

A Heterogeneous Formulation of the Himeno et al. Human Ventricular Myocyte Model for Simulation of Body Surface ECGs

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Multi-scale computational modeling of cardiac electrophysiology has fostered our understanding of the genesis of the ECG. While current models capture the relevant processes under physiological and many disease conditions with high fidelity, proper representation of the conditions in the extracellular milieu remains challenging. The recent human ventricular myocyte model by Himeno et al. is one of the first biophysical models which faithfully represents the dependence of the action potential (AP) duration on the extracellular calcium level.

Here, we present a heterogeneous formulation of the Himeno cellular model and integrate it into a multi-scale framework to compute body surface ECGs. We propose three variants of the Himeno model to account for transmural heterogeneity. The ionic current level parameter sets representing subendocardial, midmyocardial (M), and subepicardial cell types were informed by the experimental data presented with the O'Hara-Rudy model and tuned to match AP level features such as repolarization stability. As shown in previous work by Keller et al., an apico-basal gradient of I_{Ks} conductance is a likely mechanism causing concordant T-waves. Therefore, we increased the I_{Ks} conductance in the Himeno et al. model at the apex by a factor of 3.5 compared to the base to obtain an APD shortening of 12.5%.

The model setup comprising transmural and apico-basal heterogeneity yielded a physiological ventricular ECG comparable to previous setups building on the ten Tusscher-Panfilov cellular model. Our novel setup allows to study, for the first time, how realistic changes of the AP under hypo- and hypercalcaemic conditions translate to changes in the ECG. Resulting QT shortening under hypocalcaemic conditions matched human experimental data both qualitatively and quantitatively.

In conclusion, the setup presented here provides a tool to study the effect of altered calcium levels in the extracellular milieu of the heart, as occurring during renal failure, across multiple spatial scales mechanistically.