this field of research, pointing out the possible future developments but at the same time the technical limitations that still represent a burden on it.

## REFERENCES

- [1] R. J. Solomonoff, "Artificial intelligence, social effects, future developments," *Hum. Syst. Manage.*, vol. 32, no. 2, pp. 149–153, 1985.
- [2] J. Moore, "The dartmouth college artificial intelligence conference: The next fifty years," *AI Mag.*, vol. 27, no. 4, pp. 87–91, 2006.
- [3] B. Marr. (Feb. 14, 2018). *The Key Definitions Of Artificial Intelligence (AI) That Explain Its Importance*. [Online]. Available: <https://www.to.be/publishedforbes.com/sites/bernardmarr/2018/02/14/the-key-definitions-of-artificial-intelligence-ai-that-explain-its-importance>
- [4] E. Casiraghi, M. Cossa, V. Huber, M. Tozzi, L. Rivoltini, A. Villa, and B. Vergani, "Miaquant, a novel system for automatic segmentation, measurement, and localization comparison of different biomarkers from serialized histological slices," *Eur. J. Histochem.*, vol. 61, no. 4, p. 2838, 2017.
- [5] S. K. C. Devi and T. S. Savithri, "Review: On segmentation of nodules from posterior and anterior chest radiographs," *Int. J. Biomed. Imag.*, vol. 2018, Oct. 2018, Art. no. 9752638, doi: [10.1155/2018/9752638](https://doi.org/10.1155/2018/9752638).
- [6] P. J. Hunter, A. J. Pullan, and B. H. Smaill, "Modeling total heart function," *Annu. Rev. Biomed. Eng.*, vol. 5, no. 1, pp. 147–177, 2003, doi: [10.1146/annurev.bioeng.5.040202.121537](https://doi.org/10.1146/annurev.bioeng.5.040202.121537).
- [7] N. A. Trayanova, "Whole-heart modeling: Applications to cardiac electrophysiology and electromechanics," *Circulat. Res.*, vol. 108, no. 1, pp. 113–128, 2011.
- [8] Y. Feng, X. Chen, and J. Zhao, "Create the individualized digital twin for noninvasive precise pulmonary healthcare," in *Significances Bioengineering & Biosciences*, vol. 1, no. 2. New York, NY, USA: Crimson Publishers, 2018, doi: [10.31031/SB.2018.01.000507](https://doi.org/10.31031/SB.2018.01.000507).
- [9] P. Campadelli, E. Casiraghi, C. Ceruti, and A. Rozza, "Intrinsic dimension estimation: Relevant techniques and a benchmark framework," *Math. Problems Eng.*, vol. 2015, May 2015, Art. no. 759567.
- [10] K. Ashton, "That Internet of Things thing," *RFID J.*, vol. 22, no. 7, pp. 97–114, Jun. 2009.
- [11] A. Canedo, "Industrial IoT lifecycle via digital twins," in *Proc. 11th IEEE/ACM/FIP Int. Conf. Hardw./Softw. Codesign Syst. Synth.*, 2016, p. 29.
- [12] D. Laney. (2001). *3D Data Management: Controlling Data Volume, Velocity and Variety*. META Group. Accessed: Oct. 16, 2019. [Online]. Available: <http://blogs.gartner.com/doug-laney/files/2012/01/ad949-3D-Data-Management-Controlling-Data-Volume-Velocity-and-Variety.pdf>
- [13] P. Zikopoulos and C. Eaton, *Understanding Big Data: Analytics for Enterprise Class Hadoop and Streaming Data*, 1st ed. New York, NY, USA: McGraw-Hill, 2011.
- [14] M. Chen, S. Mao, and Y. Liu, "Big data: A survey," *Mobile Netw. Appl.*, vol. 19, no. 2, pp. 171–209, Apr. 2014, doi: [10.1007/s11036-013-0489-0](https://doi.org/10.1007/s11036-013-0489-0).
- [15] A. Banerjee, R. Dalal, S. Mittal, and K. P. Joshi, "Generating digital twin models using knowledge graphs for industrial production lines," in *Proc. Workshop Ind. Knowl. Graphs (ACM Web Sci. Conf.)*, 2017, pp. 1–6.
- [16] F. Tao, J. Cheng, Q. Qi, M. Zhang, H. Zhang, and F. Sui, "Digital twin-driven product design, manufacturing and service with big data," *Int. J. Adv. Manuf. Technol.*, vol. 94, nos. 9–12, pp. 3563–3576, Feb. 2018.
- [17] H. Ikävalko, P. Turkama, and A. Smedlund, "Value creation in the Internet of Things: Mapping business models and ecosystem roles," *Technol. Innov. Manage. Rev.*, vol. 8, pp. 5–15, Mar. 2018, doi: [10.22215/timreview/1142](https://doi.org/10.22215/timreview/1142).
- [18] NASA. *The Ill-Fated Space Odyssey of Apollo 13*. Accessed: Oct. 16, 2019. [Online]. Available: <https://er.jsc.nasa.gov/seh/pg13.htm>
- [19] M. Grieves. (2015). *Digital Twin: Manufacturing Excellence Through Virtual Factory Replication*. Digital Twin White Paper. Accessed: Oct. 16, 2019. [Online]. Available: [https://research.fit.edu/media/sites-specific/researchfitedu/camid/documents/1411.0\\_Digital\\_Twin\\_White\\_Paper\\_Dr\\_Grieves.pdf](https://research.fit.edu/media/sites-specific/researchfitedu/camid/documents/1411.0_Digital_Twin_White_Paper_Dr_Grieves.pdf)
- [20] M. Grieves and J. Vickers, *Digital Twin: Mitigating Unpredictable, Undesirable Emergent Behavior in Complex Systems*. Springer, 2017, pp. 85–113.
