Efficient approximation of cardiac mechanics through reduced-order modeling with deep learning-based operator approximation

Ludovica Cicci¹ | Stefania Fresca¹ | Andrea Manzoni¹ | Alfio Quarteroni¹,²

⁰MOX-Dipartimento di Matematica, Politecnico di Milano, Milan, Italy
²Mathematics Institute, École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

Correspondence
Andrea Manzoni, MOX-Dipartimento di Matematica, Politecnico di Milano, Milan, Italy.
Email: andrea1.manzoni@polimi.it

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Abstract
Reducing the computational time required by high-fidelity, full-order models (FOMs) for the solution of problems in cardiac mechanics is crucial to allow the translation of patient-specific simulations into clinical practice. Indeed, while FOMs, such as those based on the finite element method, provide valuable information on the cardiac mechanical function, accurate numerical results can be obtained at the price of very fine spatio-temporal discretizations. As a matter of fact, simulating even just a few heartbeats can require up to hours of wall time on high-performance computing architectures. In addition, cardiac models usually depend on a set of input parameters that are calibrated in order to explore multiple virtual scenarios. To compute reliable solutions at a greatly reduced computational cost, we rely on a reduced basis method empowered with a new deep learning-based operator approximation, which we refer to as Deep-HyROMnet technique. Our strategy combines a projection-based POD-Galerkin method with deep neural networks for the approximation of (reduced) nonlinear operators, overcoming the typical computational bottleneck associated with standard hyper-reduction techniques employed in reduced-order models (ROMs) for nonlinear parameterized systems. This method can provide extremely accurate approximations to parametrized cardiac mechanics problems, such as in the case of the complete cardiac cycle in a patient-specific left ventricle geometry. In this respect, a 3D model for tissue mechanics is coupled with a 0D model for external blood circulation; active force generation is provided through an adjustable parameter-dependent surrogate model as input to the tissue 3D model. The proposed strategy is shown to outperform classical projection-based ROMs, in terms of orders of magnitude of computational speed-up, and to return accurate pressure-volume loops in both physiological and pathological cases. Finally, an application to a forward uncertainty quantification analysis, unaffordable if relying on a FOM, is considered, involving output quantities of interest such as, for example, the ejection fraction or the maximal rate of change in pressure in the left ventricle.
1 | INTRODUCTION

Cardiac mechanics simulations aim at reproducing the response of the cardiac muscle under specified loading conditions and consist of large-scale differential systems governed by the equations of elastodynamics, complemented with suitable constitutive laws to correctly capture the mechanical behavior of the myocardium. Modeling the cardiac dynamics is therefore a challenging task, as the myocardium is a strongly anisotropic, incompressible material, characterized by an exponential strain energy function $^{1,2}$ and a fiber-sheet structure. $^3$ Another crucial aspect is the inclusion in the mathematical model of the active forces that drive the contraction mechanism of the muscle, which is able to contract after being electrically activated; these active properties are time-dependent and anisotropic. In the last decades, there have been substantial advances in the development of multi-physics, multi-scale mathematical models of the cardiac functions. $^{4-10}$ The availability of realistic, patient-specific simulations, both for normal and diseased hearts, allows for a quantitative understanding of cardiac physiology and raises the prospect of their use in a number of applications, for example, for improving diagnosis, providing real-time decision support, predicting prognosis and, ultimately, supporting clinical decisions. $^{11-14}$ However, the translation of cardiac simulations into the clinical practice is often hampered by the very high computational costs involved in the solution to the underlying problem by means of suitable numerical procedures, such as the finite element (FE) method. $^{15-20}$

While FE models of the heart provide valuable information, they may require up to hundreds of thousands degrees of freedom (dofs) to obtain accurate numerical results. In these cases, despite great advancements recently made in the development of highly efficient frameworks for 3D-0D electromechanics simulations, $^{9,21}$ computing even just a few heartbeats can require several minutes or hours of wall time, and usually demands access to high-performance computers. Additionally, cardiac models depend on a large set of patient-specific parameters characterizing, for example, material properties, boundary/initial conditions, geometrical features, or local fiber orientation, which are affected by uncertainty and should be properly calibrated through optimization routines. Being able to perform efficient numerical simulations in this context is indeed essential to explore multiple virtual scenarios, to quantify cardiac output biomarkers and related uncertainties, as well as to evaluate the impact of pathological conditions. All these tasks require repeated model evaluations over different input parameter values, thus relying on high-fidelity, full-order models (FOMs) can become computationally unaffordable.

Alternative numerical methods have been developed in the past decades aiming at computing reliable solutions to parameter-dependent problems at a greatly reduced computational cost, such as data-driven surrogate models and projection-based reduced-order models (ROMs). The former aim to learn, in a non-intrusive way, the hidden relation between input parameters and corresponding output quantities of interest (possibly including the solution to the problem) from usually large data sets of input–output pairs. For instance, in $^{22,23}$ surrogate models were generated via the polynomial chaos expansion approach to accelerate uncertainty quantification (UQ) studies and sensitivity analysis (SA) of left ventricular mechanics. Numerous machine learning-based models have been proposed as real-time cardiac mechanics simulators, $^{24-27}$ while statistical emulators, such as Gaussian processes, have been used to speed-up parameter inference, $^{28,29}$ to enable global sensitivity analysis studies, $^{30,31}$ or to reduce the complexity of parametric searches for high-fidelity models. $^{32}$ These models, well suited for the rapid and repeated evaluation of input–output maps, may lack of accuracy when dealing with patient-specific simulations of the cardiac activity.

On the contrary, projection-based ROMs, such as the Galerkin-reduced basis (RB) method, replace the high-fidelity problem with a reduced problem featuring lower computational complexity, still retaining the essential features of the FOM. These methods are usually characterized by a splitting of the reduction procedure into an expensive offline phase, during which multiple parametric instances of the FOM are computed to generate a basis for the reduced subspace, and an efficient online phase. A reduction strategy for the quasi-static mechanics problem is proposed in Reference $^{33}$, where proper orthogonal decomposition (POD) for basis construction is combined with suitable hyper-reduction techniques to efficiently handle nonlinear terms, whereas in References $^{34}$ POD-Galerkin ROMs exploiting the discrete empirical interpolation method (DEIM) $^{35}$ have been exploited for the efficient and accurate solution to the
time-dependent cardiac problem, on both idealized and patient-specific left ventricle geometries, albeit using a relative low number of degrees of freedom. In References 36,37, POD has been applied to reduce the structural dimension of a monolithic 3D-0D coupled structure-circulation model in a four-chamber, patient-specific geometry. Nonetheless, despite their application in a wide range of scenarios, relatively contained speed-ups are achieved by projection-based ROMs in cardiac mechanics due to the highly nonlinear nature of the problem. In all these cases, the construction of a reduced subspace to approximate the high-fidelity solution manifold does not pose serious issues, resulting in extremely low dimensional spaces even for complex material laws. Indeed, the computational bottleneck is represented by the hyper-reduction stage, namely, the assembling of the reduced nonlinear operators and their projection though DEIM.

Motivated by this observation, in this work we address the efficient solution to parameterized cardiac mechanics problems by means of our newly developed Deep-HyROMnet (deep hyper-reduced-order model network) method.38 The key idea of this strategy is to leverage a Galerkin-RB method for the dimensionality reduction of the solution space and deep neural networks (DNNs) – as the ones introduced in References 39,40 for the DL-ROM and the POD-DL-ROM techniques – to perform hyper-reduction, that is, to approximate reduced nonlinear operators efficiently. Whilst DL-ROMs aim at approximating, in a non-intrusive way, the solution dynamics, the Deep-HyROMnet method exploits DNNs to avoid expensive array assembling during the construction of the reduced Newton system. Unlike data-driven strategies, for which the predicted output is not guaranteed to satisfy the underlying PDE, Deep-HyROMnet is a fully physics-based ROM strategy, as it computes the problem solution by solving a reduced nonlinear system built by enforcing the problem equations onto a linear, low-dimensional subspace. In this work, we show how Deep-HyROMnet outperforms classical POD-Galerkin-DEIM ROMs in terms of computational speed-up for the solution to a 3D-0D coupled structure-circulation model for the left ventricle, both in physiological and pathological scenarios. By providing accurate and computationally efficient simulations of the left ventricle dynamics, the reduction strategy is successfully used to address the solution to many-query tasks, such as the ones arising in a forward UQ context.

The rest of the paper is structured as follows. In Section 2, we formulate the problem we focus on, that is, a monolithically coupled structure-circulation model for the description of the mechanical activity of the left ventricle during a whole heartbeat (Section 2.1). Then, we describe the high-fidelity full order model (Section 2.2) used to generate data for – and to assess the performance of – our reduced order model, as well as the construction of this latter through the Deep-HyROMnet technique (Section 2.3).

The numerical performances of the resulting hyper-reduced ROM are assessed both on a physiological scenario and in presence of an ischemic region inside the myocardium (Section 3). A detailed discussion on the obtained results, showing a possible application of Deep-HyROMnet in the multi-query context of forward UQ, is then reported in Section 4, whilst conclusions are drawn in Section 5.

2 | METHODS

After formulating the problem we focus on, we show how to solve it efficiently through the proposed Deep-HyROMnet technique. In particular, we recall the construction of a full-order model relying on the finite element method, we set a POD-Galerkin reduced order model, and we introduce the approximation of the reduced operators through deep neural networks.

2.1 | Mathematical models: 3D-0D mechanics-circulation model

The solution of cardiac mechanics problems involves the interaction between several biophysical phenomena contributing to the functioning of the heart, namely, electrophysiology, biochemistry, mechanics and fluid dynamics, each described by suitable models (see Figure 1) written in terms of PDEs and/or ODEs.18,19 Electrophysiology corresponds to the propagation of the electrical potential and ion dynamics, and it describes the electric activity of cardiac muscle cells; the activation of cardiomyocytes is the result of complex mechano-chemical interactions among contractile proteins,41 and is responsible for the active tension at tissue level. This latter quantity determines the coupling with the mechanical model. In this work, we focus on the mechanical behavior only, surrogating the active force generation model through an explicit, periodic, analytical active tension function. See, References 42,43,10 for a detailed presentation of a fully coupled cardiac electromechanics model.
2.1.1 | 3D elastodynamics model

Let us denote by \( \Omega_0 \subset \mathbb{R}^3 \) the reference configuration of a continuum body \( B \) at time \( t = 0 \), and by \( \Omega_t \subset \mathbb{R}^3 \) its current configuration at time \( t > 0 \). The motion of the body \( B \) is defined as the map \( \chi : \Omega_0 \to \Omega_t \), for all \( t > 0 \), such that \( x = \chi(X, t) \), where \( X \) and \( x \) denote the position vector in the reference \( \Omega_0 \) and in the current \( \Omega_t \) configurations, respectively. The deformation of the body \( B \) is described by means of the displacement field \( u(X, t) = \chi(X, t) - X \), which represents the unknown of our problem and depends on a set of model parameters, such as material coefficients, boundary/initial conditions, source terms and so on, here collectively denoted by \( \mu \in \mathcal{P} \subset \mathbb{R}^P \), where \( \mathcal{P} \) is a compact set. Hence, we have \( u = u(X, t; \mu) \). Other important quantities in the framework of continuum mechanics are the deformation gradient \( F \), the right Cauchy-Green tensor \( C \) and the Green-Lagrange strain tensor \( E \), that are defined as

\[
F = \frac{\partial \chi}{\partial X}, \quad C = F^T F, \quad E = \frac{1}{2} (C - I),
\]

respectively. Note that all the above quantities depend on the parameter vector \( \mu \), as well as on \( t \) and \( X \) – this latter being hereon undeclared. Moreover, for the sake of brevity, also the dependence on \( t \) and \( \mu \) will be sometimes omitted. The change in volume between the reference and the current configuration at time \( t > 0 \) is given by the determinant of the deformation gradient, that is, \( J = \det F \), known as the volume ratio. A motion for which \( J = 1 \) is said to be isochoric or isovolumetric. The displacement field \( u(\mu) \in \Omega_0 \times \mathbb{R}^3 \), for \( \mu \in \mathcal{P} \), can be found by solving the equation of motion given by the balance of linear momentum,

\[
\rho_0 \frac{\partial^2 u(t; \mu)}{\partial t^2} - \nabla_0 \cdot P(t; \mu, t; \mu) = b_0(t; \mu), \quad \text{in} \ \Omega_0, t > 0,
\]

when boundary and initial conditions are provided. Here, \( \rho_0 > 0 \) denotes the density of the body, \( P \) is the first Piola-Kirchhoff stress tensor and \( b_0 \) represents a body force field. Suitable constitutive laws, that is, stress–strain relationships, must be specified to describe the behavior of the given material. Furthermore, to incorporate active contraction of the tissue, we adopt an active stress approach, which assumes an additive decomposition of the stress tensor into a passive and an active contribution as

\[
P = P_p + P_a.
\]
For what concerns the passive term $P_p$, we consider the myocardium as a hyperelastic tissue, therefore we can assume the existence of a strain density function $W$ such that

$$P_p(F) = \frac{\partial V(F)}{\partial F}.$$  

In this work, we adopt the transverse isotropic constitutive model proposed in Reference 1, known as the Guccione relation, with an additional term penalizing large volume variations, so that the passive term of the Piola-Kirchoff stress tensor is given by

$$P_p = \frac{\partial}{\partial F} (W_{Guccione} + W_{vol}) = \frac{\partial}{\partial F} \left( \frac{C}{2} (e^q - 1) + \frac{K}{2} (J - 1) \ln(J) \right),$$  

with the following form for $Q = Q(F)$ to describe anisotropy with respect to a local orthonormal coordinate system (with axes parallel to the local fiber, sheet and sheet-normal directions),

$$Q = b_f E_{ff}^2 + b_s E_{ss}^2 + b_n E_{nn}^2 + b_f \left( E_{fs}^2 + E_{sf}^2 \right) + b_n \left( E_{fn}^2 + E_{nf}^2 \right) + b_{sn} (E_{sn}^2 + E_{ns}^2).$$

