Physiome Model Based State-Space Framework for Cardiac Kinematics Recovery^{*}

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Abstract. In order to more reliably recover cardiac information from noise-corrupted patient-specific measurements, it is essential to employ meaningful *a priori* constraining models and adopt appropriate optimization criteria to couple the models with the measurements. While biomechanical models have been extensively used for myocardial motion recovery with encouraging results, the passive nature of such constraints limits their ability to fully count for the deformation caused by active forces of the myocytes. To overcome such limitations, we propose to adopt a *cardiac physiome model* as the prior constraint for heart motion analysis. The model is comprised of a cardiac electric wave propagation model, an electromechanical coupling model, and a biomechanical model, and thus more completely describes the macroscopic cardiac physiology. Embedded within a multiframe state-space framework, the uncertainties of the model and the patient-specific measurements are systematically dealt with to arrive at optimal estimates of the cardiac kinematics and possibly beyond. Experiments have been conducted on synthetic data and MR image sequences to illustrate its abilities and benefits.

1 Introduction

The goal of computational cardiac analysis is to objectively and accurately recover the parameters of various cardiac functions based on the specific measurements on the patients, such as those obtained from medical imaging, electrocardiograms, blood pressures, etc [1]. Nevertheless, these non-invasive, *in vivo* measurements can only provide either sparse, or gross, or projective observations in spatial and/or temporal domains, and are usually corrupted by noises of various sources. In consequence, analysis based solely on the measurements

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is ill-posed, and thus *a priori* models obtained from invasive or *in vitro* experiments, such as those from anatomy, biomechanics, or physiology, are necessary to constrain the inverse problems.

Study on human physiology has established that, at the beginning of each cardiac cycle, the pacemaker cells in the heart generate action potentials that are conducted to the whole heart through the conduction fibers which spread throughout the myocardium [1]. The myocardial contractile cells are then excited by the action potentials and contract according to the sequence of excitations, and the heart beats in a rhythmic motion. Thus, in order to properly model the cyclic dynamics of the heart, the cardiac electric wave propagation model (E model) that describes the spatiotemporal propagation pattern of the action potentials [2], the electromechanical coupling model (EM model) which transforms the excitation into myocardium contractile stresses [3], and the biomechanical model (BM model) which captures the deformation caused by the contractile stresses through the system dynamics [4] are all required. Since the integration of these three models gives a more complete macroscopic description of the physiological behavior of the heart, we call it the *cardiac physiome model* [5]. With *a priori* physiome models and various patient-specific measurements available, it becomes possible to establish a computational cardiac information analysis paradigm to recover the physiologically and clinically useful parameters such as the electrical propagation, ventricular geometry, cardiac kinematics, and myocardial material properties of the patient's heart.

In this paper, we address one aspect of the cardiac information analysis by proposing a kinematics recovery strategy that combines the physiome model with the multiframe filtering framework. Expressing the cardiac dynamics in a state-space representation, with the physiome model providing *a priori* predictive cardiac kinematics, patient specific kinematic estimates can be obtained in minimum-mean-square-error (MMSE) sense by updating the model predictions with measurements from images and other means. With the use of the physiome model, the predictions are more meaningful and potentially more accurate compared with the strategies which are only based on BM model and image-derived passive force [6]. Experiments have been performed on synthetic data to show the importance of utilizing the physiome model, and also performed on canine MR image sequences to show its possible practical applications.

2 Methodology

The physiome model, including the E, EM and BM components, provides prior predictions of cardiac kinematics, which are then updated by various measurement data to recover patient-specific cardiac parameters.

2.1 Electric Wave Propagation Model

After leaving the Purkinje fibers, the action potentials propagate throughout the myocardium through the myocytes. To model the electric wave propagation in the myocardium, because of the relative easiness of implementation, a simplified

reaction system based on FitzHugh-Nagumo model has been used as our model [7]. It is able to reproduce basic excitation propagation pattern through:

$$\begin{aligned}\frac{\partial u}{\partial t} &= c_1 f(u, v) + \nabla \cdot (D \nabla u) \\ \frac{\partial v}{\partial t} &= b(u - dv) \\ f(u, v) &= c_1 u(u - a)(1 - u) - c_2 uv\end{aligned}\tag{1}$$

where u is the action potential that corresponds to the transmembrane voltage, v is the recovery variable, D is the diffusion tensor, $f(u, v)$ is the excitation term, and a , b , c_1 , c_2 and d are parameters that define the shape of the action potential. The diffusion tensor and the parameters are constant in time but not necessary in space, with values adopted from [7].