- [21] K. Framling, J. Holmström, T. Ala-Risku, and M. Karkkainen, "Product agents for handling information about physical objects," Helsinki Univ. Technol., Dept. Comput. Sci. Eng. Ser. B TKO-B, Espoo, Finland, 2003.
- [22] M. Shafto, M. Conroy, R. Doyle, E. Glaessgen, C. Kemp, J. LeMoigne, and L. Wang. (Nov. 2010). *Modeling, Simulation, Information Technology & Processing Roadmap*. National Aeronautics and Space Administration. Accessed: Oct. 16, 2019. [Online]. Available: [https://www.nasa.gov/pdf/501321main\\_TA11-MSITP-DRAFT-Nov2010-A1.pdf](https://www.nasa.gov/pdf/501321main_TA11-MSITP-DRAFT-Nov2010-A1.pdf)
- [23] E. Glaessgen and D. Stargel, "The digital twin paradigm for future NASA and U.S. Air Force vehicles," in *Proc. 53rd Struct., Struct. Dyn., Mater. Conf., Special Session Digit. Twin*, 2012, p. 818.
- [24] E. J. Tuegel, A. R. Ingraffea, T. G. Eason, and S. M. Spottswood, "Reengineering aircraft structural life prediction using a digital twin," *Int. J. Aerosp. Eng.*, vol. 2011, Aug. 2011, Art. no. 154798, doi: [10.1155/2011/154798](https://doi.org/10.1155/2011/154798).
- [25] E. Tuegel, "The airframe digital twin: Some challenges to realization," in *Proc. 53rd Struct., Struct. Dyn. Mater. Conf.*, 2012, p. 1812.
- [26] B. Gockel, A. Tudor, M. Brandyberry, R. Penmetsa, and E. Tuegel, "Challenges with structural life forecasting using realistic mission profiles," in *Proc. 53rd Struct., Struct. Dyn. Mater. Conf.*, 2012, p. 1812.
- [27] U.S. Air Force. (2013). *Global Horizons Final Report: United States Air Force Global Science and Technology Vision*. AF/ST TR 13-01, United States Air Force. Accessed: Oct. 16, 2019. [Online]. Available: <https://www.hsdsl.org/?view&did=741377>
- [28] C. Leiva. (Oct. 22, 2018). *What is the Digital Thread?* iBaseT. Accessed: Oct. 16, 2019. [Online]. Available: <https://www.ibaset.com/blog/what-is-the-digital-thread/>
- [29] ItBase. (Dec. 23, 2018). *Enabling the Digital Thread: Unify Design, Manufacturing and ERP in a Closed Loop Digital Thread That Streamlines Operations, Improves Quality and Boosts Productivity*. Accessed: Oct. 16, 2019. [Online]. Available: [https://info.ibaset.com/enable-the-digital-thread?utm\\_campaign=eBook%20Enabling%20the%20Digital%20Thread&utm\\_source=In-Text%20Link%20for%20Blogs,%20last%20accessed%202027/07/2019](https://info.ibaset.com/enable-the-digital-thread?utm_campaign=eBook%20Enabling%20the%20Digital%20Thread&utm_source=In-Text%20Link%20for%20Blogs,%20last%20accessed%202027/07/2019)
- [30] D. J. L. Siedlak, O. J. Pinon, P. R. Schlais, T. M. Schmidt, and D. N. Mavris, "A digital thread approach to support manufacturing-influenced conceptual aircraft design," *Res. Eng. Des.*, vol. 29, no. 2, pp. 285–308, 2018, doi: [10.1007/s00163-017-0269-0](https://doi.org/10.1007/s00163-017-0269-0).
- [31] M. Brettel, N. Friederichsen, M. Keller, and M. Rosenberg, "How virtualization, decentralization and network building change the manufacturing landscape: An industry 4.0 perspective," *Int. J. Mech., Ind. Sci. Eng.*, vol. 8, no. 1, pp. 37–44, 2014.
- [32] M. Hermann, T. Pentek, and B. Otto, "Design principles for industrie 4.0 scenarios," in *Proc. HICSS*, 2016, pp. 3928–3937, doi: [10.1109/HICSS.2016.488](https://doi.org/10.1109/HICSS.2016.488).
- [33] J. Vachálek, L. Bartalský, O. Rovny, D. Šišmišová, M. Morhč, and M. Lokšík, "The digital twin of an industrial production line within the industry 4.0 concept," in *Proc. PC*, 2017, pp. 258–262, doi: [10.1109/PC.2017.7976223](https://doi.org/10.1109/PC.2017.7976223).
- [34] M. Mabkhot, A. M. Al-Ahmari, B. Salah, and H. Alkhalefah, "Requirements of the smart factory system: A survey and perspective," *Machines*, vol. 6, no. 2, p. 23, 2018.
