Solving Hodgkin-Huxley equations using the compact difference scheme - tapering dendrite

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Summary

Dendritic processing is now considered to be important in pre-processing of signals coming into a cell. Dendrites are involved in both propagation and backpropagation of signals\(^1\). In a cylindrical dendrite, signals moving in either direction will be similar. However, if the dendrites taper, then this is not the case any more. The picture gets more complex if the ion channel distribution along the dendrite is also non-uniform. These equations have been solved using the Chebyshev pseudo-spectral method \(^2\). Here we look at non-uniform dendritic voltage gated channels in both cylindrical and tapering dendrites. For back-propagating signals, the signal is accentuated in the case of tapering dendrites. We assume a Hodgkin-Huxley formulation of ion channels and solve these equations with the compact finite-difference scheme. The scheme gives spectral-like spatial resolution while being easier to solve than spectral methods. We show that the scheme is able to reproduce the results obtained from spectral methods. The compact difference scheme is widely used to study turbulence in airflow, however it is being used for the first time in our laboratory to solve the equations involving transmission of signals in the brain.

Introduction

Dendritic morphology plays an important role in determining both orthodromic and antidromic propagation \(^3,4,5,6,7,8,9\). Additionally, the distribution of channels especially non uniform sodium channels in the dendrites influences the propagation of the signal. It is a combination of passive cable properties of dendritic membranes, sodium channel density and the diameter of the dendrite that influences the spike initiation in dendrites\(^10,11\). Additionally, tapering optimises charge transfer from all dendritic synapses to the dendritic root\(^12\).

In this paper we use the compact difference scheme to solve the Hodgkin Huxley equations as they pertain to a tapering unbranched dendrite with a point soma. There are two types of taper under consideration: linear and exponential. The distribution of sodium and potassium channels follows an exponentially decaying function along the dendrite. The problem has been solved using the Chebyshev pseudo-spectral method\(^2\). Assuming that there are just sodium, potassium and leak channels, these equations take the following form

\[
C_m \frac{\partial V}{\partial t} = \gamma_0(x) \frac{\partial^2 V}{\partial x^2} + \gamma_1(x) \frac{\partial V}{\partial x} - I_{ion} + I_{in}(x,t)
\]

\(1\)

\[
\gamma_0(x) = \frac{1}{2 R_i} \frac{r(x)}{\sqrt{(1 + r'^2(x))}}
\]

\(2\)

\[
\gamma_1(x) = \frac{1}{R_i} \frac{r'(x)}{\sqrt{(1 + r'^2(x))}}
\]

\(3\)

where \(r(x)\) is the radius of the dendrite, \(r'(x) = dr/dx\), \(C_m\) is the constant membrane capacitance, \(R_i\) is the constant axial resistivity, \(I_{ion} = I_{Na} + I_{K} + I_{L}\) and \(I_{in}\) is the injected current.

\[
I_{Na} = g_{Na}(x)n^3h(V - E_{Na}), I_{K} = g_{K}(x)n^4(V - E_{K}), I_{L} = g_{L}(V - V_{L})
\]

\(4\)
Equations for evaluating \( g_{Na} \) and \( g_K \) are given in reference 2. The evolution equations for the potassium activation particle \( n \) and sodium activation particle \( m \) and inactivation particle \( h \) are given by:

\[
\frac{dn}{dt} = \alpha_n(V)(1 - n) - \beta_n(V)n
\]  

\[
\frac{dm}{dt} = \alpha_m(V)(1 - m) - \beta_m(V)m
\]  

\[
\frac{dh}{dt} = \alpha_h(V)(1 - h) - \beta_h(V)h
\]

\( \alpha_n, \beta_n, \alpha_m, \beta_m, \alpha_h, \beta_h \) are evaluated from formulae given in reference 2.

