Towards a Digital Twin of the Cardiovascular System

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Abstract: As medicine aims to become smarter, more pervasive, and more personalised, the concept of the Digital Twin has become a cornerstone of the entire base and applied research. The advantages of having Digital Twins to understand, predict and communicate complex mechanisms and functionalities have become of paramount importance in modern and future medicine. This paper presents an approach for the construction of a Digital Twin for the cardiovascular system. The approach, with the objective of being as lightweight and explainable as possible, is based on the integration of partial differential equation models and of realistic data. This integration can overcome both the rigidity of traditional model-based methods and the computational demands of modern deep learning approaches. A technical integration of a smart backend with a frontend based on virtual reality visor is presented in the paper.

1 INTRODUCTION

In a society where the use of high-tech devices in daily life is accessible to everyone, various research fields contribute to the ambitious goal of improving life. The impact achieved by the Internet of Things (IoT) massive employment in Cyber Physical Systems (CPSs) has been concretised into the availability of large amounts of data, enabling the application of sophisticated analysis techniques (Ramasamy et al., 2022). In this framework, medical applications are acquiring a role of significant importance. The availability of huge amounts of data from different sources contributes to having a holistic and complete view of medical problems, supporting the definition of more realistic predictive models. This ambitious purpose, integrated into the real clinical practice, is translated into the definition of innovative Decision Support Systems (DSSs) that contribute to achieve personalised medicine objectives (Marques et al., 2024).

In the direction of personalised approaches to disease diagnosis and therapy, efforts are devoted to Artificial Intelligence (AI)-based techniques that use Internet of Medical Things (IoMT) and wearable devices to adapt models, training them on patient data (Alshamrani, 2022). One of the principal strengths of Data-Driven (DD) techniques is flexibility, intended as the ability to tailor the model to the specific scenario, extracting the knowledge directly from the data and making the prediction more adherent to the real practice (Yu et al., 2021).

In this context, Digital Twins (DTs) play a crucial role. A DT is a virtual replica that monitors and interacts with a twinned physical system to predict and react to meaningful events, also aiming at an optimisation of the system itself (Campanile et al., 2023). One of the characteristics, that contributes to the great success achieved by DTs in the last decade, is its capability to enable holistic views of a problem (Hemamalini et al., 2024). This property allows the integration of data and information from different sources: from the vital parameters recorded by IoMT sensors and medical diagnostic data — such as Magnetic Resonance Imaging (MRI), Computed Tomography (CT) — towards the long-term information regarding follow-ups and therapies. Human Digital Twins (HDTs) are designed to replicate the patient's Health State (HS), considering his/her interaction with the physical environment and his/her responses to the treatments, enhancing and supporting personalised medicine.

The integrated view is not only limited to the in-

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formational sources, but also involves the analytics approaches. The concept of DT is based on the necessity to establish a connection between the digital and physical world. In the literature, this task is assessed by introducing a layered architecture, traditionally based on three interconnected layers (Hassani et al., 2022; Okegbile et al., 2023; Wang et al., 2022). In a previous work, we introduced a four-layers architecture for HDT to address the integration between Model Based (MB) and DD approaches (De Fazio et al., 2025). DD techniques are the key for exploiting the value of data obtained by IoT network. Despite being flexible and accurate in the predictions, the generated model is not fully explainable. In critical contexts, especially medical ones where some decisions could impact patients' HS, a clear view of the mechanisms that guided the decisions is strictly required. In other words, models' explainability is highly demanded in healthcare applications, reinforcing the medical staff reliance in AI application to support the decision-making process (Antoniadi et al., 2021). The integration of MB approaches, based on a domain-aware formal definition of the system, addresses this point, providing a transparent view of the model and including experts' knowledge. This hybrid approach, known as Scientific Machine Learning (SML), is raising interest in the scientific community and, particularly, in clinical practice.

This work introduces the Differential Equation baSed dIGital twiN (DESIGN) reference architecture for the definition of Digital Twin of the Cardio Vascular System (CVS-DT), framed in SML paradigm. In detail, the architecture is based on an Ordinary/Partial Differential Equation (O/PDE) model and Machine Learning (ML) approaches for adapting the model to real-world data. The complexity of the O/PDE system varies based on several factors. The Cardio-Vascular System (CVS) is represented using a simplified theoretical model for clarity and transparency.

The proposed architecture can be used with different modelling and DD techniques. In this paper, a more specific application for CVS-DT is presented, exploiting a set of differential equations, introduced by Zenker (Zenker et al., 2007), and the platform based on the study of Linial et al. (Linial et al., 2021).

