EFFICIENT COMPUTATION OF BRANCHED NERVE EQUATIONS

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Three simple improvements are presented which, for a given accuracy, result in a 10–20-fold decrease in computation time for simulation of arbitrarily branched active cables with Hodgkin Huxley (HH) kinetics. The first improvement takes advantage of the essentially tridiagonal character of the matrix equation for each branch of a 'tree' network and solves the equations as efficiently as for an unbranched cable. The second improvement evaluates the HH membrane conductances at the midpoint of a time step, Δt, to maintain full second order accuracy, $0(\Delta t^2)$, with no increase in the number of computational steps. The third improvement makes use of 'premultiplied' HH rate function tables for very efficient second order correct integration of HH membrane conductance.

Introduction

In order to fully understand and interpret electrical activity (excitation and impulse propagation) in neurons and neuron networks, it is necessary to solve the equations describing current flows. This paper presents several improvements to the usual methods of solving the Hodgkin Huxley (HH) (1952) branched cable equations which result in a significant decrease in computation time for a given accuracy. This makes such simulations convenient on even small computers. Although these improvements are illustrated with reference to HH kinetics, the concepts involved are immediately generalizable to other kinetic systems incorporated into the cable equations.

Statement of problem

The one dimensional HH cable equation,

$$\frac{1}{2\pi a}\frac{\partial}{\partial x}\left(\frac{\pi a^2}{R_a}\frac{\partial V}{\partial x}\right) = C_m\frac{\partial V}{\partial t} + I_{\mathrm{HH}} \tag{1}$$

is used to describe a single branch of an arbitrary tree structure. Here, a is the branch radius (in general a function of x), V is the potential across the membrane (mV), C_m is specific membrane capacitance ($\mu F/\mathrm{cm}^2$), R_a is axial

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resistivity (Ω cm) and I_{HH} is the HH membrane current* (amps/cm^2). Each of the three terms in Eqn. 1 has the units of current/area. The quantity in parentheses on the left hand side of Eqn. 1 is the axial current in the branch. When branches are connected together to form a node, conservation of charge requires that the axial currents flowing into the node equals the membrane current flowing out of the node.

$$\frac{1}{(\text{node area})} \sum_{\substack{\text{branches} \\ \text{into} \\ \text{node}}} \pm \left(\frac{\pi a^2}{R_a} \frac{\partial V}{\partial x} \right) = C_m \left. \frac{\partial V}{\partial t} \right|_{\text{node}} + I_{HH} \tag{2}$$

Here, the $\pm$ merely cautions that the direction of the axial current must be taken into account in the sum. A special case of Eqn. 2 is the 'sealed end' boundary condition in which one end of a branch does not connect to any other branch. In the limit as the end area approaches 0, this condition is commonly written,

$$\left. \frac{\partial V}{\partial x} \right|_{\text{end}} = 0 \tag{3}$$

*In the HH formalism the ionic current is defined as

$$I_{HH} = \bar{g}_{Na} m^3 h (V - E_{Na}) + \bar{g}_K n^4 (V - E_K) - g_L (V - E_L)$$

where m, h, and n are voltage and time dependent variables varying between 0 and 1 satisfying equations of the type

$$\frac{dm}{dt} = \alpha_m - (\alpha_m + \beta_m) m$$

The α's and β's are rate functions in units of ms^{-1} and at 6.3°C are given by

$$\alpha_m = \frac{0.1(-V + 25)}{e^{(-V+25)/10} - 1}$$

$$\beta_m = 4e^{-V/18}$$

$$\alpha_h = 0.07e^{-V/20}$$

$$\beta_h = 1/(e^{(-V+30)/10} + 1)$$

$$\alpha_n = \frac{0.01(-V + 10)}{e^{(-V+10)/10} - 1}$$

$$\beta_n = 0.125e^{-V/80}$$

The rate functions must be multiplied by a factor of three for every 10°C increase in temperature. Other constants are $\bar{g}_{Na} = 0.120\ \Omega/\text{cm}^2$, $\bar{g}_k = 0.036$, $g_L = 0.0003$, $E_{Na} = 115$ mV, $E_K = -12$, and $E_L = 10.598$.