- [35] D. Riener. (Apr. 8, 2017). *Powering a&d Business Agility With Digital Integration*. Siemens. Accessed: Oct. 16, 2019. [Online]. Available: <https://community.plm.automation.siemens.com/5/Digital-Transformations/Powering-A-&-D-business-agility-with-digital-integration/ba-p/426885>
- [36] D. Riener. (Nov. 9, 2017). *How the Digital Thread Transforms Verification Management*. Siemens. Accessed: Oct. 16, 2019. [Online]. Available: <https://community.plm.automation.siemens.com/5/Digital-Transformations/How-the-digital-thread-transforms-verification-management/ba-p/431699>
- [37] W. Kritzinger, M. Karner, G. Traar, J. Henjes, and W. Sihl, "Digital twin in manufacturing: A categorical literature review and classification," *IFAC-PapersOnLine*, vol. 51, no. 11, pp. 1016–1022, 2018.
- [38] R. Y. Zhong, X. Xu, E. Klotz, and S. T. Newman, "Intelligent manufacturing in the context of industry 4.0: A review," *Engineering*, vol. 3, no. 5, pp. 616–630, 2017.
- [39] Y. Lu, C. Liu, K. I.-K. Wang, H. Huang, and X. Xu, "Digital Twin-driven smart manufacturing: Connotation, reference model, applications and research issues," *Robot. Comput.-Integr. Manuf.*, vol. 61, Feb. 2020, Art. no. 101837.
- [40] P. Zheng, H. Wang, Z. Sang, R. Y. Zhong, Y. Liu, C. Liu, K. Mubarok, S. Yu, and X. Xu, "Smart manufacturing systems for Industry 4.0: Conceptual framework, scenarios, and future perspectives," *Frontiers Mech. Eng.*, vol. 13, no. 2, pp. 137–150, 2018.

- [41] M. Holler, F. Uebenickel, and W. Brenner, "Digital twin concepts in manufacturing industries—A literature review and avenues for further research," in *Proc. 18th Int. Conf. Ind. Eng. (IJIE)*, 2016, pp. 1–9.
- [42] C. Wohlin, "Guidelines for snowballing in systematic literature studies and a replication in software engineering," in *Proc. EASE*, vol. 38, 2014, pp. 1–10.
- [43] J. Ríos, J. Hernández, M. Oliva, and F. Mas, "Product avatar as digital counterpart of a physical individual product: Literature review and implications in an aircraft," in *Transdisciplinary Lifecycle Analysis of Systems (Advances in Transdisciplinary Engineering)*, vol. 2, 2015, pp. 657–666.
- [44] D. Kiritsis, "Closed-loop PLM for intelligent products in the era of the Internet of Things," *Comput.-Aided Des.*, vol. 43, pp. 479–501, May 2011.
- [45] S. Boschert and R. Rosen, "Digital twin—The simulation aspect," in *Mechatronic Futures*. Basel, Switzerland: Springer, 2016, pp. 59–74.
- [46] E. Negri, L. Fumagalli, and M. Macchi, "A review of the roles of digital twin in CPS-based production systems," *Procedia Manuf.*, vol. 11, pp. 939–948, 2017, doi: [10.1016/j.promfg.2017.07.198](https://doi.org/10.1016/j.promfg.2017.07.198).
- [47] G. N. Schroeder, C. Steinmetz, C. E. Pereira, and D. B. Espindola, "Digital twin data modeling with automationML and a communication methodology for data exchange," *IFAC-PapersOnLine*, vol. 49, no. 30, pp. 12–17, 2016.
- [48] K. M. Alam and A. El Saddik, "C2PS: A digital twin architecture reference model for the cloud-based cyber-physical systems," *IEEE Access*, vol. 5, pp. 2050–2062, 2017.
- [49] K. Hribernik, T. Wuest, and K.-D. Thoben, "Towards product avatars representing middle-of-life information for improving design, development and manufacturing processes," in *Digital Product and Process Development Systems*, G. L. Kovács, D. Kochan, Eds. Berlin, Germany: Springer, 2013, pp. 85–96.
- [50] J. Ríos, M. F. Mas, M. Oliva, and J. C. Hernandez, "Framework to support the aircraft digital counterpart concept with an industrial design view," *Int. J. Agile Syst. Manage.*, vol. 9, no. 3, pp. 212–231, 2016.
- [51] V. Hempel, *Healthcare Solution Testing for Future Digital Twins in Healthcare*. Accessed: Oct. 16, 2019. [Online]. Available: <https://www.dr-hempel-network.com/digital-health-technology/digital-twins-in-healthcare/>
- [52] A. M. Madni, C. C. Madni, and S. D. Lucero, "Leveraging digital twin technology in model-based systems engineering," *Systems*, vol. 7, no. 1, p. 7, 2019, doi: [10.3390/systems7010007](https://doi.org/10.3390/systems7010007).
- [53] R. Rosen, G. Von Wichert, G. Lo, and K. D. Bettenhausen, "About the importance of autonomy and digital twins for the future of manufacturing," *IFAC-PapersOnLine*, vol. 48, no. 3, pp. 567–572, 2015.
- [54] T. Gabor, L. Belzner, M. Kiermeier, M. T. Beck, and A. Neitz, "A simulation-based architecture for smart cyber-physical systems," in *Proc. ICAC*, Jul. 2016, pp. 374–379, doi: [10.1109/ICAC.2016.29](https://doi.org/10.1109/ICAC.2016.29).
- [55] S. Boschert, C. Heinrich, and R. Rosen, "Next generation digital twin," in *Proc. TMCE*, 2018, pp. 209–218.
