Action Potential Propagation

MNS CP Project WS ‘19/20
with Roopa, Andrey, and Luke

Outline

- Introduction to the cable equation
- Method of solving the partial differential equation
- Usage with the Hodgkin-Huxley model
- Initiation of an action potential
- Propagation in a myelinated axon

Motivation

1. Create a model of an axon with various biological parameters that allow us to simulate action potential conduction.

2. Understand the impact of myelination on the spiking characteristics, as well as propagation velocity.

3. Illustrate what affect multiple action potentials within the same axon simultaneously has.

The Cable Equation

The Cable Equation

$$c_m \frac{\partial V}{\partial t} = \frac{1}{2ar_L} \frac{\partial}{\partial x}\left(a^2 \frac{\partial V}{\partial x}\right) - i_m + i_e$$

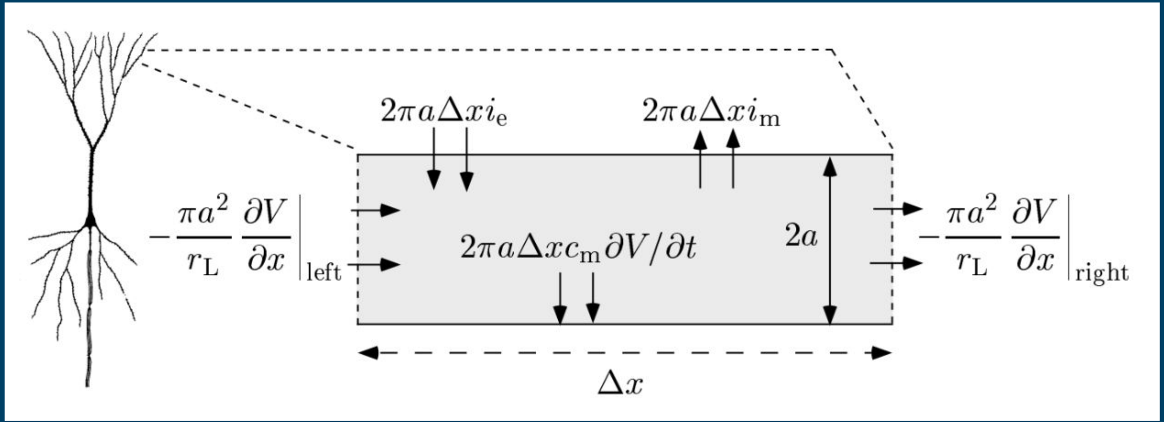

Figure 6.6 Dayan & Abbott, 2001

The Cable Equation

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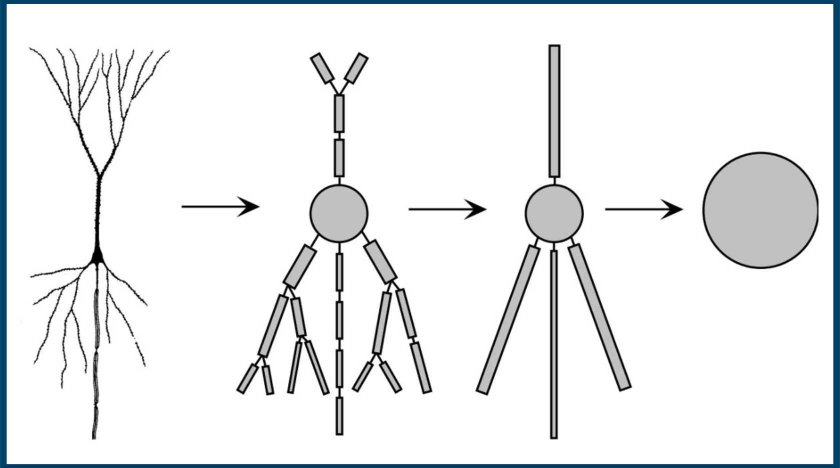
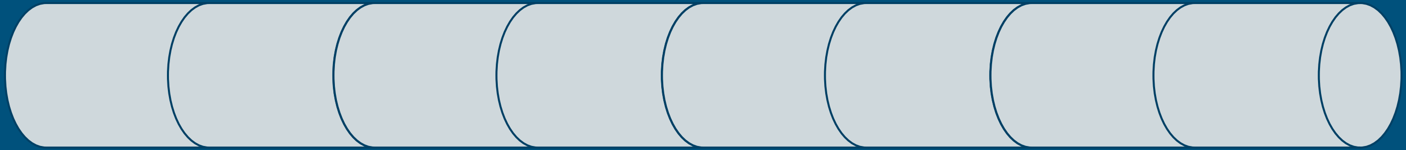


