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PERSONALIZATION OF A CARDIAC COMPUTATIONAL MODEL USING CLINICAL MEASUREMENTS

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Summary. Important features in cardiac mechanics that cannot easily be measured in the clinic, can be computed using a computational model that is calibrated to behave in the same way as a patient's heart. To construct such a model, clinical measurements such as strain, volume and cavity pressure are used to personalize the mechanics of a cardiac computational model. The problem is formulated as a PDE-constrained optimization problem where the minimization functional represents the misfit between the measured and simulated data. The target parameters are material parameters and a spatially varying contraction parameter. The minimization is carried out using a gradient based optimization algorithm and an automatically derived adjoint equation. The method has been tested on synthetic data, and is able to reproduce a prescribed contraction pattern on the left ventricle.

1 INTRODUCTION

Abnormal stresses are hypothesized to be a key driver in remodelling processes associated with heart failure[1]. However, it is impossible to measure stresses *in vivo* in a human heart. This necessitates the use of computational models in cardiac stress calculation. A key step to making calculated stresses useful for clinical practice is patient specificity. This means that the calculated stresses should come from a computational model that has been calibrated to behave in the same way as a patient's heart.

In this study, we combine strain data obtained using 4D echocardiography methods, with left ventricular pressure and volume measurements in order to match simulated ventricular mechanics to those observed in a patient. We formulate this matching as a mathematical optimization problem in which we minimize the difference between simulated and measured strains and volumes. As a result, we obtain patient specific stress maps that can be used as guidance in the decision making for cardiac treatments.

2 THE MECHANICAL MODEL

We model the heart as a continuum body with a reference configuration taken at the beginning of the passive filling phase. To model the active contraction of the heart we introduce a single spatially varying parameter $\gamma = \gamma(\mathbf{x}, t)$, and apply the active strain formulation[3]. This is based on a multiplicative decomposition of the deformation gradient,

$$\mathbf{F} = \mathbf{F}_e \mathbf{F}_a, \tag{1}$$

where $\mathbf{F}_e$ is the elastic part and $\mathbf{F}_a$ the active part of the deformation gradient. Under the assumption that the active contraction is volume preserving and results in a shortening in the fiber direction, the active deformation gradient takes the following form

$$\mathbf{F}_a = (1-\gamma)\mathbf{f}_0 \otimes \mathbf{f}_0 + \frac{1}{\sqrt{1-\gamma}}(\mathbf{I} - \mathbf{f}_0 \otimes \mathbf{f}_0). \tag{2}$$

The parameter γ is modeled as a smooth function over the domain and represents the relative shortening of the fibers.

The myocardium is modeled as an incompressible, hyperelastic material. We use a transversally isotropic version of the strain energy density function proposed by Holzapfel and Ogden[2],

$$\mathcal{W}(\mathbf{C}_e) = \frac{a}{2b}\left(e^{b(I_1-3)} - 1\right) + \frac{a_f}{2b_f}\left(e^{b_f(I_{4,\mathbf{f}_0}-1)_+^2} - 1\right). \tag{3}$$

Here I_1 is the first isotropic invariant of the elastic part of the right Cauchy-Green tensor $\mathbf{C}_e = \mathbf{F}_e^T\mathbf{F}_e$, $I_{4,\mathbf{f}_0} = \mathbf{f}_0 \cdot (\mathbf{C}_e\mathbf{f}_0)$ is the quasi-invariant with a preferred direction along the fibers $\mathbf{f}_0$ and $(\cdot)_+ = \max\{\cdot, 0\}$.

3 PERSONALIZED SIMULATION

Left ventricular epicardial and endocardial surfaces are provided through 4D echocardiography. We use these two surfaces to generate and attach an artificial right ventricle using an in-house algorithm. The mesh generation is done using Gmsh[4]. Since measuring the myocardial fiber orientation is currently not possible using echocardiography methods, we apply the rule-based method proposed by Bayer et. al[5] for assigning myocardial fiber orientation. Cavity volume and average regional strain for the left ventricle were measured in the left ventricle (LV) during a cardiac cycle using 4D echocardiography[6]. Left ventricular pressure data were obtained invasively by catheterization of each patient during later surgery. The pressure and volume data has been synchronized in order to produce a pressure volume loop for each patient. The average regional strain is measured in the circumferential(e_c), radial(e_r) and longitudinal(e_l) direction relative to the LV. The heart Ω, is partitioned into 18 regions, $\Omega = \bigcup_{k=0}^{17} \Omega_k$, with $\Omega_{\text{LV}} = \bigcup_{k=1}^{17} \Omega_k$, and $\Omega_{\text{RV}} = \Omega_0$. The average regional strain over the region Ω_j in the direction e_k can be approximated as