- [56] Q. Qi and F. Tao, "Digital twin and big data towards smart manufacturing and industry 4.0: 360 degree comparison," *IEEE Access*, vol. 6, pp. 3585–3593, 2018, doi: [10.1109/ACCESS.2018.2793265](https://doi.org/10.1109/ACCESS.2018.2793265).
- [57] F. Tao and M. Zhang, "Digital twin shop-floor: A new shop-floor paradigm towards smart manufacturing," *IEEE Access*, vol. 5, pp. 20418–20427, 2017, doi: [10.1109/ACCESS.2017.2756069](https://doi.org/10.1109/ACCESS.2017.2756069).
- [58] F. Tao, M. Zhang, Y. Liu, and A. Y. C. Nee, "Digital twin driven prognostics and health management for complex equipment," *CIRP Ann.*, vol. 67, no. 1, pp. 169–172, 2018.
- [59] K. Rajratna, V. Bavane, S. Jadhao, and R. Marode, *Digital Twin: Manufacturing Excellence Through Virtual Factory Replication*. Global Journal of Engineering Science and Researches, 2018, pp. 6–15, doi: [10.5281/zenodo.1493930](https://doi.org/10.5281/zenodo.1493930).
- [60] J. Lee, E. Lapira, B. Bagheri, and H.-A. Kao, "Recent advances and trends in predictive manufacturing systems in big data environment," *Manuf. Lett.*, vol. 1, no. 1, pp. 38–41, Oct. 2013, doi: [10.1016/j.mfglet.2013.09.005](https://doi.org/10.1016/j.mfglet.2013.09.005).
- [61] J. Guo, N. Zhao, L. Sun, and S. Zhang, "Modular based flexible digital twin for factory design," *J. Ambient Intell. Humanized Comput.*, vol. 10, no. 3, pp. 1189–1200, 2018, doi: [10.1007/s12652-018-0953-6](https://doi.org/10.1007/s12652-018-0953-6).
- [62] M. Abramovici, J. C. Göbel, and P. Savarino, "Reconfiguration of smart products during their use phase based on virtual product twins," *CIRP Ann.*, vol. 66, no. 1, pp. 165–168, 2017, doi: [10.1016/j.cirp.2017.04.042](https://doi.org/10.1016/j.cirp.2017.04.042).
- [63] K. Bruynseels, F. S. di Sio, and J. van den Hoven, "Digital twins in health care: Ethical implications of an emerging engineering paradigm," *Frontiers Genet.*, vol. 9, p. 31, Feb. 2018, doi: [10.3389/fgene.2018.00031](https://doi.org/10.3389/fgene.2018.00031).
- [64] T. Marshall. (Sep. 6, 2016). *VPH: The Ultimate Stage Before Your Own Medical Digital Twin*. Accessed: Oct. 16, 2019. [Online]. Available: <https://www.linkedin.com/pulse/vph-ultimate-stage-before-your-own-medical-digital-twin-marchal/?trk=mp-reader-car>
- [65] F. Michelfeit, "Exploring the possibilities offered by digital twins in medical technology," *Siemens Healthcare GmbH-Communc. RSNA*, 2018. [Online]. Available: [https://static.healthcare.siemens.com/siemens\\_hwem\\_hwem\\_ssxa\\_websites-context-root/wcm/idc/groups/public/@global/@press/documents/download/mda4/nzm4/~edisp/exploring-the-possibilities-offered-by-digital-twins-in-medical-technology-05899262.pdf](https://static.healthcare.siemens.com/siemens_hwem_hwem_ssxa_websites-context-root/wcm/idc/groups/public/@global/@press/documents/download/mda4/nzm4/~edisp/exploring-the-possibilities-offered-by-digital-twins-in-medical-technology-05899262.pdf)
- [66] K. Warmefjord, R. Sderberg, L. Lindkvist, B. Lindau, and J. S. Carlson, "Inspection data to support a digital twin for geometry assurance," in *Proc. ASME*, 2017, vol. 101, vol. 2, Art. no. V002T02A101, doi: [10.1115/IMECE2017-70398](https://doi.org/10.1115/IMECE2017-70398).
- [67] B. A. Talkhestani, N. Jazdi, W. Schlg, and M. Weyrich, "Consistency check to synchronize the digital twin of manufacturing automation based on anchor points," *Procedia CIRP*, vol. 72, pp. 159–164, 2018.
- [68] T. H.-J. Uhlemann, C. Lehmann, and R. Steinhilper, "The digital twin: Realizing the cyber-physical production system for industry 4.0," *Procedia CIRP*, vol. 61, pp. 335–340, 2017.
- [69] T. H.-J. Uhlemann, C. Schock, C. Lehmann, S. Freiberger, and R. Steinhilper, "The digital twin: Demonstrating the potential of real time data acquisition in production systems," *Procedia Manuf.*, vol. 9, pp. 113–120, 2017.
- [70] J. Um, S. Weyer, and F. Quint, "Plug-and-simulate within modular assembly line enabled by digital twins and the use of automationML," *IFAC-PapersOnLine*, vol. 50, no. 1, pp. 15904–15909, 2017.
- [71] F. Ameri and R. Sabbagh, "Digital factories for capability modeling and visualization," in *Proc. APMS*, 2016, pp. 69–78, doi: [10.1007/978-3-319-51133-7\\_9](https://doi.org/10.1007/978-3-319-51133-7_9).
- [72] S. Luscienski, "Digital twinning for smart industry," in *Proc. EAI*, 2018, pp. 1–9, doi: [10.4108/eai.6-11-2018.2279986](https://doi.org/10.4108/eai.6-11-2018.2279986).
