Multiscale Evaluation of a Human-Like Atrioventricular Nodal Model

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The atrioventricular (AV) node plays a central role in cardiac conduction by delaying atrial-to-ventricular activation, supporting subsidiary pacemaking, and filtering rapid atrial impulses. Despite its importance, human AV-nodal electrophysiology remains difficult to study experimentally, and most available computational formulations are based on non-human data or non-nodal cell types. In this work, we developed and evaluated a human-like AV nodal model using a multiscale computational framework. Starting from the human atrial Skibsbye cell model, we optimized ionic parameters toward reported AV-nodal biomarkers, including spontaneous rate, maximum diastolic potential, action-potential amplitude, peak voltage, upstroke velocity, and repolarization duration. The resulting model, denoted hAV, was then compared against rabbit nodal, human atrial, ventricular, and Purkinje reference models using single-cell biomarkers, integrated ionic-current fluxes, and APD restitution. Finally, hAV was embedded in a three-dimensional AV conduction-axis tissue model including atrial tissue, fast and slow pathways, compact AV node, and His–Purkinje system to assess emergent conduction behavior under different pacing rates. At the cellular level, hAV reproduced key AV-nodal features, including spontaneous activity, a depolarized diastolic potential (-67.55 mV), low upstroke velocity (7.25 V/s), prolonged repolarization (APD90 249.04 ms), and a spontaneous rate of 52.10 bpm. Ionic-current flux analysis placed hAV in an intermediate regime distinct from atrial, ventricular, rabbit nodal, and Purkinje-like phenotypes, while restitution analysis showed a broader and more complex dynamic profile than the reference models. At the tissue scale, the model reproduced preferential fast-path conduction at baseline and rate-dependent 2:1 filtering during rapid atrial pacing. These results support hAV as a physiologically plausible and computationally robust basis for multiscale simulation of human AV-nodal electrophysiology.