Here, $E_{ij}, i, j \in \{f, s, n\}$ are the components of the Green-Lagrange strain tensor $E = E(F)$, the material constant $C > 0$ is used for scaling the stresses and the coefficients $b_f, b_s, b_n$ are related to the material stiffness in the fiber, sheet and cross-fiber directions, respectively. Finally, the bulk modulus $K > 0$ is the penalization term controlling the incompressibility of the myocardial tissue. Since active properties are time-dependent and anisotropic, that is, with more active stress generated along the local muscle fiber direction, we model the tissue stretch along the reference fiber direction $f_0 \in \mathbb{R}^3$ only, and define

$$P_a(F) = T_a(t; \mu) \left( F f_0 \otimes f_0 \right),$$  

where $T_a$ represents the active tension generated at cellular level. A parameterized surrogate model for the active tension, introduced to avoid the coupling with the electrophysiology model, is described in Section 2.1.3. From now on, since the deformation gradient can be calculated as $F = I + \nabla_0 u$, we write for the stress tensor $P = P(u(t; \mu), t; \mu)$.

The strong formulation of the nonlinear parameterized initial-boundary value problem for cardiac mechanics that we consider reads as follows: given $\mu \in \mathcal{P}$, find the displacement field $u(\mu) : \Omega_0 \times [0, T) \rightarrow \mathbb{R}^3$ such that

$$\begin{align*}
\rho_0 \partial_t^2 u(t; \mu) - \nabla \cdot P(u(t; \mu); \mu) &= 0 & \text{in } \Omega_0 \times (0, t_f), \\
P(u(t; \mu); t, \mu) \mathbf{N} - p_{LV}(t; \mu) \| J(t; \mu) F^{-T}(t; \mu) \| v(t; \mu) &= 0 & \text{on } \Gamma_{0}^{\text{base}} \times (0, t_f), \\
P(u(t; \mu); t, \mu) \mathbf{N} + K^{sp} u(t; \mu) + C^{sp} \dot{u}(t; \mu) &= 0 & \text{on } \Gamma_{0}^{\text{epi}} \times (0, t_f), \\
P(u(t; \mu); t, \mu) \mathbf{N} = -p_{LV}(t; \mu) J(t; \mu) F^{-T}(t; \mu) \mathbf{N} & = 0 & \text{on } \Gamma_{0}^{\text{endo}} \times (0, t_f), \\
u(t; \mu) = u_0(t; \mu) & = 0 & \text{on } \Gamma_{0} \times \{0\},
\end{align*}$$

where $\mathbf{N}$ is the normal unit vector. The computational boundary $\partial \Omega_0$ is divided into the inner endocardium $\Gamma_{0}^{\text{endo}}$, the outer epicardium $\Gamma_{0}^{\text{epi}}$ and the ventricular base $\Gamma_{0}^{\text{base}}$, the latter representing the artificial boundary resulting from truncation of the heart below the valves in a short axis plane. The boundary conditions on $\Gamma_{0}^{\text{base}}$ are energy-consistent and provide an explicit expression for the stresses at the base, being

$$v(t; \mu) = \frac{\int_{\Gamma_{0}^{\text{endo}}} J(t; \mu) F^{-T}(t; \mu) \mathbf{N} d\Gamma}{\int_{\Gamma_{0}^{\text{base}}} \| J(t; \mu) F^{-T}(t; \mu) \| d\Gamma}.$$
The Robin boundary conditions at the epicardium aim at modeling the interaction between the ventricle and the pericardium, that is the fibroelastic sac containing the heart, and are given by \( K_{\text{epi}} = K_\perp (N \otimes N) + K_\parallel (I - N \otimes N) \) and \( C_{\text{epi}} = C_\perp (N \otimes N) + C_\parallel (I - N \otimes N) \), where the local values of stiffness \( K_{\text{epi}} \) and viscosity \( C_{\text{epi}} \) of the epicardial tissue, in the normal (\( \perp \)) and tangential (\( \parallel \)) directions, are reported in Table A2. Finally, Neumann boundary conditions account for the action of the blood pressure \( p_{LV}(t;\mu) \) at the endocardium. Figure 2 reports the unloaded computational geometry with indication of the boundaries (left), the geometry obtained when the left ventricle is loaded by a value of pressure corresponding to the end-diastolic pressure \( p_{ED} = 10 \text{ mmHg} \) (center), and one of the corresponding meshes used in the numerical test cases of Section 3 (right).

**Remark 1.** To correctly start the numerical simulations, the end-diastolic configuration of the left ventricle must be computed, and the corresponding displacement used as initial condition for problem (3). This is done by solving the quasi-static problem obtained by setting to zero the time-dependent terms on the reference configuration \( \Omega_0 \).

To provide meaningful numerical simulations of the left ventricle activity between two consecutive heartbeats, and then to characterize the complete cardiac cycle from a mechanical point of view, we rely on a lumped-parameter model for blood circulation, see Section 2.1.2. This strategy allows us to take into account the action of blood pressure inside the chamber.

### 2.1.2 0D blood external circulation model

Several haemodynamics models have been proposed in the literature to account for the presence of blood inside the cardiac chamber, see, References 10,47,48,49 just to mention a few examples. Among these, in the context of coupled problems, lumped-parameter fluid models have been extensively considered,37,50,51 since they provide good approximation results at a greatly reduced cost. In this work, we adopt the following 0D model, as done in References 42,43. Starting from the configuration in which the ventricle is full of blood, and both the mitral valve and the aortic valve are closed, the four phases of the cardiac cycle (see the Wiggers diagram52 in Figure 3) are described as follows:

1. **Isovolumetric contraction:** the endocardial pressure rapidly grows from the end-diastolic pressure \( p_{ED} \) to the value measured in the aorta, in such a way that the volume remains unchanged;
2. **Ejection:** as soon as the aortic valve opens, the ejection phase starts and the evolution of the pressure \( p_{LV}(t;\mu) \) is governed by a two-element windkessel model,48 with capacitance \( C_p \) and resistance \( R_p \):

\[
\begin{align*}
C_p & \frac{d}{dt} p_{LV}(t;\mu) = - \frac{p_{LV}(t;\mu)}{R_p} - \dot{V}_{LV}(\mathbf{u}(t;\mu);t,\mu), \quad t \in (T_{AVO},T_{AVC}], \\
p(T_{AVO};\mu) &= p_{AVO}.
\end{align*}
\]

![Figure 2](image)  
**Figure 2** Patient-specific left ventricle geometry in the unloaded (left) and loaded (center) configurations, and the computational grid (right).
Here, $T_{AVO}$ and $T_{AVC}$ are the aortic valve opening and closing times, respectively, and $p_{AVO}$ is the pressure measured in the aorta at the beginning of the ejection phase. This phase is characterized by a decrement of the volume due to the contraction of the ventricle;

3. *Isovolumetric relaxation*: when the aortic valve closes, the ventricle relaxes and the pressure drops. As both the ventricular valves are closed, no change of volume is experienced;

4. *Filling*: finally, as the pressure inside the ventricle falls below the one in the atrium, the mitral valve opens and the ventricle begins to fill again, so that the pressure linearly increases to the end-diastolic pressure $p_{ED}$, concluding the cardiac cycle.

### 2.1.3 Surrogate active force generation model

To surrogate the input provided to tissue mechanics by the active force generation model, we need to define the active tension $T_a(t; \mu)$ modeling the contraction of cardiomyofiber bundles in reference fiber direction. In this work, this is done by interpolating the average tension computed from the solution to a fully-coupled electromechanics (EM) problem, and multiplying the obtained function by a scaling factor, in order to introduce a parametric dependence. Furthermore, we differentiate between physiological and pathological tissues, characterized by the presence of a necrotic region, by means of an indicator function. We point out that a uniform activation of the cardiac myocytes in the healthy tissue is considered.

To be more specific, let

$$B_r = B(\mathbf{X}, r) = \{ \mathbf{X} \in \Omega_0 \mid \| \mathbf{X} - \mathbf{X} \|_2 < r \} \subset \mathbb{R}^3$$

be an idealized ischemic region with center $\mathbf{X} \in \Omega_0$ and radius $r > 0$, and define $B_r^c$ to be its complement, thus corresponding to the healthy tissue. The active tension in (2) is approximated as

$$T_a(\mathbf{X}, t; \mu) = T_a(t; \mu),$$

for physiological cases, and as

$$T_a(\mathbf{X}, t; \mu) = T_a(t; \mu) \chi_{B_r^c}(\mathbf{X}),$$
for pathological ones, where we assume zero activation in the dofs belonging to the necrotic region to model the passive behavior of the cardiomyocytes. Here, $T_a(t; \mu)$ is a prescribed time-dependent function computed as follows:

1. For a fixed set of physiological parameters, a 3D EM problem coupled with circulation and active force generation models is solved for a single heartbeat in the time interval $(0, t_f^{EM})$.

2. Then, the spatial average of the active tension coming from the EM simulation is computed

$$r_a^{EM}(t) = \text{avg}_{X \in \Omega_0} T_a^{EM}(X, t), \quad (5)$$

and a cubic spline interpolation of $r_a^{EM}(t)$ is performed to obtain the corresponding time-dependent function $r_a^M(t)$, reported in Figure 4.

3. finally, given $T_a > 0$, for $t \in (0, t_f)$, the active tension is defined as

$$T_a(t; \mu) = \frac{T_a}{\max_{t \in (0, t_f^{EM})} r_a^M(t)} r_a^M\left(\frac{t}{t_f} - \frac{t_0}{t_f}\right)$$

and a cubic spline interpolation of $r_a^M(t)$ is performed to obtain the corresponding time-dependent function $r_a^M(t)$, reported in Figure 4.

2.2 Full-order model

The core models described so far, mutually exchanging pressure and volume, must be suitably coupled to provide physically meaningful simulations of the cardiac cycle, leading to a 3D-0D coupled structure-windkessel problem. In this section, we outline the corresponding full-order model obtained by relying on the FE method (in space) and implicit time schemes, which avoid restrictions on the time step due to the highly nonlinear terms of the strain energy density function.

