Revisiting Saltatory Conductance

Comparing Conductance in Myelenated and Unmyelenated Axons

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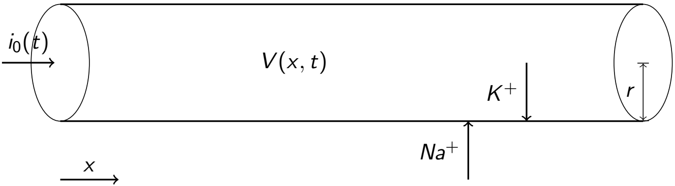
Numerical Methods 2, Spring'18

Outline

Outline

Hodgkin-Huxley Equations



$$
\begin{aligned}
V &= \text{voltage } (mV) \\
t &= \text{time } (msec) \\
x &= \text{distance along the axon } (cm) \\
i_0(t) &= \text{stimulating current} \\
r &= \text{radius of the cable} = 0.005 \ (cm) \\
\rho &= \text{axoplasmic resistivity}
\end{aligned}
$$

Hodgkin-Huxley Equation

$$C\frac{\partial V}{\partial t} = \frac{r}{2\rho}\frac{\partial^2 V}{\partial x^2} - \overline{g_{Na}}m^3h(V - E_{Na}) - \overline{g_K}n^4(V - E_K) - \overline{g_L}(V - E_{LP}) \tag{1}$$

$$\frac{dm}{dt} = \alpha_m(V)(1-m) - \beta_m(V)m \tag{2}$$

$$\frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n \tag{3}$$

$$\frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)h \tag{4}$$

$$\begin{aligned} C &= \text{capacitance per unit area}(\mu F/cm^2) \\ \overline{g_{Na}}, \overline{g_K} &= \text{membrane conductances}(k\Omega/cm^2) \\ m, h, n &= \text{activation and inactivation variables} \\ \alpha, \beta &= \text{activation functions} \\ E &= \text{Rest Potential} \end{aligned}$$

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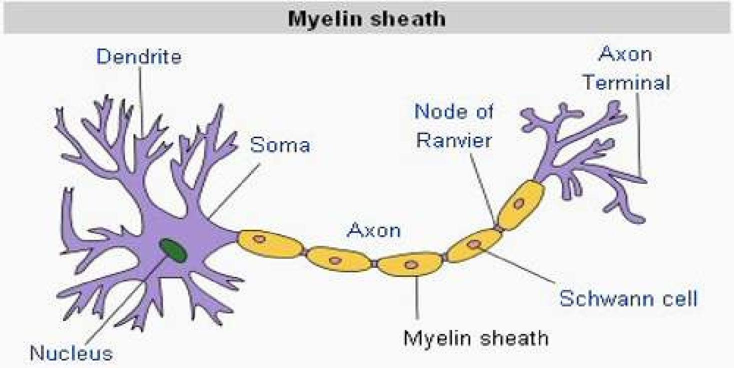
Myelenation



Modified Model

$$C_A \frac{\partial V}{\partial t} = \frac{r_A}{2\rho_A}\frac{\partial^2 V}{\partial x^2} - \overline{g_{Na}} m^3 h (V - E_{Na}) - \overline{g_K} n^4 (V - E_K) - \overline{g_L}(V - E_{LP}) \tag{5}$$

$$C_P \frac{\partial V}{\partial t} = \frac{r_P}{2\rho_P}\frac{\partial^2 V}{\partial x^2} - \overline{g_{LP}}(V - E_{LP}) \tag{6}$$

$$\frac{dm}{dt} = \alpha_m(V)(1 - m) - \beta_m(V) m \tag{7}$$

$$\frac{dn}{dt} = \alpha_n(V)(1 - n) - \beta_n(V) n \tag{8}$$

$$\frac{dh}{dt} = \alpha_h(V)(1 - h) - \beta_h(V) h \tag{9}$$

Boundary Condition

Starting Junction:

$$i(t) = -\frac{\pi r_A^2}{\rho_A}\frac{\partial V(0,t)}{\partial x} \tag{10}$$

$$i(t) = \begin{cases} i_0 & \text{if } t_1 \leq t \leq t_2 \\ 0 & \text{otherwise} \end{cases} \tag{11}$$

