AUTOMATIC IMAGE-TO-MODEL FRAMEWORK FOR PATIENT-SPECIFIC ELECTROMECHANICAL MODELING OF THE HEART

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ABSTRACT

A key requirement for recent advances in computational modeling to be clinically applicable is the ability to fit models to patient data. Various personalization techniques have been proposed for isolated sub-components of complex models of heart physiology. However, no work has been presented that focuses on personalizing full electromechanical (EM) models in a streamlined, consistent and automatic fashion, which has been evaluated on a large population. We present an integrated system for full EM personalization from routinely acquired clinical data. The importance of mechanical parameters is analyzed in a comprehensive sensitivity study, revealing that myocyte contraction and Young's modulus are the main determinants of model output variation, what lead to the proposed personalization strategy. On a large, physiologically diverse set of 15 patients, we demonstrate the effectiveness of our framework by comparing measured and calculated parameters, yielding left ventricular ejection fraction and stroke volume errors of 6.6% and 9.2 mL, respectively.

1. INTRODUCTION

Heart failure, a common form of cardiovascular disease with significant mortality and morbidity rates, is a major threat to public health in the Western world [1]. Although its causes are manifold, cardiomyopathies (diseases affecting the myocardium) are prevailing, yet challenging to diagnose and treat. Thus, complex models of heart function are being investigated for providing more information from clinical data [2] and for predicting therapy outcome or disease course [3].

Over the last decades, personalization approaches using inverse problem techniques such as filtering-based algorithms [4], gradient-descent or more sophisticated gradient-free methods [2] have been proposed for isolated sub-components of complex cardiac models. For instance, [2, 5] propose approaches for electrophysiology (EP) personalization. [4, 6] focus on mechanics. However, only few authors (e.g. [3], semi-automatic method evaluated on two patients) propose methods for full EM personalization. To the best of our knowledge, no comprehensive framework has been presented to personalize full electromechanics in a streamlined, consistent and automatic fashion on a large number of cases.

We propose a novel integrated system for full EM personalization. Our modular framework allows for fast generation of reproducible patient-specific models by estimating model parameters from routinely acquired clinical data. Volumetric images are exploited to personalize anatomy and hemodynamics. Clinical ECG features are used to automatically estimate patient-specific parameters for a phenomenological EP model [7], and active and passive biomechanical parameters are personalized automatically. Finally, we show quantitative results and discuss the importance of individual mechanical model parameters in a comprehensive sensitivity analysis, which we used to enhance our personalization strategy.

2. METHODOLOGY

Below, we describe the individual modules of the proposed pipeline (Fig. 1). Clinical data is required for personalization, including 12-lead ECG for patient-specific EP and dynamic cardiac images to obtain ventricular volume and to create the anatomical model. Furthermore, arterial and ventricular pressure measured during cardiac catheterization are utilized. In total, 17 parameters are personalized: 5 Windkessel parameters each for both arteries, 3 regional diffusivity values and the time during which the ion channels are closed for EP, and for patient-specific biomechanics, tissue elasticity and left (LV) and right (RV) ventricular myocyte contraction are estimated.

2.1. Anatomy Personalization

First, patient-specific heart morphology is obtained from volumetric imaging data (e.g. MRI, 3D US, CT or C-arm CT). To that end, we employ a robust, data-driven machine learn-

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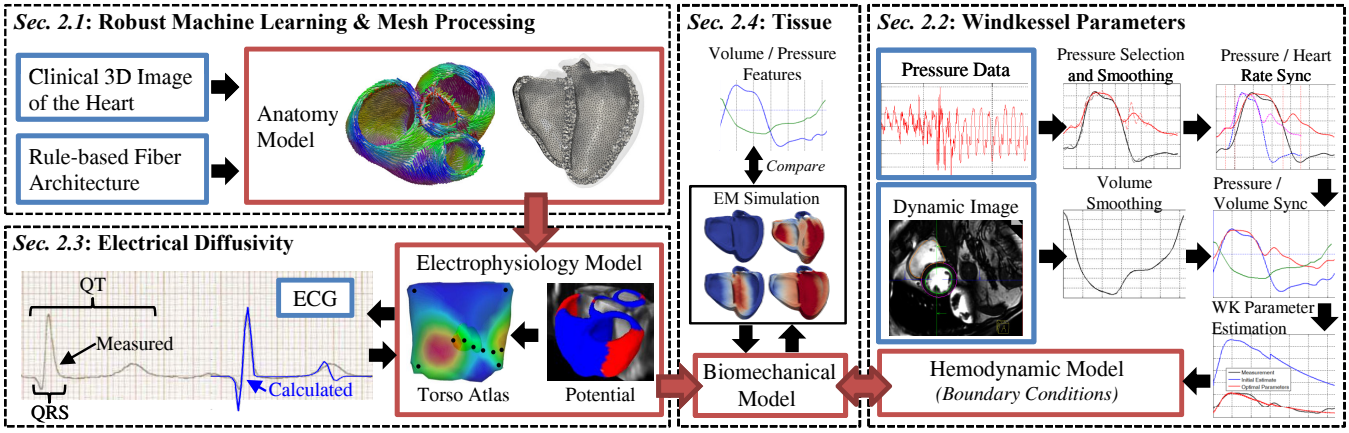