Let $T_h$ be a tetrahedral (or an hexahedral) mesh on the reference domain $\Omega_0 \subset \mathbb{R}^3$, and $P_r(\tau)$ (or $Q_r(\tau)$) be the set of polynomials of degree smaller than or equal to $r \in \mathbb{N}$ over a mesh element $\tau \in T_h$. Given the finite-dimensional space of real-valued functions $\mathcal{X}_h = \left\{ v \in C^0(\Omega_0) : v \big| \tau \in P_r(\tau) \text{ (or } Q_r(\tau) \text{) } \forall \tau \in T_h \right\}$, we define the FE space of degree $r \geq 1$ as

$$V_h = \left\{ \eta \in H^1(\Omega_0) \right\}^3 \big| \eta = 0 \text{ on } \Gamma_0^D \bigcap [\mathcal{X}_h]^3 = \text{span}\{\varphi_i\}_{i=1}^N,$$
whose dimension $N_h = 3\dim(\mathcal{X}_h)$ corresponds to the total number of structural dofs. Hence, the semi-discrete Galerkin-FE approximation of problem (3) reads: for each $t \in (0, t_f)$, find $\mathbf{u}_h(t; \mu) \in V_h$ such that

$$
\begin{align*}
&\left\{ \rho_0 \mathcal{M}_h(t; \mu) \dot{\mathbf{u}}_h(t; \mu) + \mathcal{F}_{\mathcal{C}}(\mathbf{u}_h(t; \mu)) + \mathcal{F}_{\mathcal{K}}(\mathbf{u}_h(t; \mu)) + \mathcal{S}(\mathbf{u}_h(t; \mu); \mu) = \mathcal{F}_{p_{LV}}(p_{LV}(t; \mu); \mu), \\
&\mathbf{u}_h(0; \mu) = \mathbf{u}_{h,0}(0; \mu), \mathbf{u}_{h}(0; \mu) = \mathbf{u}_{h,0}(0; \mu),
\end{align*}
$$

where $\mathbf{u}_{h,0}(0; \mu) = \left[ (\mathbf{u}_0(0; \mu), \phi_1) \right]_{L^2(\Omega_h)}^{N_h}$, $\mathbf{u}_{h,0}(0; \mu) = \left[ (\mathbf{u}_0(0; \mu), \phi_1) \right]_{L^2(\Omega_h)}^{N_h}$, and

$$
[M]_{ij} = \int_{\Omega_h} \mathbf{q}_j \cdot \mathbf{q}_i \, d\Omega, \quad [\mathcal{F}_{\mathcal{C}}]_{ij} = \int_{\Gamma_{ext}} \mathcal{C}^{ep} \mathbf{q}_j \cdot \mathbf{q}_i \, d\Gamma, \quad [\mathcal{F}_{\mathcal{K}}]_{ij} = \int_{\Gamma_{ext}} \mathcal{K}^{ep} \mathbf{q}_j \cdot \mathbf{q}_i \, d\Gamma,
$$

$$
[S(\mathbf{u}_h(t; \mu); \mu)]_{i} = \int_{\Omega_h} \mathbf{p}(\mathbf{u}_h(t; \mu)) : \nabla \mathbf{q}_i \, d\Omega,
$$

$$
[\mathcal{F}_{p_{LV}}(p_{LV}(t; \mu); \mu)]_{i} = p_{LV}(t; \mu) \left( \int_{\Gamma_{flow}} \| J(t; \mu) F^{-T}(\mu) N \| \mathbf{v}(t; \mu) : \mathbf{q}_i \, d\Gamma - \int_{\Gamma_{flow}} J(t; \mu) F^{-T}(\mu) N \cdot \mathbf{p}(\mathbf{u}_h(t; \mu)) d\Gamma \right),
$$

for all $i, j = 1, \ldots, N_h$. Furthermore, we introduce a uniform partition $\{ t^0, \ldots, t^{N_t} \}$ of the time interval $(0, t_f)$, with time step $\Delta t$. The vector of nodal displacements of the fully-discretized problem and the left ventricular pressure at time $t^k$, for $k = 1, \ldots, N_t$, are denoted as $\mathbf{u}_h^k(\mu) \in \mathbb{R}^{N_h}$ and $p_{LV}^k(\mu)$, respectively. Time derivatives computed at time $t^k$ are approximated as

$$
\dot{\mathbf{u}}(t^k; \mu) \approx \frac{\mathbf{u}_h^k(\mu) - \mathbf{u}_h^{k-1}(\mu)}{\Delta t} \quad \text{and} \quad \ddot{\mathbf{u}}(t^k; \mu) \approx \frac{\mathbf{u}_h^k(\mu) - 2\mathbf{u}_h^{k-1}(\mu) + \mathbf{u}_h^{k-2}(\mu)}{\Delta t^2}.
$$

To ease the notation of what follows, we define

$$
\left( \mathbf{x}_h^{k,j} \right) := \left( \mathbf{u}_h^k(\mu), p_{LV}^k(\mu), t^k; \mu \right),
$$

where the superscript “$(j)$” denotes quantities computed at the $j$-th iteration of the Newton method used for the solution of the algebraic nonlinear system arising at each time step. Note that $\mathbf{x}_h^{k,j}(\mu) := (\mathbf{u}_h^k(\mu), \mu)_j$, $\forall j \geq 0$, during the non-isochoric phases.

During ventricular ejection (phase 2) and filling (phase 4), the structural and the circulation problems are segregated, meaning that the two models are solved in sequence, one after the other. In particular, in the ejection phase, the current pressure $p_{LV}^k(\mu)$ is updated by solving the two-element windkessel model (4) before addressing the mechanics problem. For simplicity, we assume

$$
\dot{V}_{LV}(\mathbf{u}_h^k(\mu); t^k, \mu) \approx \frac{V_{LV}(\mathbf{u}_h^{k-1}(\mu); t^{k-1}, \mu) - V_{LV}(\mathbf{u}_h^{k-2}(\mu); t^{k-2}, \mu)}{\Delta t},
$$

where the ventricular volume at time $t^k$, for $k \in \{k - 1, k - 2\}$, is computed as

$$
V_{LV}(\mathbf{u}_h^k(\mu); t^k, \mu) = \frac{1}{3} \int_{\Gamma_{flow}} J(t^k; \mu) (\mathbf{X} + \mathbf{u}_h^k(\mu) - \mathbf{b}_h^k(\mu)) \cdot F^{-T}(t^k; \mu) N dl_{\Gamma_0},
$$

where $\mathbf{b}_h^k(\mu) = \frac{1}{\Delta t} \int_{t^{k-1}}^{t^k} (\mathbf{X} + \mathbf{u}_h^k(\mu)) d\Gamma_0$. See, Reference 43 for further details on the derivation of formula (6). The corresponding problem at time $t^k$ for the unknown $\mathbf{u}_h^k(\mu)$, $k = 1, \ldots, N_t$, is the nonlinear system

$$
\mathbf{R}(\mathbf{u}_h^k(\mu), p_{LV}^k(\mu), t^k; \mu) = 0 \quad \text{in} \mathbb{R}^{N_h},
$$
where the high-fidelity residual vector is defined as

\[
\mathbf{R}(\mathbf{u}_h^k(\mu), p_{LV}^k(\mu), t^k; \mu) := \left( \frac{\rho_0}{\Delta t^2} \mathcal{M} + \frac{1}{\Delta t} \mathcal{F}_{cp} + \mathcal{F}_{k} \right) \mathbf{u}_h^k(\mu) - \left( \frac{2\rho_0}{\Delta t^2} \mathcal{M} + \frac{1}{\Delta t} \mathcal{F}_{cp} \right) \mathbf{u}_h^{k-1}(\mu) + \frac{\rho_0}{\Delta t^2} \mathcal{M} \mathbf{u}_h^{k-2}(\mu) + \mathbf{S}(\mathbf{u}_h^k(\mu); \mu) - \mathcal{F}_{p_{LV}}(p_{LV}^k(\mu); \mu).
\]

This problem is solved by means of the Newton method, leading to a sequence of linear systems of the form

\[
\partial_\mu \mathbf{R}(\mathbf{u}_h^k(\mu)) \delta \mathbf{u}_h^j(\mu) = -\mathbf{R}(\mathbf{u}_h^k(\mu)),
\]

for \( j \geq 0 \), where \( \partial_\mu \mathbf{R} \) is the directional derivative of the structural residual. At each iteration \( j \), the current solution is then updated as \( \mathbf{u}_h^{k+1}(\mu) = \mathbf{u}_h^k(\mu) + \delta \mathbf{u}_h^j(\mu) \).

On the other hand, during isovolumetric contraction (phase 1) and isovolumetric relaxation (phase 3), the elastodynamics problem is solved together with the volume constraint \( V_{LV}^k = V_{LV}^{k-1} \). At each time step, this results in a nonlinear saddle-point system for the unknowns \( \mathbf{u}_h^k(\mu) \) and \( p_{LV}^k(\mu) \) of the form

\[
\begin{align*}
\mathbf{R}(\mathbf{u}_h^k(\mu), p_{LV}^k(\mu), t^k; \mu) &= \mathbf{0}, \\
V_{LV}(\mathbf{u}_h^k(\mu), t^k; \mu) &= V_{LV}(\mathbf{u}_h^{k-1}(\mu), t^{k-1}; \mu),
\end{align*}
\]

that can be solved by means of the Schur complement reduction. By applying the Newton method, at each time step we end up with a sequence of linear systems under the form

\[
\begin{pmatrix}
\partial_\mu \mathbf{R}(\mathbf{u}_h^k(\mu)) & \partial_p \mathbf{R}(\mathbf{u}_h^k(\mu)) \\
\partial_\mu \mathbf{R}^\text{vol}(\mathbf{u}_h^k(\mu)) & 0
\end{pmatrix}
\begin{pmatrix}
\delta \mathbf{u}_h^j(\mu) \\
\delta p_{LV}^j(\mu)
\end{pmatrix}
= -
\begin{pmatrix}
\mathbf{R}(\mathbf{u}_h^k(\mu)) \\
\mathbf{R}^\text{vol}(\mathbf{u}_h^k(\mu))
\end{pmatrix},
\]

for \( j \geq 0 \). Here \( \mathbf{R}^\text{vol}(\mathbf{u}_h^k(\mu)) := V_{LV}(\mathbf{u}_h^k(\mu)) - V_{LV}(\mathbf{u}_h^{k-1}(\mu), t^{k-1}; \mu) \in \mathbb{R} \) denotes the residual related to the volume constraint.

To summarize, the discrete nonlinear parameterized FOM for the coupled 3D-0D problem can be written as: given \( \mu \in \mathcal{P} \) and \( \mathbf{u}_h^0(\mu) \), for \( k = 1, \ldots, N_t \), find \( \mathbf{u}_h^k(\mu) \in \mathbb{R}^{N_{dofs}} \) and \( p_{LV}^k(\mu) > 0 \) such that

\[
\begin{bmatrix}
\mathbf{R}(\mathbf{u}_h^k(\mu), p_{LV}^k(\mu), t^k; \mu) \\
\mathbf{R}^\text{vol}(\mathbf{u}_h^k(\mu), p_{LV}^k(\mu), t^k; \mu)
\end{bmatrix} = \mathbf{0},
\]

(7)

where \( \mathbf{R}^\text{vol} \) is discarded during phases 2 and 4 of the cardiac cycle.

### 2.3 The deep-HyROMnet technique for cardiac mechanics problems

The numerical solution of problem (7) entails very high computational costs as soon as \( N_t \), which depends on the space discretization, becomes too large. This is extremely challenging, if not prohibitive, when the solution to the forward problem is required repeatedly, such as in the context of UQ, parameter estimation or model calibration. To reduce the computational burden associated with the solution of the FOM, we tackle the 3D-0D coupled problem described in the previous section by means of the Deep-HyROMnet technique recently introduced in Reference 38. We point out that, since blood circulation is modeled through a lumped-parameter model and the volume constraint only requires to add few dofs to the mechanics problem, the 0D circulation model does not need to be reduced, similarly to the approach adopted in Reference 37. The idea of the Deep-HyROMnet technique is to enhance by DNNs the construction
of a POD-Galerkin ROM, employing a DNN architecture to approximate reduced residual vectors and Jacobian matrices once a Galerkin projection has been performed, as opposite to classical hyper-reduction techniques. Hence, two stages are involved in the assembly of Deep-HyROMnets, namely, the construction of a POD-Galerkin ROM and the training of DNNs for the approximation of the ROM nonlinear operators.

2.3.1 | POD-Galerkin reduced-order model

Exploiting the RB method,\textsuperscript{54,55} we aim at approximating the elements of the high-fidelity discrete solution manifold

$$\mathcal{M}_h = \{ \mathbf{u}_h^k(\mu) \in \mathbb{R}^{N_h}, k = 1, \ldots, N_t | \mu \in \mathcal{P} \}$$

through a linear combination of (possibly few) global, problem-dependent, reduced basis functions, that is,

$$\mathbf{V} \mathbf{u}_h^k(\mu) \approx \mathbf{u}_h^k(\mu).$$

Here, we denote by $\mathbf{V} \in \mathbb{R}^{N_h \times N}$, with $N \ll N_h$, the matrix collecting (column-wise) the nodal values of the RB functions, and by $\mathbf{u}_h^k(\mu) \in \mathbb{R}^N$ the coordinates of the reduced-order approximation found by solving, for each $k = 1, \ldots, N_t$, a low-dimensional nonlinear problem, as later described. In this work, the reduced basis $\mathbf{V}$ is built by performing POD on the snapshots matrix $\mathbf{S}_u$ of mechanical displacements obtained by solving the FOM problem (7) for $n_s \in \mathbb{N}$ parameter vectors, that is,

$$\mathbf{S}_u = [\mathbf{u}_h^1(\mu_1) | \ldots | \mathbf{u}_h^{N_s}(\mu_1) | \ldots | \mathbf{u}_h^1(\mu_{n_s}) | \ldots | \mathbf{u}_h^{N_s}(\mu_{n_s})].$$

The values $\mu_1, \ldots, \mu_{n_s}$ are selected, for example, by means of the Latin Hypercube Sampling (LHS). Thus, a reduced basis of dimension $N$ is obtained by performing the singular value decomposition of $\mathbf{S}_u$, and collecting the first $N$ left singular vectors. This yields an orthonormal basis that, among all $N$-dimensional orthonormal basis, minimizes the least square error of the snapshot reconstruction. The size $N$ is selected as the minimum integer satisfying the condition

$$\sum_{i=1}^{N} \sigma_i^2 \geq 1 - \varepsilon_{\text{POD}}^2$$

for a given tolerance $\varepsilon_{\text{POD}} > 0$, where $\sigma_1 \geq \ldots \geq \sigma_r \geq 0$ are the singular values of $\mathbf{S}_u$, with $r = \text{rank}(\mathbf{S}_u)$.

