Title: Reproducing hiPSC-CM in vitro 2D culture in silico

Authors:
Noita O, Forouzandehmehr A, Ahola A, Koivumäki JT, Hyttinen J

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Abstract
Cardiomyocytes (CM) work in tandem to achieve synchronous well-paced behaviour with constant need of energy, a process that conditions such as ischemia disrupts. Human induced pluripotent stem cell derived CM (hiPSC-CM) 2D multi-electrode array (MEA) studies have shown that ischemia can reduce conduction velocity to 52 %, or even to < 20 %. In silico models of single hiPSC-CM have been frequently studied e.g., Paci et al.. We developed an in silico hiPSC-CM 2D tissue conduction propagation model and validated it against these in vitro models.

To model hiPSC-CM 2D tissue in silico, Paci2013 model was imported from CellML into OpenCARP EasyML. Cells were positioned in a 2-dimensional grid. Cell concentration is set to 93 000 cells/cm2, i.e. the shortest distance between two cells is 32.79 µm resembling in vitro culture. Ischemia was introduced to the model by adjusting single cell model parameters that ischemia is known to alter. With two severities of ischemia in cells, the 2D model shows conduction velocity reduction to 57% and 40% respectively.

Our results correspond to results of in-vitro ischemia in literature, however, we were not able to gain the in-vitro results in deeper ischemia with changes only in the cell model parameters. This hints that changes in prolonged ischemia might also cause changes in the connectivity between cells, not just in cellular electrophysiology. Our developed model augments MEA studies by enabling fast iteration of experiments and can be used to predict the efficiency of drugs.