In Silico heart model: electromechanical coupling

N. Filipovic[a,b1], S. Djorovic[a,b], V. Geroski[a,b], M. Milosevic[a], and M. Kojic[a,c]

[a] *BioIRC Kragujevac, Serbia;* [b]*Faculty of Engineering, University of Kragujevac, Serbia;* [c]*Houston Methodist Research Institute, The Department of Nanomedicine, Houston, TX, USA*

Keywords*:* in silico, heart, fluid-structure interaction, electrophysiology, drug release

1. Introduction

[1]Sudden cardiac death and arrhythmia represent a major worldwide public health problem, accounting for 15–20 % of all deaths. Computer modelling can help to better understand heart function. Computer simulation with biophysical background can explain experimental observations and make better understanding how organ-scale arrhythmogenic phenomena (ectopic heartbeats, conduction failure, electrical turbulence, etc.) and contractile dysfunction emerge from pathological effects at the tissue, cell and protein levels [1].

2. Methods

2.1 Fluid-structure interaction of left ventricle model

The pressure-volume (P-V) diagram of the left ventricle is given from ultrasound echocardiographic. Volume at the end of systole is called endsystolic (normally 60[*mL*]), and the volume of the blood pumped out in a single cycle is the strike volume. Duration of systole is dependent on the heart frequency and with the frequency of 75/*min* it lasts 0.3[*s*].

The left ventricle is represented by 3D deformable body. We model blood flow during filling phase by applying the fluid-solid interaction method. The ventricle wall is modeled by 3D brick 8-node solid elements, with fibers which have three-dimensional direction. The Navier-Stokes equations are solved using the ALE formulation for fluid with large displacements of the boundary. Also, a remeshing procedure is employed for the fluid domain in accordance with the motion of the ventricle wall. Boundary conditions for blood flow are: impermeable walls; no slip at the wall; the aortic pressure is prescribed at the outlet section according to the integrated lumped parameter model of systemic net [2]. It is considered that blood behaves as a Newtonian fluid (ρ = 1.05 *x* 10^3 [*kg*/m^3], μ = 3.65 x 10^{-3} [*kg*/*ms*]). The time step used in the calculation is Δt=0.005[*s*].

The ventricle wall model is simulated by muscle material model. Muscle fiber orientation is defined by direction vector in 3D prescribed through input data. It has two components: in radial plane and circumferential direction. In this way we approximate in our FE model the real counter-rotating fibers within the heart wall [2]. It is assumed that initially the blood is at rest. The outlet blood pressure is used as the boundary condition. At the same time the wall muscle fibers are activated according to the activation function taken from specific patient measurement.

2.2 Smeared finite element model formulation for Purkinje network

We used the composite smeared finite element as (CSFE) which is generalized in [3]. It represents a FE which contains separate domains which correspond to physical domains to be modeled. In case of electrophysiology, there is also the domain of the nerve network.

Continuum fields within the CSFE are coupled by 2-node connectivity elements at each FE node. These elements take into account transport characteristics of walls or membrane transport in case of cells, as 1D domain. The “mass” matrices can be expressed as

$$M_{11} = M_{22} = \frac{1}{3} c_{mJ} A_J h, \quad M_{12} = M_{21} = \frac{1}{6} c_{mJ} A_J h \qquad (1)$$

where c_{mJ} is capacitance coefficient of the wall in case of electrical field [4]. The terms A_J and h are the interface area belonging to the node J and wall/membrane thickness, respectively. The wall transport matrix is

$$K_{11} = K_{22} = -K_{12} = -K_{21} = D_{wall} A_J \qquad (2)$$

where D_{wall} is the wall/membrane transport coefficient.

The governing balance equation of electrical flow within neural fibers relies on the so-called cable theory. For the axial current flow along a nerve without lateral flow, the basic relation is

$$I_x = -G_a \frac{\partial V_e}{\partial x} \qquad (3)$$

where I_x is the current density along the fiber axis x, G_a is axial conductivity and V_e is electric potential. In case of large neural fibers, there is practically only the axial flow, and the FE model consists of the 1D elements with a standard form (1) of balance equations.