The POD-Galerkin low-dimensional problem is obtained by performing a Galerkin projection of the structural residual onto the reduced subspace spanned by the columns of $\mathbf{V}$, and reads: given $\mu \in \mathcal{P}$, for $k = 1, \ldots, N_t$, find $\mathbf{u}_N^k(\mu) \in \mathbb{R}^N$ and $P_{LV}^k(\mu) > 0$ such that

$$\begin{bmatrix} \mathbf{V}^T \mathbf{R}(\mathbf{Vu}_N^k(\mu), P_{LV}^k(\mu), t^k; \mu) \\ \mathbf{R}^{\text{vol}}(\mathbf{Vu}_N^k(\mu), P_{LV}^k(\mu), t^k; \mu) \end{bmatrix} = 0, \quad k = 1, \ldots, N_t.$$  

The corresponding reduced Newton system at time $t^k$, for $k = 1, \ldots, N_t$, reads:

- for the ejection and filling phases: given an initial guess $\mathbf{u}_N^{k,(0)}(\mu)$, find $\mathbf{u}_N^{k,(j)}(\mu)$ such that, for $j \geq 0,$
\[
\begin{aligned}
&V^T \partial_u R \left( \star_{N}^{k(j)} \right) V \delta u_N^{(j)} = -V^T R \left( \star_{N}^{k(j)} \right), \\
&u_N^{k(j+1)}(\mu) = u_N^{k(j)}(\mu) + \delta u_N^{(j)}(\mu),
\end{aligned}
\]

until \( \| V^T R \left( \star_{N}^{k(j+1)} \right) \|_2 / \| V^T R \left( \star_{N}^{k(0)} \right) \|_2 < \epsilon_{\text{newt}} \), where \( \epsilon_{\text{newt}} > 0 \) is a prescribed tolerance;

- for the isovolumetric phases: given initial guesses \( u_N^{k(0)}(\mu) \) and \( p_{LV}^{k(0)}(\mu) \), find \( u_N^{k(j)}(\mu) \) and \( p_{LV}^{k(j)}(\mu) \) such that, for \( j \geq 0 \),

\[
\begin{aligned}
&\begin{pmatrix}
V^T \partial_u R \left( \star_{N}^{k(j)} \right) V \\
\partial_u R^{\text{vol}} \left( \star_{N}^{k(j)} \right) V
\end{pmatrix} \begin{pmatrix}
\delta u_N^{(j)}(\mu) \\
\delta p_{LV}^{(j)}(\mu)
\end{pmatrix} = -\begin{pmatrix}
V^T R \left( \star_{N}^{k(j)} \right) \\
R^{\text{vol}} \left( \star_{N}^{k(j)} \right)
\end{pmatrix},
\end{aligned}
\]

then update

\[
u_N^{k(j+1)}(\mu) = u_N^{k(j)}(\mu) + \delta u_N^{(j)}(\mu)
\]

and

\[
p_{LV}^{k(j+1)}(\mu) = p_{LV}^{k(j)}(\mu) + \delta p_{LV}^{(j)}(\mu),
\]

until \( \| V^T R \left( \star_{N}^{k(j+1)} \right) \|_2 / \| V^T R \left( \star_{N}^{k(0)} \right) \|_2 < \epsilon_{\text{newt}} \), where \( \epsilon_{\text{newt}} > 0 \) is a prescribed tolerance.

Similarly to the previous section, we have used the notation

\[
\begin{pmatrix}
\star_{N}^{k(j)}
\end{pmatrix} := \left( \begin{array}{c}
V u_N^{k(j)}(\mu), p_{LV}^{k(j)}(\mu), t^{k(\cdot)}(\mu)
\end{array} \right),
\]

where \( p_{LV}^{k(j)}(\mu) := p_{LV}^{k(j)}(\mu), \forall j \geq 0 \) during ejection and filling. Finally, as initial guess we assume \( u_N^{0(0)}(\mu) = V^T u_0(\mu) \), and \( u_N^{k(0)}(\mu) = u_N^{k-1}(\mu) \), for \( k = 1, \ldots, N_t \).

### 2.3.2 Deep learning-based approximation of ROM operators

Since the reduced arrays appearing in the Newton systems, namely,

\[
V^T R \in \mathbb{R}^{N \times 1}, \ V^T \partial_u RV \in \mathbb{R}^{N \times N}, \ V^T \partial_p R \in \mathbb{R}^{N \times 1}, \ R^{\text{vol}} \in \mathbb{R}^{1 \times 1}, \ \partial_u R^{\text{vol}} V \in \mathbb{R}^{1 \times N},
\]

are evaluated on \( V u_N^{k(j)}(\mu) \) and \( p_{LV}^{k(j)}(\mu) \), they have to be recomputed for every new \( j \geq 0 \) and \( k = 1, \ldots, N_t \). Due to non-linearity, this requires to assemble the corresponding high-fidelity arrays at each Newton iteration before projecting them onto the reduced subspace, thus entailing a computational cost that still depends on the FOM dimension. To overcome this limitation when constructing ROMs for parametrized systems, suitable hyper-reduction techniques providing \( N_u \)-independent approximations of the nonlinear terms are usually taken into account. In particular, the empirical interpolation method (EIM)\(^{56,57}\) and its discrete version DEIM\(^{55}\) represent standard hyper-reduction techniques in the context of the RB method. These strategies rely on the assembling of the nonlinear quantities onto a reduced mesh obtained as a subset of the original one. Nonetheless, when applied in the context of cardiac mechanics, they still suffer from severe computational burdens, as a large reduced mesh is required to correctly capture the great variability of the residual vectors; see, Reference 33, and the analysis recently carried out in Reference 34.
To enhance the efficiency of POD-Galerkin hyper-reduced-order models, we perform a deep learning-based approximation of the reduced nonlinear terms arising in the ROM problem (9), avoiding the expensive assembling stage. Given the triplet

$$\mathcal{G} = (\mu, t^k, j) \in \mathcal{P} \times \{t, \ldots, t^{Nt}\} \times \mathbb{N}$$

made of the input parameters $\mu \in \mathcal{P}$, the current time step $t^k$ and the Newton iteration $j \geq 0$, we efficiently approximate the $N$-dimensional ROM operators evaluated on $(\ast_N^{k,j})$ by exploiting a DNN architecture to learn the following nonlinear maps:

$$\rho_N : (\mu, t^k, j) \mapsto V^T R (\ast_N^{k,j}),$$
$$\iota_N : (\mu, t^k, j) \mapsto V^T \partial_u R (\ast_N^{k,j}) V,$$
$$\pi_N : (\mu, t^k, j) \mapsto V^T \partial_R (\ast_N^{k,j}),$$
$$v_N : (\mu, t^k, j) \mapsto \partial_R \ast_{\text{red}} (\ast_N^{k,j}) V, R_{\text{red}} (\ast_N^{k,j}).$$

This strategy ensures an efficient decomposition into a costly (offline) training phase, which is performed once and for all, and a very inexpensive (online) testing phase, during which the problem solution is computed for a specific input vector, after the reduced operators have been approximated. To be more specific,

- **Offline**: FOM snapshots are collected for the construction of the reduced basis $V$. Then, the reduced nonlinear datasets are built by performing POD-Galerkin ROM simulations for a set of $n' \in \mathbb{N}$ parameter values randomly chosen, and the DNNs are trained on this data.

- **Online**: for each new instance of the input parameter $\mu \in \mathcal{P}$, the output of the DNNs is efficiently evaluated to assemble the reduced Newton system at each iteration, and the low-dimensional problem is solved. More precisely, for $k = 1, \ldots, N_t$, given $u_N^{k,0}(\mu)$ and $p_{LV}^{k,0}(\mu)$, for $j \geq 0$, one needs to predict $\rho_N$, $\iota_N$, $\pi_N$ and $v_N$, and then find $\delta u_N^{(j)}(\mu) \in \mathbb{R}^N$ and $\delta p_{LV}^{(j)} > 0$ such that

$$\iota_N(\mu, t^k, j) \delta u_N^{(j)} = -\rho_N(\mu, t^k, j)$$

for the ejection and filling phases, or

$$\begin{pmatrix} \iota_N(\mu, t^k, j) & \pi_N(\mu, t^k, j) \\ v_N^{\text{red}}(\mu, t^k, j) & 0 \end{pmatrix} \begin{pmatrix} \delta u_N^{(j)} \\ \delta p_{LV}^{(j)} \end{pmatrix} = - \begin{pmatrix} \rho_N(\mu, t^k, j) \\ v_N^{\text{red}}(\mu, t^k, j) \end{pmatrix}$$

for the isovolumetric phases, until $\| \rho_N(\mu, t^k, j + 1) \|_2 / \| \rho_N(\mu, t^k, 0) \|_2 < \varepsilon_{\text{met}}$. Here, $v_N^{\text{red}}$ and $u_N^{\text{red}}$ denote the first $N$ entries and the last component of $u_N$, respectively, such that $v_N^{\text{red}}(\mu, t^k, j) \approx \partial_u R_{\text{red}} (\ast_N^{k,j}) V$ and $u_N^{\text{red}}(\mu, t^k, j) \approx R_{\text{red}} (\ast_N^{k,j})$. As an additional stopping criterion, we consider an upper bound on the number of Newton iterations per time step, that is $j \leq N_{\text{met}}$ must hold. The value for $N_{\text{met}}$ can be estimated when solving repeatedly the POD-Galerkin ROM for the generation of the training datasets.

The linear systems (10) and (11) can be assembled very efficiently, requiring only $O(10^{-3})$ s on a standard laptop, while both the FOM and the POD-Galerkin ROM would require up to $O(1)$ s for each Newton iteration. Since this operation is performed $O(N_t N_{\text{met}})$ times during each cardiac cycle, relying on the Deep-HyROMnet strategy allows us to achieve speed-ups with respect to the FOM of more than two orders of magnitude, outperforming traditional hyper-reduction techniques such as DEIM, as shown in Section 3.

We remark that the different DNNs are trained independently of each other. As a consequence, the approximation of $V^T \partial_u R (\ast_N^{k,j}) V$, that is, the output of the DNN $\iota_N$ evaluated on $(\mu, t^k, j)$, is not the derivative of
\( \rho_N(\mu, t^k, j) \approx V^T R(\star_N^{k,j}) \). Strategies taking into account a direct dependence of the Jacobian matrix on the corresponding residual vector, for example, by relying on Broyden-based methods, have been tested in Reference 58, although leading to less satisfying results when compared to Deep-HyROMnet.

### 2.3.3 DNN architectures

Reduced residual vectors and Jacobian matrices are approximated through a map composed by two DNN architectures, namely, a convolutional autoencoder (CAE) that performs a further dimensionality reduction of the data, and a deep feedforward neural network (DFNN) that ultimately provides the low-dimensional representation of the operator as a function of the input triple \( \theta = (\mu, t^k, j) \). In this section, we briefly review the approximation of the reduced residual vector by means of DNNs, that is

\[
\rho_N(\mu, t^k, j) \approx V^T R(\star_N^{k,j}) \in \mathbb{R}^N.
\]

A similar procedure can be set up for the approximation of the other nonlinear terms, including the reduced Jacobian matrix \( V^T \partial_q R(\star_N^{k,j}) V \), as explained in Remark 5.

The Deep-HyROMnet approximation of the ROM residual \( V^T R(\star_N^{k,j}) \) takes the form

\[
\rho_N(\mu, t^k, j) = \left( f_N^D(\cdot; \theta_D) \circ \phi_D^q(\cdot; \theta_{DF}) \right) (\mu, t^k, j) := R_N(\mu, t^k, j; \theta_{DF}, \theta_D),
\]

where:

- the map \( \phi_D^q(\cdot; \theta_{DF}) : \mathbb{R}^{P+2} \rightarrow \mathbb{R}^q \) is a DFNN that provides a low-dimensional representation

\[
\phi_D^q(\mu, t^k, j; \theta_{DF}) := R_q(\mu, t^k, j; \theta_{DF}).
\]

Here, the latent dimension \( q \) is as close as possible to the input size \( P + 2 \) and \( \theta_{DF} \) denotes the vector of parameters, collecting all the corresponding weights and biases of each layer;

- \( f_N^D(\cdot; \theta_D) : \mathbb{R}^q \rightarrow \mathbb{R}^N \) is the decoder function of a CAE, depending on the vector \( \theta_D \) of weights and biases, yielding

\[
f_N^D(\theta_D) := R_N(\mu, t^k, j; \theta_{DF}, \theta_D).
\]

The encoder function of the CAE is considered during the training stage only, and it is exploited to map the reduced residual \( V^{-T} R \left( V u_N^{k,j}(\mu, t^k; \mu) \right) \) associated to \( (\mu, t^k, j) \) onto a low-dimensional representation

\[
f^E_q \left( V^{-T} R \left( V u_N^{k,j}(\mu, t^k; \mu) \right) ; \theta_E \right) := \hat{R}_q(\mu, t^k, j; \theta_E),
\]

where \( f^E_q(\cdot; \theta_E) : \mathbb{R}^N \rightarrow \mathbb{R}^q \) denotes the encoder function and \( \theta_E \) the corresponding vector of parameters. The architecture used during the training phase is summarized in Figure 5; during the testing phase, the encoder function \( f^E_q \) is discarded.

