

Computer Simulations of 3D Action Potential Propagation in a Branched Cable Network

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Abstract

This project will focus on the propagation of action potentials along a tree structure. Specifically, the properties of action potentials along a parent branch as they lead into daughter branches will be modeled and observed. Hodgkin Huxley partial differential equations for electrical signaling in axons and dendrites and a numerical methodology (Crank-Nicolson) that solves equations like these on an arbitrary tree of cables will be employed. This is a continuous-time dynamical system of nonlinear differential equations used for approximating electrical properties of cells with excitable nature such as how action potentials in neurons are initiated and propagated. An applied instantaneous current at the terminal end of a branch will initiate propagation of action potentials heading towards a junction that splits off into daughter branches and the question that will be investigated is under what conditions the propagating wave fails or succeeds to enter to daughter branches.

1 Introduction

In an arbitrary neuron structure, there are axons and dendrites that share various physical and electrical properties of a cylindrical cable of a certain resistance with a current flowing through it. Arbitrary connections of various cables can form networks that allow signals to propagate and spread, allowing communication within the cell. Neurons also have the ability to make changes in the membrane potential by adjusting conductances of sodium and potassium channels along the surface of the cables. The electrical activity of neurons is responsible for sensation, action and thought, and is thus a fundamental physiological mechanism of great importance.

2 Methods

2.1 Mathematical Model

In order to model the tree structure of a neuron, we begin by using partial differential equations for an electrical cable in space and time. We define $i(x, t)$ to be the axial current along the cable at a particular position and time respectively and $I(x, t)$ to be the transmembrane current (positive perpendicular outward from the cable). $v(x, t)$ is the transmembrane voltage and r is the radius of the cylinder. We can use current conservation to note that:

$$i(x_1, t) - i(x_2, t) = \int_{x_1}^{x_2} I(x, t)(2\pi r)dx \quad (1)$$

$$\int_{x_1}^{x_2} \left(\frac{\partial i}{\partial x} + I2\pi r \right) dx = 0 \quad (2)$$

$$\frac{\partial i}{\partial x} + I2\pi r = 0 \quad (3)$$

Transmembrane current is given by the following equation:

$$I = C \frac{\partial v}{\partial t} + g(v - E) \quad (4)$$

where C is the membrane capacitance per unit area, g is the membrane conductance per unit area, and E is the reversal potential which will be defined later. Next we have the equation for axial current given by:

$$i = \frac{-\pi r^2}{\rho} \frac{\partial^2 v}{\partial x^2} \quad (5)$$

where ρ is the resistivity of the internal medium. Substituting the two current equations (4) and (5) back into (3) yields the following:

$$C \frac{\partial v}{\partial t} + g(v - E) = \frac{r}{2\rho} \frac{\partial^2 v}{\partial x^2} \quad (6)$$

Next we note that the ionic transmembrane current $g(v - E)$ actually has three components that flow through different membrane channels, namely sodium and potassium channels as well as leakage:

$$g(v - E) = g_{\text{Na}}(v - E_{\text{Na}}) + g_{\text{K}}(v - E_{\text{K}}) + g_{\text{L}}(v - E_{\text{L}}) \quad (7)$$

and from this we observe that

$$g = g_{\text{Na}} + g_{\text{K}} + g_{\text{L}} \quad (8)$$

$$E = \frac{g_{\text{Na}}E_{\text{Na}} + g_{\text{K}}E_{\text{K}} + g_{\text{L}}E_{\text{L}}}{g_{\text{Na}} + g_{\text{K}} + g_{\text{L}}} \quad (9)$$

Next we will consider the conductance dynamics. Hodgkin and Huxley characterized the membrane channels. Each potassium channel has four identical voltage dependent gates that open and close independently of each other. The rate constants for opening and closing a gate are given by known voltage dependent functions $\alpha_n(v)$ and $\beta_n(v)$ respectively. Sodium channels have three gates of one type and one gate of another type with rate constants $\alpha_m(v)$, $\beta_m(v)$ and $\alpha_h(v)$, $\beta_h(v)$. Conductances obey the following, where $s = m, n, h$ is the probability that the respective gate is open and \bar{g} means the conductance when all gates are open:

$$g_{\text{Na}} = \bar{g}_{\text{Na}} m^3 h \quad (10)$$

$$g_{\text{K}} = \bar{g}_{\text{K}} n^4 \quad (11)$$

$$g_{\text{L}} = \bar{g}_{\text{L}} \quad (12)$$

and we get the following differential equations for the three different gating variables:

$$\frac{\partial s}{\partial t} = \alpha_s(v)(1 - s) - \beta_s(v)s \quad (13)$$

The last thing we need to consider is the boundary conditions. Consider a junction in which L cables come together and are numbered $l = 1, 2, \dots, L$. At the terminal end of a branch, $L = 1$. We can inject a current $i_0(t)$ at the junction. We measure position x away from the junction and at the junction $x = 0$. The boundary conditions are the voltage is continuous and current adds up. In order to discretize the junctions, there is only one node needed there. Let the junction voltage be $v_0(t)$.