When current is injected at the point soma \( (x = 0) \) only, \( I_{in} \) is omitted from equation 1 but appears in the boundary condition. Then in nondimensional form equation 1 is:

\[
C_m \frac{\partial V}{\partial T} = \gamma_0(x) \frac{\partial^2 V}{\partial X^2} + \gamma_1(x) \frac{\partial V}{\partial X} - I_{ion}
\]

where \( T = t/\tau_m \), \( X = x/\lambda \), \( \lambda = \lambda_{nontapered}(1 + ((2px)/d_1))^{1/2} \) cm, \( \rho \) is defined in equations 13, 15, \( d_1 \) is the diameter at the nontapering end, \( \tau_m = R_mC_m10^3 \) msec.

**Spatial discretisation:** Using compact finite difference schemes to solve the cable equation

Both the first and second derivative are approximated using the compact difference scheme. The equations used for approximating the second derivative are given in reference 14. Here we describe the equations used to approximate \( V' \).

\[
\beta V'_{i-2} + \alpha V'_{i-1} + V'_i + \alpha V'_{i+1} + \beta V'_{i+2} = \frac{c(V_{i+3} - V_{i-3})}{6h} + \frac{b(V_{i+2} - 2V'_i + V_{i-2})}{4h} + \frac{a(V_{i+1} - V_{i-1})}{h}, \quad (2 < i < N - 1)
\]

where \( V'_i \) represents the finite difference approximation to the first derivative at node \( i \) and \( N \) is the maximum number of nodes in any given grid. The relations between the coefficients \( a, b, c \) and \( \alpha, \beta \) are derived by matching the Taylor series coefficients of various orders. We take (ref.13, equation 2.1.7)

\[
\alpha = \frac{1}{3}, \beta = 0, a = \frac{14}{9}, b = \frac{1}{9}, c = 0
\]

When \( \alpha = 1/3 \), the leading order truncation error becomes \( \frac{4}{3}h^6d^7V/dx^7 \) making it sixth-order accurate. (ref.13 - Table 1) For boundaries the formula chosen is (ref. 13, equation 4.1.1):

\[
V''_1 + \alpha V''_2 = \frac{aV_1 + bV_2 + cV_3 + dV_4}{h}
\]
For third order accuracy, the coefficients are (ref.13, 4.1.3):

\[a = \frac{(11 + 2\alpha)}{6}, \quad b = \frac{(6 - \alpha)}{2}, \quad c = \frac{(2\alpha - 3)}{2}, \quad d = \frac{(2 - \alpha)}{6}\]

The leading order truncation error (on the r.h.s of equation 10) is \((2(\alpha - 3)/4!)h^3d^4V/dx^4\).

Equations 10, 11 from reference 14 and equations 9 and 10 applied at interior points results in a matrix problem \(AV'' = B\) where A is tridiagonal and \(V''\) can be obtained easily.

**Time discretisation**

The values for \(V''\) and \(V'\) calculated from the compact-difference scheme were used to integrate the result in time using an explicit time stepping scheme - forward Euler. The scheme and its implementation is discussed in reference 14. Stability conditions requires the choice of the time step to be

\[\Delta T < \frac{\Delta X^2C_m\lambda^2}{\tau_m\gamma_0(X = 0)}\]

\(\gamma_0(X = 0)\) is maximum over the dendrite. \(\Delta T\) varies as shown in (ref.14, Table 1). The numerical integration in time has been done with an explicit scheme. Since spatial derivatives are obtained with a compact scheme, which is an implicit formula that requires the solution of a linear system, implicit time-stepping is not possible. Implicit time-stepping is desirable in the case of stiff equations. A work-around is to use a predictor-corrector scheme which uses an explicit step estimate from the predictor step in a corrector step which is also an explicit step. Computations were performed on a Toshiba Satellite Pro laptop using Octave in a Linux(Ubuntu) environment. The data used for simulations is given in (Table 1) and captions of (Fig. 2) and (Fig. 3).