Active-Passive/Pasive-Active Interface:

$$0 = \frac{\pi r_A^2}{\rho_A}\frac{\partial V_A}{\partial x} + \frac{\pi r_P^2}{\rho_P}\frac{\partial V_P}{\partial x} \tag{12}$$

End Junction:

$$0 = \frac{\pi r_A^2}{\rho_A}\frac{\partial V(L,t)}{\partial x} \tag{13}$$

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Discretization

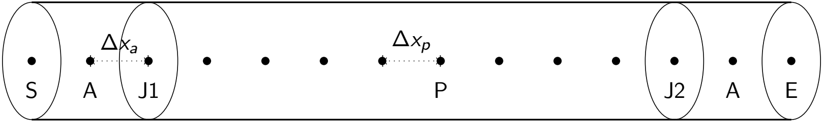
$$V_j^k = V(j\Delta x, k\Delta t) \tag{14}$$

$$s_j^{k+1/2} = s(j\Delta x, (k+1/2)\Delta t) \tag{15}$$

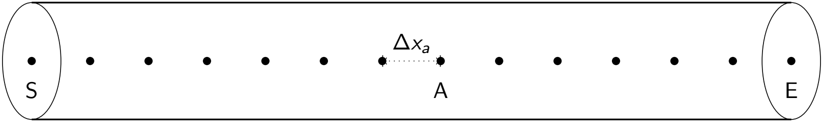
where s = m,n and h

Spatial Discretization

Myelenated Cable



Unmyelenated Cable



Discretization

$$\frac{s_j^{k+1/2} - s_j^{k-1/2}}{\Delta t} = \alpha_s(V_j^k)\left(1 - \frac{s_j^{k+1/2} + s_j^{k-1/2}}{2}\right) - \beta_s(V_j^k)\left(\frac{s_j^{k+1/2} + s_j^{k-1/2}}{2}\right) \quad (16)$$

Points A and P

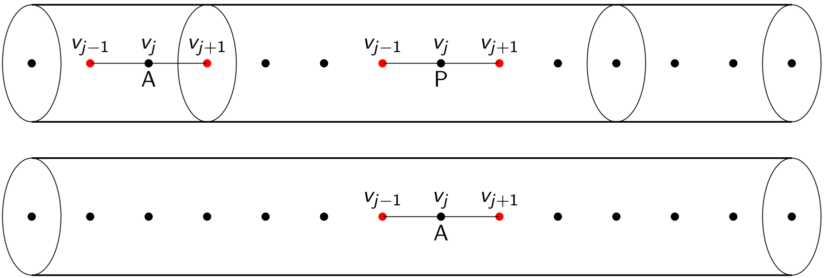
$$C_A \frac{V_j^{k+1} - V_j^k}{\Delta t} = -g_j^{k+1/2}\left(\frac{V_j^{k+1} + V_j^k}{2} - E_j^{k+1/2}\right) + \frac{r_A}{2\rho_A}\left(D^+D^-\frac{V^{k+1} + V^k}{2}\right)_j$$

$$C_P \frac{V_j^{k+1} - V_j^k}{\Delta t} = -g_{LP}\left(\frac{V_j^{k+1} + V_j^k}{2} - E_{LP}\right) + \frac{r_P}{2\rho_P}\left(D^+D^-\frac{V^{k+1} + V^k}{2}\right)_j$$

where

$$(D^+D^-\Phi)_j = \frac{\Phi_{j+1} - 2\Phi_j + \Phi_{j-1}}{\Delta x^2} \quad (17)$$

Spatial Discretization



Spatial Discretization

Discretization of the Junction Points involves expanding the $\partial V/\partial x$ term by Taylor series and substituting the second derivative using the Cable equation. Following this procedure the following junction equations are obtained

Start Point

$$i_0^{k+1/2} + \left(\frac{\pi r_A^2}{\rho_A}\right)\left(\frac{v_1^{k+1} + v_1^k - v_0^{k+1} - v_0^k}{2\Delta x}\right) = r_A \Delta x_A \left(C_A \frac{V_0^{k+1} - V_0^k}{\Delta t} + g_1^{k+1/2}\left(\frac{V_0^{k+1} + V_0^k}{2} - E_1^{k+1/2}\right)\right)$$