$$v_0(t) = v_1(t) = \dots = v_L(0, t) \quad (14)$$

$$i_0(t) = A_0 \left(C \frac{\partial v_0}{\partial t} + g_0(v_0 - E_0) \right) + \sum_{l=1}^L \left(\frac{-\pi r_l^2}{\rho} \right) \frac{\partial v_l}{\partial x_l}(0, t) \quad (15)$$

where

$$A_0 = \sum_{l=1}^L \frac{1}{2} (2\pi r_l \Delta x_l) \quad (16)$$

2.2 Computational Model Experiment

The tree that we consider for this study has a parent branch that leads into two daughter branches. We apply a constant step current $i_0(t)$ at $t = 0$ at the terminal end of the parent branch and particularly choose a value so that we achieve repetitive firing of action potentials that propagate towards the junction. To understand what happens when the current reaches the junction we look to the concept of equivalent cylinders introduced by Rall in 1962. The key assumptions here are that the distribution of the membrane channels are identical on each of the daughter branches and the terminals of the daughter branches are at equal distances electrically from the center junction. That is, the dimensionless length, which is the physical length scaled by the space constant λ , also known as the electrotonic length l , should be the same for each daughter branch to begin. The solutions for voltage along the daughter branches will be identical in this special case and the idea here derived by Rall is that the way the signal proceeds through to the daughter branches is equivalent to the way it would proceed through just one daughter branch with a scaled diameter and the same electrotonic length:

$$\sum_{i=1}^J d_i^{\frac{3}{2}} = d_{\text{new}}^{\frac{3}{2}} \quad (17)$$

where d_{new} is the diameter of the scaled daughter branch and d_i for $i = 1, \dots, J$ is the diameter of daughter branch i in the original tree.

Since we can scale an arbitrary number of finite branches down to just one, it is obvious that if we have propagating action potentials traveling toward the junction that leads into one daughter, that propagation will either fail or succeed at the junction. That means that in the equivalent tree case with numerous branches, the qualitative property that we should observe is an "all or none" phenomena, where current will either enter all daughters successfully or none of them. The way to predict whether propagation will fail or succeed is to compare the geometric ratios of the diameters using the $\frac{3}{2}$ rule. If, for a parent branch diameter d_P and daughter branches with diameter d_i :

$$\sum_{i=1}^J d_i^{\frac{3}{2}} \leq d_P^{\frac{3}{2}} \quad (18)$$

then propagation will succeed. If on the other hand

$$\sum_{i=1}^J d_i^{\frac{3}{2}} >> d_P^{\frac{3}{2}} \quad (19)$$

then we expect propagation to fail because there is too much membrane area to excite. Lastly, if

$$\sum_{i=1}^J d_i^{\frac{3}{2}} = d_P^{\frac{3}{2}} \quad (20)$$

propagation proceeds as if it were unbranched. This is a result called impedance matching.

For differential propagation, or the deviation from "all or none", to occur, it is only possible if the electrotonic lengths of the daughter branches are different. For example, by making the terminal of one branch very proximal to the junction electrically, while placing the terminal of another branch to be very far, an action potential can be excited in the branch with the proximal terminal but not the branch with the distal terminal.

3 Numerical Methods for the Hodgkin-Huxley Equations

To solve the differential equations presented in the model we use a generalized tridiagonal system on a tree of nodes. Consider an arbitrary connected graph G with no loops. The nodes of this graph may be numbered $1, \dots, N$ arbitrarily and pick node 1 to be the root. Between the root and any other node, there is a unique chain of nodes that connects them because of the fact that there are no loops. Any two successive nodes in this chain are called neighbors. Let $R(i)$ be the node that immediately precedes i or in other words is the rootward neighbor of i . The rootward neighbor is unique. We say $R(1) = 0$ for the root. Now let's consider the set of leafward neighbors of a node i , $L(i)$ which is the set of all neighbors of i except $R(i)$. If $L(i) = \emptyset$, then i is a "leaf node" or a terminal junction. A generalized tridiagonal system on the tree defined above is a linear system of the form:

$$-a_i v_{R(i)} + b_i v_i - \sum_{j \in L(i)} c_j v_j = W_i \quad (21)$$

Now let

$$v_j^k = v(j\Delta x, k\Delta t) \quad (22)$$

$$s_j^{k+\frac{1}{2}} = s(j\Delta x, (k + \frac{1}{2})\Delta t) \quad (23)$$

where $s = m, n, h$. Then for the interior spatial nodes, the differential equations (6) and (13) can be solved using the Crank-Nicolson method:

$$\frac{s_j^{k+\frac{1}{2}} - s_j^{k-\frac{1}{2}}}{\Delta t} = \alpha_s(v_j^k) \left(1 - \frac{s_j^{k+\frac{1}{2}} + s_j^{k-\frac{1}{2}}}{2}\right) - \beta_s(v_j^k) \left(\frac{s_j^{k+\frac{1}{2}} + s_j^{k-\frac{1}{2}}}{2}\right) \quad (24)$$

$$C \frac{v_j^{k+1} - v_j^k}{\Delta t} + g_j^{k+\frac{1}{2}} \left(\frac{v_j^{k+1} + v_j^k}{2} - E_j^{k+\frac{1}{2}}\right) = \frac{r}{2\rho} (D^+ D^- \frac{v^{k+1} + v^k}{2})_j \quad (25)$$

For boundary junction nodes we use the same numerical method to solve (15):

$$i_0^{k+\frac{1}{2}} = A_0 \left(C \frac{v_0^{k+1} - v_0^k}{\Delta t} + g_0^{k+\frac{1}{2}} \left(\frac{v_0^{k+1} + v_0^k}{2} - E_0^{k+\frac{1}{2}} \right) \right) + \sum_{l=1}^L \left(\frac{-\pi r_l^2}{2\rho \Delta x_l} \right) (v_{l1}^{k+1} + v_{l1}^k - v_0^{k+1} - v_0^k) \quad (26)$$

This method in (22) couples the junction point to its immediate neighbor nodes only, the same way (20) and (21) does for the interior nodes. This gives us a system of equations for v^{k+1} and coefficients a, b, c, W for the tridiagonal system.

4 Results

The main results produced were simulations that demonstrated the various cases discussed in the computational model section of this report. They empirically confirm the theory regarding Rall's derivations. The following exclusively considers the simplest tree case that would demonstrate the principles discussed above, where we have one parent that leads into multiple daughters. The more complex examples can be reduced down to this anyways, using the equivalent cylinder idea in succession.

4.1 All or none phenomena

Let l_1 and l_2 be the electrotonic lengths of the daughter branches. When $l_1 = l_2$ we expect an identical solution for the voltage along the respective branches. The two cases for success and failure are show in snapshots at instantaneous moments in time during the simulation where at $t = 0$ a step

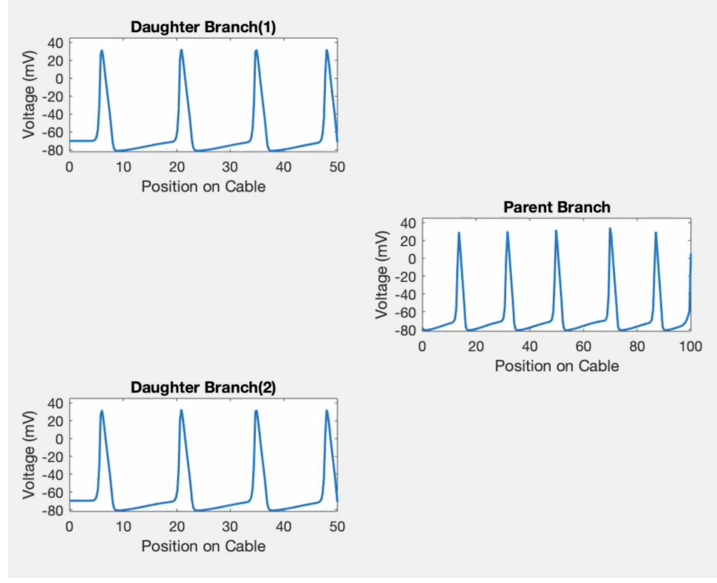


Figure 1: Time snapshot of the simulation shows the case where $\sum_{i=1}^J d_i^{\frac{3}{2}} \ll d_P^{\frac{3}{2}}$ resulting in successful entering of the signal into the daughter branches (direction of propagation is right to left).

