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Numerical solution of calcium-mediated dendritic branch model

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ABSTRACT

The standard algorithms for spatial discretizations of calcium-mediated dendritic branch models via finite difference methods are quite accurate, but they are also extremely slow. To improve computational efficiency we apply spatial discretization using a spectral collocation method. Simulations using the spectral collocation method are compared to the finite difference approach using a model for calcium-mediated restructuring with spine pruning. We find that the spectral collocation method is about fifteen times more efficient to achieve similar accuracy than the finite difference approach even though spectral collocation requires more steps.

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1. Introduction

Dendrities are extensively branched neuronal processes specialized for receiving and processing the vast majority of excitatory synaptic inputs in the central nervous system. The most common synaptic specializations of dendrites are dendritic spines. Spines are protrusions from the dendrite of usually no more than two microns, often ending in a bulbous head that is attached to the dendritic shaft by a narrow stem. There can be hundreds of spines on a single dendritic branch.

Experimental evidence is overwhelming (including *in vitro* optical recordings) that spines change their physical structure in response to synaptic activity. The time scale of restructuring can range from seconds to hours, and hundreds of spines on a single branch may morph simultaneously but at different rates. Conversely, slow structural changes in spines influence how electrical activity (millisecond time scale) spreads or propagates in the cell. Resolving such interactions will lead to much improved understanding of the input–output properties of dendrites and how morphological change in dendrites both influences, and is influenced by, electrical and chemical activity in the cell.

Recently, computational models of restructuring spines on a dendritic branch have been formulated and studied [17,18]. The models are an extension of Baer and Rinzel's cable-theoretic approach for a dendrite with many spines [1,2,4,12–14,19]. The governing system consists of a linear second-order parabolic partial differential (passive cable equation) coupled to a system of ordinary differential equations representing the spine dynamics (electrical, chemical, and physical) at location X on a dendrite of electrotonic length L. The computational difficulty with these models is that the equations need to be solved

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over long time intervals to observe the slow changes in dendritic morphology while retaining resolution on the millisecond time scale to capture membrane potential dynamics. Simulations using a spatial discretization via finite difference methods are accurate, but are simply too slow.

In this paper we demonstrate, for a continuum spine model, that spatial discretization using a spectral collocation method is about fifteen times faster than the finite difference approach. We choose as our example problem, a continuum spine model for calcium-mediated restructuring and spine pruning [18]. The approach is to compare discretization of the spatial variable X using a second order finite difference method on the uniform grid $X_i = (i-1)\,\delta X$, $i = 0, 1, \ldots, N+1$, to a pseudospectral discretization method based on the Chebyshev–Gauss–Lobatto points on the interval $[0, L]$ where L in the electrotonic (dimensionless) length of the cable.

Boundary conditions for these two methods are handled quite differently. For the finite difference method, the boundary conditions are discretized by introducing grid points to the left of 0 and the right of L. In the case of the pseudospectral method the boundary conditions are discretized by computing first the approximation to the derivative of V_d (cable's membrane potential) by $D\,V_d$ where D is the differentiation matrix of the first order, and then replacing the first and last component of the resulting vector by the Neumann boundary conditions. The remaining system of ordinary differential equations is restricted to the grid X_i, $i = 1, 2, \ldots, N$.

This overall process leads to a system of stiff differential equations which are solved using the code `ode15s` from the Matlab ODE suite [16]. Using this approach, we are able to resolve variations in membrane potential dynamics in the cable and spine heads. If necessary, we may restrict maximum stepsize of integration by setting the appropriate parameter *MaxStep* in OPTIONS using `odeset`. A key result is that the pseudospectral method requires a much smaller number of spatial gridpoints than required by the finite difference method to achieve comparable accuracy.

The plan of the paper is as follows. In Section 2 the calcium-mediated model is presented followed in Sections 3 and 4 by the descriptions of the finite difference and spectral collocation methods for the numerical discretization of this model. Numerical experiments comparing the two numerical approaches are presented in Section 5. Finally, in Section 6, some concluding remarks are given and plans for future research are briefly outlined.

2. Description of the calcium-mediated model

Following the derivation in [18], our model for a dendritic branch with spines is based on the dimensionless cable equation for the transmembrane potential V_d along a dendrite of dimensionless length L with both ends sealed. We assume that this branch is studded with a population of dendritic spines where $\bar{n}$ represents the spine density along the cable in units of spines per unit of electrotonic length. The spines deliver current to the dendrite, and I_{ss} represents the stem current flowing through an individual spine stem. This leads to an equation of the form

$$\begin{cases} \tau_m \dfrac{\partial V_d}{\partial t} = \dfrac{\partial^2 V_d}{\partial X^2} - V_d + R_\infty \bar{n} I_{ss}, & 0 < X < L,\ t > 0, \\ \dfrac{\partial V_d}{\partial X}(0,t) = -R_\infty I_1, & t > 0, \\ \dfrac{\partial V_d}{\partial X}(L,t) = R_\infty I_2, & t > 0. \end{cases} \tag{2.1}$$

Here τ_m is the membrane time constant, and R_∞ is the cable input resistance. For each spine, the spine head is modeled as an isopotential compartment where the equation for the transmembrane potential V_{sh} is a current balance equation for the capacitive, ionic (I_{ion}), synaptic (I_{syn}) and spine stem (I_{ss}) currents given by

$$C_{sh} \frac{\partial V_{sh}}{\partial t} = -I_{\text{ion}} - I_{\text{syn}} - I_{ss}. \tag{2.2}$$

Here C_{sh} is the capacitance of an individual spine. The terms for the ionic currents I_{ion} and the synaptic current I_{syn} are described in detail later in this section.

The spine stem current I_{ss} for an individual spine has the form

$$I_{ss} = \frac{V_{sh} - V_d}{R_{ss}},$$

where R_{ss} is the spine stem resistance. Changes in R_{ss} reflect activity-dependent changes in the spine stem structure. These structural changes are mediated by activity-induced changes in the intraspine calcium level C_a described by the equation of the form

$$\frac{\partial C_a}{\partial t} = -\varepsilon_1 (C_a - C_{\min}) + \frac{|I_{ss}|}{\kappa_c}. \tag{2.3}$$

Observe that the rate of increase for the intraspine calcium level is proportional to $|I_{ss}|$ which is a measure of activity. In the absence of activity, C_a decays to a minimum value. The equation for the change in stem resistance for spines along the cable is

$$\frac{\partial R_{ss}}{\partial t} = -\varepsilon_2 (R_{ss} - R_{\min}) \left(1 - \frac{R_{ss}}{R_{\max}}\right) \left(\frac{C_a}{C_{\min}} - 1\right) \left(\frac{C_a}{C_{\text{crit}}} - 1\right). \tag{2.4}$$