A 3D-0D closed-loop Model of the Heart and the Circulatory System ⋆

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1. INTRODUCTION

In industrialized countries, cardiovascular diseases are the primary cause of mortality and morbidity. Due to the complex multiphysics nature of cardiovascular function, the optimal treatment remains challenging. In the recent years, personalized computer models of electrophysiology (EP) became an important tool to predict intervention outcomes or to improve therapy stratification and planning. Problems of cardiac electromechanics (EM) are even more challenging. Beside the deformation of the heart, also the bi-directional interaction with the systemic and pulmonary vascular system plays a major role in EM simulations. A fully coupled fluid-structure interaction problem would yield the most detailed insights but is computationally expensive. Simpler lumped models of the circulatory system are able to predict physiological behaviors at a much lower computational cost. In this work, we discuss the coupling of a 3D bi-ventricular model with the closed-loop 0D *CircAdapt* model and we show its ability to predict physiological behaviors under experimental standard protocols.

2. METHODS

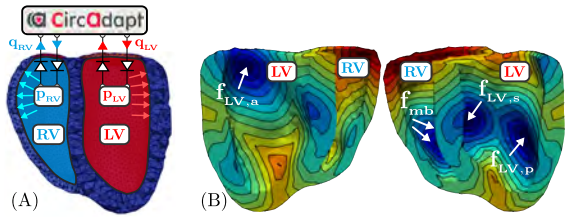

Fig. 1. (A) Bi-ventricular model setup and (B) activation sequence induced by five fasciles used for EP.

2.1 3D Electromechanical PDE Model

The tissue is modeled as a nearly incompressible, hyperelastic, orthotropic material with a nonlinear stress-strain relation using Cauchy's equation of motion

$$\rho_0 \ddot{\mathbf{u}} - \nabla \cdot \mathbf{FS}(\mathbf{u}) = \mathbf{0} \quad in \quad \Omega_0 \times (0,T) \tag{1}$$

for a final time $T > 0$, where $\mathbf{F}$ denotes the deformation gradient, $\mathbf{S}$ is the second Piola-Kirchhoff stress tensor, ρ_0 is the tissue density and Ω_0 denotes the reference configuration. Normal stress boundary conditions are applied at the endocardium

$$\mathbf{FS}(\mathbf{u})\mathbf{N} = -p\, J\, \mathbf{F}^{-\top}\, \mathbf{N} \quad on \quad \Gamma_{0,\text{endo}} \times (0,T) \tag{2}$$

with pressure p, outer normal vector $\mathbf{N}$ of the reference enodicardial surface $\Gamma_{0,\text{endo}}$ and the Jacobian determinant $J = \det\mathbf{F}$. Appropriate spring type boundary conditions are imposed at the remaining boundary of the geometry, see Fig. 1(A).

Passive and active tissue properties are simulated by decomposing the total stress $\mathbf{S}$ into a passive $\mathbf{S}_p$ and active $\mathbf{S}_a$ part, i.e. $\mathbf{S} = \mathbf{S}_p + \mathbf{S}_a$. The passive stress is modeled by the constitutive equation

$$\mathbf{S}_p = 2\frac{\partial \Psi(\mathbf{C})}{\partial \mathbf{C}}$$

with the right Cauchy-Green strain tensor $\mathbf{C} = \mathbf{F}^\top\mathbf{F}$ and the strain-energy function Ψ which is given by

$$\Psi(\mathbf{C}) = \frac{\kappa}{2}\big(\log\, J\big)^2 + \frac{a}{2}\big(\exp(\mathcal{Q}) - 1\big). \tag{3}$$

The first term in (3) penalizes local volume changes scaled by the bulk modulus $\kappa \gg 0\,\text{kPa}$ and the second term models a Fung-type material with a scaling factor $a > 0$ and $\mathcal{Q}$ according to Usyk et al. (2000).

Active stress $\mathbf{S}_a$ is assumed to be orthotropic with full contractile force along myocyte fiber direction $\mathbf{f}_0$ plus 40 % contractile force in sheet direction $\mathbf{s}_0$, i.e.

$$\mathbf{S}_a = S_a(\mathbf{f}_0 \cdot \mathbf{C}\mathbf{f}_0)^{-1}\mathbf{f}_0 \otimes \mathbf{f}_0 + 0.4\, S_a(\mathbf{s}_0 \cdot \mathbf{C}\mathbf{s}_0)^{-1}\mathbf{s}_0 \otimes \mathbf{s}_0$$

with a simplified phenomenological length dependent active stress transient S_a, see Niederer et al. (2011).

The EP, which serves as a trigger for the active stress generation, was modeled by a recently developed reaction-Eikonal approach which combines a standard reaction-diffusion model based on the monodomain equation with an Eikonal model, see Neic et al. (2017).

2.2 0D CircAdapt ODE Model

The *CircAdapt* model, see Arts et al. (2005), is a lumped 0D model enabling real-time simulations of the entire

⋆ The project received funding fom the European Union's Horizon 2020 research and innovation programme and the Austrian Science Fund (FWF).

cardiovascular system by concatenating modules (tubes, valves, chambers, ...) yielding a system of 26 ordinary differential equations. A detailed description of the model and the underlying equations can be found in Augustin et al. (2021).