While this paper generalises the results of a previous work designed for heartbeat prediction (Marrone, 2024), it presents novel original contributions, here summarised:

- presenting the DESIGN reference architecture for the CVS, extending the previous paper, oriented to the heartbeat prediction;
- using a more complex characterisation of the patient is possible, considering "systemic" parameters such as pressure, Heart Failure (HF), etc.;
- capability of modelling medical actions as therapies or drug administration, and the possibility to view the effect of patient's variables evolution.

Regarding these points, the paper is structured as follows: Section 2 presents a brief review of the works that encompass architectures and mathematical models underlying the definition of CVS-DTs; Section 3 reports the DESIGN reference architecture and detail the role of architecture elements; Section 4 defines the perspectives on how to conjugate the reference architecture and the Generative ODE modeling with Known Unknowns (GOKU) tool; Section 5 illustrates client-server architecture based on the microservice architectural pattern; Section 6 draws some conclusion and future perspectives.

2 RELATED WORK

This section provides a brief review of the literature, investigating two primary aspects adopted in the presented work: the development of a CVS-DT and the mathematical modelling of the CVS in general.

2.1 Digital Twins of CVS

The adoption of DT for the cardiovascular system will provide useful computational tools for both research and clinical practice. However, this requires reliable, well-defined models and methods for the different stages of the process (Coorey et al., 2022).

A Vascular Coordinate System (VCS) is presented in (Romero et al., 2025). It provides a clear and precise method for defining positions in a vascular section. The VCS model has been tested in several applications, including the development of a robust, low-dimensional, patient-specific vascular model used to study the phenotypic variability of the thoracic aorta in a cohort of patients. Point correspondences were used to construct a hemodynamic atlas of the aorta based on fluid simulations using the Navier-Stokes equations with the finite volume method.

While a Longitudinal Haemodynamic Mapping Framework (LHMF) is proposed in (Tanade et al., 2024), designed to capture personalised 3D blood flow dynamics over a timescale of months. This realised 3D coronary DT is continuously updated with data from wearable devices. In addition, hemodynamically similar heartbeats are grouped to minimise redundant simulations and enable accurate reconstruction of Longitudinal Hemodynamic Maps (LHM).

The study described in (Hermida et al., 2024) uses

DTs to improve the understanding and prenatal diagnosis of Coarctation of the Aorta (CoA). A statistical model of the shape of the fetal aortic arch is constructed from cardiac MRI data of 188 fetuses. A DT approach is proposed, which is capable of performing Computational Fluid Dynamics (CFD) simulations of the three-dimensional hemodynamics of the aortic arch to predict specific biomarkers and outcomes. In detail, analyses show that changes in arch shape and left-right ventricular output balance resulted in qualitatively similar haemodynamic changes. This approach highlights the importance of a combined anatomical and functional diagnosis in CoA.

A dynamic DT for healthcare, designed to optimise individual care pathways, particularly for women at risk of cardiovascular complications, is presented in (Mulder et al., 2022). This DT evolves over time, adapting to life conditions and patient needs, such as fertility prevention or acute disease management. Its dynamism makes it possible to update goals and forecasts based on up-to-date data specific to each stage of life. This capability to stay connected to the real system is possible due to wearable devices for continuous monitoring, enabling early intervention and improving the relevance of predictions compared to standard intermittent measurements.

The study (Chakshu et al., 2021) proposes, instead, a DT-based methodology for inverse analysis of the cardiovascular system using Recurrent Neural Networks (RNN), using a virtual database of patients. Blood pressure waveforms in different vessels are inversely reconstructed using Long Short-Term Memory (LSTM) models from non-invasive measurements on the carotid, femoral and brachial arteries. The system is used to detect and assess the severity of Abdominal Aortic Aneurysms (AAA). Data from accessible sites are used to predict pressure in other areas, and a Neural Network (NN) model analyses these predictions to identify and characterise aneurysms.

2.2 CVS Mathematical Models

CVS mathematical and numerical modelling has attracted considerable interest from the research community over the last 25 years. In this context, several studies exist in the literature. In (Quarteroni et al., 2017) an in-depth review of the main mathematical modelling of the CVS is presented. In detail, several models, describing arterial circulation and heart function with its electrical and mechanical activities, are presented.

An adaptive step method is proposed in (García-Mollá et al., 2014) for large Ordinary Differential Equation (ODE) systems on Graphics Processing Units (GPUs) for simulating electrical cardiac activity. The study compares the performance of the proposed adaptive methods with fixed-step methods and finds that while fixed-step methods can achieve higher speed, adaptive-step methods demonstrate superior accuracy and robustness.

A multiscale approach is presented in (Lagana et al., 2005), which is, instead, designed to prescribe appropriate and realistic boundary conditions for the 3D model of the circulation following the Norwood procedure. This method enhances a more accurate reproduction of realistic conditions compared to the classical approach, allowing the monitoring of both local and global haemodynamics.