The second order correct ($0(\Delta x^2, \Delta t^2)$), numerically stable, finite difference form of Eqn. 1 occurs often in the literature (Cooley and Dodge, 1956; Joyner *et al.*, 1978) and is expressed by

$$A_{i,i+1}V_{i+1}(t+\Delta t/2) - (A_{i,i+1}+A_{i,i-1})V_i(t+\Delta t/2) + A_{i,i-1}V_{i-1}(t+\Delta t/2)$$
$$= \frac{2C_m}{\Delta t}(V_i(t+\Delta t/2) - V_i(t)) + I_{HH}(t+\Delta t/2) \tag{4}$$

with

$$A_{i,i+1} = \frac{1}{2\pi a_i \Delta x}\frac{\pi a_{i+1/2}^2}{R_a \Delta x} \tag{5}$$

and

$$A_{i,i-1} = \frac{1}{2\pi a_i \Delta x}\frac{\pi a_{i-1/2}^2}{R_a \Delta x} \tag{6}$$

The subscript on 'a' denotes the branch position in units of Δx at which the radius is to be evaluated. Note that each term of Eqn. 4 is evaluated at $t + \Delta t/2$. This tridiagonal system of equations advances V from time t to time $t + \Delta t/2$ by what is called a fully implicit time step. Subsequently, if V is advanced to time $t + \Delta t$ via an explicit time step through the equation,

$$V(t+\Delta t) = 2V(t+\Delta t/2) - V(t), \tag{7}$$

then the advance over the full interval from t to $t + \Delta t$ is equivalent to the Crank-Nicholson method (Crank and Nicholson, 1947). This method is numerically stable for any Δt and is thus appropriate for stiff systems. Alternate implicit and explicit half time steps avoid the computational overhead involved in the usual Crank–Nicholson equation where $(V(t+\Delta t) + V(t))/2$ is substituted for $V(t+\Delta t/2)$ in Eqn. 4. At a branch node the finite difference form of Eqn. 2 is similar to Eqn. 4, except that the number of coupled voltage variables at the node is one more than the number of connecting branches.

1. Efficient solution of a branched cable system

For a given Δx, if Δt is taken small enough so that the off diagonal matrix elements in Eqn. 4 are much smaller than the diagonal elements, then Eqn. 4 can be solved most efficiently by a relaxation technique (Gerald, 1970). More than adequate accuracy for neurophysiological purposes can be obtained using a Δt of 25 μs, however, and in that case Gaussian elimination becomes more efficient. This section describes efficient use of Gauss elimination for solution of

the branched cable equation. By taking note of the relationships between the branch segments in the corresponding coefficient matrix, we have developed a method of solution with a minimum number of matrix manipulations.

Figure 1 illustrates the coefficient matrix for a particular nerve 'tree'. Application of the Gaussian method of elimination (Gerald, 1970) involves upper triangularization of the coefficient matrix followed by back substitution. By judicious application of the upper triangularization 'function' to selected tridiagonal parts of the coefficient matrix, one can eliminate each far off diagonal element in a single step. This results in much increased computational efficiency and is a generalization of the method used by Zeevi (1971) for three intersecting branches.

Conceptually, the upper triangularization of a tree structure proceeds as follows. Choose any branch, which is not connected at both ends to other branches, and number its finite difference segments so that the unconnected end is the last segment. The first segment of this 'trunk' is called a node. All branches connecting to this node have their segments numbered so that their last segment connects to the node. Their first segments are also called nodes, and this segment-numbering process continues until the segments of all branches of the tree are numbered. The last numbered branches, 'twigs', all have one end (the first segment of the twigs) unconnected. As implied by the formulation of Eqn. 2, a node is the center of a Wye network. This is simpler and generates fewer matrix coefficients than having the first segment of the trunk and the last segments of the branches connected together in the equivalent Delta network.

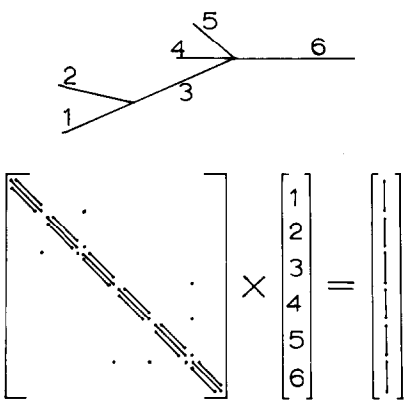

Fig. 1. An example of a branched cable and the form of its finite difference matrix equation. The position of the branches in the matrix equation is reflected in the membrane voltage vector, V_j. Most of the equations for a branch form a tridiagonal system but connected branches can generate non-zero far off diagonal elements.

