Analysis of axonal and dendritic signal propagation - finite difference and finite element techniques

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The prevalent model to describe propagation of neural membrane voltage responses to ion currents is the cable equation. The cable equation is a parabolic-type partial differential equation, which is frequently studied with the use of compartmental models. This paper explores other solution techniques for this type of partial differential equation, specifically the finite difference and finite element methods, and compares these methods to the traditional compartmental model solutions.

I. INTRODUCTION

The dynamics of neuron behavior is most commonly modeled by the Hodgkin-Huxley formulation, which describes the time rate of change of neural membrane voltage. The original model was based on the giant squid axon, and postulates that the membrane voltage changes due to a combination of ion currents through ion channels with voltage-dependent membrane conductances.[1]

$$\frac{dV}{dt} = \frac{1}{C_m}\Big(g_{Na}(V_{Na} - V) + g_K(V_K - V) + g_L(V_L - V) + I\Big) \tag{1}$$

Here, V is the membrane potential (mV), C_m is the specific membrane capacitance ($\mu F/cm^2$), I is an applied current (mA), V_L is the leakage reversal potential, V_K is the potassium reversal potential, V_{Na} is the sodium reversal potential, g_L is the leakage conductance density (mS/cm^2), and g_K and g_{Na} are the potassium and sodium conductance densities, which are generally functions of additional dynamical variables. Given initial conditions for the voltage and the other dynamical variables, the Hodgkin-Huxley equations give a fully deterministic and continuous model to describe the dynamics of a neural membrane.

This model does not describe how the membrane potential propagates down the axon and dendritic structure of a neuron, and thus communicates a signal to neighboring neurons in a network. For this, the voltage equation must be modified by an additional term, which describes the spatial dependence of the voltage. This equation is called the cable equation, and is of the form:[2]

$$\frac{\partial V}{\partial t} = \frac{1}{C_m}\left(\frac{a}{2R}\frac{\partial^2 V}{\partial x^2} - gV + J\right) \tag{2}$$

Where a is the cable (axonal or dendritic) diameter, R is the membrane resistance, and all currents (ionic, leakage, etc ...) are captured in J. In general, all parameters appearing on the right hand side of this equation are functions of space and time. This equation, coupled with the Hodgkin-Huxley dynamics, then gives a full description of the dynamics of action potential propagation down an axon.

Equations of the form given by equation (2) are called parabolic partial differential equations (PDEs). This type of PDE is characterized by one temporal derivative and two spatial derivatives. Without the nonlinear dynamics associated with the ion currents (J term), the solution to equation (2) is similar to that for the more familiar heat and diffusion equations. The typical mathematical solution for parabolic PDEs is by the finite difference or finite element methods.

II. DISCUSSION

The majority of neuronal models are solved using compartmental methods. Compartmental methods do not use the full PDE formulation, but instead utilize the ordinary differential equations (ODEs) associated with Hodgkin-Huxley like dynamics with additional coupling terms to related the spatial dependence between compartments. Thus, the dynamical variables within each compartment are spatially constant, and this set of coupled equations can be solved using the usual methods for ODEs. This approach is valid for cases where the local geometry of the axonal and dendritic structure is not important, but is a mathematically distinct problem than the original PDE cable equation.

A. Finite Difference Method

The finite difference method is similar to compartmental models, but explicitly discretizes both space and time in order to reduce the system of equations to a linear algebra form. For space discretization, various methods are used which show different convergence and stability characteristics. The most basic discretization is the forward-Euler method:[3]

$$C_m \frac{V_i^{t+1} - V_i^t}{\Delta t} = \frac{d}{4R_i} \frac{V_{i+1}^t - 2V_i^t + V_{i-1}^t}{\Delta x^2} - G_m V_i^t - J_i^t \tag{3}$$

Here, the subscripts denote the spatial coordinates, and the superscripts denote the time coordinates. The forward-Euler method is an explicit method, meaning that knowledge of the voltage at a given time step will allow the calculation of the voltage at the subsequent time step. Therefore, this method is very easy to implement, but it unfortunately has undesirable numerical properties. If the constant λ is defined by $\lambda = a\Delta t / 2RC(\Delta x)^2$, then the forward-Euler method is known to be numerically unstable when $\lambda > 1/2$. Since this inequality includes both Δt and Δx, increased spatial fidelity will typically require increased temporal fidelity in order to maintain solution stability. Thus, the forward-Euler method can be computationally intensive, and is seldom utilized.