Figure 6.15 Dayan & Abbott, 2001

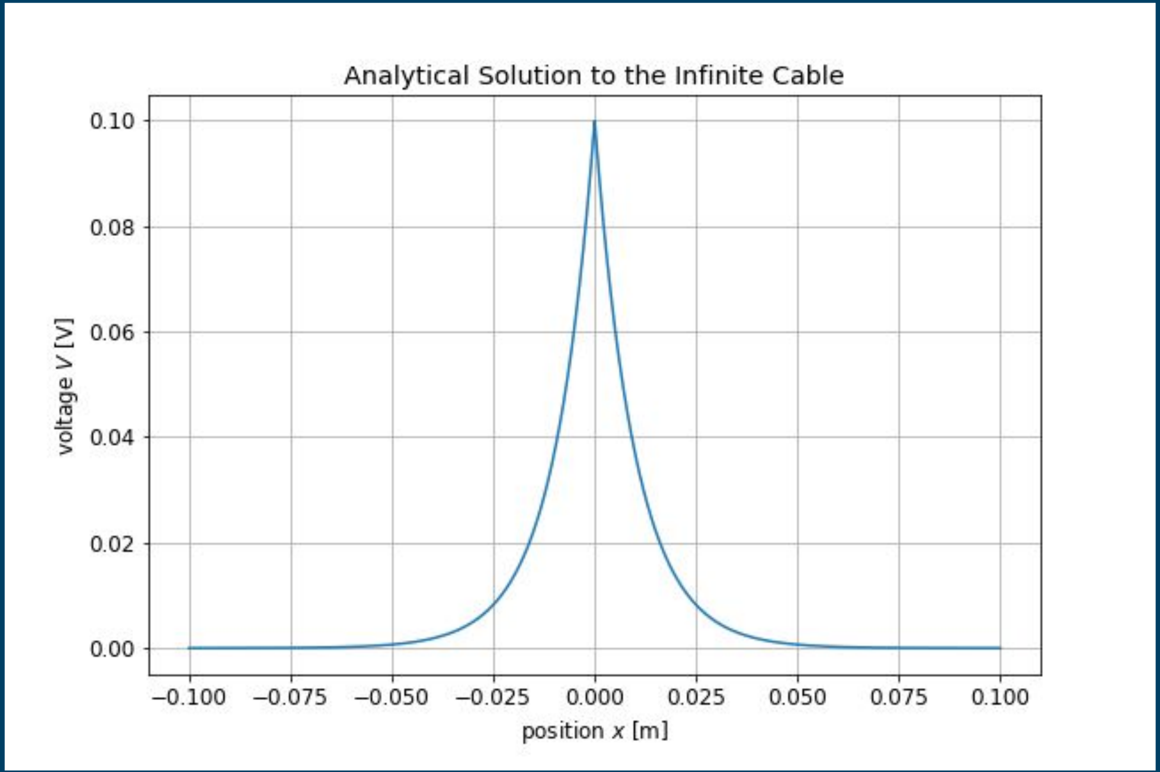
The Cable Equation

$$c_m \frac{\partial V}{\partial t} = \frac{1}{2ar_L} \frac{\partial}{\partial x}\left(a^2 \frac{\partial V}{\partial x}\right) - i_m + i_e$$



Assumptions:

- Constant axon radius *a*
- Identical compartment size
- No branching



The Analytical Solution to the Infinite Cable

Cable equation reduces to ODE in static case

$$c_m \frac{\partial v}{\partial t} = \frac{1}{2ar_L}\frac{\partial}{\partial x}\left(a^2 \frac{\partial v}{\partial x}\right) - i_m + i_e$$

Current is steady, implying no change over time, therefore: $\frac{\partial v}{\partial t} = 0$

$$0 = \frac{1}{2ar_L}\frac{\partial}{\partial x}\left(a^2 \frac{\partial v}{\partial x}\right) - i_m + i_e$$

Rearranging terms: $$\frac{dv}{dx^2} = \frac{2r_L}{a}(i_m - i_e)$$

Substituting: $i_m = \frac{V - V_{rest}}{r_m} = \frac{v}{r_m}$

$$\frac{dv}{dx^2} = \frac{2r_L}{ar_m}(v - i_e r_m) \Rightarrow \lambda^2 \frac{dv}{dx^2} = v - i_e r_m$$

[$i_e = 0$ everywhere except the site of injection (x=0)]

$$\lambda^2 \frac{\partial v}{\partial x^2} = v$$

$$v(x) = B_1 e^{(-x/\lambda)} + B_2 e^{(x/\lambda)}$$

At ends of cable, B = 0. Iat x=0, as we want the solution to be continuous, B1=B2=B, and the solution: $v(x) = Be^{(-|x|/\lambda)}$

