Adjoint Based Personalization of Mechanical Models for Quantification of Right Ventricular Failure in Pulmonary Hypertension

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Abstract

Individualized analysis of cardiac mechanics offers promise for improved diagnosis and treatment of patients. However, while detailed models and constitutive laws accurately describing myocardial behavior exist, efficiently fitting these models to data is made difficult by the number of interacting parameters that are often needed. Although numerous techniques, from trial and error to advanced optimization, can be used to fit data, challenges still exist, often due to the computational requirements when many control parameters are needed.

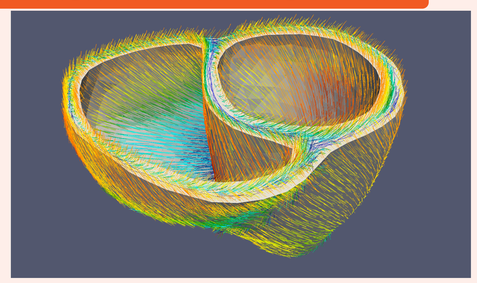
Here we discuss the use of adjoint methods as an attractive, efficient means to rapidly assimilate data sets into personalized models of cardiac mechanics. These adjoint-based optimization techniques allow us to fit models at a cost that does not significantly depend upon the numbers of parameters to be fit, and thereby provide an excellent means to assimilate data at a relatively low computational cost. These methods are enabled by the new generation of software tools that automatically create physical models and derive adjoint equations for problems of interest.

We test this method in the clinical case of pulmonary hypertension. For a cohort of healthy and hypertensive patients, we use an efficient pipeline to create biventricular models directly from medical imaging, and assimilate strain data and pressure measurements. Our results indicate that in early PH, peak contractility of the right ventricle as measured by active strain is increased compared to the normal contraction of a healthy patient. However, as the RV remodels and increases in size, we are able to observe a sharp decrease in contraction as the ventricle fails.

Methods

Data acquisition and pre-processing

Cine magnetic resonance (MR) images were obtained from 12 patients diagnosed with pulmonary hypertension (PH) and 6 healthy control subjects. Ventricular, atrial and artery pressure were 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 from the MR images by segmentation of the biventricular geometry. These measurements were used to construct pressure-volume loops of the RV and LV for the PH patients and the normal subject. Hyperelastic warping was used to estimate corresponding strain traces through the cycle. 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,

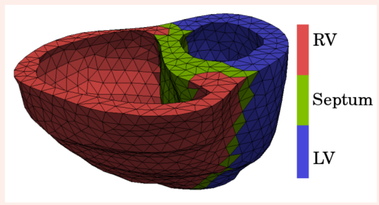
$$\mathsf{F} = \mathsf{F}_\mathsf{e}\mathsf{F}_\mathsf{a}.$$

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** $\mathcal{I}_1^\mathsf{e} = \mathrm{tr}\mathsf{C}_\mathsf{e}$ and $\mathcal{I}_{4,\mathbf{f}_\circ}^\mathsf{e} = \mathbf{f}_\circ \cdot \mathsf{C}_\mathsf{e}\mathbf{f}_\circ$ of the elastic part of right Cauchy-Green tensor $\mathsf{C}_\mathsf{e} = \mathsf{F}_\mathsf{e}^T\mathsf{F}_\mathsf{e}$:

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

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

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



◁ **Figure:** We spatially resolve the contraction γ, and the linear isotropic parameter a to be a constant on each segment. This introduces additional degrees of freedon 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:

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

where

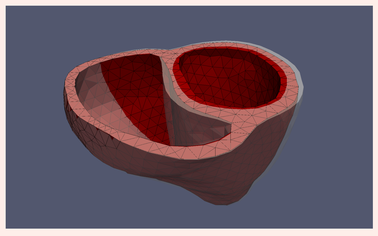
$$\Pi(\mathbf{u}, p, \mu) = \int_\Omega \left[\mathcal{W}(\mathsf{F}_\mathsf{e}(\mathbf{u})) - p(\det(\mathsf{F}_\mathsf{e}(\mathbf{u})) - 1)\right] \mathrm{d}V + \Pi_{\text{ext}}(\mathbf{u}).$$

▷ 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:

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

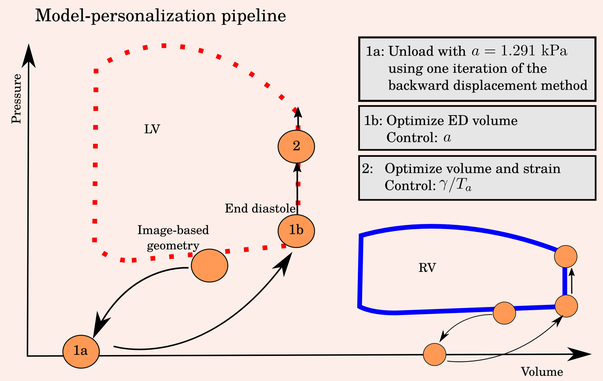
▷ The optimization is done using a **gradient-based optimzation** method, where the functional gradient $D\mathcal{J}(\mathbf{u}(\mu), \mu)$ is computed by solving an automatically derrived adjoint equation using Dolfin-Adjoint.