To overcome this stability concern, the backward-Euler method is used. This method is an implicit method, meaning that knowledge of the voltage at a given time step will allow the calculation of the voltage at the previous time step. For the cable equation, the backward-Euler discretization is:

$$C_m \frac{V_i^{t+1} - V_i^t}{\Delta t} = \frac{d}{4R_i} \frac{V_{i+1}^{t+1} - 2V_i^{t+1} + V_{i-1}^{t+1}}{\Delta x^2} - G_m V_i^{t+1} - J_i^{t+1} \tag{4}$$

The backward-Euler method does not have the numerical instabilities that the forward-Euler method suffers from, and thus Δt and Δx can be chosen independently. Both the forward- and backward-Euler methods have error of $O(\Delta t) + O((\Delta x)^2)$.[4]

The third commonly used discretization method is the Crank-Nicolson method.[5] For this method, the right hand side is the average of the forward- and backward-Euler methods. This is again in implicit method with no numerical instabilities (similar to the backward-Euler method), but the Crank-Nicolson method has numerical accuracy of $O((\Delta t)^2) + O((\Delta x)^2)$.

$$C_m \frac{V_i^{t+1} - V_i^t}{\Delta t} = \frac{1}{2}\left(\frac{d}{4R_i} \frac{V_{i+1}^{t+1} - 2V_i^{t+1} + V_{i-1}^{t+1}}{\Delta x^2} - G_m V_i^{t+1} - J_i^{t+1} + \frac{d}{4R_i} \frac{V_{i+1}^t - 2V_i^t + V_{i-1}^t}{\Delta x^2} - G_m V_i^t - J_i^t \right) \tag{5}$$

Thus, with any of these finite difference discretizations, the cable equation can be transformed into a system of equations that can be solved using linear algebra. For instance, the backward-Euler discretization, equation (4), can be rewritten in matrix form (with $J_i^{t+1} = 0$) as

$$V^{t+1} = B_b V^t \tag{6}$$

where the matrix B_b is given by:

$$B_b = [I - \frac{\lambda}{C_m} B - \frac{G}{C_m}]^{-1} \tag{7}$$

with G being a diagonal matrix with the nodal conductances on the diagonal, and the matrix B is a tri-diagonal matrix with -2 along the diagonal and ones on the off-diagonals. The boundary conditions for the problem are handled by the first and last rows of this matrix. The choice of boundary conditions depends on the physical situation to be modeled. The matrix described here implements Dirichlet boundary conditions, i.e., the voltage is clamped at the ends of the cable. For von Neumann boundary conditions ($\partial V / \partial x = 0$ on the boundary), the diagonal terms for the first and last row will change to be -1.

Computationally, the solution to the cable equation using finite differences involves solving this linear algebra problem. For the case of the forward-Euler discretization, this is simple, as no matrix inversion is necessary. As shown by equation (7), the backward-Euler method requires inversion, which can become computationally intensive for large problems. This extended computing time is typically preferred so as to avoid the stability issues with the explicit method.

B. Finite Element Method

Whereas the finite difference method approximates a PDE and solves it, the finite element method approximates the solution to a PDE. The finite element method is based on the variational form of the PDE and approximates the exact solution by a piecewise polynomial function. It more easily adapts to the geometry of the underlying problem domain than the finite difference method, and also can reduce to a finite linear system of equations.[4] For simple geometries, such as a one-dimensional cable in the cable equation, finite element methods can reduce to the same linear algebraic equations of the finite difference method. Finite element methods appear to be rarely used in axonic and dendritic modeling of the cable equation.

Altenberger et al used a finite element approach to model specific geometric aspects of action potential transmission.[6] They first showed that the numerical solutions of the cable equation using their finite element technique matched previously published solutions using compartment and finite differences methods, then proceeded to use the finite element methodology to model more complex morphology of the axon. For example, they varied the perimeter and cross sectional area along the cable, and determined the effects on action potential propagation.