This numbering process ensures that all far off diagonal coefficients in the lower triangular portion of the matrix are associated with the first (node) equation of a branch. Also, all far off diagonal elements of the upper triangular portion are associated with the last equation of a branch's tridiagonal system. The coefficient matrix in Fig. 1 was constructed using branch 6 as the trunk.

Now, upper triangularize each twig of the tree. The last equation for each twig can then be used to eliminate, in a single step, one far lower triangular element in the node equation of the branch that the twig connects to (the upper triangular element in the last equation of each twig affects only the diagonal element of the node equation). When all lower diagonal elements of a node have been eliminated, the branch, of which this node is the first segment, can then be upper triangularized. This process continues until the truck is upper triangularized. Back substitution to solve for $V(t + \Delta t/2)$ is then standard*.

The procedure discussed in this section is not valid for modeling nerve networks containing feedback loops involving only electrical synapses. In that case the usual procedure must be employed to move the lower triangular coefficient connecting the pre- to the postsynaptic segment by one column at a time. The upper triangularization process will also create an upper triangular element at each step due to coupling of the post- to the presynaptic segment

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*To solve the matrix equation, $A_{i,j}V_j = \text{RHS}_i$, illustrated in Fig. 1 do the procedure TRIANG for the 6 branches in the order 1, 2, 4, 5, 3, 6 and then do the procedure BKSUB for the branches in the order 6, 3, 4, 5, 1, 2.

Procedure TRIANG

Do for i = second segment of the branch to the last segment of the branch

$$A_{i,i} = A_{i,i} - A_{i-1,i}(A_{i,i-1}/A_{i-1,i-1})$$

$$\text{RHS}_i = \text{RHS}_i - \text{RHS}_{i-1}(A_{i,i-1}/A_{i-1,i-1})$$

If the last segment, j, of the branch is connected to a node, k, then

$$A_{k,k} = A_{k,k} - A_{j,k}(A_{k,j}/A_{j,j})$$

$$\text{RHS}_k = \text{RHS}_k - \text{RHS}_j(A_{k,j}/A_{j,j})$$

Procedure BKSUB

If the last segment, j, of the branch is connected to a node, k

then, $V_j = (\text{RHS}_j - V_k A_{j,k})/A_{j,j}$

else, $V_j = \text{RHS}_j/A_{j,j}$

Do for i = next to last segment of the branch to the first segment of the branch

$$V_i = (\text{RHS}_i - V_{i+1}A_{i,i+1})/A_{i,i}$$

that must be taken into account during back substitution. Feedback loops involving at least one chemical synapse, however, can still be handled efficiently for the following reasons. To second order, the presynaptic potential at $t + \Delta t/2$ is independent of the postsynaptic potential at $t + \Delta t/2$, and there is no matrix element coupling the post- to the presynaptic segment. Thus, upper triangular matrix elements are not created during the upper triangularization process. Furthermore, to second order, the presynaptic potential does not directly affect the postsynaptic potential at $t + \Delta t/2$. Instead, the presynaptic potential controls the postsynaptic conductance via a kinetic scheme, and this case can be handled by the method detailed in the next section.

One other case involving loops occurs when simulating a voltage clamped neuron with the voltage recording and current injection electrodes at different places. Here again, one far off diagonal coefficient must be moved toward the diagonal one column at a time. This is not so vicious as the electrical synapse loop, however, since the electrodes would usually be placed in the same branch only a few segments apart**.

2. Second order accuracy in calculation of ionic currents

For complete second order accuracy in the simulation of Eqn. 1, it is also necessary for I_{HH} to be evaluated at the midpoint of the time step, $t + \Delta t/2$. At first sight, since I_{HH} is a non-linear function of V, it would seem necessary to find $I_{HH}(t + \Delta t/2)$ by some form of iterative procedure in which successive approximations to $I_{HH}(t + \Delta t/2)$ are computed until the entire Eqn. 1 is satisfied at $t + \Delta t/2$ (Cooley and Dodge, 1966). To avoid these iterations, most investigators have abandoned complete second order accuracy by using I_{HH} at time t (Joyner *et al.*, 1978). However, the non-linear nature of I_{HH} as a function of V occurs only through the voltage sensitive rate functions in the computation of m, h, and n. Thus, if the conductances at time $t + \Delta t/2$ can be placed in the coefficient matrix which multiplies the membrane potential, second order accuracy can be maintained without the use of successive approximations. This can be done by evaluating the HH rate equations for m, h, and n at time t (we already know $V(t)$) to obtain the second order correct expression,

$$\frac{m(t+\Delta t/2) - m(t-\Delta t/2)}{\Delta t} = \alpha_m(V(t)) - (\alpha_m(V(t)) + \beta_m(V(t)))\frac{m(t+\Delta t/2) + m(t-\Delta t/2)}{2} \quad (8)$$