A scientific machine learning approach to constructing a comprehensive surrogate model that integrates cardiac and cardiovascular functions is presented in (Salvador et al., 2024). This method involves training a system of Latent Neural Ordinary Differential Equationss (LNODEs) to learn the pressure-volume transients of a HF patient while varying 43 model parameters. These parameters capture cardiac electrophysiology, active and passive mechanics, and cardiovascular fluid dynamics. The training uses 400 3D-0D closed-loop electromechanical simulations. The LNODEs framework enables global sensitivity analysis and parameter estimation with uncertainty quantification, completing the process within 3 hours of computation on a single processor.

3 THE DESIGN APPROACH

This section outlines the proposed approach, starting from a reference scenario. In this scenario, a doctor and a patient are interacting: the patient is monitored, to retrieve his/her vital parameters, and the doctor decides which is the best action to perform for the patient's health, according to his/her HS. The main aim of the proposed architecture is to provide a system that could be:

- **R1:** fed by the patient's current data;
- **R2:** queried by the doctor to understand the possible evolutions of the patient's HS;
- **R3:** used as a what-if tool by the doctor to "test in-silico" the effect of possible actions (e.g., interventions, drug administration).

Figure 1 presents a reference architecture of the DESIGN approach.

At the centre of the approach, there is the definition of a set of **O/PDE** models, which are stored in the

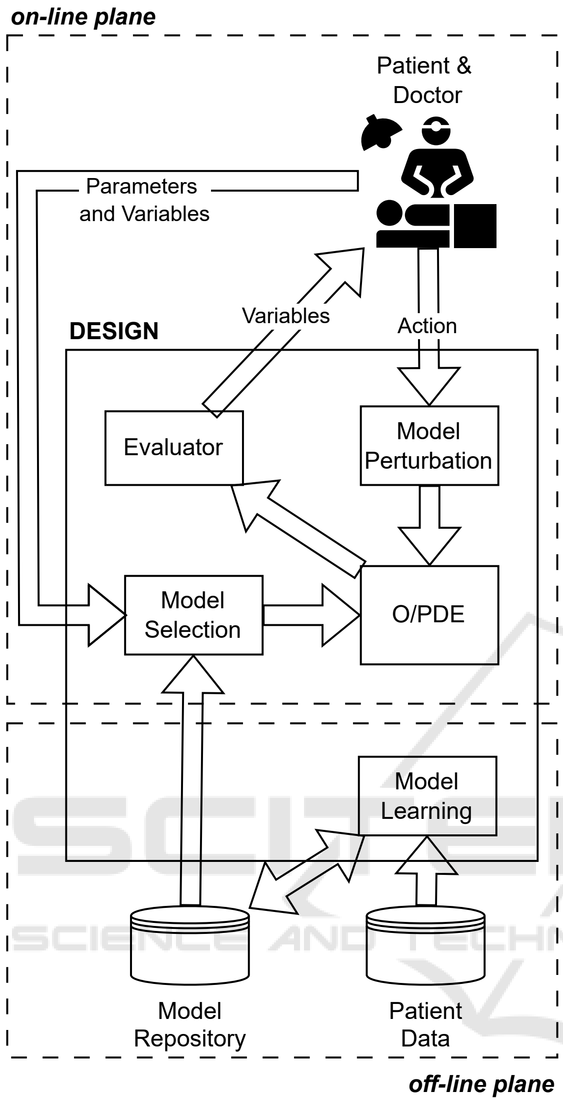

Figure 1: The overall approach.

Model Repository. These models describe the evolution in time of a set of variables, $\mathcal{X}$, subject to the value of some parameters, $\mathcal{P}$. It is worth underlining that the nature of these models is not strictly bounded to the O/PDE, since other possible forms fit in the DESIGN approach (e.g., ML or Petri Net (PN) models, or hybrid approaches).

The approach is then structured of two different planes, named **off-line plane** and **on-line plane**. The off-line plane is used to tune the models to obtain a usable Model Repository, while the on-line plane uses the trained models, choosing the proper values of the parameters in $\mathcal{P}$, and interacting with the doctor-patient scenario.

The Off-Line Plane. The off-line plane set of elements contains a tool, the *Model Learning*, and two repositories, *Patient Data* and *Model Repository*. By collecting and pre-processing patients' historical data, the Model Learning tool is responsible for analysing data and generating — also starting from pre-existing partial models stored in the Model Repository — one or more models describing the phenomenon under study. Once a model is generated by fitting the data, it is stored in the Model Repository.

