A coupled model of mitochondrial metabolism and cardiac electrophysiology

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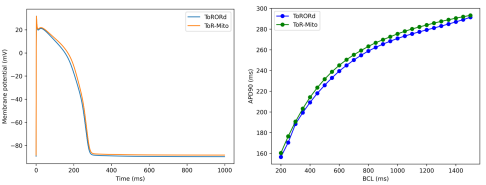
Existing human 3D electrophysiology models do not usually include mitochondrial energetics due to computational complexity. Here, we developed (ToR-Mito) a coupled mitochondrial–electrophysiology framework and evaluated whether it preserves baseline ventricular electrical behavior across cell-level and 3D biventricular heart model simulations. We coupled the human ventricular electrophysiology model (ToR-ORd) with the Cortassa mitochondrial (2017) model. ATP produced by the mitochondrial model was supplied as the principal input to the electrophysiology model, while ADP, cytosolic calcium, and sodium computed by ToR-ORd were passed back to the mitochondrial model. We also included the ATP-sensitive I_{KATP} channels. Both ToR-ORd and ToR-Mito models were simulated for 1000 beats under healthy conditions across basic cycle lengths (BCLs) ranging from 50 to 1500 ms. After cell-level simulations, both models were further evaluated on a 3D slab and on a biventricular (BiV) geometry using monodomain representation.



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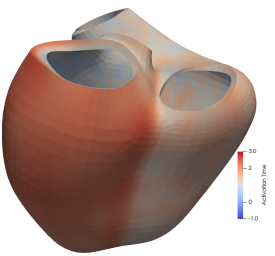

C

Both models reproduced similar action potential morphology at all BCLs. Only a 1.63% difference was observed during repolarization at a BCL of 1000 ms, with a slight 4.43 ms prolongation of APD90 in ToR-Mito (Figure A). Restitution curve analysis showed similar restitution behavior in both models, with a mean difference of 1.83% (Figure B). In 3D slab simulations, both models exhibited the same conduction velocity of 50 cm/s. In the BiV geometry, activation time mapping demonstrated consistent propagation patterns at the organ level (Figure C), while ToR-Mito increased simulation time by ~12% compared with ToR-ORd.

ToR-Mito preserves baseline ventricular electrophysiological behavior across cell and organ-level simulations, providing a foundation for future studies of mitochondrial–electrophysiological coupling.