- [73] B. Smarslok, A. Culler, and A. Mahadevan, "Error quantification and confidence assessment of aerothermal model predictions for hypersonic aircraft," in *Proc. AIAA*, 2012, p. 1817, doi: [10.2514/6.2012-1817](https://doi.org/10.2514/6.2012-1817).
- [74] J. Yang, W. Zhang, and Y. Liu, "Subcycle fatigue crack growth mechanism investigation for aluminum alloys and steel," in *Proc. AIAA*, 2013, p. 1499, doi: [10.2514/6.2013-1499](https://doi.org/10.2514/6.2013-1499).
- [75] E. M. Kraft, "The air force digital thread/digital twin-life cycle integration and use of computational and experimental knowledge," in *Proc. AIAA*, 2016, p. 0897.
- [76] P. K. Majumdar, M. F. Haider, and K. Reifsnider, "Multi-physics response of structural composites and framework for modeling using material geometry," in *Proc. AIAA*, 2013, p. 1577, doi: [10.2514/6.2013-1577](https://doi.org/10.2514/6.2013-1577).
- [77] B. Bielefeldt, J. Hochhalter, and D. Hartl, "Computationally efficient analysis of SMA sensory particles embedded in complex aerostructures using a substructure approach," in *Proc. ASME*, 2015, Art. no. V001T02A007, doi: [10.1115/SMASIS2015-8975](https://doi.org/10.1115/SMASIS2015-8975).
- [78] H.-K. Wang, R. Haynes, H.-Z. Huang, L. Dong, and S. N. Atluri, "The use of high-performance fatigue mechanics and the extended Kalman/particle filters, for diagnostics and prognostics of aircraft structures," *Comput. Model. Eng. Sci.*, vol. 105, no. 1, pp. 1–24, 2015.
- [79] C. Y. Liao and S. N. Atluri, "A finite element alternating method for evaluation of stress intensity factors fpr part-circular cracks subjected to arbitrary loadings," *Comput. Methods Appl. Mech. Eng.*, vol. 91, nos. 1–3, pp. 1253–1270, 1991.
- [80] L. Dong, R. Haynes, and S. N. Atluri, "On improving the celebrated Paris' power law for fatigue, by using moving least squares," *Comput., Mater. Continua*, vol. 45, no. 1, pp. 1–15, 2015.
- [81] C. Li, S. Mahadevan, Y. Ling, S. Choze, and L. Wang, "Dynamic Bayesian network for aircraft wing health monitoring digital twin," *AIAA J.*, vol. 55, no. 3, pp. 930–941, 2017.
- [82] Y. Bazilevs, X. Deng, A. Korobenko, F. L. di Scalea, M. D. Todd, and S. G. Taylor, "Isogeometric fatigue damage prediction in large-scale composite structures driven by dynamic sensor data," *J. Appl. Mech.*, vol. 82, no. 9, 2015, Art. no. 091008.
- [83] B. R. Seshadri and T. Krishnamurthy, "Structural health management of damaged aircraft structures using digital twin concept," in *Proc. AIAA*, 2017, p. 1675, doi: [10.2514/6.2017-1675](https://doi.org/10.2514/6.2017-1675).
- [84] A. J. Zakrajsek and S. Mall, "The development and use of a digital twin model for tire touchdown health monitoring," in *Proc. AIAA*, vol. 2017, p. 0863.

- [85] K. Polyniak and J. Matthews. (Oct. 26, 2016). *The Johns Hopkins Hospital Launches Capacity Command Center to Enhance Hospital Operations*. John Hopkins Medicine. Accessed: Oct. 16, 2019. [Online]. Available: [https://www.hopkinsmedicine.org/news/media/releases/the\\_johns\\_hopkins\\_hospital\\_launches\\_capacity\\_command\\_center\\_to\\_enhance\\_hospital\\_operations](https://www.hopkinsmedicine.org/news/media/releases/the_johns_hopkins_hospital_launches_capacity_command_center_to_enhance_hospital_operations)
- [86] S. Scharff. (Sep. 10, 2010). *From Digital Twin to Improved Patient Experience*. Siemens Healthineers. Accessed: Oct. 16, 2019. [Online]. Available: <https://www.siemens-healthineers.com/news/mso-digital-twin-mater.html>
- [87] G. Clapworthy, M. Viceconti, P. V. Coveney, and P. Kohl, "Editorial," *Philos. Trans. Roy. Soc. A Math., Phys. Eng. Sci.*, vol. 366, no. 1878, pp. 2975–2978, 2008, doi: [10.1098/rsta.2008.0103](https://doi.org/10.1098/rsta.2008.0103).
- [88] *The Living Heart Project*. Accessed: Oct. 16, 2019. [Online]. Available: <https://www.3ds.com/products-services/simulia/solutions/life-sciences/the-living-heart-project>
- [89] C. Copley. (2018). *Medical Technology Firms Develop 'Digital Twins' for Personalized Health Care*. Accessed: Oct. 16, 2019. [Online]. Available: <https://www.theglobeandmail.com/business/article-medical-technology-firms-develop-digital-twins-for-personalized>
- [90] X. Chen, Y. Feng, W. Zhong, and C. Kleinstreuer, "Numerical investigation of the interaction, transport and deposition of multicomponent droplets in a simple mouth-throat model," *J. Aerosol Sci.*, vol. 105, pp. 108–127, Mar. 2016.