$$\tilde{\varepsilon}_{k,j} = \int_{\Omega^j} e_k^T \nabla \mathbf{u} \cdot e_k \; dx, \tag{4}$$

where $\mathbf{u}$ is the displacement. Let N be the number of discrete measurements during a cardiac cycle, and let N_{ED} be the number of points from the beginning of the passive filling to end diastole. For point $i = 1, \cdots, N$ we define the strain misfit functional as,

$$I^i_{\text{strain}} = \sum_{j=1}^{17} \left\| \mathbf{W}(\boldsymbol{\varepsilon}^i_j - \tilde{\boldsymbol{\varepsilon}}^i_j) \right\|_2, \;\; \boldsymbol{\varepsilon}^i_j = \begin{bmatrix} \varepsilon^i_{c,j} \\ \varepsilon^i_{r,j} \\ \varepsilon^i_{l,j} \end{bmatrix}, \; \mathbf{W} = \text{diag}(\omega_{c,j}, \omega_{r,j}, \omega_{l,j}). \tag{5}$$

The weights $\omega_{k,j}$ are based on the quality of the strain measurement over the region Ω_j in the direction e_k. The LV volume misfit functional is defined as

$$I^i_{\text{vol}} = \frac{|V_i - \tilde{V}_i|}{V_i}, \;\; \tilde{V}_i = \frac{1}{3} \int_{\partial \Omega_{\text{endo LV}}} (\mathbf{I} + \mathbf{u}) \cdot J \mathbf{F}^{-T} \mathbf{N} \; dS, \tag{6}$$

where $\partial\Omega_{\text{endo LV}}$ is the surface inside the left ventricular cavity. Because of noise in the measurements, optimizing the strain only, does not necessarily lead to the correct volume. On the other hand, optimizing only the volume, does not capture regional differences that may be present due to a diseased heart. We therefore combine the mismatch between the strain and volume into one single mismatch functional of the form

$$I^i_{\alpha} = \alpha I^i_{\text{vol}} + (1 - \alpha) I^i_{\text{strain}}. \tag{7}$$

The parameter α controls how much weight is given to the volume matching versus the strain matching.

During the passive filling there is assumed to be little or no active contraction. This makes this phase suitable for estimating the material parameters. We select the material parameter set $\mathbf{m} = (a, b, a_f, b_f)$ that minimizes the misfit functional for a given value of α. In other words, we solve the following problem

$$\begin{aligned} \underset{\mathbf{m}}{\text{minimize}} \quad & \sum_{i=0}^{N_{\text{ED}}} I^i_{\alpha} \\ \text{subject to} \quad & R(\mathbf{u}, p) = 0. \end{aligned} \tag{8}$$

Here $R(\mathbf{u}, p) = 0$ denotes the force balance equation. From end diastole and throughout the rest of the cardiac cycle we fix the material parameters so that γ determines the motion. Thus, we are searching for γ that solves the following optimization problem:

$$\begin{aligned} \underset{\gamma(\mathbf{x}, i)}{\text{minimize}} \quad & I^i_{\alpha} + \lambda \|\nabla \gamma\|^2_{L^2(\Omega)} \\ \text{subject to} \quad & R(\mathbf{u}, p) = 0, \\ & \gamma(\mathbf{x}, i) \in [0, 1), \;\; \mathbf{x} \in \Omega, i = N_{\text{ED}} + 1, \cdots, N. \end{aligned} \tag{9}$$

Here we have also introduced a regularization parameter λ that penalizes high values of the gradient $\nabla\gamma$.

The solver is fully parallelized and based on the open–source framework FEniCS [7]. To solve the PDE-constrained optimization problem we use a gradient based optimization algorithm [8] where the gradient is computed by solving the automatically derived adjoint equation [9].

4 CONCLUSION

Using clinical measurements coming from 4D echocardiography together with invasive pressure measurements, we are able to personalize the mechanics of a cardiac computational model. The model has been tested on synthetic data with a prescribed sequence of contraction parameters. Results show that the model is able to reproduce a similar contraction pattern on the LV when $\alpha \in [0, 1)$. This model can therefore be used to visualize patient specific stress maps which may provide clinicians with useful information about the heart's condition.

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