Fig. 1. Personalization pipeline: from clinical data to patient-specific EM models (blue/red box: input data/model component).

ing approach [8] in order to estimate meshes of the endocardia and epicardium automatically. Appending them yields a closed surface of the biventricular myocardium. The closed contour at end-diastasis is transformed into a tetrahedral volume using a mesher algorithm[1]. Next, myocardium fibers are mapped onto the patient-specific anatomy using a rule-based system [9]: Below the basal plane, fiber elevation angles vary linearly from epi- to endocardium (typically from $-70°$ to $+70°$, adjustable by user). An extrapolation of the angles up to the valves is performed based on geodesic distances.

2.2. Hemodynamics Personalization

A lumped model of cardiac hemodynamics [9] is employed, which mimics the four cardiac phases by alternating endocardial boundary conditions. During filling and ejection, atrial and arterial pressure is applied directly, while in between (isovolumetric contraction and relaxation), an isovolumetric constraint based on an efficient projection-prediction method [9] is enabled to keep the ventricular volume constant. Arterial and atrial pressures are calculated using a 3-element Windkessel (WK) and an elastance model, respectively.

The hemodynamics personalization consists in estimating the WK parameters of both arteries, namely artery compliance, characteristic and peripheral resistance, remote pressure and initial pressure. To that end, we rely on the arterial pressure measured during cardiac catheterization and the volume curve derived from MRI. First, we interactively select a cardiac cycle among the pressure trace and low-pass filter the arterial and ventricular pressure. Next, the pressure curve is automatically adjusted to match the heart rate at the MRI acquisition. As a simple temporal scaling would not be physiologically coherent, we apply the following algorithm. First, we stretch the systolic portion of the pressure curve such that the ejection time (ET) observed in the pressure measurement (time during which ventricular pressure is higher or equal than arterial pressure) matches the ET measured on the volume curve (time during which the ventricular flow is negative). Then, we interactively shift the pressure curve such that it is synchronized with the volume curve smoothed using a low-pass filter. Finally, the parameters of the WK model are estimated automatically using the simplex method. The cost function writes $\frac{1}{N}\sum_{i=1}^{N}\left(\mathbf{p}_m[i]-\mathbf{p}_c[i]\right)^2+\omega_{\text{min}}^2+\omega_{\text{max}}^2$, where $\mathbf{p}_m$ and $\mathbf{p}_c$ are the time-sequence of measured and computed artery pressure, respectively. N is the number of samples and ω_{min}, ω_{max} are penalty terms $(\min \mathbf{p}_m - \min \mathbf{p}_c)$, $(\max \mathbf{p}_m - \max \mathbf{p}_c)$. The simplex method is used to automatically estimate all the parameters but the initial pressure. The latter is obtained automatically from the computed pressure curve over several cycles such that the first computed pressure cycle is close to the steady state.

2.3. Electrophysiology Personalization

Cardiac EP models ranging from simplified Eikonal models to highly detailed ionic models are available [9]. With its parameters closely related to the shape of the action potential, we use the Mitchell-Schaeffer (MS) [7] phenomenological model in this study as a good compromise between model complexity and computational efficiency. It is solved using LBM-EP [7], a near-real-time solver for patient-specific cardiac EP based on an efficient GPU implementation of the Lattice-Boltzmann method. Its main free parameters, which need to be personalized in order to generate realistic EP, comprise tissue diffusivity c, determining the speed of the electrical wave propagation throughout the heart, and the time during which the ion channels are closed τ_{cl}. In this study, we model fast regional diffusivity for the left c_{L} and right c_{R} endocardium to mimic the Purkinje network, and slower diffusivity $c_{\text{M}} \leq c_{\text{L}}$, $c_{\text{M}} \leq c_{\text{R}}$ for the myocardium.

A major goal in the development of our framework was to be usable without the need for specialized data such as contact mapping catheters as in [2]. Hence, the EP parameter

[1] http://www.cgal.org - computational geometry algorithms library

estimation is solely based on routinely acquired 12-lead ECG data. In order to calculate ECG signals from the simulated EP, we follow a similar approach as in [5], where we *(i)* register the anatomical heart model to a torso atlas, *(ii)* calculate the mapping of potentials on the anatomical model to the atlas, and *(iii)* compute signals on pre-defined torso lead positions.