The On-Line Plane. The on-line plane is responsible for setting up, running and evaluating the output of the DT. Once the patient's monitored data is generated, both parameters and variables are used to understand which model, in the Model Repository, adequately fits the data. This task is responsible for the *Model Selection* block, which produces the O/PDE model. Once the model is chosen and tuned with the specific features of the patient, the *Evaluator* analyses the model and provides the doctor the possible future evolution of the patient's HS, by computing model variables. As a last step, the doctor could define a possible treatment plan to improve the patient's HS by supposing one or more actions to perform; the *Model Perturbation* block affects the parameters and/or the variables of the model and allows the doctor to understand the effect of his/her hypotheses.

The O/PDE Model Structure To provide a detailed technical description of the approach, this section outlines the following model structure.

Let $x(t) =< x_1(t), x_2(t), \ldots, x_n(t) >$ denote the variables of the O/PDE system, referred to as the **Variable Vector**. Its temporal evolution explicitly depends on a set of parameters characteristic of the phenomenon under investigation, collected in the vector $p(t) =< p_1(t), p_2(t), \ldots, p_m(t) >$, referred to as the **Parameter Vector**. This dependence can be expressed as a vector of functional relationships $f_P(t; x(t))$, referred to as the **Dynamics Function**. When the vector $p(t)$ is set, it defines a specific configuration of the phenomenon under study (e.g., in case of the CVS, this could represent a particular heart condition or a heart undergoing a specific medical treatment). Once a configuration is defined, the goal is to estimate the temporal evolution of the phenomenon through the integration of the O/PDE system.

This function is explicated in a system of k differential equations regarding the time variable t, as shown in Eq. 1[1]:

[1]This system is based on the hypothesis that $k \leq n$. The

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$$\begin{cases} \frac{dx_1}{dt} = f_{1,P}(t; x_1, x_2, \ldots, x_n) \\ \frac{dx_2}{dt} = f_{2,P}(t; x_1, x_2, \ldots, x_n) \\ \ldots \\ \frac{dx_k}{dt} = f_{k,P}(t; x_1, x_2, \ldots, x_n) \end{cases} \tag{1}$$

The three presented blocks map the three functionalities described at the beginning of this section (see Table 1).

Table 1: Mapping between functionalities and blocks.

Use Case	Block
R1	Model Selection
R2	Evaluator
R3	Model Perturbation

In Section 5, a concrete architecture is reported, and its realisation is described. While the reported example and the entire paper are devoted to the CVS, it is clear that the overall approach described in this section can be extended also to other systems (e.g., renal system, hepatic system).

4 BUILDING A CARDIOVASCULAR SYSTEM DIGITAL TWIN

This section shows how the general approach presented in Section 3 can be customised into Differential Equation baSed dIGital twiN for Cardio-Vascular System ($DESIGN_{CVS}$) for the realisation of a CVS-DT, possibly exploiting existing platforms. In particular, the GOKU approach presented in (Linial et al., 2021) has been chosen as the best candidate for realising $DESIGN_{CVS}$.

Hence, this section is structured as follows:

- the O/PDE model underlying this example, which is the one presented by Zenker (Zenker et al., 2007), is presented in Subsection 4.1;
- the GOKU approach and workflow and the adaptation of GOKU to the $DESIGN_{CVS}$ are presented in Subsection 4.2;
- the execution of the experiments and the discussion of the results in the proposed demonstration are presented in Subsection 4.3.

system can be completed by other $n-k$ equations, needed to uniquely determine the solution, and that can be of a different nature (e.g., non-differential).

4.1 The Zenker's -ODE Model

As outlined in Section 2, significant research has been conducted on the development of a O/PDE system to represent the functioning of the CVS. This approach is built upon the proposal by Zenker et al. (Zenker et al., 2007). It introduces a simplified representation of the CVS focused on monitoring key variables, reported in Table 2, according to patient parameters.

Table 2: Variables used in the CVS O/PDE.

Name	Description	Unit
P_a	Artherial Pressure	$mmHg$
P_v	Venous Pressure	$mmHg$
S	Baroreflex's response	—
S_V	Stroke volume	ml
R_{TPR}	TPR value	$mmHg \cdot s/ml$
f_{HR}	Heart Rate (HR) value	Hz

Consequently, $x(t) = x^O(t)?x^H(t)$ means that the Variable Vector is constituted by two sub-vectors concatenated by the ? operator. More in detail, $x^O(t) =< P_a(t), P_v(t), f_{HR}(t) >$ refers to the variables in $\mathcal{X}_O$ while $x^H(t) =< R_{TPR}(t), S(t), S_V(t) >$ refers to the variables in $\mathcal{X}_H$.

Table 3, instead, describes the Parameter Vector and the meaning of each parameter.

Table 3: System Parameter Vector used in the CVS O/PDE.