To find B: current injected = current diffusing away from x

In the region around x: $\frac{dv}{dx} = -\frac{B}{\lambda} e^{\left(\frac{-|x|}{\lambda}\right)}$, where $e^{\left(\frac{-|x|}{\lambda}\right)}$ is approx. = 1, giving $-B/\lambda$. (Other side is B/λ)

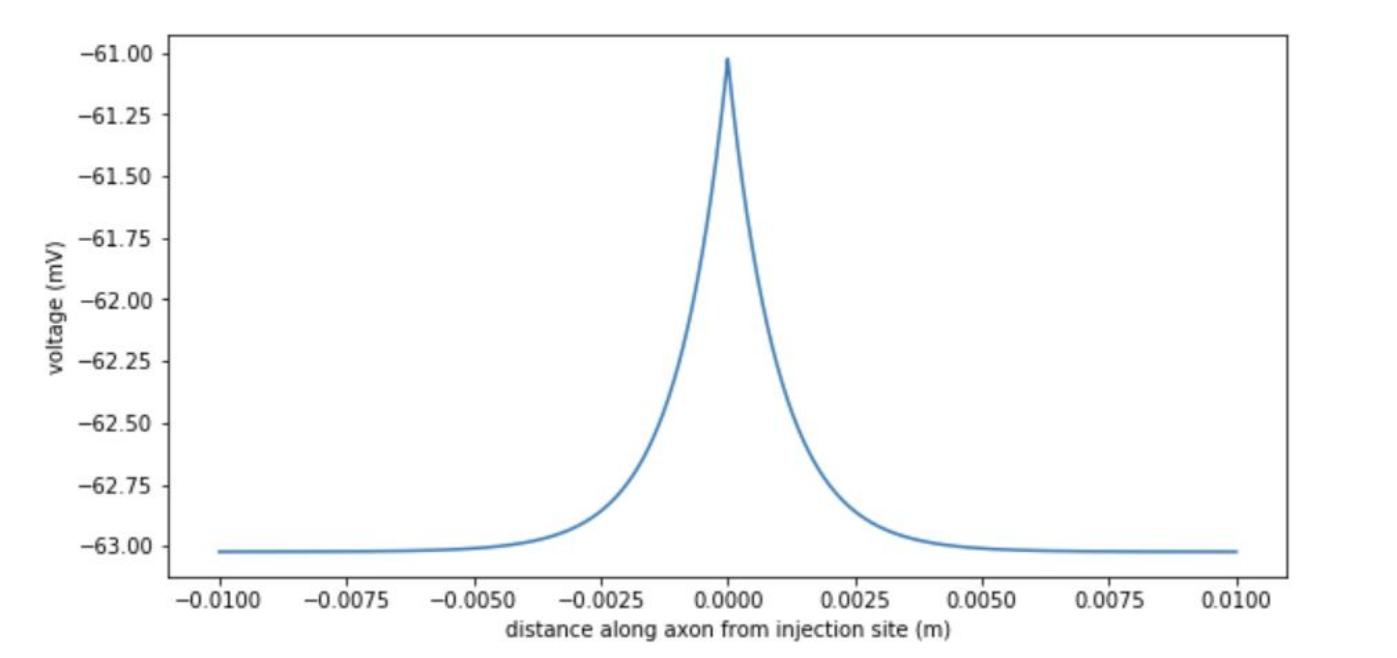
Second derivative: $\frac{d^2 v}{dx^2} = -\frac{2B}{\lambda \Delta x}$

Substituting in cable equation: $-2\lambda^2 B/\lambda\Delta x = -r_m I_e/2\pi a x$, which gives: $B = I_e R_\lambda/2$

Therefore: $v(x) = \frac{I_e R_\lambda}{2} e^{(-|x|/\lambda)}$

Numerical solution:

Membrane voltage along axon (steady current injection in middle of axon)



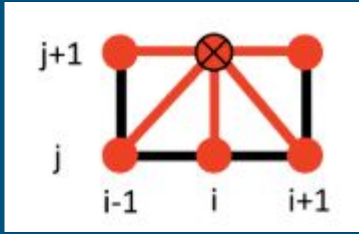
Numerical Solution of PDEs

Crank-Nicolson Method: Theory

- For problems which involve an update in both time and space, to increase accuracy, "implicit“ methods of numerical analysis are preferred, e.g. the Crank-Nicolson scheme.
- time derivative evaluated with the "forward differencing" approach, but spatial derivative evaluated at a time in between the current and next time point
- get a system of linear equations to be solved simultaneously

$$\frac{\partial v}{\partial t} = \frac{\partial v}{\partial x^2}$$

$$\frac{v_{i,j+1} - v_{i,j}}{\Delta t} = \frac{v_{i+1,j+1/2} - 2v_{i,j+1/2} - v_{i-1,j+1/2}}{\Delta x^2}$$
$$= \left(\frac{v_{i+1,j+1} - 2v_{i,j+1} - v_{i-1,j+1}}{\Delta x^2} + \frac{v_{i+1,j} - 2v_{i,j} - v_{i-1,j}}{\Delta x^2} \right)$$