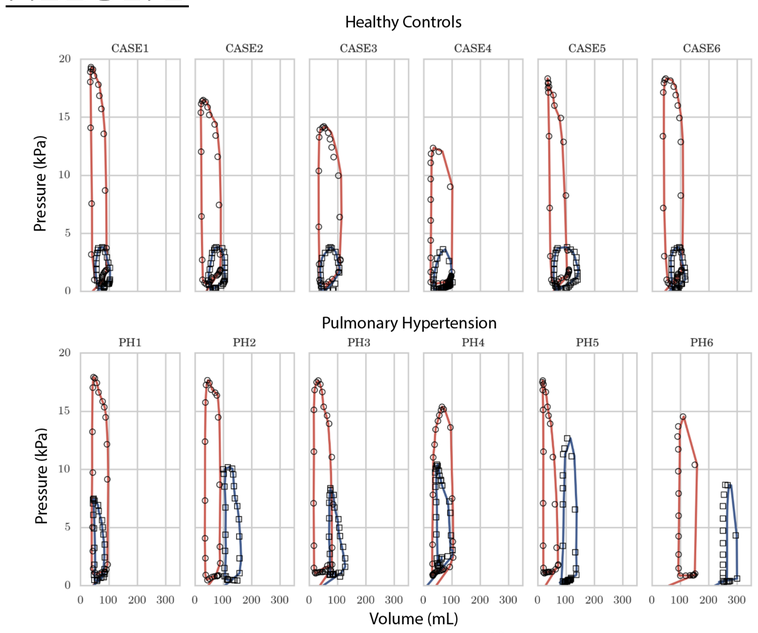
△ **Figure:** Showing the unloaded geometry in red, overlayed with the (loaded) image-based geometry for one of the healthy controls.

▷ In order to account for the non-zero internal pressure in the image based geometry, we apply an algorithm for estimating the **unloaded stress-free configuration**. For the case of a biventricular geometry, buckling may occur due to the thin RVFW and a high RV pressure. For this reason, we start by applying 1 iteration of the backward displacement method with initial values prescribed for the material parameters followed by the material parameter estimation.

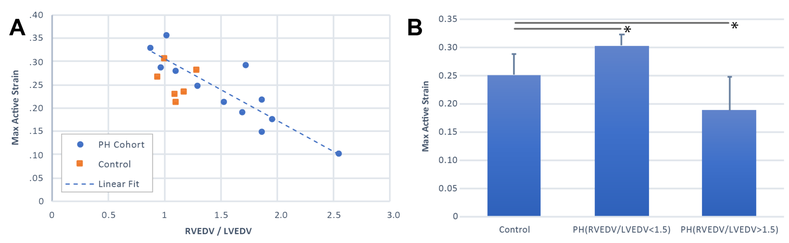
▷ **Figure:** The image based geometry corresponds to an image taken at mid diastole. An estimate of the unloaded geometry was found by applying 1 iteration of the backward displacement method followed by an estimation of a by minimizing the fit of the end diastolic volumes (EDV). During systole, both cavity volumes and circumferential strain were used in the optimization to determine the amount of active contraction, γ. The resulting time profile of the fit γ was used to asses ventricular contraction.



Results



◁ **Figure:** Here we show PV samples for both control and patient cohorts with the LV (open circles) and RV (open squares) measurements compared to fit simulations (red and blue lines respectively).



△ **Figure:** Above in (A) we show the fit max contraction (gamma) for each simulation as a function of the ration of end diastolic RV to LV volume. All control simulations show end diastolic volume ratios near one, while PH patients have high variation as the ventricles remodel. We show a linear decrease in max contractility as a function of remodeling. In (B) we show that PH patients with a similar ratio of ED RV to LV volume as control patients have significantly increased contractility, while those with increased RV remodelling have decreased contraction.

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Source code repository Based on FEniCS

FEniCS project

Dolfin-Adjoint dolfin-adjoint.org

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