Parameter	Description	Unit
K_{width}	Baroreflex curve's slope	-
τ_{baro}	Baroreflex's response time	s
T_{sys}	Time of systolic phase	s
$f_{HR_{min}}$	HR min value	Hz
$f_{HR_{max}}$	HR max value	Hz
$I_{external}$	External blood flow	ml/s
$V_{ed,0}$	Initial telediastolic volume	ml
$S_{V_{Mod}}$	Possible modification in S_V	ml
K_{elv}	Ventricular compliance constant	$1/ml$
$P_{a,set}$	Baroreflex target pressure	$mmHg$
$cprsw_{min}$	PRSW min slope	$mmHg$
$cprsw_{max}$	PRSW max slope	$mmHg$
$P_{v,0}$	Initial venous pressure	$mmHg$
C_a	Arterial compliance	$ml/mmHg$
C_v	Venous compliance	$ml/mmHg$
R_{valve}	Atrial valve resistance	$mmHg \cdot s/ml$
$R_{TPR_{min}}$	TPR min value	$mmHg \cdot s/ml$
$R_{TPR_{max}}$	TPR max value	$mmHg \cdot s/ml$
$R_{TPR_{Mod}}$	Possible modification in R_{TPR}	$mmHg \cdot s/ml$

The specific model is reported in three equations, Eq. 2, Eq. 3, and Eq. 4.

$$\frac{dS(t)}{dt} = \frac{1}{\tau_{baro}} \left(1 - \frac{1}{1 + e^{-k_{width}(P_a(t) - P_{a,set})}} - S(t) \right) \tag{2}$$

$$\begin{cases} R_{TPR}(t) = S(t)(R_{TPR_{max}} - R_{TPR_{min}}) + R_{TPR_{min}} + R_{TPR_{Mod}} \\ f_{HR}(t) = S(t)(f_{HR_{max}} - f_{HR_{min}}) + f_{HR_{min}} \end{cases} \tag{3}$$

$$\begin{cases} \frac{dS_v(t)}{dt} = I_{external} \\ \frac{dP_a(t)}{dt} = \frac{1}{C_a}\left(\frac{P_a(t)-P_v(t)}{R_{TPR}(t)} - S_v(t)\cdot f_{HR}(t)\right) \\ \frac{dP_v(t)}{dt} = \frac{1}{C_v}\left(-C_a\frac{dP_a(t)}{dt} + I_{external}\right) \end{cases} \tag{4}$$

This specific O/PDE model has an appropriate integration process, which is expressed in the following steps:

1. a solution of $S(t)$ is found (Eq. 2);
2. R_{TPR} and $f_{HR}(t)$ are easily computed (Eq. 3);
3. the rest of the equations are solved (Eq. 4).

4.2 Implementing the $DESIGN_{CVS}$ Approach

The GOKU approach aims to integrate the defined O/PDE system into a hybrid DD architecture to forecast the CVS's HR value (Linial et al., 2021). This mixing of methods is conformant with the main objective of that work, which is to cope with uncertainty in the estimation of the whole parameter vector as well as the sub-vector of the hidden variables.

More in details, the GOKU architecture employs a Virtual Auto Encoder (VAE) model, with the aim to infer part of the model from observable variables:

- learning the patient's HS in terms of initial conditions $x^O(t_0)$ of the O/PDE system, its specific parametrisation $p(t_0)$, and the relationship between the system's solution $x^O(t_1)$ with the final output $x^H(t_1)$;
- the input of the VAE stage consists of a triplet of values $x^O(t_0)$, which is used to compute the initial state of the O/PDE system, including the System Parameter Vector $\mathcal{P}$;
- subsequently, the O/PDE system is solved, and the solution is used to infer the triplet $x^O(t^*)$.

Starting from this background knowledge, the DESIGN architecture "instantiation" on CVS here proposed is shown in the Figure 2, offering the advantage of predicting the future state by integrating the previously defined O/PDE system and exploiting some of the GOKU components.

With respect to the three phases of the GOKU approach, DESIGN maps each phase into one of its components:

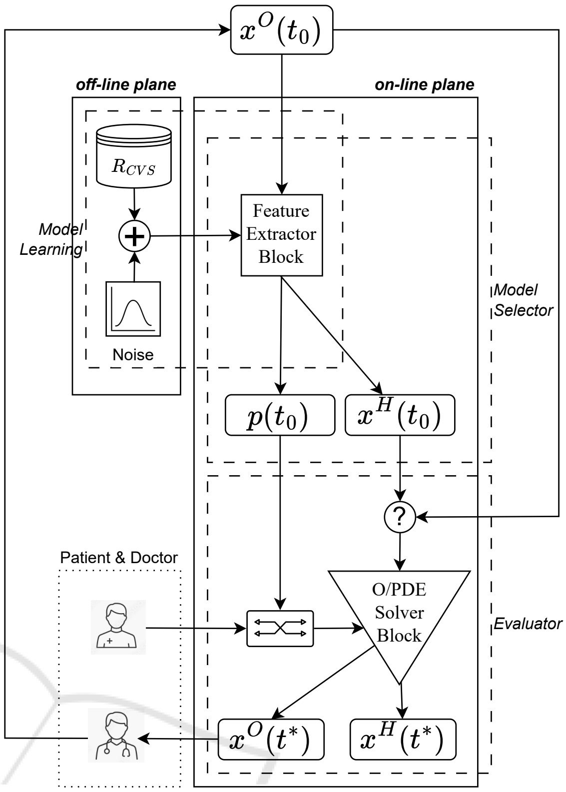


Figure 2: DESIGN architecture representation.