Crank-Nicolson Method: Application

Coupled equations are solved as follows:

$$c_m \frac{dV_\mu}{dt} = -i_m^\mu + \frac{I_e^\mu}{A_\mu} + g_{\mu,\mu+1}(V_{\mu+1} - V_\mu) + g_{\mu,\mu-1}(V_{\mu-1} - V_\mu)$$

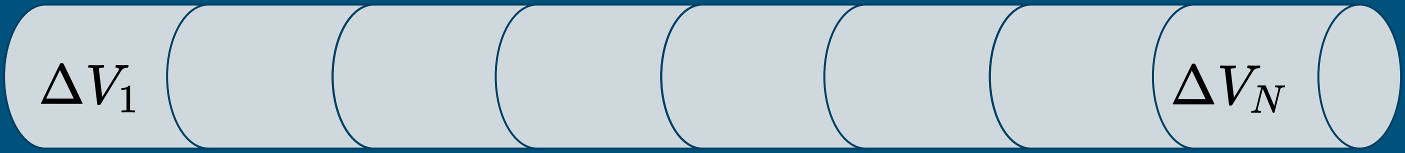
1. starting from compartment #1, we get the voltage, ΔV_μ, in terms of $\Delta V_{\mu+1}$.
2. At the last compartment , using the boundary condition, we obtain ΔV_N, and substitute it in the previous equation, and continue solving backwards until compartment #1.

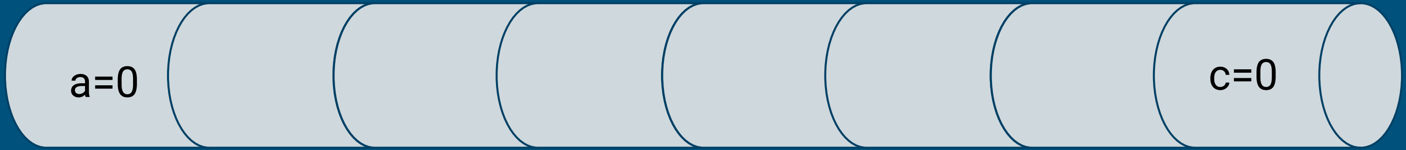
$$\frac{dV_\mu}{dt} = A_\mu V_{\mu-1} + B_\mu V_\mu + C_\mu V_{\mu+1} + D_\mu$$

$$A_\mu = \frac{g_{\mu,\mu-1}}{c_m} \quad B_\mu = \frac{\sum_i g_i^\mu + g_{\mu,\mu+1} + g_{\mu,\mu-1}}{c_m}$$

$$C_\mu = \frac{g_{\mu,\mu+1}}{c_m} \quad D_\mu = \frac{\sum_i g_i^\mu E_i + \frac{I_e^\mu}{A_\mu}}{c_m}$$

$$\Delta V_\mu = (A_\mu V_{\mu-1}(t + z\Delta t) + B_\mu V_\mu(t + z\Delta t) + C_\mu V_{\mu+1}(t + z\Delta t) + D_\mu)\Delta t$$





$$\Delta V_\mu = (A_\mu V_{\mu-1}(t+z\Delta t) + B_\mu V_\mu(t+z\Delta t) + C_\mu V_{\mu+1}(t+z\Delta t) + D_\mu)\Delta t$$

$$V_\mu(t+z\Delta t) = V_\mu(t) + z\Delta V_\mu$$

$$\Delta V_\mu = a_\mu \Delta V_{\mu-1} + b_\mu \Delta V_\mu + c_\mu \Delta V_{\mu+1} + d_\mu$$

$$a_\mu = A_\mu z\Delta t$$

$$b_\mu = B_\mu z\Delta t$$

$$c_\mu = C_\mu z\Delta t$$

$$d_\mu = (D_\mu + A_\mu V_{\mu-1}(t) + B_\mu V_\mu(t) + C_\mu V_{\mu+1}(t))\Delta t$$