End Point

$$\left(\frac{\pi r_A^2}{\rho_A}\right)\left(\frac{v_{n-2}^{k+1} + v_{n-2}^k - v_{n-1}^{k+1} - v_{n-1}^k}{2\Delta x}\right) = r_A \Delta x_A \left(C_A \frac{V_{n-1}^{k+1} - V_{n-1}^k}{\Delta t} + g_1^{k+1/2}\left(\frac{V_{n-1}^{k+1} + V_{n-1}^k}{2} - E_1^{k+1/2}\right)\right)$$

Active-Passive Junction

The active to passive and passive to active interface points depend on their neighboring points and therefore have the properties of both the myelenated and unmyelenated cable.

$$\begin{aligned}\left(\frac{\widetilde{A}_j C}{\Delta t} + \frac{\widetilde{A}_j \widetilde{g}_j^{k+1/2}}{2} + D_P + D_A\right) V_j^{k+1} - D_P V_p^{k+1} - D_A V_A^{k+1} = \\ \left(\frac{\widetilde{A}_j C}{\Delta t} + \frac{\widetilde{A}_j \widetilde{g}_j^{k+1/2}}{2} - D_P - D_A\right) V_j^k + D_P V_P^k + D_A V_A^k\end{aligned} \tag{18}$$

Active-Passive Junction

where

$$
\begin{aligned}
\widetilde{A}_j &= \pi r_P \Delta x_P + \pi r_A \Delta x_A \\
\widetilde{g}_j &= \frac{1}{\widetilde{A}_j}(r_P \Delta x_P g_P + r_A \Delta x_A g_A) \\
\widetilde{E}_j &= \frac{1}{\widetilde{A}_j \widetilde{g}_j}(r_P \Delta x_P g_P E_P + r_A \Delta x_A g_A E_A) \\
D_A &= \frac{\pi r_A^2}{2\Delta x_A \rho_A} \\
D_P &= \frac{\pi r_P^2}{2\Delta x_P \rho_P}
\end{aligned}
$$

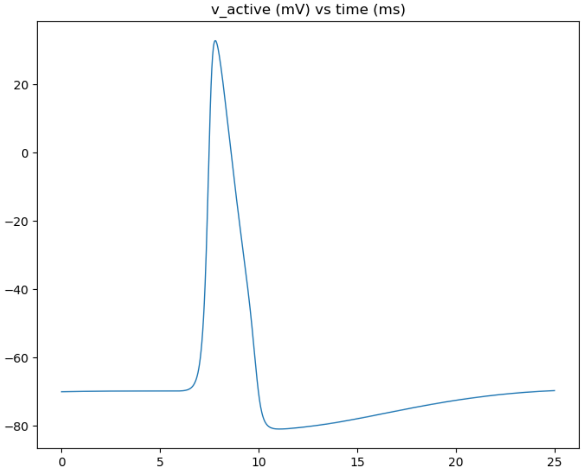
Tridiagonal System

These equations result in a tridiagonal system of the following form which can be solved by a back substitution algorithm in $O(n)$

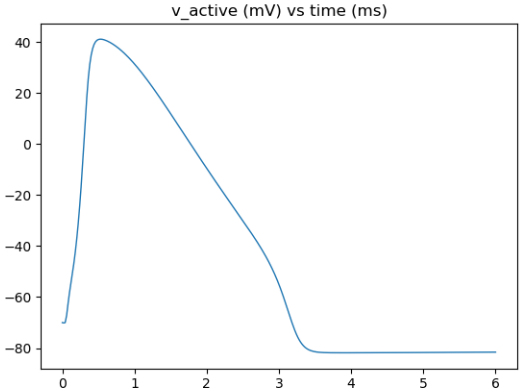
$$\begin{bmatrix} b_1 & c_1 & 0 & 0 & \dots & 0 \\ a_1 & b_2 & c_2 & 0 & \dots & 0 \\ 0 & a_2 & b_3 & c_3 & \dots & 0 \\ \vdots & \ddots & \ddots & \ddots & & \vdots \\ 0 & \dots & & 0 & a_{n-1} & b_n \end{bmatrix} \begin{bmatrix} \vdots \\ V_{j-1}^{k+1} \\ V_j^{k+1} \\ V_{j+1}^{k+1} \\ \vdots \end{bmatrix} = \begin{bmatrix} \vdots \\ d_{j-1}(V^k) \\ d_j(V^k) \\ d_{j+1}(V^k) \\ \vdots \end{bmatrix}$$

