Role of the Instantaneous Component of the Funny Current in Murine Sinoatrial Node Pacemaking

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Introduction: The cardiac pacemaker current (I_f) is responsible for the diastolic depolarization phase of action potentials of cardiac pacemaking cells in the sinoatrial node (SAN). Mathematical formulations of I_f have focused on the time-dependent current, assuming the instantaneous component was caused by various leak channels. New experimental data suggests that I_f is the superposition of two components, one part being time-dependent and the other instantaneous.

Method: Using experimental current-voltage data the formulation of I_f in the Kharche model of the murine SAN cell was modified to include an instantaneous component. Using the newly updated model the role of the instantaneous component of I_f on action potential morphology was studied by reducing the conductance of this channel. The role of I_f on cardiac conduction was also studied using a 1D chain of cells.

Results: In simulation, at the single cell level, combined blocking of the instantaneous and time-dependent components by 50% increased the cycle length (CL) by ~200 ms and reduced the slope of the diastolic depolarization (SDD) phase by 0.05 V/s. Applying the same block in isolation to the instantaneous component resulted in an increase in CL and decrease in SDD of ~90 ms and 0.04 V/s respectively. An isolated block of the time-dependent component by 50% had a minimal effect on both CL and SDD. Independently blocking the instantaneous component and total I_f in the 1D model resulted in a reduction in the conduction velocity.

Conclusion: This new formulation of I_f represents a significant improvement to the Kharche model, highlighting the important role of I_f, especially the instantaneous component, in both pacemaking and the conduction of pacemaking action potentials in the murine SAN.