Solve ΔV_μ equation sequentially for each compartment, in terms of $\Delta V_{\mu+1}$

$$\Delta V_{\mu-1} = \frac{c_{\mu-1}\Delta V_\mu + d'_{\mu-1}}{1-b'_{\mu-1}}$$

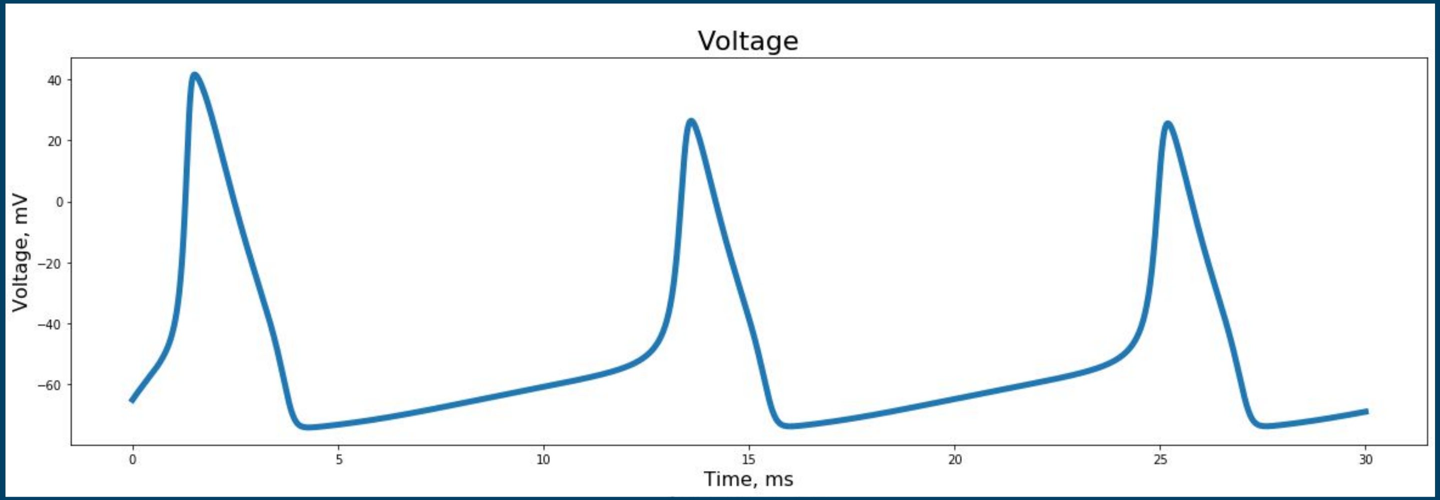
At end of cable use boundary condition to find ΔV_N, and substitute backwards to get all ΔV_μ

