MECHANICAL ANALYSIS OF PULMONARY HYPERTENSION VIA ADJOINT BASED DATA ASSIMILATION OF A FINITE ELEMENT MODEL

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INTRODUCTION

Pulmonary hypertension (PH) is associated with an elevated pressure in the pulmonary arterial system. Without treatment, PH can quickly lead to decompensated RV failure and death. Our current understanding of PH has largely been obtained through animal models, which do not fully reproduce the etiology of human PH.

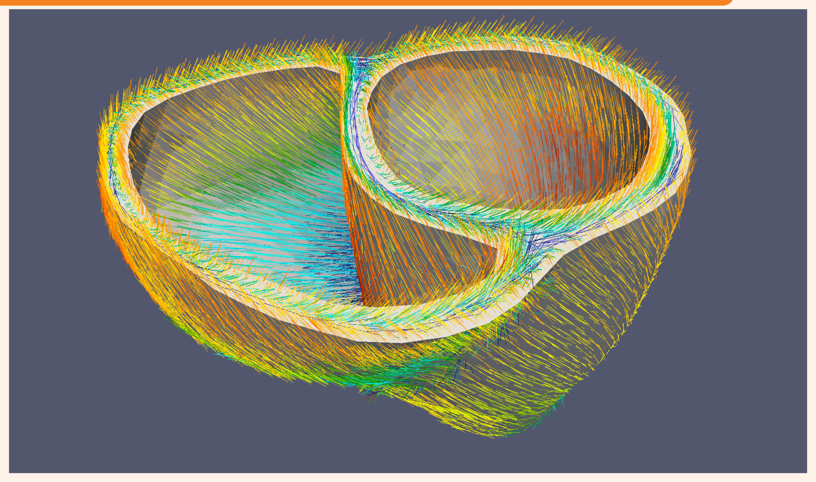
To overcome this limitation, we describe an inverse computational analysis framework that uses patient data consisting of MR images and pressure measurements to quantify the biomechanical alteration in ventricular mechanics associated with PH.

The framework was developed based on an adjoint-gradient based data assimilation method that can efficiently handle optimization in high dimensional parameter spaces.

METHODS

DATA ACQUISITION AND PRE-PROCESSING

Cine magnetic resonance (MR) images were obtained from three patients diagnosed with pulmonary hypertension (PH) and two healthy controls subjects. Ventricular, atrial and artery pressure were also measured in the PH patients by right heart catheterization. The ventricular pressure from the healthy controls was estimated based on previous studies. Left and right ventricular (LV and RV) volumes were measured at different time frames in a cardiac cycle from the MR images by segmentation of the biventricular geometry. These measurements (as well as the pressure estimation for normal human subjects) were used to construct pressure-volume loops of the RV and LV for the PH patients and the normal subject. Biventricular finite element (FE) geometries for the PH patients and normal subject were reconstructed from the corresponding MR images at atrial systole.



△ **Figure:** Myocardial fiber architecture are assigned using the Laplace-Dirichlet Rule Based algorithm, with a helix fiber angle of 60° and −60° on the endo- and epicardium respectively.

MECHANICAL MODELING

▷ The myocardium is modeled as an **incompressible, hyperelastic material** with a transversely isotropic version of the Holzapfel and Ogden strain energy density function. The active contraction of the muscle is modeled though the **active strain** framework, which is based on a multiplicative decomposition of the deformation gradient tensor,

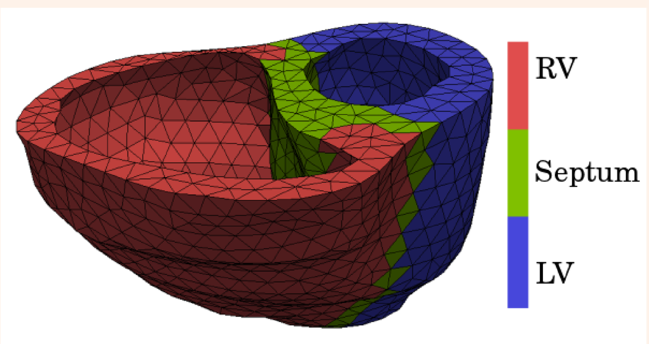
$$\mathrm{F} = \mathrm{F}_{\mathrm{e}}\mathrm{F}_{\mathrm{a}}.$$