- [91] Y. Feng, J. Zhao, X. Chen, and J. Lin, "An in silico subject-variability study of upper airway morphological influence on the airflow regime in a tracheobronchial tree," *Bioengineering*, vol. 4, no. 4, pp. 90–93, 2017.
- [92] X. Chen, Y. Feng, W. Zhong, B. Sun, and F. Tao, "Numerical investigation of particle deposition in a triple bifurcation airway due to gravitational sedimentation and inertial impaction," *Powder Technol.*, vol. 323, pp. 284–293, Jan. 2017.
- [93] Y. Feng, J. Zhao, C. Kleinstreuer, Q. Wang, J. Wang, D. Wu, and J. Lin, "An in silico inter-subject variability study of extra-thoracic morphology effects on inhaled particle transport and deposition," *J. Aerosol Sci.*, vol. 123, pp. 185–207, May 2018.
- [94] Y. Feng, "Targeting a tumour," in *Proc. 12th ANSYS Advantage-Healthcare*, 2018, pp. 42–45.
- [95] J. M. Ospel, G. Gascou, V. Costalat, L. Piergallini, K. A. Blackham, and D. W. Zumofen, "Comparison of pipeline embolization device sizing based on conventional 2D measurements and virtual simulation using the Sim&Size software: An agreement study," *Amer. J. Neuroradiol.*, vol. 40, pp. 524–530, Mar. 2019, doi: [10.3174/ajnr.A5973](https://doi.org/10.3174/ajnr.A5973).
- [96] M. Holtmannspotter, M. Martinez-Galdamez, M. Isokangas, R. Ferrara, and M. Sanchez, "Simulation in clinical practice: First experience with Sim&Cure before implantation of flow diverter (pipeline) or Web-device for the treatment of intracranial aneurysm," in *Proc. ABC/WIN*, Val d'Isère, France, 2017. [Online]. Available: [https://sim-and-cure.com/wp-content/uploads/2018/01/91aa70\\_01fd87e567ec49e9907a061bd780c76b.pdf](https://sim-and-cure.com/wp-content/uploads/2018/01/91aa70_01fd87e567ec49e9907a061bd780c76b.pdf)
- [97] B. Schleich, N. Anwer, L. Mathieu, and S. Wartzack, "Shaping the digital twin for design and production engineering," *CIRP Ann.*, vol. 66, no. 1, pp. 141–144, 2017, doi: [10.1016/j.cirp.2017.04.040](https://doi.org/10.1016/j.cirp.2017.04.040).
- [98] S. P. A. Datta, "Emergence of digital Twins—Is this the march of reason?" *J. Innov. Manage.*, vol. 5, no. 3, pp. 14–33, 2017.
- [99] T. R. Gruber, "A translation approach to portable ontology specifications," *Knowl. Acquisition*, vol. 5, pp. 199–220, Jun. 1993.
- [100] S. Heymans, L. Ma, D. Anicic, Z. Ma, N. Steimetz, Y. Pan, J. Mei, A. Fokoue, A. Kalyanpur, A. Kershnerbaum, E. Schonberg, K. Srinivas, C. Feier, G. Hench, B. Wetzelstein, and U. Keller, "Ontology reasoning with large data repositories," in *Ontology Management*. Boston, MA, USA: Springer, 2008, pp. 89–128.
- [101] S. Borgo, "An ontological approach for reliable data integration in the industrial domain," *Comput. Ind.*, vol. 65, no. 9, pp. 1242–1252, 2014.
- [102] C. Legat, C. Seitz, S. Lamparter, and S. Feldmann, "Semantics to the shop floor: Towards ontology modularization and reuse in the automation domain," *IFAC Proc.*, vol. vol., 47, no. 3, pp. 3444–3449, 2014.
- [103] P. Witherell, I. R. Grossé, S. Krishnamurti, and J. C. Wileden, "AIERO: An algorithm for identifying engineering relationships in ontologies," *Adv. Eng. Inf.*, vol. 27, pp. 555–565, Oct. 2013, doi: [10.1016/j.aei.2013.06.003](https://doi.org/10.1016/j.aei.2013.06.003).
- [104] P. A. Vikhar, "Evolutionary algorithms: A critical review and its future prospects," in *Proc. ICGTSPICC*, 2016, pp. 165–261, doi: [10.1109/ICGTSPICC.2016.7955308](https://doi.org/10.1109/ICGTSPICC.2016.7955308).
- [105] D. Abbott, *Applied Predictive Analytics: Principles and Techniques for the Professional Data Analyst*. Hoboken, NJ, USA: Wiley, 2014.
- [106] A. Gandomi and M. Haider, "Beyond the hype: Big data concepts, methods, and analytics," *Int. J. Inf. Manage.*, vol. 35, no. 2, pp. 137–144, 2015.
- [107] S. Poornima and M. Pushpalatha, "A journey from big data towards prescriptive analytics," *ARPN J. Eng. Appl. Sci.*, vol. 11, pp. 11465–11474, Oct. 2016.
- [108] J. Davis, T. Edgar, J. Porter, J. Bernaden, and M. Sarli, "Smart manufacturing, manufacturing intelligence and demand-dynamic performance," *Comput. Chem. Eng.*, vol. 47, pp. 145–156, Dec. 2012.