Hodgkin-Huxley model

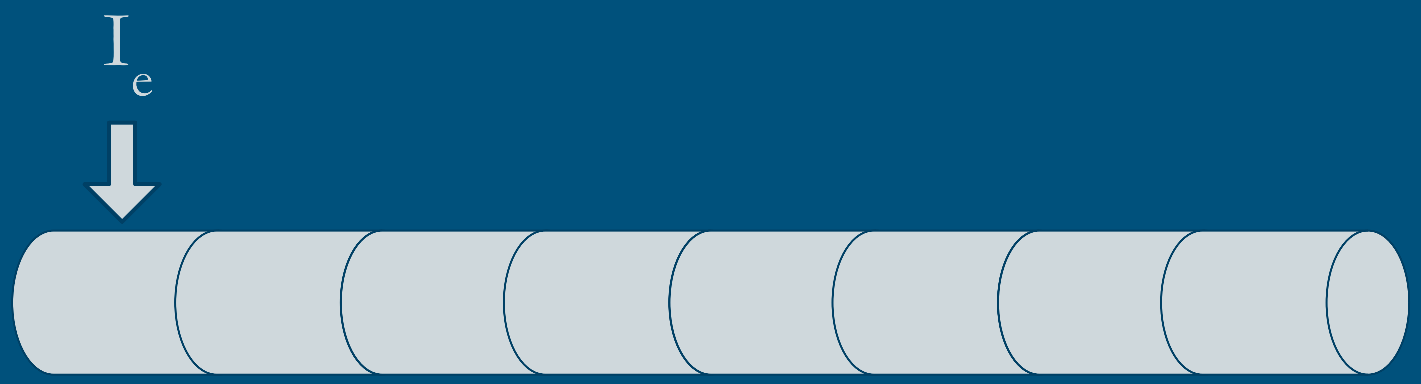
The Hodgkin-Huxley Model

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

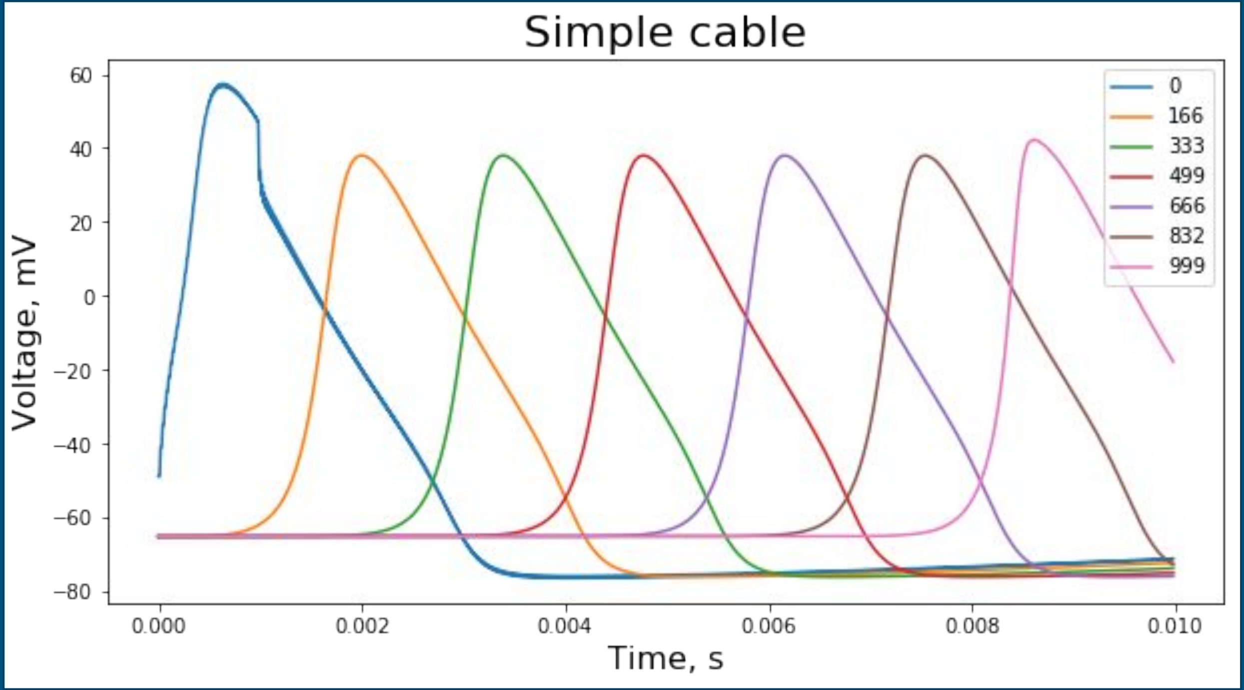
$$\frac{dx}{dt} = \alpha_x(V)(1 - x) - \beta_x(V)x$$

