

Accelerating stabilization of whole-heart models after changes in ion concentrations

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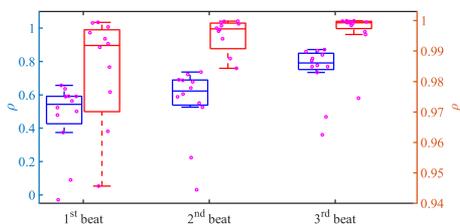
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Parameter changes in membrane models can cause long-term drift in model variables. To reduce the cost of whole-heart simulations with such changes one can perform the stabilization in models of isolated cells and then copy the state variables to the full model, but it can then still take many beats to stabilize. We investigated the causes of this and tested methods to stabilize faster.

Simulations were performed with modified concentrations of extracellular potassium ($[K^+]_o$, 3 to 6.2 mM) and calcium ($[Ca^{2+}]_o$, 1.4 to 3.2 mM), and cycle length (0.6 to 1.2 s) in a modified Ten Tusscher-Panfilov 2006 model. Isolated cells parameterized to mimic endocardial, mid-myocardial, and epicardial myocytes were simulated for 1000 beats. Their final state was then copied to all nodes of the corresponding type in a model of the whole human ventricles, which was run for 10 beats. The state variables of each node, except for the activation gate of the sodium current, were frozen until the sodium current activated. Twelve-lead ECGs were simulated. Model stability was evaluated in terms of action potential duration and T-wave characteristics.

We found that changes in $[K^+]_o$ caused drift over more than 500 beats, while changes in $[Ca^{2+}]_o$ caused shorter drift. Stabilization of the whole-heart model took 4 to 6 beats. Freezing of the membrane state had no effect in our scenarios. Changes in the whole-heart model were most prominent in the midmyocardial and epicardial layers and not, as we expected, at their interfaces.



Median and 25th/75th percentiles of the correlation coefficient (ρ) between the 12-lead ECGs of the first three beats and the 10th beat, with (red) and without (blue) initialization for 1000 beats. Each purple dot represents an individual ECG lead.