- [109] J. Kiendl, K.-U. Bletzinger, J. Linhard, and R. Wchner, "Isogeometric shell analysis with kirchhoff-love elements," *Comput. Methods Appl. Mech. Eng.*, vol. 198, pp. 3902–3914, Nov. 2009, doi: [10.1016/j.cma.2009.08.013](https://doi.org/10.1016/j.cma.2009.08.013).
- [110] H. Sohn, C. R. Farrar, F. Hemez, and J. Czarnecki, "A review of structural health monitoring literature: 1996–2001," Los Alamos National Laboratory, New Mexico, NM, USA, Tech. Rep. LA-13976-MS, 2004.
- [111] D. E. Goldberg, *Genetic Algorithms in Search, Optimization & Machine Learning*. Reading, MA, USA: Addison-Wesley, 1989.
- [112] Genetics Home Reference. (May 14, 2019). *What is Precision Medicine?* U.S. National Library of Medicine. Accessed: Oct. 16, 2019. [Online]. Available: <https://ghr.nlm.nih.gov/primer/precisionmedicine/definition>
- [113] J. L. Jameson and D. L. Longo, "Precision medicine—Personalized, problematic, and promising," *Obstetrical Gynecological Surv.*, vol. 70, no. 10, pp. 612–614, 2015.
- [114] S. Kohler, "Personalized medicine and global health," *Public Health Forum*, vol. 25, no. 3, pp. 244–248, 2017, doi: [10.1515/pubhef-2017-0032](https://doi.org/10.1515/pubhef-2017-0032).
- [115] S. Kohler, "Precision medicine—moving away from one-size-fits-all," *Acad. Sci. South Africa*, vol. 14, pp. 12–15, Nov. 2018.
- [116] M. Viceconti, A. Henney, and E. Morley-Fletcher, "In silico clinical trials: How computer simulation will transform the biomedical industry," *Int. J. Clin. Trials*, vol. 3, no. 2, pp. 37–46, 2016.
- [117] R. H. Choplin, J. M. Boehme, and C. D. Maynard, "Picture archiving and communication systems: An overview," *RadioGraphics*, vol. 12, no. 1, pp. 127–129, 1992, doi: [10.1148/radiographics.12.1.1734458](https://doi.org/10.1148/radiographics.12.1.1734458).
- [118] J. D. Kelleher, B. M. Namee, and A. D'arcy, *Fundamentals of Machine Learning for Predictive Data Analytics: Algorithms, Worked Examples, and Case Studies*. Cambridge, MA, USA: MIT Press, 2015.
- [119] L. Zhu, B. R. Barricelli, and C. Iacob, "A meta-design model for creative distributed collaborative design," *Int. J. Distrib. Syst. Technol.*, vol. 2, no. 4, pp. 1–16, 2011, doi: [10.4018/ijdst.201100101](https://doi.org/10.4018/ijdst.201100101).
- [120] C. Ardito, B. R. Barricelli, P. Buono, M. F. Costabile, A. Piccinno, S. Valtolina, and L. Zhu, "Visual mediation mechanisms for collaborative design and development," in *Proc. UAHCI, LNCS*, vol. 6765, 2011, pp. 3–11, doi: [10.1007/978-3-642-21672-5\\_1](https://doi.org/10.1007/978-3-642-21672-5_1).
- [121] L. Zhu, P. Mussio, B. R. Barricelli, and C. Iacob, "A habitable space for supporting creative collaboration," in *Proc. CTS*, 2010, pp. 617–622, doi: [10.1109/CTS.2010.5478455](https://doi.org/10.1109/CTS.2010.5478455).
- [122] J. Abdelnour-Nocera, B. R. Barricelli, A. Lopes, P. Campos, and T. Clemmensen, "Human work interaction design: Analysis and interaction design methods for pervasive and smart workplaces," in *IFIP Advances in Information and Communication Technology*, vol. 468. New York, NY, USA: Springer, 2015.
- [123] B. R. Barricelli, F. Cassano, D. Fogli, and A. Piccinno, "End-user development, end-user programming and end-user software engineering: A systematic mapping study," *J. Syst. Softw.*, vol. 149, pp. 101–137, Mar. 2019, doi: [10.1016/j.jss.2018.11.041](https://doi.org/10.1016/j.jss.2018.11.041).
- [124] B. R. Barricelli and S. Valtolina, "A visual language and interactive system for end-user development of Internet of Things ecosystems," *J. Vis. Lang. Comput.*, vol. 40, pp. 1–19, Jun. 2017, doi: [10.1016/j.jvlc.2017.01.004](https://doi.org/10.1016/j.jvlc.2017.01.004).
- [125] B. R. Barricelli and S. Valtolina, "A semiotic approach to EUD for the Internet of Things," in *Proc. CoPDA2015, CEUR-WS*, vol. 1641, 2015, pp. 45–51.
- [126] B. R. Barricelli and S. Valtolina, "Designing for end-user development in the Internet of Things," in *Proc. IS-EUD, LNCS*, vol. 9083, 2015, pp. 9–24, doi: [10.1007/978-3-319-18425-8\\_2](https://doi.org/10.1007/978-3-319-18425-8_2).
- [127] G. Desolda, C. Ardito, and M. Matera, "Empowering end users to customize their smart environments: Model, composition paradigms, and domain-specific tools," *ACM Trans. Comput.-Hum. Interact.*, vol. 24, no. 2, pp. 1–52, 2017, doi: [10.1145/3057859](https://doi.org/10.1145/3057859).