2.3 0D-3D Coupling and Numerical Framework

To couple the ODE with the PDE model, the 0D cavities in the *CircAdapt* model are replaced by the 3D models discussed in Sec. 2.1. Furthermore, the pressure p within the cavities is introduced as an additional unknown and a supplementary equation enforcing the equality of the cavity volume is added in order to close the formulation. The resulting nonlinear saddle point problem reads

$$\begin{aligned} K(\mathbf{u},t) + G(p,t) &= 0 \\ V^{\mathrm{PDE}}(\mathbf{u},t) - V^{\mathrm{ODE}}(p,t) &= 0 \end{aligned} \tag{4}$$

where V^{PDE} is the cavity volume of the PDE model, V^{ODE} is the cavity volume predicted by the *CircAdapt* model and K and G are operators realizing (1) and (2), respectively.

The saddle point problem (4) is linearized by applying a Newton scheme and solved within the Cardiac Arrhythmia Research Package (CARP) framework, see Vigmond et al. (2008), using a finite element approach.

3. RESULTS

To demonstrate the predictive power of the coupled model, physiological experiments such as altering loading conditions and contractility are performed with a bi-ventricular PDE model. Therefore, 20 heart beats with tuned model parameters are simulated to arrive a stable limit cycle which matches measured baseline conditions. The response of the model to changes in (A) systemic afterload, (B) left aterial preload and (C) left ventricular contractility are probed by changing (A) the systemic resistance, (B) the cross sectional area of the pulmonary vein and (C) the peak active stress, respectively. The response of the coupled model on the pressure-volume diagram is depicted in Fig. 2 (acute response) and Fig. 3 (limit cycle response).

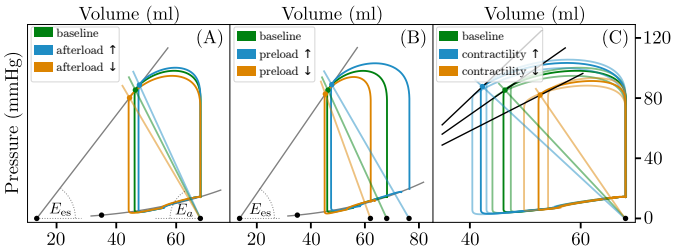

Fig. 2. Acute response to changes in (A) afterload, (B) preload and (C) contractility.

4. DISCUSSION

The coupled model is capable to reproduce the expected physiological behaviors in the left ventricular pressure-volume diagram, see Fig. 2 and Fig. 3. Altering afterload is reflected in pivoting the slope of the arterial elastance

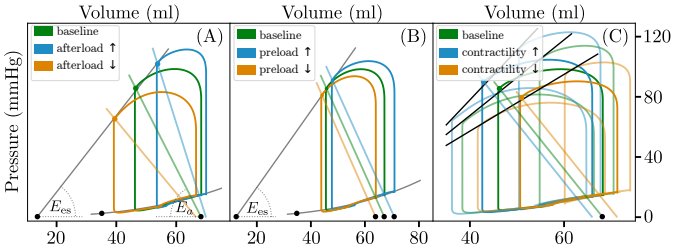

Fig. 3. Limit cycle response to changes in (A) afterload, (B) preload and (C) contractility.

curve E_a. Only marginal affects are observed in the acute case, Fig. 2(A), but significant changes are witnessed after stabilization to a limit cycle, Fig. 3(A). Changing preload conditions increased/decreased the stroke volume (SV) of the left ventricle due to the Frank-Starling mechanism and shifted E_a according to the changed end-diastolic volume. The slope of the end-systolic pressure volume relation E_{es} remains the same as under baseline conditions, see Fig. 2(B) and Fig. 3(B). Altering contractility increased/decreased the SV and E_{es} (sampled by perturbing afterload) is steepened/flattened as expected. In the acute response, Fig. 2(C), E_a was affected but after stabilization E_a was the same for all states, see Fig. 3(C).

REFERENCES

Arts, T., Delhaas, T., Bovendeerd, P., Verbeek, X., and Prinzen, F.W. (2005). Adaptation to mechanical load determines shape and properties of heart and circulation: the CircAdapt model. *American Journal of Physiology-Heart and Circulatory Physiology*, 288(4), H1943–H1954. doi:10.1152/ajpheart.00444.2004.

Augustin, C.M., Gsell, M.A., Karabelas, E., Willemen, E., Prinzen, F.W., Lumens, J., Vigmond, E.J., and Plank, G. (2021). A computationally efficient physiologically comprehensive 3D-0D closed-loop model of the heart and circulation. *Computer Methods in Applied Mechanics and Engineering*, 386, 114092. doi: 10.1016/j.cma.2021.114092.

Neic, A., Campos, F.O., Prassl, A.J., Niederer, S.A., Bishop, M.J., Vigmond, E.J., and Plank, G. (2017). Efficient computation of electrograms and ECGs in human whole heart simulations using a reaction-eikonal model. *Journal of Computational Physics*, 346, 191–211. doi:10.1016/j.jcp.2017.06.020.

Niederer, S.A., Plank, G., Chinchapatnam, P., Ginks, M., Lamata, P., Rhode, K.S., Rinaldi, C.A., Razavi, R., and Smith, N.P. (2011). Length-dependent tension in the failing heart and the efficacy of cardiac resynchronization therapy. *Cardiovascular Research*, 89(2), 336–343. doi:10.1093/cvr/cvq318.

Usyk, T.P., Mazhari, R., and McCulloch, A.D. (2000). Effect of laminar orthotropic myofiber architecture on regional stress and strain in the canine left ventricle. *Journal of Elasticity*, 61(1-3), 143–164. doi: 10.1023/A:1010883920374.

Vigmond, E.J., Weber dos Santos, R., Prassl, A.J., Deo, M., and Plank, G. (2008). Solvers for the cardiac bidomain equations. *Progress in Biophysics and Molecular Biology*, 96(1-3), 3–18. doi: 10.1016/j.pbiomolbio.2007.07.012.