



*The Effect of Residual Calcium on the Stochastic Gating of  
Calcium-regulated Calcium Channels*

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Abstract

Single channel models of intracellular Ca channels such as the inositol 1,4,5-trisphosphate (IP<sub>3</sub>) receptor and ryanodine receptor (RyR) often assume that Ca-dependent transitions are mediated by a constant background [Ca] as opposed to a dynamic [Ca] representing the formation and collapse of a localized Ca domain. This assumption neglects the fact that Ca released by open intracellular Ca channels may influence subsequent gating through the processes of Ca-activation or Ca-inactivation. We study the effect of such "residual Ca" from previous channel opening on the stochastic gating of minimal and realistic single channel models coupled to a restricted cytoplasmic compartment. Using Monte-Carlo simulations we determine how the steady-state open probability of single channel models of Ca-regulated Ca channels depends on the time constant for Ca domain formation and collapse. The Monte Carlo approach is extended to model Ca release site composed of multiple two-state Ca-activated channels in a preliminary study of the dynamics of Ca puffs or sparks terminated by stochastic attrition---the spontaneous closing of the coupled channels in the absence of a slow closed (i.e., refractory) state.