- the Model Learning starts from the definition of a relation between the sets $\mathcal{P}$ and $\mathcal{X}$ with the specific objective of representing the dataset (see Eq.5).

$$R_{CVS} \subseteq \mathcal{X}_O \times \mathcal{X}_H \times \mathcal{P} \tag{5}$$

  As this dataset can be synthetic, noise could be added as well, to let the training of a *Feature Extractor Block*.
- the Model Selector is based on this *Feature Extractor Block*, being able to infer from observable variables $x^O(t_0)$ at a certain instant of time t_0. This block extracts the parameters $p(t_0)$ and the hidden variables $x^H(t_0)$ at t_0.
- the Evaluator exploits the *ODE Solver Block*. This block gets as input the given initial observed variables $x^O(t_0)$ as well as the initial inferred hidden variables $x^H(t_0)$, under the configuration determined by $p(t_0)$. The *ODE Solver Block*, by implementing the solution process reported in Subsection 4.1. Once the ODE model is solved, the time series $x^O(t^*)$ and $x^H(t^*)$ with $t^* > t_0$ are generated. $x^O(t^*)$ is then reported to the DT user.

In addition, $DESIGN_{CVS}$ incorporates a dual adaptation mechanism to address the following needs:

- Patient Adaptation: over time, a patient's HS may change (e.g., due to the onset of haemorrhage).

This adaptation mechanism is implemented considering the feedback from the DT user to $x^O(t_0)$.

- Medical Intervention: medical staff may intervene after analysing the patient's vital parameters (e.g., by administering a treatment). This mechanism is embedded in the change of the parameters by the DT user. Such changes are then mixed with the original parameter to determine the configuration of the *ODE Solver Block*.

4.3 Use Case and Discussion

This subsection presents a first attempt of integrating between $DESIGN_{CVS}$ and GOKU. To accomplish this task, three distinct CVS HSs have been detected. In detail, the *Healthy_config*, which represents the CVS of a healthy patient, the *Unhealthy_config*, which represents the CVS of a patient with mild HF, and the *Bleeding_config*, representing the CVS of a patient during a haemorrhage, are considered. Table 4 reports the configuration's details, while the parameter values for each configuration are shown in Table 5.

Table 4: Sample CVS configurations.

ID	Description
C_{HE}	This is the configuration corresponding to a healthy patient.
C_{UH}	This is the configuration corresponding to an unhealthy patient, suffering from mild HF.
C_{BL}	This is the configuration corresponding to a patient, who is bleeding due to some trauma or other causes.

A simulation process, inspired by the approach in (Linial et al., 2021), was used to generate a dataset consisting of 1000 samples, each representing a different patient. Each sample is composed of a time series of length 400 seconds, capturing the temporal evolution of key vital parameters, including P_a, P_v, S_V, and f_{HR} (see Table 6).

Then, the GOKU prototype is used to simulate these CVS configurations. The results obtained from the simulations are summarized in Table 7.

As reported in Table 7, $x^O(t^*)$ has been accurately defined, demonstrating an appropriate response to the proposed configurations. Specifically:

- P_a in C_{HE} exhibits an average trend around 78.8 $mmHg$, corresponding to a healthy patient. It slightly increases to approximately 97.6 $mmHg$ in C_{HF}, which represents a patient with mild HF. Moreover, it significantly drops to 70.7 $mmHg$ in C_{BL}, simulating a severe haemorrhage;

Table 5: Parameter Vector for each configuration.