Let calcQT, calcQRS and calcEA be procedures which run an EP simulation on a patient-specific anatomical model using the provided parameters and then calculate named ECG feature. We deploy methods to automatically derive the duration of the QRS and QT complex (Δ_{QRS}, Δ_{QT}), and electrical axis (α) from the lead signals [5]. $\Delta_{\text{QRS},m}$, $\Delta_{\text{QT},m}$ and α_m are measured values extracted from clinical ECG images. In Algorithm 1, we outlined our proposed inverse framework for the personalization of stated MS parameters. Standard values from literature are used for initialization. The optimization steps (lines 2 and 4) are performed using NEWUOA [10], a robust gradient-free optimization technique.

Algorithm 1 EP Personalization Workflow

Require: Initial τ_{cl}^0 and diffusivity c_{M}^0, c_{L}^0, c_{R}^0
1: $\tau_{\text{cl}}^1 = \tau_{\text{cl}}^0 + \Delta_{\text{QT},m} - \text{calcQT}(\tau_{\text{cl}}^0, c_{\text{M}}^0, c_{\text{L}}^0, c_{\text{R}}^0)$
2: $\kappa^* = \text{argmin}_\kappa \left(\Delta_{\text{QRS},m} - \text{calcQRS}(\tau_{\text{cl}}^1, \kappa(c_{\text{M}}^0, c_{\text{L}}^0, c_{\text{R}}^0))\right)$
3: $(c_{\text{M}}^*, c_{\text{L}}^1, c_{\text{R}}^1) = \kappa^*(c_{\text{M}}^0, c_{\text{L}}^0, c_{\text{R}}^0)$
4: $c_{\text{L}}^*, c_{\text{R}}^* = \text{argmin}_{c_{\text{L}}, c_{\text{R}}} \left(\alpha_m - \text{calcEA}(\tau_{\text{cl}}^1, c_{\text{M}}^*, c_{\text{L}}, c_{\text{R}})\right)$
5: $\tau_{\text{cl}}^* = \tau_{\text{cl}}^1 + \Delta_{\text{QT},m} - \text{calcQT}(\tau_{\text{cl}}^1, c_{\text{M}}^*, c_{\text{L}}^*, c_{\text{R}}^*)$
6: **return** personalized EP parameters τ_{cl}^*, c_{M}^*, c_{L}^* and c_{R}^*

2.4. Biomechanics Personalization

The EP signal is coupled with myocardial tissue mechanics through models of active and passive tissue behavior to compute realistic cardiac motion. Therefore, the dynamics equation $\mathbf{M}\ddot{\mathbf{u}} + \mathbf{C}\dot{\mathbf{u}} + \mathbf{K}\mathbf{u} = \mathbf{f}_a + \mathbf{f}_p + \mathbf{f}_b$ needs to be solved (e.g. using finite-element methods). $\ddot{\mathbf{u}}$, $\dot{\mathbf{u}}$ and $\mathbf{u}$ denote accelerations, velocities and displacements of the mesh nodes, and $\mathbf{M}$, $\mathbf{K}$ and $\mathbf{C}$ are the mass, internal elastic stiffness and Rayleigh damping matrix, respectively. $\mathbf{f}_a$, $\mathbf{f}_p$ and $\mathbf{f}_c$ model active stress, ventricular pressure and boundary conditions.

In this study, a phenomenological model is utilized for the active myocyte contraction, which is—to a large extent—governed by σ [9], the maximum asymptotic strength of the active contraction. We rely on transverse isotropic linear elasticity to model passive myocardial properties using co-rotational linear tetrahedra to cope with large deformations (mainly observed during systole). Young's modulus E with respect to the fiber architecture, and Poisson ratio $\nu = 0.48$, a measure of tissue incompressibility, are the main parameters. Please note that σ is estimated independently for left and right ventricular mechanics.

The procedures calcPr and calcPrVol (Algorithm 2) return time-sequences of computed pressure (and volume) data from a forward simulation of the full EM model given the provided parameters. p_{PV} denotes the pulmonary vein pressure. NEWUOA is used to optimize the cost function $\xi = \boldsymbol{\lambda} \cdot (\varepsilon_{\text{EF}}, \varepsilon_{\text{SV}}, \varepsilon_{\min \mathbf{v}}, \varepsilon_{\max \mathbf{v}}, \varepsilon_{\min \mathbf{p}}, \varepsilon_{\max \mathbf{p}})^\top$, which determines the similarity between measured $(\mathbf{p}_m, \mathbf{v}_m)$ and calculated $(\mathbf{p}_c, \mathbf{v}_c)$ pressure and volume curves by comparing a weighted sum of features derived thereof: ejection fraction (EF), stroke volume (SV), and min/max pressure/volume ($\min \mathbf{v}$, etc.), $\varepsilon_X = (X_m - X_c)^2$. To cope with the distinct units, we set $\boldsymbol{\lambda} = 10^{-4} \cdot (10^4, 1, 1, 1, 1, 1)$. In order to minimize transient effects, two heart cycles are computed and measurements derived from the second cycle.