2.2 Electromechanical Coupling Model

When a myocyte is excited by the action potential, it generates the active force for the contraction of the heart through *electromechanical coupling*. Although realistic complex models are available [4, 3], because of the computational efficiency, a simple ordinary differential equation proposed in [8] has been used as our electromechanical coupling model:

$$\frac{\partial \sigma_c}{\partial t} = \sigma_0 |u|_+ - |u| \sigma_c \tag{2}$$

where σ_c is a scalar related to the contraction stresses, σ_0 is a constant, and $|u|_+$ is the positive value of the normalized action potential u .

With σ_c obtained by solving Equation (2), the contraction stress tensor can be obtained by $\sigma_c f \otimes f$, with f the fiber orientation vector and $\otimes$ the tensor product. Then the active force R_c can be obtained as $R_c = \int_V \text{div}(\sigma_c f \otimes f) dV$, with V the volume of the heart [9].

2.3 Biomechanical Model

The biomechanical model relates the active forces generated by the EM model with the resulted deformation of the myocardium. According to the anatomical literatures, the structure and the composition of the heart are very complicated. As a result, anisotropic material models are essential for the sensible description of myocardial characteristics.

Myocardium is assumed to be elastic. For both isotropic and anisotropic elastic materials, their stress-strain relation obeys the Hooke's Law:

$$\mathbf{S} = C\epsilon, \tag{3}$$

where $\mathbf{S} = [S_{11} \ S_{22} \ S_{33} \ S_{12} \ S_{13} \ S_{23}]^T$ and $\epsilon = [\epsilon_{11} \ \epsilon_{22} \ \epsilon_{33} \ \epsilon_{12} \ \epsilon_{13} \ \epsilon_{23}]^T$, with S_{ij} the components of the second Piola-Kirchhoff stress tensor, ϵ_{ij} the components of the Green-Lagrangian strain tensor, and C the stiffness matrix.

Because of the tubular shapes of the myocytes [4], we assume that the tissues of the myocardium are transversely isotropic. Let C_o be the 3D stiffness matrix of a point with 0° polar and azimuthal angles as its fiber orientation:

$$C_o = \begin{bmatrix} \frac{1}{E_f} & -\frac{\nu_f}{E_{cf}} & -\frac{\nu_f}{E_{cf}} & 0 & 0 & 0 \\ -\frac{\nu_f}{E_{cf}} & \frac{1}{E_{cf}} & -\frac{\nu_{cf}}{E_{cf}} & 0 & 0 & 0 \\ -\frac{\nu_f}{E_{cf}} & -\frac{\nu_{cf}}{E_{cf}} & \frac{1}{E_{cf}} & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{1}{G} & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{1}{G} & 0 \\ 0 & 0 & 0 & 0 & 0 & \frac{2(1+\nu_{cf})}{E_{cf}} \end{bmatrix}^{-1}$$

where E_f , E_{cf} , ν_f , ν_{cf} are the Young's moduli and Poisson's ratios along and cross the fiber respectively, $G \approx E_f/(2(1+\nu_f))$ describes the shearing property.¹

With C_o defined, the stiffness matrix at any point with known fiber orientation can be obtained using the tensor transformation:

$$C_{rot} = T^{-1}C_oRTR^{-1} \quad (4)$$

where T is the transformation matrix related to the fiber orientations, and R is the matrix responsible for the transformation between the strain tensor components and the engineering strain tensor components [6].

2.4 Cardiac System Dynamics Under Finite Deformation

The displacement-based total Lagrangian (TL) system dynamics of the heart under finite deformation can be written in the following form [6]:

$${}^t_0\mathbf{M} {}^{t+\Delta t}\ddot{\mathbf{U}} + {}^t_0\mathbf{C} {}^{t+\Delta t}\dot{\mathbf{U}} + {}^t_0\tilde{\mathbf{K}} \Delta\mathbf{U} = {}^{t+\Delta t}\mathbf{R}_c + {}^{t+\Delta t}\mathbf{R}_b - {}^t_0\mathbf{F} \quad (5)$$

where ${}^t_0\mathbf{M}$ is the mass matrix, ${}^t_0\mathbf{C}$ is the damping matrix, and ${}^t_0\tilde{\mathbf{K}}$ is the strain incremental stiffness matrix which contains the internal stresses as well as the material and deformation properties at time t . ${}^{t+\Delta t}\mathbf{R}_c$ is the force vector containing the contractile active force produced by the E and EM models, ${}^{t+\Delta t}\mathbf{R}_b$ is the force vector for enforcing boundary conditions, and ${}^t_0\mathbf{F}$ is the nodal force vector for finite deformation only and is related to the internal stresses at time t . ${}^{t+\Delta t}\ddot{\mathbf{U}}$, ${}^{t+\Delta t}\dot{\mathbf{U}}$ and $\Delta\mathbf{U}$ are the respective acceleration, velocity and incremental displacement vectors at time $t + \Delta t$.

