

**MARKOV CHAIN MODELS OF COUPLED
INTRACELLULAR CALCIUM CHANNELS: KRONECKER
STRUCTURED REPRESENTATIONS AND BENCHMARK
STATIONARY DISTRIBUTION CALCULATIONS**

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Mathematical models of calcium release sites derived from Markov chain models of intracellular calcium channels exhibit collective gating reminiscent of the experimentally observed phenomenon of stochastic calcium excitability (i.e., calcium puffs and sparks). We present a Kronecker structured representation for calcium release site models and perform benchmark stationary distribution calculations using numerical iterative solution techniques that leverage this structure. In this context we find multi-level methods and certain preconditioned projection methods superior to simple Gauss-Seidel type iterations. Response measures such as the number of channels in a particular state converge more quickly using these numerical iterative methods than occupation measures calculated via Monte Carlo simulation.

1. Introduction

The stochastic gating of voltage- and ligand-gated ion channels in biological membranes that is observed by single channel recording techniques is often modeled using discrete-state continuous-time Markov chains (CTMCs).^{1,2} While these single channel models can be relatively simple (e.g., two physicochemically distinct states) or complex (hundreds of states), most include only two conductance levels (closed and open). For example, a transition state diagram for a three-state calcium (Ca^{2+})-regulated channel activated by sequential binding of two Ca^{2+} ions is given by



