

A Novel Computational Model of Pacemaker Activity in the Mouse Atrioventricular Node Cell

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The development of computational electrophysiology and mathematical modeling are nowadays capable of reproducing the action potential (AP) and properties of impulse conduction in a variety of species and cell types. Although many action potential models have been developed for most heart regions [1], for the atrioventricular node (AVN) there are few experimental data and the cellular electrophysiology basis of AVN pacemaking is not completely understood. To date, only two models are available and were developed by Inada et al. [2] for rabbit AVN cells and by Marger et al. [3] for mouse. Since the AVN acts as a subsidiary pacemaker and controls impulse conduction between atria and ventricle, understanding its electrophysiological properties is an important and complex issue.

For these reasons, we aimed to develop a new mouse model of pacemaking in AVN cells by introducing equations to calculate calcium handling to an existing model of AP in mouse AVN single-cell. Preliminary work, started by Marger et al. [3], was able to simulate the AP of mouse AVN single cell but did not contain subcellular compartments or the dynamics of intracellular ions' concentrations.

The equations describing calcium handling are based on the AP mouse SAN single-cell model from Kharche's work [4]. The cell's compartmentalization has been updated as follows: the sarcoplasmic reticulum, divided into junctional and network spaces, the calcium subspace (which is 1% of the total cell volume), and the cytosol. The calcium subspace is considered as a different cell compartment because of the different calcium concentration found when the release takes place. The current equations have been fitted with the experimental data available in the literature. Moreover, our model was able to reproduce almost all the AP hallmarks and was used for simulating the effects of different currents block (If, Cav1.3-mediated I_{CaL}, and I_{Kr}).

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