**Remark 2.** The input of the encoder function, that is, \( V^{-T} R \), is reshaped into a square matrix by rewriting its elements in row-major order, thus obtaining \( (V^{-T} R)_{\text{reshape}} \in \mathbb{R}^{\sqrt{N} \times \sqrt{N}} \). If \( \sqrt{N} \) is not an integer number, the input is zero-padded,\(^59\) and the additional elements are subsequently discarded.
Let
\[ S_\rho = \frac{V^T R(V u_N^{k(j)}(\mu), t^k; \mu))}{C_0} \]
be the reduced residual snapshots matrix collecting column-wise ROM residuals computed for \( n_0 \) parameters \( \mu \in \mathcal{P} \) sampled with the LHS technique, at different time instances \( t^1, \ldots, t^{N_t} \); and for each Newton iteration \( j \geq 0 \), such that \( N_{\text{train}} \approx n_0 s N_t N_{\text{nwt}} \). Moreover, we define the parameter matrix of the corresponding triples as
\[ M = \left[ (\mu, t^k, j) \right]_{\ell=1}^{n_0} \in \mathbb{R}^{(P+2) \times N_{\text{train}}}. \]

The training stage consists in the solution of the following minimization problem:
\[ \min_{\theta} J(\theta) = \min_{\theta} \frac{1}{N_{\text{train}}} \sum_{\ell=1}^{n_0} \sum_{k=1}^{N_t} \sum_{j=0}^{N_{\text{nwt}}} L(\mu, t^k, j; \theta), \]
where \( \theta = (\theta_D, \theta_{DF}, \theta_E) \), and the loss function is given by
\[ L(\mu, t^k, j; \theta) = \frac{1}{2} \left\| V^T R(V u_N^{k(j)}(\mu), t^k; \mu) - R_N(\mu, t^k, j; \theta_{DF}, \theta_D) \right\|^2 + \frac{1}{2} \left\| R_q(\mu, t^k, j; \theta_E) - R_q(\mu, t^k, j; \theta_{DF}) \right\|^2. \] (12)

For further details on the training and testing algorithms, we refer to.\(^{38}\)

**Remark 3.** Relying on the transformation \( \text{vec}: \mathbb{R}^{N \times N} \rightarrow \mathbb{R}^{N^2} \), obtained by stacking the columns of the \( N \)-dimensional matrix over each other, the matrix \( V^T \partial_u R(\mu, k(j)) \) can be reshaped as a vector of dimension \( N^2 \), so that the same procedure described so far for the residual vector can be easily adapted to the approximation of the Jacobian matrix as well. In particular, we first obtain the approximation
\[ \bar{r}_N(\mu, t^k, j) \approx \text{vec}(V^T \partial_u R(\mu, k(j)) V) \in \mathbb{R}^{N^2}, \]
and finally revert the vec operation to obtain \( \mathbf{1}_N(\mu, t^k, j) = \text{vec}^{-1}(\mathbf{i}_N(\mu, t^k, j)) \).

The design of the DNNs employed in this work, reported in Tables 1 and 2, has proven to be robust in many applications, such as cardiac electrophysiology\(^{60,40}\) and fluid mechanics,\(^{61}\) as well as micro electro-mechanical systems\(^{62}\); the performances of the Deep-HyROMnet technique have been extensively assessed in structural mechanics problems.\(^{38}\) The approximation properties of such networks have been theoretically analyzed in References \(^{63,64}\), where a complexity analysis in terms of typical hyper-parameters has been also provided.

Indeed, during the online phase, one can vary only the parameters considered during training, as the DNNs architecture directly depends on both the number of input parameters and the size of the RB basis. Nonetheless, when only the size of the FOM is varied, for example, by considering finer computational meshes, suitable pre-training strategies can be adopted.

### 3 | NUMERICAL RESULTS

In this section, we present the numerical results obtained using the Deep-HyROMnet strategy for the solution to the 3D-0D structure-windkessel model, in both physiological and pathological scenarios. In order to evaluate the accuracy of the ROM with respect to the FOM, the following time-averaged \( L^2 \)-errors of the displacement vector are used,

\[
    e_{\text{abs}}(\mu) = \frac{1}{N_t} \sum_{k=1}^{N_t} \| \mathbf{u}_N^k(\mu) - \mathbf{V} \mathbf{u}_N^k(\mu) \|_2^2 \quad \text{and} \quad e_{\text{rel}}(\mu) = \frac{1}{N_t} \sum_{k=1}^{N_t} \frac{\| \mathbf{u}_N^k(\mu) - \mathbf{V} \mathbf{u}_N^k(\mu) \|_2^2}{\| \mathbf{u}_N^k(\mu) \|_2^2},
\]

whilst model efficiency is assessed through the wall time ratio, corresponding to the speed-up achieved by the ROM with respect to the FOM. Simulations have been performed in serial on a PC desktop computer with 3.70GHz Intel Core i5-9600K CPU and 16GB RAM using the code implemented in Python in our software package pyfe\(^x\), which

| Layer | Input dimension | Output dimension | Kernel size | # filters | Stride | Padding |
|-------|----------------|------------------|-------------|-----------|--------|--------|
| 1     | 5,5            | [5,5]            | 8           | 1         |        | SAME   |
| 2     | 5,5            | [5,5]            | 16          | 2         |        | SAME   |
| 3     | 5,5            | [5,5]            | 32          | 2         |        | SAME   |
| 4     | 5,5            | [5,5]            | 64          | 2         |        | SAME   |
| 5     | 64             |                  |             |           |        |        |
| 6     | 64             |                  |             |           |        |        |

| Layer | Input dimension | Output dimension | Kernel size | # filters | Stride | Padding |
|-------|----------------|------------------|-------------|-----------|--------|--------|
| 1     | q              | 64               |             |           |        | SAME   |
| 2     | 64             |                  |             |           |        | SAME   |
| 3     | 5,5            | [5,5]            | 64          | 2         |        | SAME   |
| 4     | 5,5            | [5,5]            | 32          | 2         |        | SAME   |
| 5     | 5,5            | [5,5]            | 16          | 2         |        | SAME   |
| 6     | 5,5            | [5,5]            | 1           | 1         |        | SAME   |
contains a Python binding with the in-house Finite Element library lifeX (https://lifex.gitlab.io/lifex). The latter is a high-performance C++ library developed within the iHEART project at MOX-Politecnico di Milano, and based on the deal.II (https://www.dealii.org) Finite Element core. For the computation of the directional derivatives of the structural residual $R$, we rely on the useful tool of automatic differentiation provided in the deal.II library. Training and testing of the DNNs have been carried out on a Tesla V100 32GB GPU. In particular, while the solution of the reduced Newton systems (9) and the reconstruction of the high-dimensional displacement vector $V_{u_N}$ are done on CPU, the generation of the approximated reduced nonlinear operators is done on GPU. In this way, we fully exploit the potentiality of using the DNNs in the hyper-reduction strategy.

3.1 Parametric and discretization setting

In order to test the performances of the Deep-HyROMnet technique in cardiac mechanics, we consider a subset of the patient-specific parameters to be unknown, and thus left free to vary. In particular, we set $\mu = \begin{bmatrix} R_p, T_a \end{bmatrix}$ for healthy scenarios, and $\mu = \begin{bmatrix} R_p, \bar{T}_a, r \end{bmatrix}$ when we assume the presence of an ischemic region. All other parameters are fixed, and their values are reported in Table 3 or listed in the Appendix A. Figure 6 shows the active tension and the ischemic region obtained for maximum and minimum values of $T_a$ and the scar radius $r$, respectively. The admissible ranges for the input parameters have been chosen based on values usually considered, see, References 23, 27, 66; as a matter of fact, a good variability of the problem solution is obtained, as we can observe from the displacements at time $t = 0.25$ s shown in Figures 7 and 8, corresponding to different values of the input parameters vector close to the boundary of the parameter space.

|                         | Physiological scenario 1 | Physiological scenario 2 | Pathological scenario |
|-------------------------|--------------------------|---------------------------|-----------------------|
| $\mu$                   | $\begin{bmatrix} R_p, T_a \end{bmatrix}$ | $\begin{bmatrix} R_p, T_a \end{bmatrix}$ | $\begin{bmatrix} R_p, \bar{T}_a, r \end{bmatrix}$ |
| FE                      | $Q_1$                    | $Q_1$                     | $Q_1$                 |
| $t_f$ [s]               | 0.8                      | 0.8                       | 0.8                   |
| $\Delta t$ [s]         | $2.5 \cdot 10^{-1}$     | $2.5 \cdot 10^{-1}$     | $2.5 \cdot 10^{-1}$  |
| $N_h$                   | 18,501                   | 107,175                   | 107,175               |
| $N$                     | 35                       | 35                        | 63                    |
| $n_s$                   | 15                       | 15                        | 15                    |
| $n_f$                   | 25                       | 25                        | 45                    |

**TABLE 3** Parameters of the numerical simulations, for different test cases.

**FIGURE 6** Active tension (left) and ischemic region (right) for the maximum and minimum values in the parameter space.
We underline that, when dealing with cardiac mechanics—especially in a nearly-incompressible regime—numerical instabilities and volumetric locking phenomena can possibly occur, leading to an inaccurate computation of strain and stress. In this regard, several formulations or stabilization techniques have been investigated; see, Reference 21 and references therein for a comprehensive review. A possible strategy to obtain more accurate results is
the use of higher order polynomials to approximate the displacement field, such as second-order FEs.\textsuperscript{67} However, using quadratic functions (at least in the context of matrix-based schemes) entails a much larger amount of degrees of freedom, such that we experienced burdensome computational costs when solving the FOM. For this reason, we decided to rely on the less expensive trilinear FEs, which proved to be sufficiently accurate for the purposes at hand – that is, to demonstrate the applicability of the Deep-HyROMnet technique to complex problems in cardiac mechanics – despite relying on suitable refined meshes. We point out that no instabilities in time have been observed. It should be mentioned that, in this work, we rely on hexahedral (\(\mathbb{Q}\)) FE, rather than the more practical and commonly used tetrahedral (\(\mathbb{P}\)) ones, since only meshes consisting of quadrilaterals or hexahedra are allowed in the deal.II library (version 9.3.3), as motivated in Reference \textsuperscript{65}. Nonetheless, we recall that the reduction strategy, acting at the algebraic level, works irrespectively of the chosen FE degree and type. On the other hand, matrix-free methods, largely adopted in fluid mechanics, have been successfully applied in the context of cardiac electrophysiology,\textsuperscript{68} as well as to problems arising in finite-strain solid mechanics.\textsuperscript{69,70} However, the investigation of these methods is beyond the scope of this work.

Regarding instead time discretization, we consider a uniform time step \(\Delta t = 2.5 \cdot 10^{-3}\) s and a final time \(t_f = 0.8\) s, which in our case corresponds to the simulation of a single heartbeat, so that the total number of time iterations is equal to \(N_t = 320\).

Since the number of Newton iterations required for the ROM solution to converge is rather small – say, between 2 and 4 for the cases at hand –, we fix \(N_{\text{nlit}} = 6\). This may be due to the fact that the employed time step makes the solution at the previous time step a good initial guess for the Newton iterations at the current time step. As the time step is reduced, the nonlinearity also gets less pronounced, because the linear mass matrix term gets divided by \(\Delta t^2\), and hence grows bigger as \(\Delta t\) gets smaller.

The number \(n_s\) of samples for the computation of the RB matrices has been chosen taking into account the computational cost required for the generation of the high-fidelity snapshots, both in terms of memory and run time. Moreover, by performing simulations on a coarse mesh, no particular improvement has been observed for \(n_s \geq 15\). Of course, this value is problem dependent, as increasing the number of unknown input parameters would require a larger value for \(n_s\) to accurately sample the parameter space \(\mathcal{P}\). However, adaptive sampling techniques can be employed to further enhance the reduction strategy. A similar argument applies to the choice of \(n_t'\), having to provide the sufficient amount of training data to the DNNs.

Finally, we employ the so-called Bayer-Blake-Plank-Trayanova algorithm\textsuperscript{71} to construct the fiber distribution, whilst for the baseline EM simulation used in the definition of the active tension (see Section 2.1.3), we rely on the high-fidelity model implemented in Reference \textsuperscript{10}, where the same ventricular geometry reported in Figure 2 is employed. The input values used are listed in Tables A2 and A1.