Here F_{a} is the active deformation induced by cell contraction, and F_{e} is the elastic deformation that stores all the energy, so that the strain energy density function depends on the **elastic invariants** $\mathcal{I}_1^{\mathrm{e}} = \mathrm{tr}\mathrm{C}_{\mathrm{e}}$ and $\mathcal{I}_{4,\mathbf{f}_\circ}^{\mathrm{e}} = \mathbf{f}_\circ \cdot \mathrm{C}_{\mathrm{e}}\mathbf{f}_\circ$ of the elastic part of right Cauchy-Green tensor $\mathrm{C}_{\mathrm{e}} = \mathrm{F}_{\mathrm{e}}^T\mathrm{F}_{\mathrm{e}}$:

$$\mathcal{W}(\mathrm{C}_{\mathrm{e}}) = \frac{a}{2b}\left(e^{b(\mathcal{I}_1^{\mathrm{e}}-3)} - 1\right) + \frac{a_{\mathrm{f}}}{2b_{\mathrm{f}}}\left(e^{b_{\mathrm{f}}(\mathcal{I}_{4,\mathbf{f}_\circ}^{\mathrm{e}}-1)_+^2} - 1\right)$$

▷ We assume that the active deformation is volume preserving and results in a shortening in the fiber direction $\mathbf{f}_\circ$. By introducing a **single activation parameter** γ, which represents relative local active fiber shortening, we get

$$\mathrm{F}_{\mathrm{a}} = (1-\gamma)\mathbf{f}_\circ \otimes \mathbf{f}_\circ + \frac{1}{\sqrt{1-\gamma}}\left(\mathrm{I} - \mathbf{f}_\circ \otimes \mathbf{f}_\circ\right).$$



◁ **Figure:** We spatially resolve the activation γ, and the linear isotropic parameter a to be a constant on each segment. This introduces additional degrees of freedom to fit data from both the LV and RV, and at the same time keeping the number of parameters at a minimum to ensure identifiable parameters.

▷ The model is discretized using Taylor-Hood finite elemets with quadratic finite elements for the displacement $\mathbf{u}$ and linear finite elements for the hydrostatic pressure p.

▷ The solver is implemented using the **open-source** finite element framework FENICS.

DATA ASSIMILATION

▷ To constrain the mechanical model to clinical data, we formulate the problem as a **PDE-constrained optimzation** problem, where the objective functional represents the mismatch between simulated and observed data, and the constraint is given by the force balance equation in the mechanical model:

$$\underset{\mu}{\text{minimize}} \quad \mathcal{J}(\mathbf{u}, \mu)$$
$$\text{subject to } \delta\Pi(\mathbf{u}, p, \mu) = 0,$$

where

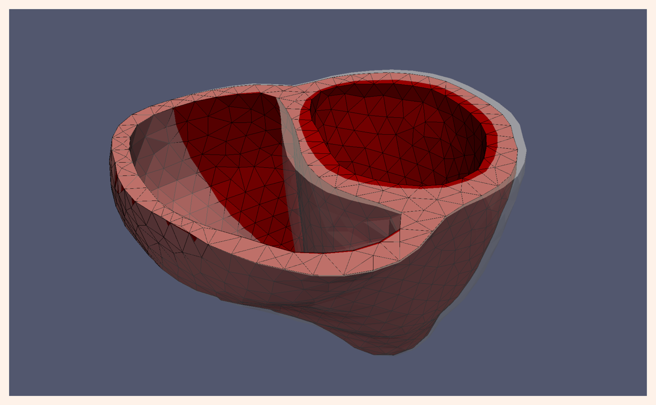
$$\Pi(\mathbf{u}, p, \mu) = \int_\Omega \left[\mathcal{W}(\mathrm{F}_{\mathrm{e}}(\mathbf{u})) - p(\det(\mathrm{F}_{\mathrm{e}}(\mathbf{u})) - 1)\right] \mathrm{d}V + \Pi_{\mathrm{ext}}(\mathbf{u}).$$

▷ Here μ is the control variable which is the linear isotropic parameter a in the strain energy density function during the passive optimization, and the activation parameter γ during the active optimzation.