[1] Corresponding author. Email: fica@kg.ac.rs

In case when there is the lateral flow through the wall, that flow can be expressed in the form (taking that current going out of the fiber is positive),

$$I_{mem} = G_m\left(V_e^{in} - V_e^{ext}\right) + C_m\left(\frac{\partial V_e^{in}}{\partial t} - \frac{\partial V_e^{ext}}{\partial t}\right) + I_{ion} \quad (4)$$

where G_m and C_m are the wall conductivity and capacitance, respectively; V_e^{in} and V_e^{ext} are potentials within fiber and in the surrounding; and I_{ion} is ionic current due to flow of various charged molecules through the wall, which depends on the membrane potential [5].

3. Results and discussion

The intraventricular pressure drop between valvular (outlet) pressure p_{valv} and pressure at the apex p_{apex} inside the ventricle is given in Fig. 1.

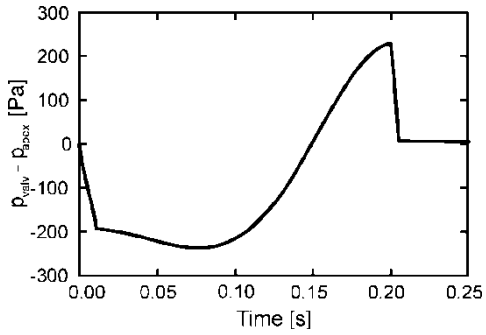

Figure 1: Intraventricular pressure drop $p_{valv}(t)$ - $p_{apex}(t)$ calculated during blood ejection phase (period between aortic valve opening and closure)

We considered smeared model coupled Purkinje network and drug release through coronary arteries. We included diffusion, convection and binding phenomena. This 3D model of drug distribution includes anisotropic diffusion properties, and the development of sophisticated nonlinear saturable binding models (Figure 2).

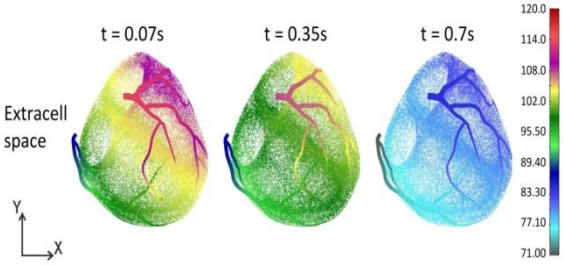

Figure 2: Drug distribution through coronary arteries

4. Conclusions

The ventricle wall model is simulated by muscle material model. Muscle fiber orientation is defined by direction vector in 3D prescribed through input data in radial plane and circumferential direction. Purkinje network was simulated with smeared finite element method which gives similar results as detailed nerve network but much faster in CPU time. We analyse coupled Purkinje network and drug release through coronary arteries. Simulated electrical field can be used in every day clinical practice electro-mechanical coupling and modeling the mechanics of the heart.

5. Acknowledgements

This work is supported by the SILICOFCM project that has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 777204. This research was also funded by Ministry of Education and Science of Serbia, grants OI 174028 and III 41007.
Note: This article reflects only the author's view. The European Commission is not responsible for any use that may be made of the information it contains.

6. References

[1] N.A. Trayanova, Mathematical approaches to understanding and imaging atrial fibrillation significance for mechanisms and management. *Circ Res,* 114:1516–1531. 2014

[2] A. Redaelli, F.M. Montovecchi, Computational evaluation of intraventricular pressure gradients based on a fluid-structure approach, *J. Biomech. Engrg.:* 118, 529-537. 1996

[3] M. Kojic, Smeared concept as a general methodology in finite element modeling of physical fields and mechanical problems in composite media, *J. Serb. Soc. Comp. Mech.*, 12,2: 1-16. 2018

[4] M. Kojic, M. Milosevic, V. Simic, A. Ziemys, N. Filipovic, M. Ferrari, Smeared multiscale finite element model for electrophysiology and ionic transport in biological tissue, *Computers in Biology and Medicine*, 108: 288-304. 2019

[5] T.O'Hara, L. Virag, A. Varro & Y. Rudy, Simulation of the undiseased human cardiac ventricular action potential: model formulation and experimental validation. *PLoS Comput Biol* **7**, e1002061. 2011