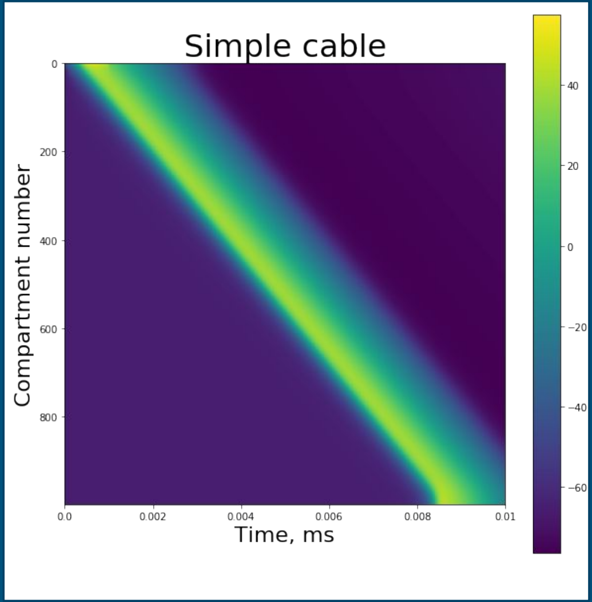


Initiating an action potential



Initiating an action potential





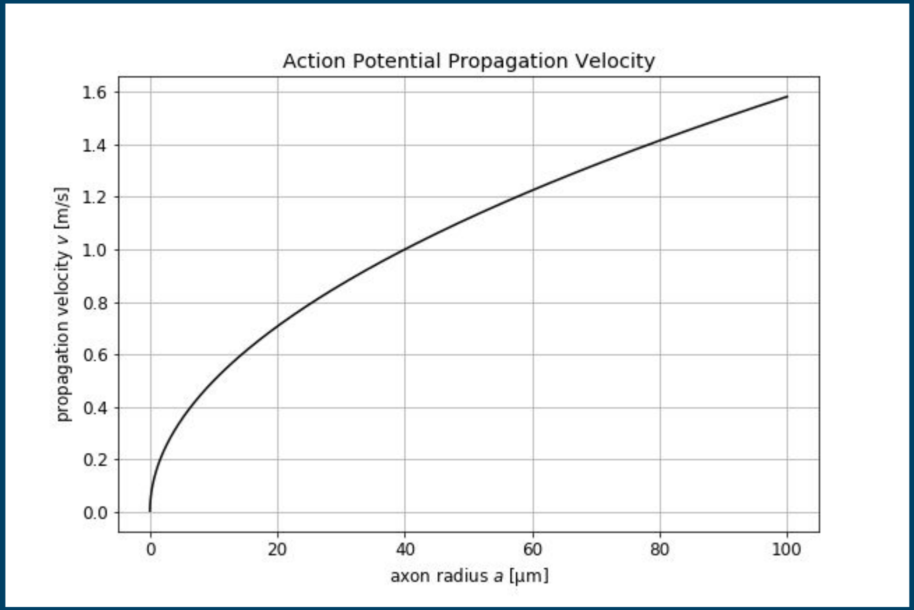
$$v \equiv \frac{x}{t_{max}} = \frac{2\lambda}{\tau_m}$$

$$\tau_m = r_m c_m$$

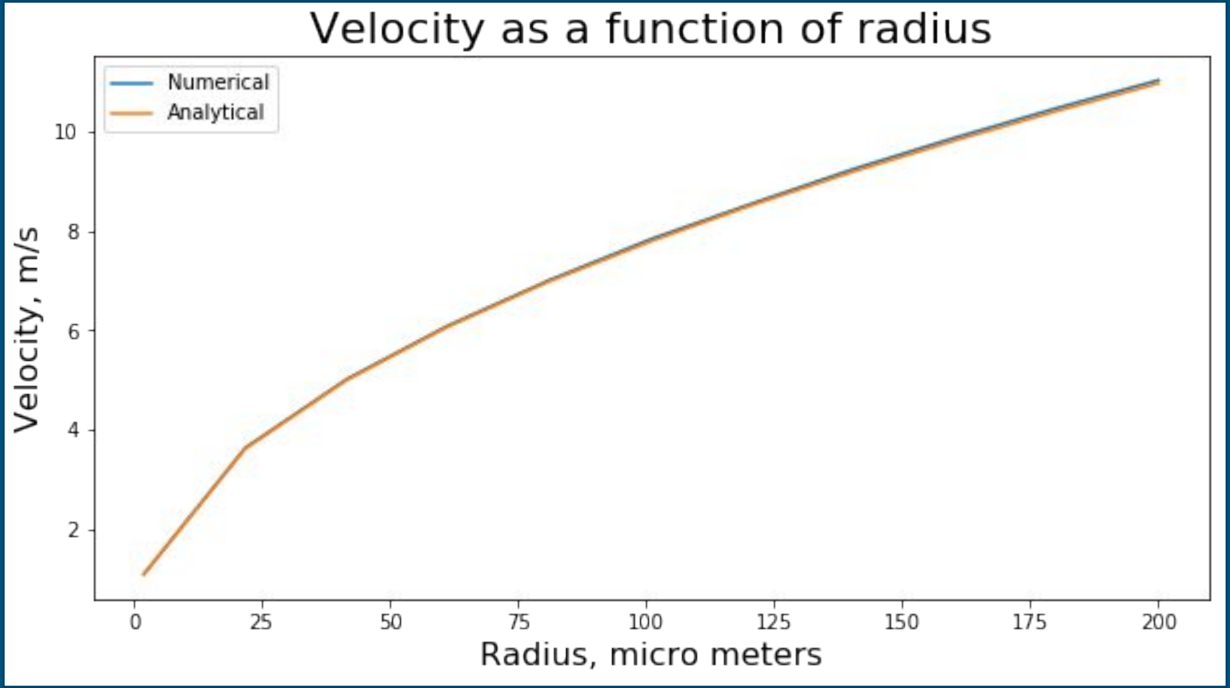
$$\lambda = \sqrt{\frac{r_m a}{2 r_L}}$$

$$v = \frac{2}{r_m c_m}\sqrt{\frac{r_m a}{2 r_L}} = \frac{1}{c_m}\sqrt{\frac{2a}{r_m r_L}}$$