▷ The cost functional at timepoint i consist of the mismatch between the simulated volume and circumferential strain and a regularization term:

$$\mathcal{J}(\mathbf{u}^i, \mu^i) = \alpha_{\text{volume}} \sum_{k\in\{\text{LV,RV}\}} \left(\frac{V_k^i - \tilde{V}_k^i}{V_k^i}\right)^2 + \alpha_{\text{strain}} \sum_{k\in\{\text{LV,Septum,RV}\}} \left(\varepsilon_k^i - \tilde{\varepsilon}_k^i\right)^2 + \alpha_{\text{regularization}}\|\mu\|^2$$

▷ The optimization is done using a **gradient-based optimzation** method, where the functional gradient $D\mathcal{J}(\mathbf{u}(\mu), \mu)$ is computed by solving an automatically derrived adjoint equation using DOLFIN-ADJOINT.



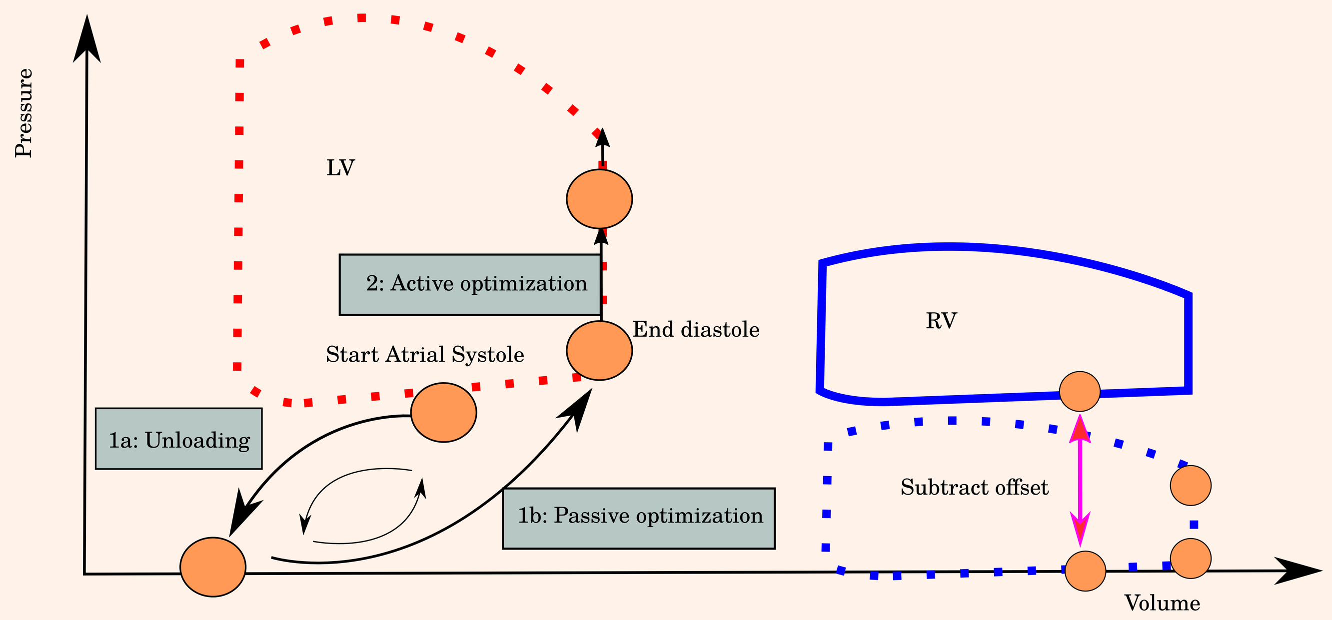
▷ In order to account for the non-zero internal pressure in the image based geometry, we iteratively apply an algorithm for estimating the **unloaded stress-free configuration**. The unloading algorithm used is based on subtracting a factor k times the displacement from the image based geometry, where k is estimated based a 1D optimization algorithm:

$$\mathrm{X}_{\mathcal{I}} = \mathrm{X}_{\mathcal{U}} + k \cdot \mathbf{d}(\mathrm{X}_{\mathcal{U}}).$$