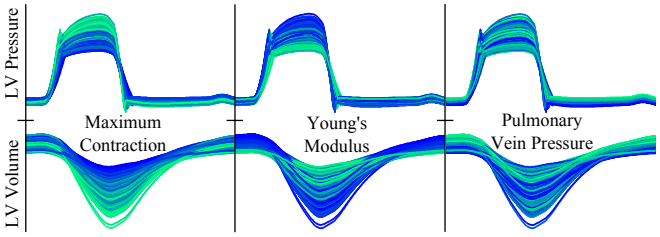

Fig. 2. Selected results of sensitivity analysis, depicting variability in volume and pressure curves introduced by varying model input parameters. Coloring is determined by the parameter value used to compute the simulation (left to right: σ, E, p_{PV}). Blue/green color means small/large values in the range of $\pm$ 50% of standard values. A clear trend is observable for σ around the minimum volume and maximum pressure, implying that these two indicators are key features for predicting σ. Similar conclusion can be drawn for E and p_{PV}.

Algorithm 2 Mechanics Personalization Workflow (LV)

Require: Initial σ^0, E^0 and p_{PV}^0
1: $p_{\text{PV}}^* = p_{\text{PV}}^0 + \min p_m - \min \text{calcPr}(\sigma^0, E^0, p_{\text{PV}}^0)$
2: $\sigma^*, E^* = \text{argmin}_{\sigma,E}\, \xi((p_m, v_m), \text{calcPrVol}(\sigma, E, p_{\text{PV}}^*))$
3: **return** personalized parameters σ^*, E^* and p_{PV}^*

3. RESULTS

We utilized the proposed personalization pipeline on 15 consecutive patients, who suffer from dilated cardiomyopathy with a large variety of disease severity. For instance, the maximum LV pressure ranges from 78 mmHg to 177 mmHg, and measured LV EFs range from 10.5% to 59.8%. This makes personalization a particularly challenging task and thus, robust estimation techniques are essential.

Model sensitivity: A comprehensive sensitivity analysis (including Sobol indices computed using DAKOTA[2]) on both passive and active biomechanical model parameters (Fig. 2) revealed that maximum contraction σ and elasticity E are most crucial for changes in ventricular volume and pressure.

[2]http://dakota.sandia.gov - multilevel framework for sensitivity analysis

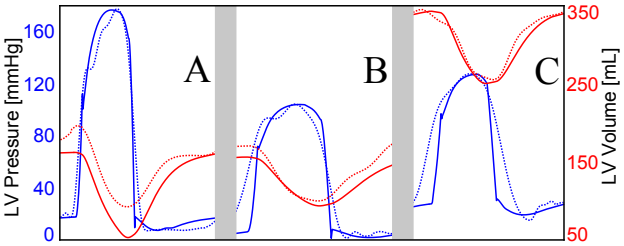

Fig. 3. Pressure (blue) and volume (red) curves (dotted: measured, line: calculated) after personalization for three cases.

Furthermore, pressure originating from the pulmonary vein p_{PV} (LV) or vena cava (RV) is dominating diastolic ventricular pressure. Fast GPU-based solvers [9, 7] enabled this large-scale experiment, which was carried out using 800 model simulations and led to the proposed personalization strategy.

Quantitative results: Known clinical indicators and methods to estimate their complements from our simulations allow for quantitative evaluation of our multi-step inverse optimization algorithms for estimating the electrophysiological and biomechanical model parameters as described in Algorithms 1 and 2. For instance, by comparing known and estimated EP features after personalization, namely Δ_{QRS} and Δ_{QT} durations, we measured mean absolute errors of 9.5 ± 8.2 ms and 4.0 ± 2.9 ms, respectively. In terms of the full patient-specific electromechanical model simulation, our method yielded low errors for clinical indicators such as stroke volume and ejection fraction of 9.2 ± 11.9 mL and $6.6 \pm 6.9\%$, respectively, indicating overall good convergence towards the corresponding observed values. Plots of calculated pressure and volume curves from three patients overlaid on top of the measured curves (Fig. 3) further confirm the validity of our personalization results. Likewise, Fig. 1 depicts a good match for one patient between ECG lead signal from measured data versus the signal computed from the personalized EP model.

4. CONCLUSION

Thanks to the modular architecture of our pipeline, we are not limited to a single model. For instance, in this study, linear elasticity is used. However, more sophisticated models of passive biomechanical properties, such as orthotropic models [9], can be inherited with little effort. This will allow for generating more realistic results in some cases (e.g. improve match between volume curves). The next step will be to further extend the dataset to validate our framework, and to evaluate the predictive power of our model.

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