Equation (5) is the governing cardiac system dynamics for finite deformation analysis, in which the material model is included through the embedding of material matrix C_{rot} into the matrix ${}^t_0\tilde{\mathbf{K}}$. In Equation (5), when the myocytes are excited and then provide the contractile forces ${}^{t+\Delta t}\mathbf{R}_c$ through Equations (1) and (2) to the system at time $t + \Delta t$, with the known structure and material property at time t , the incremental nodal displacements $\Delta\mathbf{U}$ (thus the cardiac kinematics at time $t + \Delta t$ caused by the active force) can be readily calculated, and they will be further updated by the imaging and other measurements to obtain the patient specific estimates with the use of multiframe filtering.

¹ If E_{cf} and E_f are equal, then C_o reduces to the stiffness matrix for an isotropic material.

2.5 Optimal Multiframe Kinematics Estimation: Coupling of Physiome Model and Patient's Measurements

The system dynamics of Equation (5) can be solved by applying the Newmark method and the Newton-Raphson iteration, thus providing the deterministic kinematic predictions solely based on the physiome model. Nevertheless, the parameters of the physiome model, such as the fiber orientations and the Young's moduli, may not coincide with the specific physiological properties of a particular patient's heart, and thus introduces the *system uncertainties*. On the other hand, patient-specific measurements are typically corrupted by noises (*observation errors*), so they cannot be fully trusted when fed into the system. In order to properly use the patient measurements and compromise with the prior physiome model, a statistical framework is required to couple them together.

Equation (5) can be rewritten as a state-space updating equation [6]:

$$x(t + \Delta t) = A(t)x(t) + w(t + \Delta t) \quad (6)$$

where $x(t + \Delta t) = {}^{t+\Delta t}\mathbf{U}$ and $x(t) = {}^t\mathbf{U}$ are the state vectors, containing the displacements at time t and time $t + \Delta t$. $A(t)$ is the *transition matrix* relating $x(t + \Delta t)$ with $x(t)$, and is comprised by the ${}^t_0\mathbf{M}$, ${}^t_0\mathbf{C}$ and ${}^t_0\mathbf{K}$ matrices of Equation (5). $w(t + \Delta t)$ is the *input vector* which contains the force inputs including the contractile force obtained from the physiome model. Also considering the zero-mean, additive, white *process noise* $v(t)$ ($E[v(t)] = 0$, $E[v(t)v(s)'] = Q_v(t)\delta_{ts}$), Equation (6) becomes a TL-updated state-space equation which performs nonlinear state prediction (displacement) using the Newton-Raphson iteration scheme:

$$x(t + \Delta t) = A(t)x(t) + w(t + \Delta t) + v(t + \Delta t) \quad (7)$$

and $x(t + \Delta t)$ becomes statistical representation with system uncertainties.

In order to apply the patient's measurements to the physiome model, the measurements are defined to be a subset of the state vector corrupted by noises. Assuming zero-mean, additive, and white noise $e(t)$, ($E[e(t)] = 0$, $E[e(t)e(s)'] = R_e(t)\delta_{ts}$), the measurement equation becomes the following:

$$y(t + \Delta t) = Hx(t + \Delta t) + e(t + \Delta t), \quad (8)$$

where H is a known *measurement matrix* and $y(t + \Delta t)$ contains the image-derived, patient-specific displacements.

With these statistical state-space equations (Equations (7) and (8)) defined, using the multiframe filtering procedure described in [6], the prior physiome kinematic predictions can be updated by measurements to provide the optimal patient-specific estimates.

3 Experimental Results

Synthetic Data. The canine heart model of the University of Auckland², which provides both the cardiac geometry and fiber architecture obtained through

² Bioengineering Institute, University of Auckland, <http://www.bioeng.auckland.ac.nz>

Fig. 1. Synthetic data generated by applying the physiome model (E, EM and BM models) on the canine heart model of the University of Auckland. Top: deformed geometries (blue) with fiber orientations (red) (frame #5, #15, #25, #35, #45). Bottom: action potential propagation (frame #5, #15, #25, #35, #45).