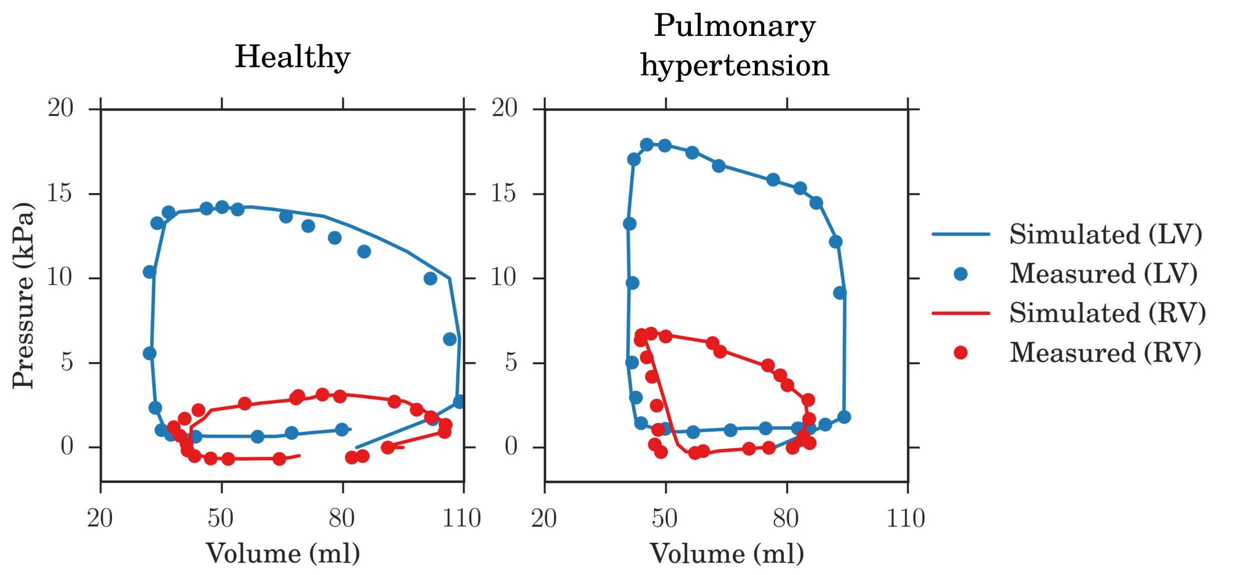
Here $\mathrm{X}_{\mathcal{I}}$ and $\mathrm{X}_{\mathcal{U}}$ are respectively the coordinates in the image-based and unloaded geometry, and $\mathbf{d}(\mathrm{X}_{\mathcal{U}})$ are the displacement obtained after inflating the unloaded geometry to the pressure in the image based geometry.

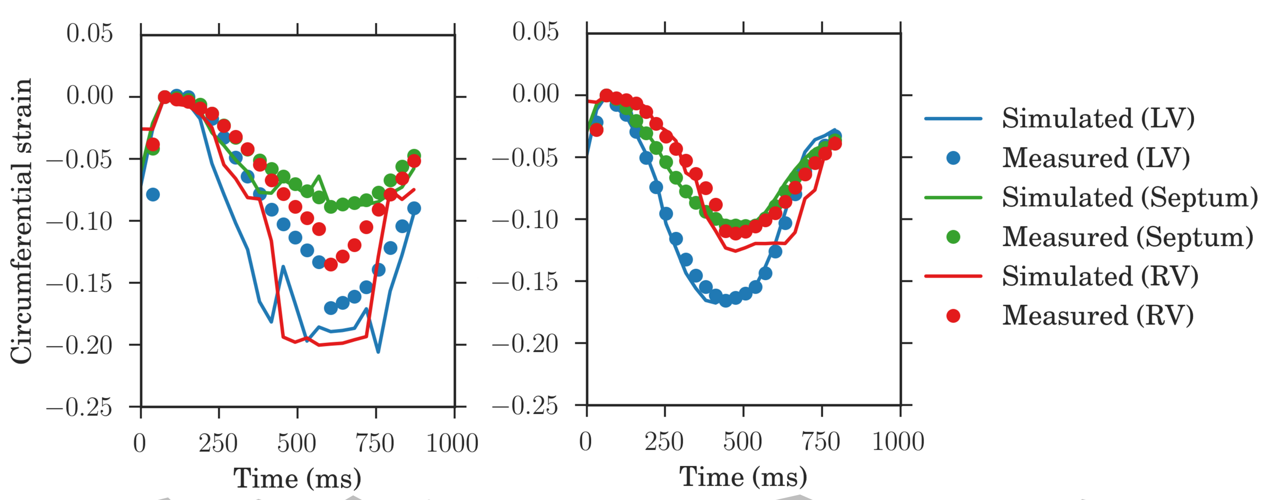
△ **Figure:** Showing the unloaded geometry in red, overlayed with the (loaded) image-based geometry for one of the healthy controls.