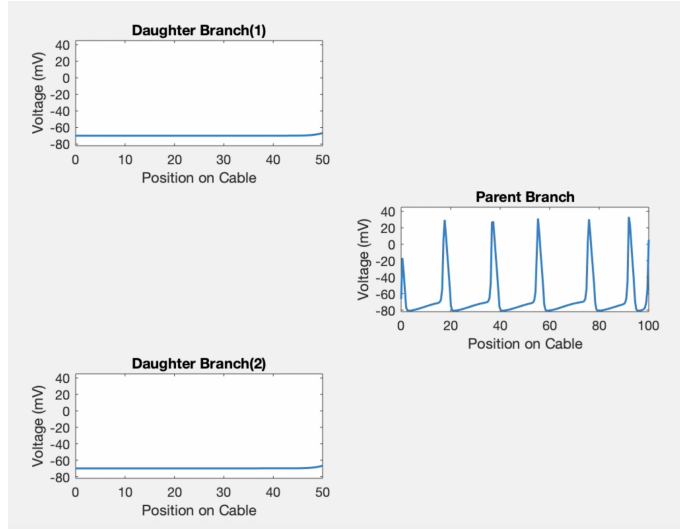


Figure 2: Time snapshot of the simulation shows the case where $\sum_{i=1}^J d_i^{\frac{3}{2}} \gg d_P^{\frac{3}{2}}$ resulting in successful entering of the signal into the daughter branches (direction of propagation is right to left).

current is applied at the terminal leaf node of the parent branch and maintained at a constant value for the entire experiment and is chosen at a value that excites repetitive firing of action potentials.

A quick quantitative check that we can do to confirm we are getting identical results on both daughter branches is to subtract the solutions of the corresponding nodes.

```

>> v(401:600)-v(201:400)
ans =
Columns 1 through 23
    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0
Columns 24 through 46
    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0
Columns 47 through 69
    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0
Columns 70 through 92
    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0
Columns 93 through 115
    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0
Columns 116 through 138
    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0
Columns 139 through 161
    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0
Columns 162 through 184
    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0
Columns 185 through 200
    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0    0

```

Figure 3: Voltage array at same time as snapshot in figure 1. Nodes 201 - 400 correspond to the nodes on daughter branch 1 while nodes 401-600 correspond to the nodes on daughter branch 2. It is clear that the solutions for the voltage are identical and even without round off error! This display is for the successful case, since the failure case is trivially constant at resting potential.

4.2 Differential Propagation

Now consider the case where $l_1 \neq l_2$, but $d_1 = d_2$. Particularly, we want to force excitation in one branch and not the other by exploiting the differences in the electrical distance of the terminals. The result in figure 4 shows that perhaps the placement of the terminals, electrically, is more important than the geometric ratios of the $\frac{3}{2}$ scaled diameters.

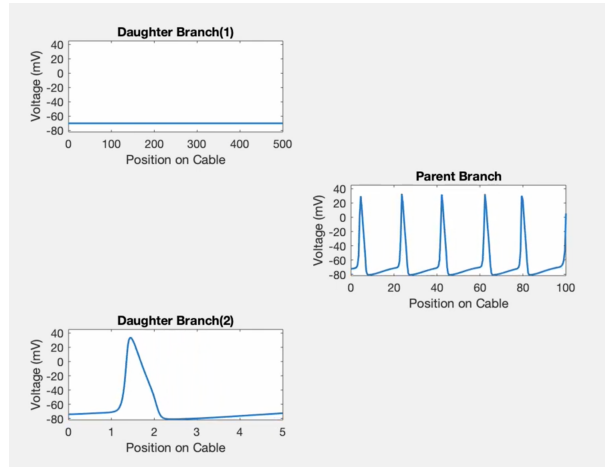


Figure 4: $l_1 \gg l_2$ resulting in successful propagation entering into the daughter branch with the terminal that is closer (electrically) to the junction (direction of propagation is right to left).

5 Conclusions

In this project, the theory introduced by Rall was empirically tested and confirmed in a computational simulation that solved electrical cable PDEs in space and time along with Hodgkin Huxley kinetics for active membranes for a general tree structure. The "all or nothing" excitability of a pair daughter branches with terminals at equal electrotonic distances from a junction receiving electrical input from a parent branch with a propagating action potential was shown by trying different geometric ratios between the scaled diameters of the parent and cumulative daughters. The differential propagation case, where the daughter branch terminals were at different electrical distances away from the junction was achieved, with the same diameter for the two daughters, by making one of the terminal ends very close to the junction and the other very far, which allows us to conclude that when we do not have equal electrotonic lengths of the daughter branches, the diameters of the cables become less important for propagation to succeed.

6 References

- [1] Peskin, Charles S. "Mathematical Aspects of Neurophysiology ." Hodgkin Huxley Equations. 2000.
- [2] Rinzel J, Rall W. Transient response in a dendritic neuron model for current injected at one branch. *Biophys J.* 1974;14(10):759-790. doi:10.1016/S0006-3495(74)85948-5