Outline

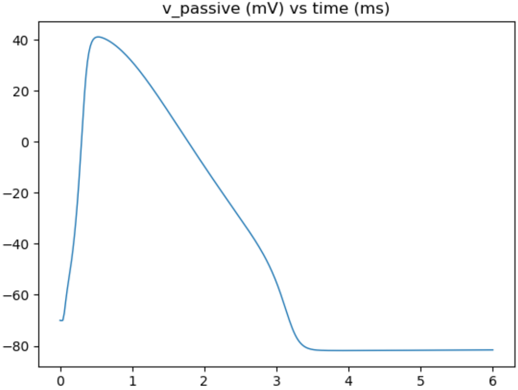
Action Potential



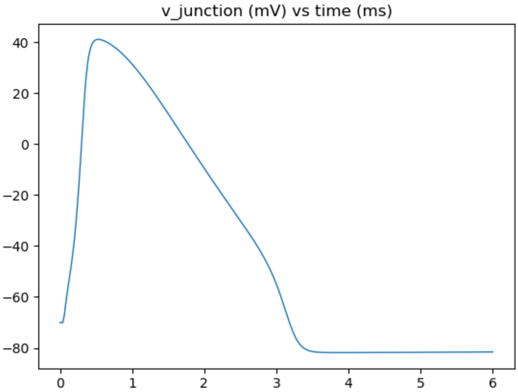
Action Potential



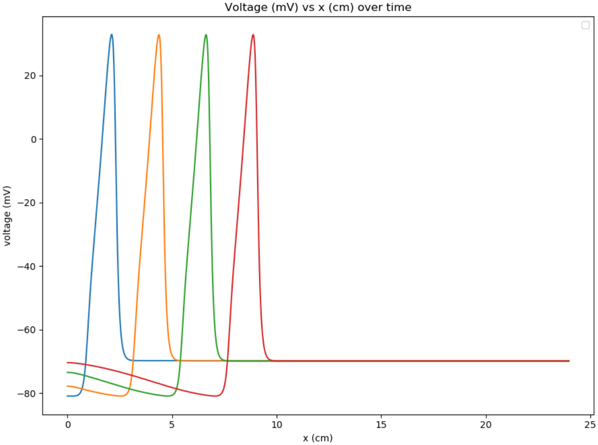
Action Potential



Action Potential

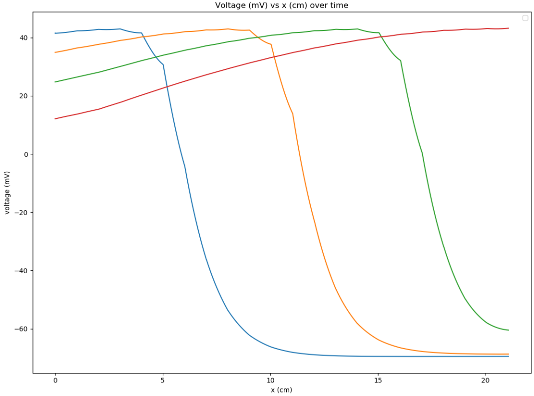


Action Potential



Frames taken at 4, 8, 12 and 16 msec

Action Potential



Frames taken at 0.4,0.8,1.2 and 1.6 msec

Outline

Unmyelenated Cable

The observed propagation speed for the myelinated cable was about 100 m/s as compared to 5 m/s for the unmyelinated cable.

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Convergence in time

t	p
0.202	1.9899
0.222	1.9618
0.244	1.9291
0.270	1.9208
0.300	1.8991
0.314	1.8991
0.332	1.8911
0.390	1.8809

Convergence in Space

x	p
0.5	2.046
0.58	2.052
0.66	2.059
0.72	2.069
0.78	2.082
0.86	2.114
0.92	2.173
0.98	2.419

Outline

Limitations

- Hyperpolarization
- Myelin-Node Length Ratio
- Convergence study in space for Myelenated Cable