- [128] G. Ghiani, M. Manca, F. Paternò, and C. Santoro, "Personalization of context-dependent applications through trigger-action rules," *ACM Trans. Comput.-Hum. Interact.*, vol. 24, no. 2, p. 14, 2017, doi: 10.1145/3057861.
- [129] R. French, C. Rayner, G. Rees, and S. Rumbles, *Organizational Behaviour*, 3rd ed. Hoboken, NJ, USA: Wiley, 2008.
- [130] E. A. Patterson and M. P. Whelan, "A framework to establish credibility of computational models in biology," *Progr. Biophys. Mol. Biol.*, vol. 129, pp. 13–19, Oct. 2016.



**BARBARA RITA BARRICELLI** had the opportunity to focus on several aspects of human-computer interaction, user-centered computing and design, software engineering and information systems domains. In particular, she developed and applied her expertise in defining methodologies in the development of interactive visual environments. She has developed a very good expertise in end-user development and meta design, and methods for collaborative knowledge-based management.

Her research is particularly focused on addressing the communication problems between different communities of practice working in common interdisciplinary work by means of interactive information systems built considering internationalization and localization needs of the end users. She applied computer semiotics theories and semiotic engineering methods for designing and developing internationalized interactive systems, localized to users' culture, gender, role played in specific contexts/domains and the digital platform in use to access systems. She has been active in this field since 2005 and applied her research in industrial design, cultural heritage, building and construction, hospitality and tourism, and medical domains. In the frame of various projects, she participated and had the opportunity to collaborate with other universities (several departments in different fields), high schools, hospitals and healthcare institutions, small and medium enterprises, and public bodies and administrations. She created a good network of relationships with researchers in several institutions in Europe and USA. She pairs off theoretical studies of general models to the design of methods and techniques and their applications (and validation) in several domains with the development of prototypes (for desktop, Web, and mobile-Android/iOS). She is the chair of IFIP TC13 WG6 human work interaction design.



**ELENA CASIRAGHI** was with the Information Technology Department, Valtion Teknillinen Tutkimuskeskus (VTT), Helsinki, Finland, developing virtual reality applications and face recognition applications (project in cooperation with Nokia). Her interest was in information technology research, in 2000. Her research work with the Department of Informatics of Milan started with the development of applications for face localization, identification, and recognition, by employing supervised and unsupervised learning algorithms. After she focused in the field of artificial intelligence to develop automatic systems for medical and biomedical image processing and pattern recognition. Since then, she has been developing several collaborations. Specifically, she was involved in digital chest radiographs, abdominal computer tomography scans, magnetic resonance images of fetal brains, mouse images produced by molecular imaging, and tissue images stained with different biological procedures and acquired by digital microscopes. She has also investigated novel learning algorithms for pattern recognition, manifold learning, and intrinsic dimensionality estimation to develop novel theories and automatic algorithms dealing with high-dimensional datasets characterized by a small cardinality

(small sample size problem). These studies led to the development of methods whose performance has been evaluated both by the comparison with the state-of-the-art techniques and tests on synthetic and real datasets related to problems in the fields of signal processing, image analysis, and bioinformatics. In the past two years, she has been collaborating with biological researchers of Consorzio Microscopic Image Analysis (MIA) with the University of Milan-Bicocca to develop automatic systems for the analysis quantification and comparison of serialized microscopic images of arteriosclerotic plaques, with the aim of investigating the main factors behind carotid plaque instability, the latest being the main cause of cerebral stroke. Due to its promising results, the developed system (called MIAQuant) has been lately adapted and generalized through the usage of machine learning techniques in order to be able to process images depicting tissue sections belonging to different body structures. Precisely, the novel system (called MIAQuant\_Learn) extracts, quantifies, and analyze the co-existence of markers characterized by any color and shape and being stained in contiguous sections extracted from any body tissue. These promising results obtained by the MIAQuant\_Learn motivate its extensive usage in oncological field to quantify and analyze cancerous tissues images produced either by Ospedale San Raffaele, Milano, or the Department of Experimental Oncology and Molecular Medicine, Fondazione IRCCS Istituto Nazionale dei Tumori.



**DANIELA FOGLI** was with the Joint Research Center of the European Commission, where she defined and experimented knowledge engineering approaches in the evaluation of reliability and safety of complex systems. She has been working in different research fields of computer science, since 1994. In the past, she had the opportunity to work in the artificial intelligence area, focusing on models and architectures for multiagent systems. In 2005, she has been a Visiting Scholar with the Center for Lifelong Learning and Design, University of Colorado at Boulder, USA. In particular, she conceived and applied an original framework to the control of autonomous mobile robots in simulated contexts. Since 2001, she has been involved in human-computer interaction. Her current research interests are thus concerned with the design and evaluation of interactive software systems, in particular, they include models and interfaces for end-user development, meta design, decision support systems, universal design, methodologies for the evaluation of web site quality, and advanced interfaces for collaborative robotics and ambient intelligence. In particular, she has contributed to the development of an original methodology to design software environments that allow domain experts to shape their software artifacts and eventually create new ones. She has applied her research in several domains such as mechanical engineering, medicine, emergency management, e-government, e-participation, collaborative web mapping, and game-based learning. She has performed her research activity in collaboration with several scholars of different universities and research centers. She is the Chair of the Steering Committee, International Symposium of End-User Development. She is serving as an Associate Editor for the *Decision Support Systems* journal.