Parameter	C_{HE}	C_{UH}	C_{BL}	Unit
C_a	4	-	-	$ml/mmHg$
C_v	111.11	-	-	$ml/mmHg$
R_{valve}	0.0025	-	-	$mmHg \cdot s/ml$
τ_{baro}	20	-	-	s
$P_{a,set}$	70	-	-	$mmHg$
K_{width}	0.1838	-	-	—
$cprsw_{min}$	25.9	-	-	$mmHg$
$cprsw_{max}$	103.8	-	-	$mmHg$
$f_{HR_{min}}$	0.6	1.2	-	Hz
$f_{HR_{max}}$	3.1	-	-	Hz
$R_{TPR_{min}}$	0.5	0.6	-	$mmHg \cdot s/ml$
$R_{TPR_{max}}$	2.1	-	-	$mmHg \cdot s/ml$
$P_{v,0}$	2.03	-	-	$mmHg$
$V_{ed,0}$	7.14	-	-	ml
T_{sys}	0.267	-	-	s
K_{elv}	0.066	-	-	$1/ml$
$S_{V_{Mod}}$	0	0.005	0.01	ml
$R_{TPR_{Mod}}$	0	-0.2	-	$mmHg \cdot s/ml$
$I_{external}$	0	-	-0.2	ml/s

Table 6: Few rows of the dataset simulated in$DESIGN_{CVS}$ architecture.

Patient Id	Time	P_a	P_v	S_v	S	f_{HR}	Conf Id
1	1	107	5.50	94.6	0.0196	71.6	C_{UH}
1	2	95.8	4.63	94.6	0.0188	73.7	C_{UH}
...	...	...	...	...	...	...	...
1000	399	82.7	4.98	94.9	0.165	58.2	C_{HE}
1000	400	72.1	6.38	94.9	0.165	63.1	C_{HE}

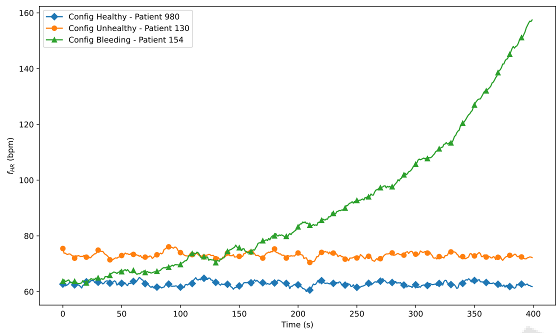
- P_v does not show substantial variations across the three configurations. However, in the cases of a healthy patient and a patient with severe haemorrhage, similar trends to those observed in P_a monitoring can be identified (1.30 $mmHg$, 1.37 $mmHg$). In contrast, for the patient with mild HF, a value close to zero is observed (0.780 $mmHg$);
- f_{HR} is particularly sensitive to the defined configuration. As expected, it remains within a normal range of around 60.8 *bpm* for a healthy patient, increases slightly for a patient with mild f_{HR} (72.8 *bpm*), and rises exponentially for a patient suffering from severe haemorrhage (95.6 *bpm*).

These variations follow a trend consistent with the physiologically realistic f_{HR} models expected for both healthy and non-healthy patients, as illustrated in Figure 3a. Figure 3b and Figure 3c respectively present the results for P_a and P_v.

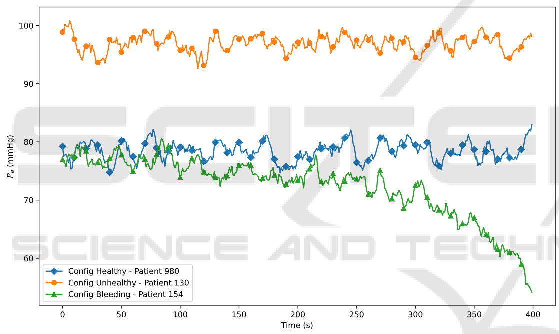
Some limitations, arising from the use of the GOKU framework, have clearly shown the path for a complete integration between the two approaches. As GOKU does not explicitly support a change in parameter' evolution, a modification of the mechanism for getting such parameters is due. Furthermore, the main mechanism of GOKU must be integrated into a

Table 7: Result Summary.

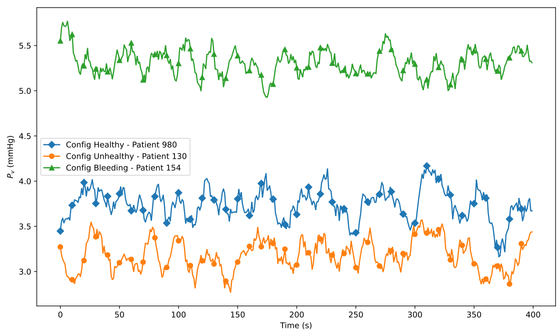
$Conf_{id}$	f_{HR} (bpm)			P_a $(mmHg)$			$P_v(mmHg)$		
	mean	min	max	mean	min	max	mean	min	max
1	60.8	47.2	73.9	78.8	53.8	102	5.14	1.30	8.81
2	72.8	59.8	86.7	97.6	72.9	121	4.39	0.780	8.20
3	95.6	52.3	186	70.7	5.61	99.2	4.88	1.37	9.01



(a) Heart Rate Trend.



(b) Arterial Pressure Trend.



