

Center for Cardiovascular Bioinformatics & Modeling

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Stochastic Modeling of Local and Global Intracellular Calcium Dynamics

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Abstract:

Although there is consensus that calcium (Ca) puffs and sparks arise from the cooperative action of multiple intracellular Ca channels, the precise relationship between single-channel kinetics and the collective phenomena of stochastic Ca excitability and oscillations is not well understood. Here we present and analyze a stochastic automata network model of instantaneously coupled Ca-regulated Ca channels that gives insight into how the stochastic dynamics of an individual Ca release site depends on channel density and the presence or absence of Ca inactivation. The relationship between such stochastic Ca release site dynamics and global Ca responses will then be discussed in the context of a novel probability density approach to modeling whole cell Ca dynamics. The method involves coupling ODEs for the bulk cytosolic and ER [Ca] to advection-reaction equations for the probability density of the [Ca] in cytosolic and luminal domains associated with each channel and conditioned on channel state. The probability density approach is computationally more efficient than explicitly spatial Monte Carlo simulations and the representation of local Ca signals inherent in the probability density approach is more realistic than conventional stochastic compartmental models.