A REDUCED MODEL OF ACTIVE CONTRACTION OF THE CARDIAC MUSCLE TISSUE

Francesco Regazzoni^{1,*}, Luca Dedè¹, Alfio Quarteroni^{1,2}

¹ MOX - Dipartimento di Matematica, Politecnico di Milano, P.zza Leonardo da Vinci 32, 20133 Milano, Italy. Email: francesco.regazzoni@polimi.it

² CMCS, Institute of Mathematics, Ecole Polytechnique Fédérale de Lausanne, Av. Piccard, CH-1015 Lausanne, Switzerland (Honorary Professor)

Key words: Cardiac Force Development, Crossbridge, Sarcomere Dynamics, Cardiac modelling

The primary role of the heart as a pump is made possible by the ability of cardiac cells to contract. The mathematical modelling of the complex phenomena behind the active contraction of cardiomyocytes is crucial for understanding heart functionality, since it represents the natural bridge between electrophysiology and mechanics [1]. The most detailed models of muscle contraction consist in Markov Chains describing the attachment-detachment of actin and myosin filaments. The centrality of the phenomenon of cooperativity between adjacent binding sites prevents applying the mean-field hypothesis in order to reduce the complexity of such models [2]; therefore, the time-consuming Monte Carlo method is typically employed in simulations, hindering the applicability of such models to the simulation of the full organ. In our work we propose a reduced ODE model for the mechanical activation of cardiac myofilaments, which is based on explicit spatial representation of nearest-neighbour interactions. Our reduced model is derived starting from the cooperative Markov Chain model presented in [3], under the assumption of conditional independence of specific sets of events. This physically motivated assumption allows to drastically reduce the number of degrees of freedom, thus reducing the computational cost by more than 10000 times [4]. We show through numerical tests that our reduced model is capable of reproducing physiological steady-state force-calcium and force-length relationships and also shows good qualitative and quantitative agreement with experimental measurements under dynamic conditions. Finally, we analyse different strategies to couple the proposed model with existing models of electrophysiology and mechanics devoting a particular care to the homogenization of the microscopic model of force generation into a macroscopic framework and we show some numerical simulations of a fully coupled electromechanical system in simple geometries.

REFERENCES

- [1] Fink, M., Niederer, S. A., Cherry, E. M. et al. Cardiac cell modelling: observations from the heart of the cardiac physiome project. *Prog Biophys Mol Biol* (2011) **104(1)**, pp. 2–21.
- [2] Rice, J.J., de Tombe P.P. Approaches to modeling crossbridges and calcium-dependent activation in cardiac muscle. *Prog Biophys Mol Biol* (2004) 85.2, pp. 179–195.
- [3] Washio, T., Okada, J., Sugiura, S., Hisada, T. Approximation for cooperative interactions of a spatially-detailed cardiac sarcomere model. *Cell Mol Bioeng* (2012) **5.1**, pp. 113–126.
- [4] Regazzoni, F., Dedè, L., Quarteroni, A. Active contraction of cardiac cells: a model for sarcomere dynamics with cooperative interactions. *MOX Report* (2017) **48**, pp 1–35.