The basis functions used are the typical piecewise linear triangular (tent) functions given by:

$$\begin{aligned} \phi_k(x) &= \frac{x - x_{k-1}}{x_k - x_{k-1}} \quad x \in (x_{k-1}, x_k) \\ &= \frac{x_{k+1} - x}{x_{k+1} - x_k} \quad x \in (x_k, x_{k+1}) \\ &= \quad 0 \qquad\quad otherwise \end{aligned} \tag{8}$$

Each of these tent functions is associated with a node x_k, where $0 = x_0 < x_1 < \ldots < x_n$. The elements are the intervals between the nodes along the axonal segment. The finite difference technique would estimate the solution at the nodes - the finite element technique estimates the solution within the element. The functions $\phi_k(x)$ collectively forma basis with respect to which the voltage, current, and any other functions (in this case area and perimeter) are represented by the expansions:

$$\begin{aligned} V(x,t) = \sum_{k=0}^{n} V_k(t)\phi_k(x), \qquad J(x,t) = \sum_{k=0}^{n} J_k(t)\phi_k(x) \\ A(x) = \sum_{k=0}^{n} A_k\phi_k(x), \qquad P(x) = \sum_{k=0}^{n} P_k\phi_k(x) \end{aligned} \tag{9}$$

The size of each element can be varied based on local geometry being modeled, and the degree of polynomial in the basis function (the given linear is the simplest case) can also be adjusted for the optimal solution to be constructed. For the Altenberger et al model, this choice of basis function results in a discretization, for instance for the left endpoint:

$$\frac{x_1 - x_0}{12}[(3P_0 + P_1)(C_m\frac{dV_0}{dt} + J_0(t)) + (P_0 + P_1)(C_m\frac{dV_1}{dt} + J_1(t)] = \frac{g_m(A_0 + A_1)}{2(x_1 - x_0)}[V_1 - V_0] \tag{10}$$

With similar discretization for nodes $0 < k < b$ and the right endpoint. These equations can then be put in vector form and integrated to determine a solution.

III. RESULTS

The finite difference solution was modeled in MATLAB, with a demonstration shown in class of the passive cable equation. With no dynamic input current variables, the solution is essentially diffusive. Both the forward- and backward-Euler cases were shown, with specific emphasis on the instabilities invoked with the forward-Euler case. These solutions are not particularly interesting - the intention of this project was definitely slanted toward learning how to use MATLAB to solve such problems.

The more interesting case is with dynamic current variables, for instance using the Morris Lecar or Hodgkin Huxley model. This involves discretization of all dynamic variable equations, with a substitution of the dynamic variable at a given timestep back in to the cable (voltage) equation. Unfortunately, I was not able to make this work correctly in MATLAB, but this should produce the propagating action potential that the cable equation solves for.

MATLAB includes a partial differential equation toolkit, which uses the finite element method to solve PDEs. I was not able to successfully run this toolkit with the passive cable equation, to compare the results to the finite difference case. However, the Altenberger et al paper is a definitive source to show how the finite element method can be used for specific problems were geometry is important. In terms of simple geometries, this method showed excellent agreement with standard published results using other methods.

IV. CONCLUSION

This project sought to determine the relative strengths and weaknesses of compartmental, finite difference, and finite element methods when applied to the cable equation. The most well-known and frequently used method is the compartmental method, which does not mathematically solve the cable equation. However, for the accuracy necessary in many neurodynamic models, compartmental models are sufficient to describe the dynamics of action potential propagation.

Finite element models could be useful in future work to model specific geometric features of axonic and dendritic structures, such as different membrane properties or flaring radii, but this level of detail is typically not necessary when modeling network behaviors except in specific cases. For simple geometries, the finite element model reduces to essentially the same linear algebra finite difference model, which will remain the predominant numerical model to describe the cable equation. The finite difference method allows for more spatial fidelity of solutions than compartmental models, and is more accurate (in a mathematical sense) solution to the cable equation. Rall[7] shows that the traditional compartmental model with compartment size shrunk to zero returns the finite difference solution. Thus, for the simple one-dimensional geometric cable models that are typically in use, all three methods essentially reduce to the same thing.

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