**Configuration simulated**

The two sets of problems attempted here are as follows:

In the first spatio temporal evolution of \(V\) was examined in cylindrical, linearly and exponentially tapering dendrites. The linear taper of the dendrite is determined by

\[r(x) = \rho x + r(0)\]

\[\rho = (r(L) - r(0))/L\]

where \(r(x)\) is the radius at any given point, \(r(0)\) is the radius at \(x = 0\) and \(r(L)\) is the radius of the dendrite at \(x = L\) and \(l\) is the length of the dendrite. Values for \(r(0), r(L)\) and \(l\) are given in (Table 1).

In the second case exponential taper is determined by:

\[r(x) = r(0)exp(-\rho x)\]

\[\rho = ln[r(0)/r(L)]/L\]
Initial and boundary conditions are the same as given in reference 14. The current injection was initially on the soma. This was followed by injections on the dendrite. This is illustrated in (Fig. 1). In the second case, the effect of dendritic geometry on propagation and back propagation of action potential was examined. Here too cylindrical, linearly and exponentially tapering dendrites were examined. The current was injected at the dendritic tip in all cases.

Results are shown in (Fig. 2) and (Fig. 3). It can be seen in (Fig. 2) that stimulus on the soma or tip of dendrite in a cylindrical dendrite leads to the cell firing once for the given parameters. However in the case of linear and exponential tapering, the cells fires multiple times when current is injected at the soma but only once when it is injected at the tip of the dendrite despite increasing the stimulus intensity by 16 (paper uses 10 times) and 14 times for the linear and exponential tapering respectively. In (Fig. 2)b, distribution of ion channels $\lambda_{Na}, \lambda_{K}$ used is $-0.0025 \times 10^4 \text{cm}^{-1}$ and in (Fig. 2)c, $\lambda_{Na}, \lambda_{K}$ used is $-0.010 \times 10^4 \text{cm}^{-1}$. These values which are slightly different from those used in reference 2 yield the same number of firing as shown in the reference. In (Fig. 3), the stimulus intensity is greater than that used in the earlier figure and elicits a train of action potentials which propagate to the soma and back-propagate to the dendritic stimulus site (blue). In (Fig. 3)a, $\lambda_{Na}, \lambda_{K}$ used is $-0.010 \times 10^4 \text{cm}^{-1}$ which is slightly higher than that used in reference 2. This yields exactly the same number of firing as shown in (Fig. 3)a. Here too tapering reduces the firing seen when stimulus is applied at the dendrite. It has also been observed that a much higher stimulus intensity than that reported in the paper has been used by us to get the desired result.

Figure 1: Soma tapering dendrite construct
Figure 2: Simulation with differing geometry and location of stimulus. Exponentially distributed Na and K channels with $\lambda_{Na} = \lambda_K = -0.0075\,\mu m^{-1}$, and $g_{Na0} = 50\,mS/cm^2$, $g_{K0} = 12.5\,mS/cm^2$, $g_L = 0.1\,mS/cm^2$ was constant throughout the soma-dendrite length. Stimulus intensity at the soma (0\,\mu m) is 300\,\mu A/cm$^2$ in all cases (A-C) while for stimulation at the end of the dendrite (400\,\mu m) the following intensities were used: 338\,\mu A/cm$^2$ with cylindric geometry (D), and 3380\,\mu A/cm$^2$ and 4657\,\mu A/cm$^2$ with linear (E) and exponential tapering (F) respectively. The duration of the stimulus was 50\,ms in all cases, starting at 5\,ms.
Figure 3: Effects of dendritic geometry on the propagation and back-propagation of action potentials along the dendrite. In all cases, a dendritic stimulus of 50ms duration, starting at 5ms was applied. The amplitude changed in each case. (A) Cylindrical geometry: a stimulus of 750µA/cm². (B) Linear tapering of dendrite: stimulus intensity is 3750µA/cm². (C) Exponential tapering of dendrite: stimulus intensity is 5250µA/cm². (D) Exponential tapering: a near threshold stimulus 4393µA/cm². Note the different time scale on this record. soma, $i = 1$, — ; end of dendrite, $i = N$, —
Tables