▷ **Figure:** The pipeline consists of first iteratively estimating the unloaded geometry and the linear isotropic parameter a. To avoid stability issues, we subtract the offset in the right ventricular pressure and unload the left ventricle only. When the volumes of the unloaded configuration in two successive iteration differ by less than 5 %, the passive optimization is terminated and the active optimization starts. In the active optimization we, fix the optimized material parameters and unloaded configuration and, estimate the active contraction γ in each measurement point.

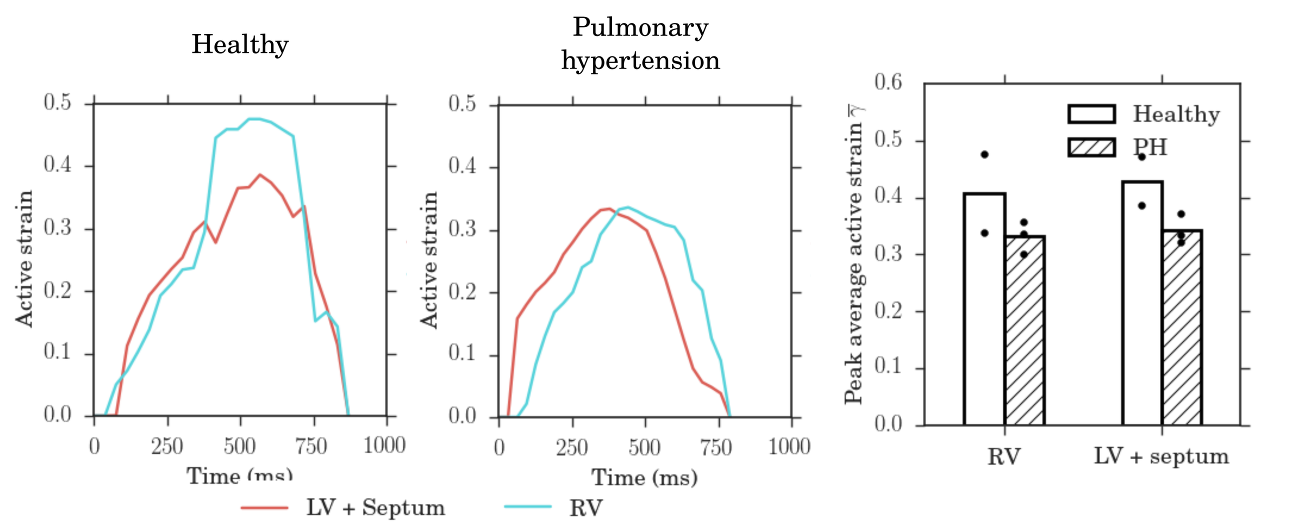


RESULTS





◁ **Figure:** On top we show the simulated PV loops in solid lines, and the measured PV loops as dots. At the bottom we show the simulatated and measured circumferential strain. In these optimization we chose $\alpha_{\text{volume}} = 0.1$, $\alpha_{\text{strain}} = 1.0$ and $\alpha_{\text{regularization}} = 10^{-4}$.



△ **Figure:** To the left we show the average acitve stain in the RV and LV + Septum for one healthy control and one patient with pulmonary hypertension. To the right we shown the peak active strain values for two healthy controls and three patients with pulmonary hypertension. The bars show the average withinh each group while each individual is plotted as a dot.

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This poster (PDF format)

Source code repository Based on FENICS

DOLFIN-ADJOINT dolfin-adjoint.org