Fig. 2. Kinematics recovery results on synthetic data in cylindrical coordinate system (frame #25, with respect to the first frame, the longitudinal-axis is the long-axis of the left ventricle). (a) Displacement magnitude (U) maps. (b) Radial strain (ϵ_{rr}) maps. (c) Circumferential strain (ϵ_{cc}) maps. (d) Radial-circumferential strain (ϵ_{rc}) maps. Left to right: ground truth, multiframe physiome model estimation, multiframe passive biomechanical model estimation.

anatomical experiments, has been used to generate the synthetic data. The physiome model (E, EM, and BM models) was applied on the heart model to provide the ground truth (see Fig. 1), and 50 frames of one cardiac cycle were obtained. The displacements on the epicardium and endocardia of every frame were extracted, and noises with 5dB SNR were added to provide the noisy measurements (y in Equation (8)), which were treated as the patient-specific motion tracking results from the cardiac images.

The kinematic parameters of the synthetic heart were recovered by the proposed multiframe physiome model and the multiframe passive biomechanical model [6]. In Fig. 2, for frame #25 as an example, it can be seen that the strains estimated using our proposed multiframe physiome model are better, especially for those parts further from the measurements, such as the septum between the left and right ventricles. This is because the roles of the models are more im-

Table 1. Deviations of the estimates from the ground truth (synthetic data).

Experiment	Multiframe Physiome Estimation	Multiframe Passive Estimation
ϵ_{rr}	0.0085 ± 0.0126	0.0228 ± 0.0337
ϵ_{cc}	0.0091 ± 0.0077	0.0120 ± 0.0150
ϵ_{zz}	0.0061 ± 0.0064	0.0101 ± 0.0122
ϵ_{rc}	0.0059 ± 0.0075	0.0104 ± 0.0123
ϵ_{cz}	0.0048 ± 0.0062	0.0066 ± 0.0079
ϵ_{zr}	0.0059 ± 0.0074	0.0098 ± 0.0136
U	0.3792 ± 0.2976	0.2266 ± 0.2621

portant for those parts without measurements. In consequence, more realistic models give more accurate estimations.

The tabulated numerical results on the deviations from the ground truth of these experiments (all 50 frames) are shown in Table.1.

Canine MRI Data. Experiments have also been conducted on canine cardiac MR image sequences to show the possible applicability of the multiframe physiome framework to clinical data. The cardiac image sequence of a normal mongrel dog consists of 16 frames over the cardiac cycle, where each 3D image frame contains 16 image slices, with 5mm inter-slice spacing, in-plane resolution of 1.64mm/pixel, and temporal resolution of 40msec/frame.

In the experiments, the canine cardiac boundaries and initial motion correspondences of the left ventricle were obtained using a simultaneous segmentation and motion tracking algorithm based on the active region model to provide the

Fig. 3. Estimated kinematics of canine MRI data in cylindrical coordinate system (frame #8, with respect to the first frame, the longitudinal-axis is the long-axis of the left ventricle). (a) Radial strain (ϵ_{rr}) maps. (b) Circumferential strain (ϵ_{cc}) maps. (c) Longitudinal strain (ϵ_{zz}) maps. (d) Radial-circumferential strain (ϵ_{rc}) maps. (e) Circumferential-longitudinal strain (ϵ_{cz}) maps. (f) Longitudinal-radial strain (ϵ_{zr}) maps. Left to right: multiframe physiome model estimation, multiframe passive biomechanical model estimation.

measurements [10]. The fiber architecture of the heart model of the University of Auckland was mapped to the canine heart, using the iterative closest points algorithm [11] followed by local registration using deformable BM model.

The kinematic estimates obtained using the proposed multiframe physiome model and the multiframe passive biomechanical model are shown in Fig. 3. Since there is no ground truth provided, numerical results are not available for comparison. Nevertheless, it has been observed that the motion tracking results (the measurements) have nearly no deformation along the long-axis of the heart (the z-axis), and this is unrealistic to a normal heart. It can be seen that, especially in Fig. 3(c), the estimates obtained through the multiframe passive biomechanical model inherit the same z-axis motion from the measurements. In contrast, the estimates obtained using our proposed algorithm is more reasonable because the physiome model gives more realistic predictions to compromise with the unrealistic measurements.

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