\textbf{Remark 4.} As stated in Remark 1, the end-diastolic configuration must be computed for every new instance of the parameter vector, in order to initiate the simulation. However, for practical reasons, we decided to solve the initial displacement problem only once and for a fixed parameter vector \(\mu^{\text{init}} = [R_p^{\text{init}}, \overline{T}_a^{\text{init}}]\). The computed displacement is thus used as initial condition for any other value of \(\mu\), that is, \(u_{h,0}(\mu) = u_{h,0}(\mu^{\text{init}})\) and \(\dot{u}_{h,0}(\mu) = \dot{u}_{h,0}(\mu^{\text{init}})\) \(\forall \mu\), both during training and testing. In particular, the reference value for \(R_p^{\text{init}}\) is taken from the literature, whilst we set \(\overline{T}_a^{\text{init}}\) such that the active tension \(T_a(\cdot; \mu^{\text{init}})\) matches the space-averaged active tension computed during the baseline EM simulation.

\subsection*{3.2 | Physiological scenario}

We first address the fast approximation of the FOM solution by means of a ROM in a physiological scenario. In this case, we choose as unknown parameters \(\mu = [R_p, \overline{T}_a] \in \mathcal{P} \subset \mathbb{R}^2\), where:

- \(R_p \in [2.5 \cdot 10^7, 4.5 \cdot 10^7]\) Pa \(\cdot\) s \(\cdot\) m\(^{-3}\) is the resistance of the windkessel model and,
- \(\overline{T}_a \in [4.5 \cdot 10^4, 6 \cdot 10^4]\) Pa is the active tension parameter.
For the sole purpose of comparing the Deep-HyROMnet approach with classical POD-Galerkin-DEIM ROMs, in terms of both accuracy and efficiency, we first consider a FOM built on a coarse hexahedral mesh with 4588 elements and 6167 vertices, featuring a high-fidelity dimension equal to $N_h = 18501$. Later on, we will consider a finer mesh to properly account for the solution features required by the application at hand.

During the offline stage, we compute the solution snapshots for $n_s = 15$ parameter samples, each requiring around 25 min using the FOM, and apply POD for the construction of the reduced basis $V \in \mathbb{R}^{N_h \times N}$. In Table 4, we report three different values for the POD tolerance $\varepsilon_{\text{POD}}$ and the corresponding RB dimension $N$. Since the input of the encoder function of the DNN architecture is reshaped into a square matrix (see Remark 2), we choose $N$ such that $\sqrt{N+1} \in \mathbb{N}$, that is, $N = 35$, in order to avoid the introduction of too many additional terms when zero-padding. The reduced basis is then built through the randomized singular value decomposition (SVD), using that is, a non-deterministic, version of SVD which exploits random sampling to construct a low-dimensional subspace to capture most of the energy of the data matrix, and then manipulates the associated reduced matrix with classical deterministic algorithms, to obtain the desired low-rank approximation.

Once the ROM is built, we perform $n_s' = 25$ simulations to collect the data required to train the DNNs, and to build the DEIM residual basis. In particular, we store the training data in the following snapshots matrices

\[
\begin{align*}
S_p & \in \mathbb{R}^{N \times 1 \times N_{\text{train}}}, & S_p & = \left[V^T R \left(V_{N}^{k(j)}(\mu_{\ell}), t^k; \mu_{\ell} \right)\right]_{\ell,j}, \\
S_\ell & \in \mathbb{R}^{N \times N \times N_{\text{train}}}, & S_\ell & = \left[V^T \partial_\ell R \left(V_{N}^{k(j)}(\mu_{\ell}), t^k; \mu_{\ell} \right)\right]_{\ell,j}, \\
S_v & \in \mathbb{R}^{N \times 1 \times N_{\text{train}}}, & S_v & = \left[V^T \partial_v R \left(V_{N}^{k(j)}(\mu_{\ell}), t^k; \mu_{\ell} \right)\right]_{\ell,j}, \\
S_j & \in \mathbb{R}^{1 \times (N+1) \times N'_{\text{train}}}, & S_j & = \left[\partial_j R_{\text{vol}} \left(V_{N}^{k(j)}(\mu_{\ell}), t^k; \mu_{\ell} \right)\right]_{\ell,j}.
\end{align*}
\]

where $\ell = 1, ..., n_s'$, $k = 1, ..., N_t$, $0 < j \leq N_{\text{vol}}$. Here, $N_{\text{train}}$ and $N'_{\text{train}}$ denote the total number of snapshots for the ejection/filling and the isovolumetric phases, respectively. Note that $N_{\text{train}} > N'_{\text{train}}$, since the snapshots for $S_v$ and $S_j$ are collected during phases 1 and 3 of the cardiac cycle only.

Table 5 summarizes the results obtained on a testing set of 10 input parameters using POD-Galerkin-DEIM and Deep-HyROMnet approaches. In particular, by performing POD on the ROM residual snapshots with tolerance $\varepsilon_{\text{DEIM}} = 10^{-5}$, we obtain a DEIM basis matrix of dimension 671. Indeed, convergence issues of the reduced Newton system have occurred for smaller basis dimensions. We observe that Deep-HyROMnet computes a reduced solution in 15 s, that is, almost 100 times faster than the high-fidelity FOM, which requires 25 min, whilst yielding an absolute error $\varepsilon_{\text{abs}}$ on the displacement field of order $O(10^{-2})$. On the other hand, the POD-Galerkin-DEIM ROM, despite being more

| POD-Galerkin-DEIM | Deep-HyROMnet |
|------------------|--------------|
| Speed-up | $\times 1.8$ | $\times 100$ |
| Avg. CPU time | 14 min | 15 s |
| Mean $\mu$, $\varepsilon_{\text{abs}}(\mu)$ | $2 \cdot 10^{-3}$ | $3 \cdot 10^{-2}$ |
| Mean $\mu$, $\varepsilon_{\text{rel}}(\mu)$ | $6 \cdot 10^{-3}$ | $6 \cdot 10^{-2}$ |

Note: Computational data related to POD-Galerkin-DEIM ROM and Deep-HyROMnet, for $N_h = 18501$ and $N = 35$. 

| Table 5 | Cardiac cycle, physiological scenarios. |
|--------|------------------------------------------|
| POD tolerance $\varepsilon_{\text{POD}}$ | $10^{-3}$ | $5 \cdot 10^{-4}$ | $10^{-4}$ |
| RB dimension $N$ | 27 | 35 | 58 |

Note: POD tolerances and associated RB dimension for the physiological scenario, when $N_h = 18501$. 

\[\text{TABLE 4} \quad \text{Cardiac cycle, physiological scenarios.}\]

| POD tolerance $\varepsilon_{\text{POD}}$ | $10^{-3}$ | $5 \cdot 10^{-4}$ | $10^{-4}$ |
|------------------------------------------|-----------|----------------|-----------|
| RB dimension $N$ | 27 | 35 | 58 |

Note: POD tolerances and associated RB dimension for the physiological scenario, when $N_h = 18501$. 

\[\text{TABLE 5} \quad \text{Cardiac cycle, physiological scenarios.}\]

| POD-Galerkin-DEIM | Deep-HyROMnet |
|------------------|--------------|
| Speed-up | $\times 1.8$ | $\times 100$ |
| Avg. CPU time | 14 min | 15 s |
| Mean $\mu$, $\varepsilon_{\text{abs}}(\mu)$ | $2 \cdot 10^{-3}$ | $3 \cdot 10^{-2}$ |
| Mean $\mu$, $\varepsilon_{\text{rel}}(\mu)$ | $6 \cdot 10^{-3}$ | $6 \cdot 10^{-2}$ |

Note: Computational data related to POD-Galerkin-DEIM ROM and Deep-HyROMnet, for $N_h = 18501$ and $N = 35$.
accurate than Deep-HyROMnet, still requires high computational resources, employing 14 min to simulate a single heartbeat, thus implying almost no computational speed-ups.

A finer computational mesh has been also considered to build a second FOM and test the Deep-HyROMnet capabilities on more realistic scenarios. In this second case, 30,108 elements and 35,725 vertices are used, so that the average cell diameter is equal to $h_{\text{avg}} = 0.003$ m (corresponding to the mesh size commonly used to accurately capture the myocardial displacement with expensive, high-fidelity models). The resulting FOM is characterized by $N_h = 107175$ degrees of freedom, requiring approximately 3 h 10 min for each instance of the input parameter. We consider $n_s = 15$ samples to collect the FOM solution snapshots and perform POD with different tolerances $\varepsilon_{\text{POD}}$, thus obtaining the results reported in Table 6. We observe that the minimum integer satisfying condition (8) with the same level of accuracy does not increase as $N_h$ becomes larger. As previously done, to avoid the introduction of too many additional terms in the training data for the DNNs when zero-padding, we use $N = 35$ to build the RB basis $V$ by means of the randomized SVD, and subsequently perform $n_s' = 25$ ROM simulations to build the snapshots matrices (13) required for training the DNNs. In order to reduce the training time for the neural networks, we rely on a suitable pre-training strategy, that is, the optimal weights and biases found for the DNNs when $N_h = 18501$ are used to initialize the corresponding networks for the larger FOM-dimension.

When using a finer mesh, Deep-HyROMnet takes 68 s on average to compute the displacement dynamics for a complete heartbeat, being 165 faster than the FOM. Similarly to the coarser mesh, the time-averaged $L^2$-absolute error $\varepsilon_{\text{abs}}(\mu)$, computed over 10 testing parameter configurations, is equal to $4 \cdot 10^{-2}$ and the $L^2$-relative error $\varepsilon_{\text{rel}}(\mu)$ is $5 \cdot 10^{-2}$. The results are summarized in Table 10.

### Table 6  Cardiac cycle, physiological scenarios.

| POD tolerance $\varepsilon_{\text{POD}}$ | $10^{-3}$ | $5 \cdot 10^{-4}$ | $10^{-4}$ |
|-------------------------------|-----------|------------------|-----------|
| RB dimension $N$              | 28        | 36               | 61        |

Note: POD tolerances and associated RB dimension for the physiological scenario, when $N_h = 107175$.

![Figure 9](image-url)

**FIGURE 9**  Cardiac cycle, physiological scenarios with $N_h = 107175$. Pressures, volumes and pressure-volume relationships, for the testing parameter values (unseen during training), computed using the FOM (green, solid line) and Deep-HyROMnet (blue, dotted line).
The left ventricular pressures and volumes obtained using the FOM and the Deep-HyROMnet strategy on a subset of the testing set are compared in Figure 9, showing perfect agreement of the reduced outputs of interest with the high-fidelity ones, uniformly on the subset of parameter inputs. Figures 10, 11 and 12 show the Deep-HyROMnet solution computed at different phases of the cardiac cycle, for different testing values of the parameter vector. The corresponding

**FIGURE 10** Cardiac cycle, physiological scenarios. Deep-HyROMnet displacement (top) and pointwise error – displayed on the undeformed configuration – between FOM and Deep-HyROMnet solutions (bottom) at different time instances, for $\mu_1 = [2.6000 \cdot 10^7 \text{ Pa} \cdot \text{s} \cdot \text{m}^{-1}, 5.175 \cdot 10^8 \text{ Pa}]$.

**FIGURE 11** Cardiac cycle, physiological scenarios. Deep-HyROMnet displacement (top) and pointwise error – displayed on the undeformed configuration – between FOM and Deep-HyROMnet solutions (bottom) at different time instances, for $\mu_3 = [2.4667 \cdot 10^7 \text{ Pa} \cdot \text{s} \cdot \text{m}^{-1}, 5.675 \cdot 10^8 \text{ Pa}]$.
The offline computational time required for the generation of the FOM snapshots, the collection of the training datasets and the actual training of the DNNs are reported in Table 7. Moreover, we report the break-even point, that is, the minimum number of FOM simulations that would justify the offline cost. If we assume that the DNNs are trained simultaneously, as they are independent of each other, only 43 FOM simulations are sufficient to exceed the total wall time necessary for the offline stage (that becomes 46 if the DNNs are trained sequentially). On the other hand, the solution to multi-query problems requires addressing the input–output map hundreds and even thousands times, thus making the construction of a ROM worthy.