In this equation, each term is evaluated at the midpoint of the interval from

**Advantage can also be taken of the fact that the voltage electrode passes no current and thus creates only one off diagonal element instead of two.

$t - \Delta t/2$ to $t + \Delta t/2$, and the only unknown is $m(t + \Delta t/2)$. In other words, since m, h, and n are not 'instantaneous' functions of V, the non-linear nature of the HH conductances does not require successive approximations to solve Eqn. 1 as long as V and m are evaluated a half time step apart. Figure 2 illustrates the increased accuracy that is obtained using this procedure. Since the second order calculation with $\Delta t = 25\ \mu s$ is more accurate than the first order calculation with $\Delta t = 5\ \mu s$, a five-fold relative decrease in computation time for that accuracy follows from the use of Eqn. 8.

3. 'Premultiplied' HH rate function tables

Collecting terms in Eqn. 8 yields,

$$m(t + \Delta t/2) = \left[\frac{\alpha_m}{\frac{1}{\Delta t} + \frac{1}{2}(\alpha_m + \beta_m)}\right] + \left[\frac{\frac{1}{\Delta t} - \frac{1}{2}(\alpha_m + \beta_m)}{\frac{1}{\Delta t} + \frac{1}{2}(\alpha_m + \beta_m)}\right] m(t - \Delta t/2) \tag{9}$$

Considerable improvement in computational efficiency is obtained if the terms in brackets are placed in tables as a function of V. In this case the advance of each HH variable can be accomplished by a single multiply and add after the appropriate table value has been looked up. In addition, table values may be interpolated if greater accuracy is desired (four place accuracy in rate values is

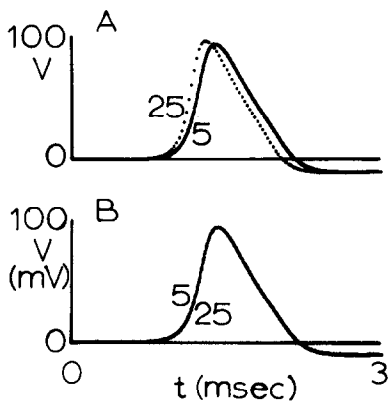

Fig. 2. Simulation of propagated action potentials (PAPs) at 16.3° in a uniform cable of diameter 500 μm and length 2.5 cm. The cable is stimulated at one end with a current of strength 15.7 μA and duration 100 μs. The time course of the membrane potential 2 cm from the point of stimulation is shown. A. PAPs computed with a Δt of 5 μs and 25 μs using first order correct ionic currents show that the simulation with $\Delta t = 25\ \mu s$ is inaccurate. B. PAPs computed with a Δt of 5 and 25 μs using the second order calculation of ionic conductance discussed in text (the two PAPs overlay). The 25 μs PAP in *B* is more accurate than the 5 μs PAP shown in A.

obtained using interpolated table entries 1 mV apart). Also, if the table value multiplying $m(t - \Delta t/2)$ is negative due to an excessively large rate at some voltage in conjunction with a too large Δt, a pure implicit method may be used to construct that particular table entry.

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References

A.L. Hodgkin and A.F. Huxley, *J. Physiol.*, **117** (1952) 500.
J.W. Cooley and F.A. Dodge, *Biophys. J.*, **6** (1966) 587.
R.W. Joyner, M. Westerfield, J.W. Moore and N. Stockbridge, *Biophys. J.*, **22** (1978) 155.
J. Crank and P.N. Nicholson, *Proc. Cambridge Phil. Soc.*, **43** (1947) 50.
G. Gerald, *Applied Numerical Analysis*, Ch. 7, Addison Wesley, 1970.
Y. Zeevi, Structural functional relationships in single neurons, *Ph.D. Thesis*, University of California, Berkeley, 1971.