Functional Roles of the L-type Calcium Channel on Cardiac Pacemaking Insights from Bifurcation Analysis

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Bifurcation analysis is a useful tool to analyze the functional roles of an ionic channel current in generating action potentials in cardiac cell models. It has assisted in understanding of the ionic mechanisms underlying the genesis of pro-arrythmogenic events and in evaluation of the functional impacts of varied parameters (i.e., ion channel conductances) on modulating the characteristics of auto-rhythmic actions potentials (APs) of cardiac pacemaker, such as the cycle length (CL), the maximal diastolic potential (MDP) and the overshoot (OS) of APs.

The objective of this study was to use bifurcation analysis to study the functional roles of the maximal channel conductance of the L-type calcium channel coded by isoforms of Cav1.2 and Cav1.3 in a novel mathematical model of murine sinoatrial node (SAN) cells developed recently. A continuous variation in the maximal channel conductance of ICaL (gCaL) was carried out to reveal the emergence and annihilation of pacemaking APs, changes in their CL, MDP and OS. Parameter value range of the channel conductance essential for generating and/or annihilating pacemaking APs were identified.

In bifurcation analysis, gCaL was varied in a range of 0   2 S. It was shown that the bifurcation branch began at gCaL =0.02 S, and terminates at 1.44 S. A gradual increase in gCaL led to a dramatic increase in the pacing rates, but a gradual decrease in the amplitude of AP due to an elevated MDP that prohibited n fully activation of the channel. At gCaL $>$1.44 S, the model reached a quiescent state, indicating the system transferring from a limit cycle state to a steady state.

In conclusion, this study demonstrates that the L-type calcium channel current contributes to cardiac pacemaking APs, especially during their diastolic and up-stroke depolarization phases.