**TABLE 7** Cardiac cycle, physiological scenarios.

|                              | Wall time × n (or n') on CPU | Wall time × #epochs on GPU |
|------------------------------|------------------------------|----------------------------|
| FOM                          | 3 h 10 min × 15               | 6 s × 2145                 |
| POD-Galerkin ROM             | 2 h 50 min × 25               | 12 s × 4952                |
| DNN for $\mathbf{V}^T \mathbf{R}$ |                              |                            |
| DNN for $\mathbf{V}^T \partial_d \mathbf{R} \mathbf{V}$ |              |                            |
| DNN for $\mathbf{V}^T \partial_p \mathbf{R}$ |              |                            |
| DNN for $[\partial_d \mathbf{R}_{\text{ref}}, \mathbf{V}, \mathbf{R}_{\text{ref}}]$ |              |                            |
| Offline time (if DNNs are trained simultaneously) | 5 d 15 h | 2.4 s × 3155 |
| Break-even point             | 43 FOM simulations            |                            |

Note: Offline computational times, when $N_h = 107175$. The second column shows the average computational time required to compute each FOM and POD-Galerkin ROM snapshots on CPU, and the average seconds per epoch necessary to train the DNNs on GPU, along with the corresponding number of snapshots and epochs, respectively. Moreover, the total offline wall time and the break-even point are reported.

Pointwise error between the FOM and the Deep-HyROMnet displacements is also reported, showing that the accuracy of the Deep-HyROMnet approximation does not deteriorate over time.
Similar to the classical Newton method, the dependence of the residual vectors on the Newton iterations is much more strong than that of the Jacobians. In fact, due to the higher variability of the data, the approximation of the ROM residual is the most challenging task. This is reflected by the accuracy of the DNNs predictions, being the training and test errors of the Jacobian matrices are almost one order of magnitude smaller than those of the residuals. For the test case at hand, with \( N_h = 107175 \), we report in Table 8 the relative error on the test set, defined as follows:

**Table 8** Cardiac cycle, physiological scenarios.

| \( W_{rel} \)                  | Relative error \( \varepsilon_{rel,W_{rel}} \) |
|-------------------------------|-----------------------------------------------|
| \( V^T R \)                   | \( 8 \cdot 10^{-2} \)                         |
| \( V^T \partial_p R \)       | \( 2 \cdot 10^{-2} \)                         |
| \( \left[ \partial_d \mathbf{R}^{\text{ref}}, \mathbf{V}, \mathbf{R}^{\text{ref}} \right] \) | \( 8 \cdot 10^{-3} \)                         |

Note: Accuracy of the DNNs on the test set, when \( N_h = 107175 \).

**Table 9** Cardiac cycle, pathological scenarios.

| POD tolerance \( \varepsilon_{\text{POD}} \) | \( 10^{-3} \) | \( 5 \cdot 10^{-4} \) | \( 10^{-4} \) |
|--------------------------------------------|---------------|-----------------|---------------|
| RB dimension \( N_h \)                    | 43            | 57              | 105           |

Note: POD tolerances and associated RB dimension for the pathological scenario, when \( N_h = 107175 \).

**Figure 13** Cardiac cycle, pathological scenarios with \( N_h = 107175 \). Pressures, volumes and pressure-volume relationships, for the testing parameter values (unseen during training), computed using the FOM (red, solid line) and Deep-HyROMnet (blue, dotted line).
ε_{\text{rel}, \mathcal{W}_N} = \frac{1}{n_s N_s} \sum_{s=1}^{n_s} \sum_{k=1}^{N_s} \sqrt{\sum_{j=1}^{N_{\text{net}}} \left\| \mathcal{W}_N \left( \mathbf{v}^{(j)}_{\mathcal{W}_N} (\mu_s, t^k; \mu_s) - \mathbf{w} (\mu_s, t^k; \theta_{\mathcal{DF}}, \theta_{\mathcal{D}}) \right) \right\|^2}.

\text{FIGURE 14}  
Cardiac cycle, pathological scenarios. Deep-HyROMnet displacement (top) and pointwise error – displayed on the undeformed configuration – between FOM and Deep-HyROMnet solutions (bottom) at different time instances, for \( \mu_s = [4.30 \times 10^7 \text{ Pa} \cdot \text{s} \cdot \text{m}^{-1}, 4.65 \times 10^4 \text{ Pa}, 0.011 \text{ m}] \).

\text{FIGURE 15}  
Cardiac cycle, pathological scenarios. Deep-HyROMnet displacement (top) and pointwise error – displayed on the undeformed configuration – between FOM and Deep-HyROMnet solutions (bottom) at different time instances, for \( \mu_s = [2.70 \times 10^7 \text{ Pa} \cdot \text{s} \cdot \text{m}^{-1}, 5.85 \times 10^4 \text{ Pa}, 0.013 \text{ m}] \).
where $W_N$ is rather $V^T R$, $\text{vec}(V^T \partial_d RV)$, $V^T \partial_p R$ or $[\partial_d R^\text{vol}, R^\text{vol}]^T$, and $f_W$ is the corresponding DNN prediction.

### 3.3 Pathological scenario

We now address the solution to the 3D-0D coupled problem in the case a portion of the cardiac tissue has been affected by myocardial ischemia, that is, a reduction of blood supply to the myocardium that may lead to the death of cells in the affected area. In this case, cells show a reduced excitability, ionic currents are altered, and tissue contractility is inhibited. However, they have never been applied to characterize the mechanical behavior of the myocardium in these scenarios, for varying conditions of the ischemic tissue. Therefore, this is the first time that such a phenomenon is investigated systematically in a broad variety of conditions. In this numerical test case, we consider as varying input parameters:

- the resistance of the windkessel model $R_p \in [2.5 \cdot 10^7, 4.5 \cdot 10^7] \, \text{Pa} \cdot \text{s} \cdot \text{m}^{-3}$,
- the active tension parameter $\tilde{T}_a \in [4.5 \cdot 10^4, 6 \cdot 10^5] \, \text{Pa}$,
- and the radius of the ischemic region $r \in [10^{-2}, 2 \cdot 10^{-2}] \, \text{m}$

which are among the most influential parameters associated with the circulation model, the active component of the structural model and the necrotic region, respectively. For the computational domain, we employ the hexahedral mesh with 35725 vertices reported in Figure 2 (right), so that the FOM obtained using $Q_1$-FE has dimension $N_h = 107175$.

The reduced basis $V$ is built by collecting high-fidelity solution snapshots for $n_s = 15$ parameter samples and performing randomized SVD using $N = 63$, so that $N$ is close to the RB dimension obtained for $\varepsilon_{\text{POD}} = 5 \cdot 10^{-4}$ and $\sqrt{N-1} \in \mathbb{N}$. In fact, a higher dimension of the reduced basis with respect to the physiological scenario is required, possibly due to the additional parameter and the presence of ischemia which causes a more involved tissue dynamics, as highlighted in Table 9. Indeed, the presence of the scar region ultimately makes the parameters-to-solution map more involved, affecting the behavior of the solution in a more pronounced way, and thus requiring a higher dimension of the basis if a global linear subspace has to be used to approximate the whole solution manifold with sufficient accuracy.

Then, $n_t = 45$ POD-Galerkin ROM simulations are performed to collect the reduced nonlinear data (13) and the DNNs are trained. Similarly to the physiological scenario, Deep-HyROMnet requires around 72s to compute a whole.
heartbeat, so that it is 156 times faster than the FOM, which for the same task to be achieved requires more than 3 h. A good approximation of the outputs of interest is obtained using our Deep-HyROMnet approach. In particular, the reduction error on the ejection fraction \( (EF) \), that is, the volumetric portion of blood ejected from the ventricle with each contraction, computed over the testing set, is less than 3.5%. The pressure-volume loops computed for inputs unseen during training are shown in Figure 13, whereas Figures 14, 15 and 16 report the Deep-HyROMnet displacement and the corresponding pointwise error for three different values of the parameter vector. For the sake of clarity, we have highlighted the computational grid corresponding to the scar region. The computational data related to the Deep-HyROMnet technique applied to both the physiological and the pathological scenarios are summarized in Table 10.

4 | DISCUSSION

4.1 | Computational efficiency and numerical accuracy

The proposed Deep-HyROMnet strategy has allowed us to obtain accurate outputs of clinical interest in a much more efficient way compared to both classical high-fidelity finite element simulations and hyper reduced order models. Regarding traditional ROMs, the need to rely on classical hyper-reduction techniques (such as, e.g., the discrete empirical interpolation method) to avoid the expensive calculation of the FOM arrays for any new parameter instance represents a severe computational bottleneck. Indeed, the high number of DEIM basis elements makes the solution of the POD-Galerkin-DEIM ROM far from being fast, taking about 14 min to simulate a single heartbeat, and thus yielding a mild computational speed-up compared to the FOM; this latter would indeed take about 25 min to perform the same task for the problem under consideration.

On the other hand, the Deep-HyROMnet method in the physiological case computes a reduced solution in 15 s on the coarser mesh – almost 100 times faster than the high-fidelity FOM – and in 68 s on the fine mesh – almost 165 times faster than the high-fidelity FOM. In both cases, the time-averaged \( L^2 \)-absolute error \( \epsilon_{abs}(\mu) \) and the \( L^2 \)-relative error \( \epsilon_{rel}(\mu) \) are of order \( 10^{-2} \) (see Table 10). Similar conclusions can be drawn in the pathological case, where the Deep-HyROMnet method computes a reduced solution in 72 s on the fine mesh – almost 160 times faster than the high-fidelity FOM – with errors of order \( 10^{-2} \) also in this case.

Taking the pressure-volume loop as the most relevant outcome of the simulation of the cardiac function from a mechanical point of view, we remark that the Deep-HyROMnet strategy produces outputs that show perfect agreement with the ones obtained with the FOM, uniformly on the parameter space; see Figure 9 for the physiological case and Figure 13 for the pathological case. Moreover, we highlight that parameter variations may have a great impact on this output of interest; as a matter of fact, its accurate approximation, over the entire parameter space, can be a demanding task. To this purpose, we report the pressure-volume loops obtained for six different values of the input vector \( \mu = [R_{ap}, Ta, \alpha, r] \in \mathcal{P} \) (see Figure 17). In particular, we observe that the end-systolic volume ranges from 43 to 84 mL, so that the \( EF \) reduces from 64% to 30%, in agreement with clinical guidelines used to identify unhealthy cases. On the other hand, the maximum value of the blood pressure goes from 92 to almost 113 mmHg, thus influencing the slope of the end-systolic pressure-volume relationship that provides an index of myocardial contractility. All these indicators

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**Table 10** Cardiac cycle.

|                     | Physiological case       | Pathological case       |
|---------------------|--------------------------|-------------------------|
| \( N_h \)           | 107175                   | 107175                  |
| FOM time            | 3 h 10 min               | 3 h 10 min              |
| \( N \)             | 35                       | 63                      |
| Speed-up            | \( \times 165 \)         | \( \times 156 \)        |
| Avg. CPU time       | 1 min 8 s                | 1 min 11 s              |
| Mean \( \mu \) \( \epsilon_{abs}(\mu) \) | \( 4.3 \cdot 10^{-2} \) | \( 7.7 \cdot 10^{-2} \) |
| Mean \( \mu \) \( \epsilon_{rel}(\mu) \) | \( 4.8 \cdot 10^{-2} \) | \( 9.3 \cdot 10^{-2} \) |

Note: Computational data related to Deep-HyROMnets in physiological and pathological scenarios.
are currently exploited in the clinical practice, see, Reference 79–81. To gain some useful knowledge about the impact of the model parameters on selected output quantities, and to show how the Deep-HyROMnet strategy can indeed enable these kinds of analysis, in the next section we focus on a possible way to perform forward uncertainty quantification on outputs of clinical interest.

4.2 Application to forward uncertainty quantification

In order to translate cardiac computational models into clinical applications, it is crucial to assess and quantify how input uncertainties impact on model predictions, and thus on selected outputs of interest. This task is carried out by performing uncertainty quantification (UQ) studies.\(^82\) The most common approach to solve UQ problems are Monte Carlo simulation (MCS) methods. However, a large number of realizations of the model are required to converge, preventing their use for large-scale problems, especially when the input–output map is computed by means of expensive high-fidelity models. To enable UQ studies for cardiac problems, several approaches have been investigated. The convergence rate of MCS can be improved, for example, by quasi-Monte Carlo and Multi-Level Monte Carlo techniques. The latter approach relies on a resolution-based hierarchy of models, such that most of the simulations are performed on the low-resolution models, and only a few on the original one. More recently, multi-level techniques have been replaced by multi-fidelity methods.\(^83,84\) In this case, the full-order model is combined with a family of reduced models, which provide efficient approximations of the problem solutions within known error bounds. A more sophisticated Bayesian multi-fidelity Monte Carlo framework is considered in Reference 85 for patient-specific biomechanical models, and in Reference 86 for the solution to UQ problems in cardiac electrophysiology. As an alternative to MCS techniques, surrogate models have been of particular interest to accelerate the UQ analysis. The polynomial chaos expansion method is adopted in Reference 22 to passive cardiac mechanics, and later extended to the whole cardiac cycle in Reference 23. In this case, the original model is replaced by a series of orthonormal polynomials over the random parameter space, which can be used to evaluate the input–output map at a low computational cost. The generalized polynomial-chaos expansion method is employed in Reference 66 to perform a forward uncertainty propagation on cardiac electromechanics problems. The probabilistic collocation method is used in Reference 87 to investigate the impact of material parameters on the passive mechanical behavior of the left ventricle, in a quasi-static framework.
In this work, we perform a qualitative – rather that quantitative – quantification of the parametric uncertainty by addressing the repeated evaluation of the inputs-to-solution map in both physiological and pathological scenarios by means of the Deep-HyROMnet technique. Although this represents a less rigorous approach to UQ studies, it allows to gain some useful knowledge about the impact of the model parameters on selected output quantities. With this aim, let us consider as quantities of interest:

- the ejection fraction, that is defined as

\[ EF = \frac{EDV - ESV}{EDV}, \]

where \( EDV \) and \( ESV \) denote the end-diastolic and the end-systolic volumes, respectively;

- the maximal rate of change in pressure

\[ \frac{dP}{dt_{\text{max}}} = \max_{t \in (0, T)} \left( \frac{dP_{LV}(t; \mu)}{dt} \right) \approx \max_{k=1, \ldots, N_t} \left( \frac{p_{LV}^k(\mu) - p_{LV}^{k-1}(\mu)}{\Delta t} \right), \]

which is a common indicator of cardiac contractility.

