World Congress on Biomechanics

Title: Population of Computational Cell and Tissue Cardiac Electromechanical Models for functional analysis

Authors: Ilsbeth van Herck[1], Henrik Finsberg[1], Cécile Daversin-Catty[2], Maite Mora[3], Beatriz Trenor[3], Hermenegild Arevalo[1], Samuel Wall[1]
Affiliations: [1]Department of Computational Physiology, Simula Research Laboratory Norway, [2]Department of Numerical Analysis and Scientific Computing, Simula Research Laboratory, Norway, [3]Centre for Research and Innovation in Bioengineering (Ci2B), Universitat Politècnica de València, Spain

Abstract:

Introduction

Cardiac computational models can fill important gaps in understanding the cardiomyocyte or cardiac tissue properties. Recent maturity in cardiac mechanical modelling enables quantitative predictive power across a range of applications. One challenge however is the tight coupling of cardiac mechanics with the underlying electrophysiological properties of the tissue, which makes modelling clinical mechanical phenomena such as drug effects difficult. More robust predictions can be achieved by modelling populations of models, which incorporate stochastic parameter variability to represent biological variation. For cardiac computational models to live up to their potential in developing safe and efficient treatments for increasingly prevalent cardiac disease, such populations of fully coupled electromechanics models will provide greater predictive power on mechanics and physiology of the heart.

Methods

A fully coupled electromechanics model of ventricular tissue is developed by coupling the O'Hara-Rudy[1] electrophysiology model and the Land[2] mechanics model. A population of models was created by varying 16 electrophysiological and 11 mechanical parameters at the cell level. The population was calibrated from 1000 to 187 models based on biomarkers derived from the action potential shape, calcium transient and active tension. The electromechanics solver is implemented by combining existing solvers for electrophysiology[3] and mechanics[4], which are both based on the open-source framework FEniCS[5]. A geometry of 20x7x3 mm is simulated with 1.0 or 0.5 mm spatial resolution for mechanics or electrophysiology respectively, with free movement in the fibre direction on one side.

Results

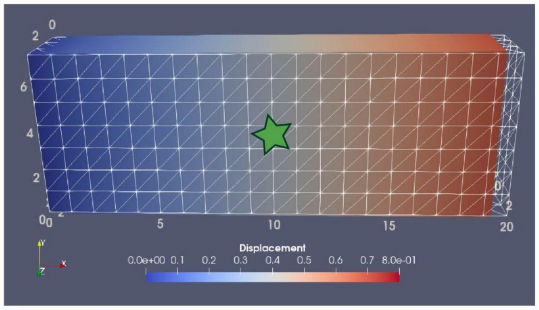
Traces from all population models were extracted at the center of the tissue in all directions (green star in top left panel) for further analysis (see figure). Electrophysiological biomarkers, such as action potential duration and systolic calcium concentration remain within calibrated and cell population model range. The maximum active tension in tissue is reduced by 65% compared to cell simulations. This reduction can be attributed to the free contraction in tissue versus fixed stretch in calibration and cell simulations. The magnitude and especially the recovery duration of active stretch varies widely across the population (see table for average±SD). This range of timing and force of contraction reinforce the need to assess cardiac function and drug effects in populations of electromechanical models.

Discussion

We present a pipeline for creating populations of strongly coupled 3D excitation-contraction models for ventricular tissue. The tissue model includes bidirectional coupling and biological variation, facilitating further investigation into the multifactorial effect of variation and drugs on the *in silico* human heart. This enables simulation of both mechanical and physiological function of the heart to aid development of safe and efficient treatment based on population statistics.

References

1. O'Hara, T. et al.; PLoS Comput Biol 2011 [doi:10.1371/journal.pcbi.1002061]
2. Land, S. et al.; J. Mol. Cell. Cardiol. 2017 [doi:10.1016/J.YJMCC.2017.03.008]
3. Logg, A. et al.; Springer 2012 [doi:10.1007/978-3-642-23099-8]
4. Rognes, M. E. et al.; Journal of Open Source Software, 2017 [doi:10.21105/joss.00224]
5. Finsberg, H. N. T.; Journal of Open Source Software, 2019 [doi:10.21105/joss.01539]



	calibration	cell	tissue
APD90 (ms)	180-440	265±25	263±25
peak Ca (μM)	0.26-2.2	0.49±0.08	0.42±0.06
peak Ta (kPa)	15-25	20±4	7±2
maximum stretch (%)	-	-	3.8±0.3
stretch recovery (ms)	-	-	383±118