Simulating HIPSC Cardiomyocyte Electromechanics with Machine Learning Surrogate Model

Olli Ylinen, Antti Ahola, Ossi Noita, Jussi Koivumäki, Jari Hyttinen

Computational Biophysics and Imaging Group, Tampere University
Tampere, Finland

Computational modelling of human induced pluripotent stem cell–derived cardiomyocytes (hiPSC-CM) enables fast iterations of experiments compared to in vitro. This complementary approach can be used for evaluating drug efficacy and safety, and modelling diseases, potentially in a patient-specific manner. Replicating in vitro results in silico benefits from population of models approach which can be computationally expensive. Calculating the dynamic steady-state with the differential equation-based models can take tens of seconds of computing time, which can become problematic when repetitive evaluations are needed. While computation time can be shortened by parallelization, solving differential equations via parallelization is impractical for large number of calculations.

One solution to overcoming computational costs in the calculation of hiPSC cardiomyocyte function is the use of surrogate models. Here, we developed a convolutional neural network-based model to estimate the steady-state, skipping most of the calculations.

The model employs 22 parameter multipliers that affect the conductances and time constants of ion channels. The model outputs 1.5 second traces of action potential, Ca^{2+} transient, active tension, L-type Ca^{2+} current and rapid delayed rectifier K^{+} current. The data were generated with the population of models approach, using the Forouzandehmehr hiPSC-CM model. The data consists of 75 000 models with a split of 10:1:4 for training, validation and testing.

We achieved average absolute errors of less than 1% of average amplitude for each model output. Using a modern laptop CPU, the model runtime decreased 1000-fold compared to the differential equation based model. In addition, the model demonstrates excellent results with cardioactive drugs. We will share the model for further use such as parameter optimization and sensitivity analysis.