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These choices are motivated by the fact that both \( EF \) and \( \frac{dP}{dt_{\text{max}}} \) are commonly used mechanical biomarkers, and are usually included among the outputs of interests in SA studies in cardiac mechanics and electromechanics simulations.\(^{23,31,88,89}\) Nonetheless, since Deep-HyROMnet computes the whole displacement at each time instance, any additional output, such as, for example, the wall thickening, the end-systolic pressure or the longitudinal fractional shortening,\(^{23,88}\) as well as other field quantities such as the axial stresses along different directions, can be considered online without the need to rebuild the ROM, see, for example, Figure 18. This is a distinguishing feature of the proposed reduction technique, compared to recent frameworks addressing NN-based or GPE-based approximations of quantities of interest, without taking into account the approximation of the field variables involved in the output evaluations.
For what concerns the varying parameters, we consider:

- the resistance of the windkessel model $R_p \in [2.5 \cdot 10^7, 4.5 \cdot 10^7] \text{Pa} \cdot \text{s} \cdot \text{m}^{-3}$,
- the active tension parameter $\tilde{T}_a \in [4.5 \cdot 10^4, 6 \cdot 10^4] \text{Pa}$, and
- the radius of the ischemic region $r \in [10^{-2}, 2 \cdot 10^{-2}] \text{m}$ for the unhealthy cases.

The following results are obtained by performing 500 Deep-HyROMnet simulations in the physiological scenario and 1000 in the pathological one, taking into account the coarser hexahedral mesh with 6167 vertices so that $N_h = 18501$. In this case, performing these studies using the FOM would have required 26 days of computations, which become almost 198 days if the finer computational grid with 35725 vertices has to be considered (reducing to less than 30 h when employing the Deep-HyROMnet approach).

Concerning the outcomes in the healthy scenario, we observe that both the resistance $R_p$ of the two-element windkessel model and the active stress parameter $\tilde{T}_a$ have a great impact on the $EF$, as shown in Figure 19 (left). Both variables are, in fact, associated with the systolic phase of the cardiac cycle: larger values of the maximum active tension lead to a greater contraction of the myocardial tissue, whereas higher values of $R_p$ correspond to a lower amount of blood that the ventricle is able to pump during ejection (phase 2 of the heartbeat). As a consequence, they both affect the $ESV$ without substantially changing the $EDV$. In particular, given a fixed value of $R_p$, the $EF$ increases as $\tilde{T}_a$ becomes higher; on the other way round, when $\tilde{T}_a$ is fixed, the $EF$ decreases as the resistance of the circulation model is increased. As an example, the minimum value $EF = 37\%$ corresponds to $\mu = [4 \cdot 10^7 \text{Pa} \cdot \text{s} \cdot \text{m}^{-3}, 4.605 \cdot 10^4 \text{Pa}]$, that is when $R_p$ and $\tilde{T}_a$ are close to their upper and lower bounds, respectively; its maximum value $EF = 78\%$ is obtained instead for $\mu = [2.6 \cdot 10^7 \text{Pa} \cdot \text{s} \cdot \text{m}^{-3}, 5.835 \cdot 10^4 \text{Pa}]$. On the other hand, from Figure 19 (right), we can conclude that the maximal rate of change in pressure is proportional to the active stress, going from $1763 \text{mmHg} \cdot \text{s}^{-1}$ to $1998 \text{mmHg} \cdot \text{s}^{-1}$ as $\tilde{T}_a$ is increased from $4.5 \cdot 10^4 \text{Pa}$ to its maximum value $6 \cdot 10^4 \text{Pa}$, whilst we observe that $R_p$ has almost no influence on $dP/dt_{\text{max}}$. These results are overall in agreement with sensitivity analysis studies reported in the literature. The scaling factor for the tension is identified to be among the parameters with greatest effect on the majority of the outputs of a fully-coupled electromechanical model in References 27,31; here, the systemic resistance is also identified as an influential parameter, although different circulation models with respect to the one employed in this paper are used, and a direct comparison is therefore not possible. Clinical studies performed on healthy subjects relate increased systemic resistance to decreased $EF$, as well as increased pressure in the ventricle. Focusing on simulations of the LV function
during the entire cardiac cycle, the results reported in Reference 23 show that both $EF$ and $dP/dt_{max}$ are highly sensitive to the reference value for the active stress. Similarly, in Reference 88, $\tilde{T}_a$ is reported to be the parameter affecting the strongest the mechanical biomarkers, especially the ejection fraction. Regarding the parameters of the 2-element Windkessel model considered, a moderated correlation with $EF$, as well as with the end-systolic pressure, is observed.

Assessing the way input variations affect the considered outputs of interest in the pathological scenario becomes more involved due to the presence of an additional parameter, and to the fact that no activation of the cardiac myocytes is assumed inside the necrotic region $B(\mathbf{X}, r)$. In Figures 20 and 21, we report the 2D views of the scatter plots associated with the computed $EF$ and $dP/dt_{max}$, respectively. Regarding the interaction between the maximum active tension $\tilde{T}_a$ and the windkessel resistance $R_p$ on their influence on the $EF$ (Figure 20, left), we can draw similar conclusions to the healthy case. On the other hand, the influence of the radius $r$ on the $EF$ is more difficult to ascertain from the analysis of the scatter plots. Finally, from the 2D-views of the scatter plots reported in Figure 21, we can assume that variations of both $R_p$ and $r$ have almost no effect on the maximal rate of change of pressure $dP/dt_{max}$, and that $\tilde{T}_a$ is the

**Figure 20** Cardiac cycle, pathological scenarios. 2D-views of the scatter plots of the $EF$ for 1000 different parameters. The colormap represents the values of the output of interest.

**Figure 21** Cardiac cycle, pathological scenarios. 2D-views of the scatter plots of the $dP/dt_{max}$ for 1000 different parameters. The colormap represents the values of the output of interest.
most influential parameter between those considered. To the extent of our knowledge, no UQ or SA studies have taken into account the size of the necrotic region among the input parameters, so that a qualitative comparison of the results is not possible.

To conclude, we have observed that the maximum value of the active tension $T_a$ has great influence on $EF$ and $dP/dt_{max}$, both in the physiological and in the pathological tests considered. This fact is in agreement with the results of SA carried out in Reference 23 for the case of a healthy left ventricle under a quasi-static assumption. The resistance $R_p$ of the circulation model, associated with the ejection phase of ventricular systole, influences the values of the $EF$, whilst it has no visible impact on the maximal rate of change of pressure. The same is true for the size of the necrosis, although its influence on the $EF$ is not easy to validate from the analysis carried out in this work.

5 | CONCLUSION

In this work, we have applied our physics-based, hyper-reduced-order modeling strategy $Deep-HyROMnet^{38}$ for the accurate and efficient approximation of nonlinear elastodynamics problems arising in cardiac mechanics. This method combines POD for the construction of a reduced basis, a Galerkin projection over the low-dimensional subspace spanned by these basis functions, and DNNs to efficiently handle the nonlinear reduced operators. We proved that Deep-HyROMnet is able to obtain an extremely good approximation of the displacement field, as well as key scalar cardiac outputs, while achieving considerable speed-ups thanks to the approximation of the nonlinear terms by means of a DNN architecture. Our method is suitable for a range of scenarios in which classical projection-based ROMs would require unaffordable computational costs.

In particular, we have shown how Deep-HyROMnets allow to address the efficient solution to cardiac mechanics problems coupled with a lumped-parameter model for blood circulation, both in physiological and pathological scenarios, outperforming POD-Galerkin-DEIM ROMs in terms of computational speed-up. Preliminary results of forward uncertainty quantification carried out on a patient-specific left ventricle allowed to gain some useful knowledge about the impact of the model parameters on possible output quantities of interest. In this context, we have observed that the active tension has great influence on both the ejection fraction and the maximal rate of change in pressure; other parameters, such as the resistance of the circulation model and the size of the necrosis, showed instead higher influence on the ejection fraction only.

By providing a reliable and computationally efficient reduction procedure, our model can be successfully used to address the solution of multi-query problems, such as, for example, forward uncertainty quantification and parameter estimation. However, some limitations of the proposed technique are worth mentioning. Since Deep-HyROMnet has been developed as an alternative to POD-Galerkin based ROMs equipped with classical hyper-reduction techniques, this approach is highly intrusive and requires access to the underlying FOM. To overcome this limitation, the analysis of non-intrusive strategies to directly learn the RB solution $u^k_N(\mu)$ at each time step $t^k$ by means of Gaussian process emulators is currently ongoing. Further investigations are needed to assess the performance of the proposed reduction strategy on even more involved scenarios. Remarkable examples include, for instance: (i) the use of finer computational meshes and smaller time steps; (ii) the introduction of a surrogate model for the computation of space- and time-dependent active tension, thus taking into account the activation of cardiac myocytes at different time instants; (iii) the inclusion of (at least) the left atrium to avoid artificial boundary conditions at the base; (iv) more and/or different input parameters, according to sensitivity analysis carried on the simulation of the whole cardiac cycle.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.
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APPENDIX A

A.1 A Reference Values for The 3D-0D Coupled Simulations
Here we report the reference values used throughout this work for the circulation and mechanics models (if not otherwise specified).

| Name                        | Parameter | Value  | Unit         |
|-----------------------------|-----------|--------|--------------|
| Circulation                |           |        |              |
| Capacitance                | \( C_p \) | \( 4.5 \cdot 10^9 \) | \( \text{m}^{-3} \cdot \text{Pa}^{-1} \) |
| Resistance                 | \( R_p \) | \( 3.5 \cdot 10^7 \) | \( \text{Pa} \cdot \text{s} \cdot \text{m}^{-3} \) |
| End-diastolic pressure     | \( p_{ED} \) | 10    | mmHg         |
| Aortic valve opening pressure | \( p_{AVO} \) | 82,50 | mmHg         |
| Mitral valve opening pressure | \( p_{MVO} \) | 5     | mmHg         |

| Name                        | Parameter | Value  | Unit         |
|-----------------------------|-----------|--------|--------------|
| Cardiac mechanics           |           |        |              |
| Tissue density              | \( \rho_0 \) | \( 10^3 \) | kg \cdot m\(^{-3}\) |
| Robin boundary condition    | \( K_\perp \) | \( 2 \cdot 10^4 \) | Pa \cdot m\(^{-1}\) |
| Robin boundary condition    | \( K_\parallel \) | \( 2 \cdot 10^4 \) | Pa \cdot m\(^{-1}\) |
| Robin boundary condition    | \( C_\perp \) | \( 2 \cdot 10^4 \) | Pa \cdot s \cdot m\(^{-1}\) |
| Robin boundary condition    | \( C_\parallel \) | \( 2 \cdot 10^3 \) | Pa \cdot s \cdot m\(^{-1}\) |
| Passive myocardial tissue   |           |        |              |
| Hyperelastic parameter      | \( b_f \) | 8      |              |
| Hyperelastic parameter      | \( b_s \) | 6      |              |
| Hyperelastic parameter      | \( b_n \) | 3      |              |
| Hyperelastic parameter      | \( b_{fs} \) | 12     |              |
| Hyperelastic parameter      | \( b_{fs}, b_{sn} \) | 3      |              |
| Material stiffness          | \( C \) | 880    | Pa           |
| Bulk modulus                | \( K \) | \( 5 \cdot 10^4 \) | Pa           |
| Active myocardial tissue    |           |        |              |
| Maximum active tension      | \( \bar{T}_a \) | \( 5 \cdot 10^4 \) | Pa           |
| Fiber angle                 | \( \alpha_{epi} \) | -60    | deg          |
| Fiber angle                 | \( \alpha_{endo} \) | 60     | deg          |
| Fiber angle                 | \( \beta_{epi} \) | 20     | deg          |
| Fiber angle                 | \( \beta_{endo} \) | -20    | deg          |