Table 1: **Parameters of dendrite used in simulation**

| Parameter   | Values   |
|-------------|----------|
| length      | 400µ     |
| diameter d1 | 3.7µ     |
| diameter d2 | 0.3µ     |
| $R_m$       | $10^{-3}\Omega \cdot cm^2$ |
| $R_i$       | 320Ω \cdot cm |
| $C_m$       | $1^{-6}farad/cm^2$ |
| $\tau$      | 1^{-5} sec |
| $V_{Na}$    | 55 mV    |
| $V_K$       | -95 mV   |
| $V_L$       | -60 mV   |

Table 2: Resolving Efficiency $\epsilon$ of the first derivative schemes,(ref.13, Table 4)

| Scheme                  | $\epsilon = 0.1$ | $\epsilon = 0.01$ | $\epsilon = 0.001$ |
|-------------------------|------------------|-------------------|-------------------|
| Fourth order central    | 0.44             | 0.23              | 0.13              |
| Fourth order compact    | 0.59             | 0.35              | 0.20              |
| Sixth order tridiagonal | 0.70             | 0.50              | 0.35              |

Table 3: Injected current in (Fig. 2) and (Fig. 3)

| Figure | $I \mu A/cm^2$  ( paper) | $I \mu A/cm^2$  (actual) |
|--------|--------------------------|--------------------------|
| 2 e    | 3380                     | 5659                     |
| 3b     | 3750                     | 6720                     |
| 3c     | 5250                     | 5482                     |
| 3d     | 4393                     | 4810                     |

**Concluding Remarks**

In this paper we have used the compact finite difference scheme to solve the Hodgkin Huxley equations for a tapering dendrite. It has been shown that the scheme is robust and can reproduce the results seen in reference 2 in (Fig. 2) and (Fig. 3). Convergence as defined in reference 14 has been tested in (Fig. 3) (a, b, c) and it is seen that the solution is convergent. In all cases of injection of current from the dendritic end in tapering dendrites, the current used had to be changed slightly from that reported in reference 2. The values used by us are reported in (Table 3). In (Fig. 3), the plots in red are those of the action potentials generated at the soma and that in blue of those generated at the dendrite. The dendritic action potential occurs after the somatic action potential in both cylindrical and linearly tapering dendrites. In the exponentially tapering dendrite (Fig. 3), it is seen that the first dendritic action potential occurs before the somatic action potential. The second one occurs closer to the somatic...
action potential. This indicates variation in travelling speed of excitation from
dendrite to soma and back propagation.

We have provided here an alternate to the Chebyshev pseudo-spectral method
used in reference 2. This is an easier method to implement and can give spectral
like resolution depending on the scheme chosen. As shown in Table 2, for the
first derivative, at \( \epsilon = 0.001 \), the resolving efficiency of sixth order and fourth
order compact difference is higher than that of a fourth order central difference
scheme. By selecting different coefficients, this efficiency can be brought closer
to exact differentiation. The resolving efficiency for second derivative schemes
is shown in Table 3 (ref. 14). Here too it can be seen that the at \( \epsilon = 0.001 \),
the resolving efficiency of the sixth order tridiagonal and fourth order compact
scheme is higher than that of the central difference scheme.

As discussed in reference 14, implicit methods for time stepping cannot be
utilised. However, a corrector-predictor method can be used to circumvent the
issues involving this.

As discussed earlier, certain values of \( \lambda_{Na} \) and \( \lambda_K \) have had to be altered along
with the I values. In reference 14 it can be seen that both compact and fourth
order central schemes are affected similarly by these changes. Thus it is not
scheme specific.

This paper along with reference 14 thus shows that the compact scheme can be
used as an alternate method to solve the HH equations in both cylindrical and
tapering dendrites. By picking different coefficients, the spatial resolution at
given any error can be improved. It is our understanding that this is the first
time it has been used to solve these equations.

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Supplementary Information is available in the online version of the paper.

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