(c) Venous Pressure Trend.

Figure 3: Plots of heart rate, arterial pressure, and venous pressure.

continuous mechanism for patient's monitoring, closing the loop of interaction between the $DESIGN_{CVS}$ architecture and the medical staff.

5 TOWARDS A CLIENT-SERVER ARCHITECTURE

Figure 4 illustrates a client-server architecture based on the microservice architectural pattern, to fully implement the reference architecture of DESIGN.

The Server exposes four main endpoints:

- *training*, which is used to train a CVS O/PDE model. With the *training* application, a user may select a specific O/PDE model from the Model Repository, and a subset of data in the Patient Data repository, to train the model, according to the GOKU workflow. This service may use another internal service — *simulation* — that could be adopted to augment data. As in (Linial et al., 2021), O/PDE integration can be used to generate time series — with a proper noise level — on which Deep Learning (DL) models are trained;
- *instantiate*, this endpoint is used to instantiate a new patient, with a specified set of parameter values. The Model Selector — which is responsible for serving this endpoint — instantiates from the Model Repository the specified model and adds this instantiation into a Patient Cache, which contains current patient models and their evolutions. The service returns a `patient_id` to the client;
- *step*, this endpoint needs the specification of the `patient_id` from the client. The service retrieves the patient model from the Patient Cache and then integrates the instantiated equations to simulate the evolution of the $x(t)$ Variables Vector;
- *perturb*, this endpoint changes the values of one or more parameters in $\mathcal{P}$, present in the Patient Cache, according to a specified `patient_id`.

Due to compatibility with the GOKU framework and to the high flexibility of the language, the Python language is a preferable choice to implement the server.

A client ends the architecture, opening to be integrated into the Virtual Reality / Augmented Reality (VR/AR) visor. The integration of VR/AR visors will boost the impact of the DT, giving to its usage also the capability to practically see the effects of

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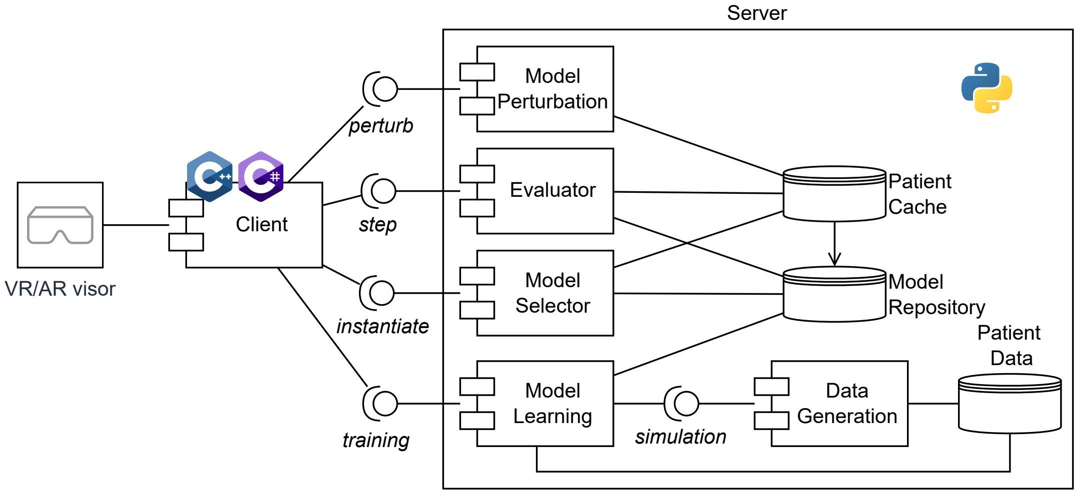

Figure 4: The DESIGN microservice architecture.

Variable Vector changes. To make this solution easy to integrate into existing VR/AR platforms — e.g., Unity, Unreal Engine — high-performance languages as C#/C++ are perfect candidates to implement this tool.

6 CONCLUSION AND FUTURE WORK

This paper presents a reference architecture for a CVS-DT, and an adaption of an existing prototype for an effective implementation of such software. By means of the proposed methods and techniques, medical staff can query a model of a CVS — related to a specific patient — and can obtain information regarding the patient's HS. The proposed architecture can also enable what-if analysis on possible treatments and drug administrations.

First future research efforts will be devoted to the completion of the DESIGN tool and to the integration of real-world and simulated data. Furthermore, the application to other human body systems is another possible research task. Of course, exploring new body mechanisms/systems and defining further variables/parameters to study, implies considering other O/PDE models.

From the technological point of view, the building of a full demonstrator, based on IoT sensors, capable of interacting with the physical world as well as with the DESIGN platform is to build. This scenario would bring the possibility to run tests with physical subjects (i.e., human beings and/or Human Patient Simulators (HPSs)).

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