$$v \propto \sqrt{a}$$

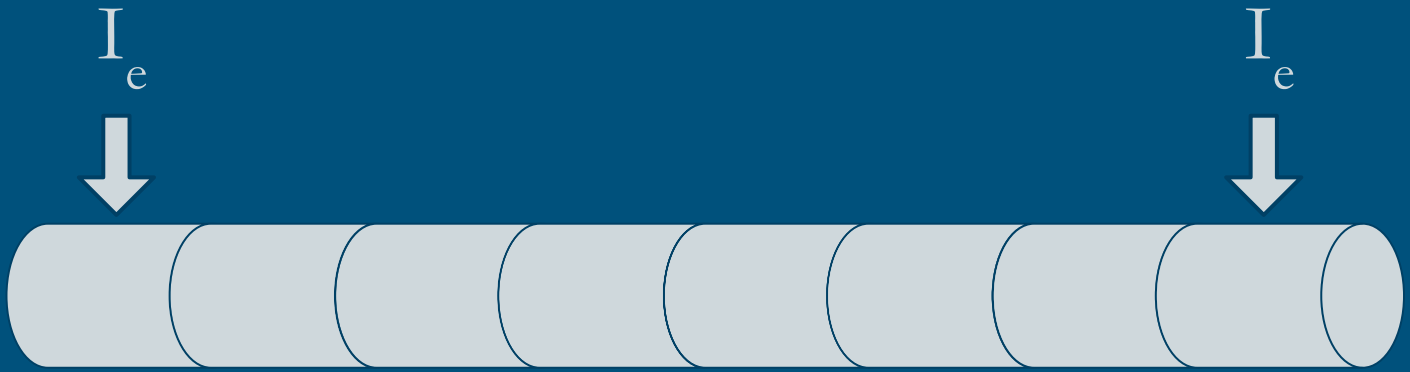


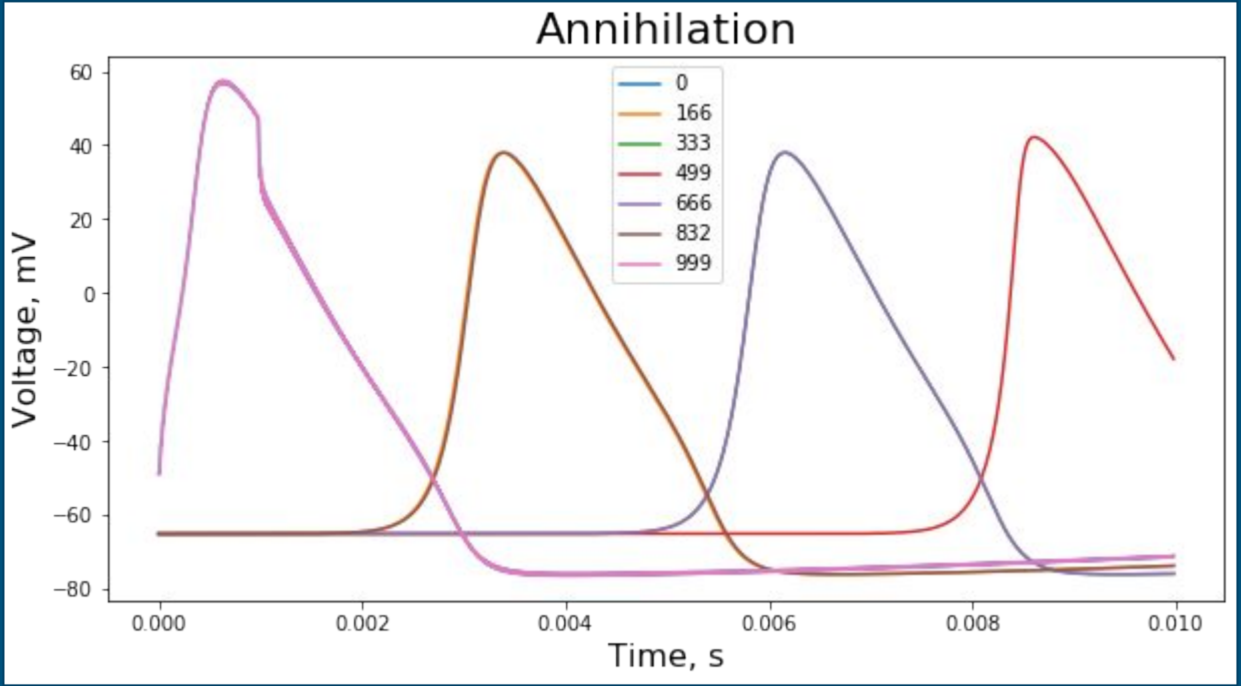
Action Potential Propagation Velocity - Analytically

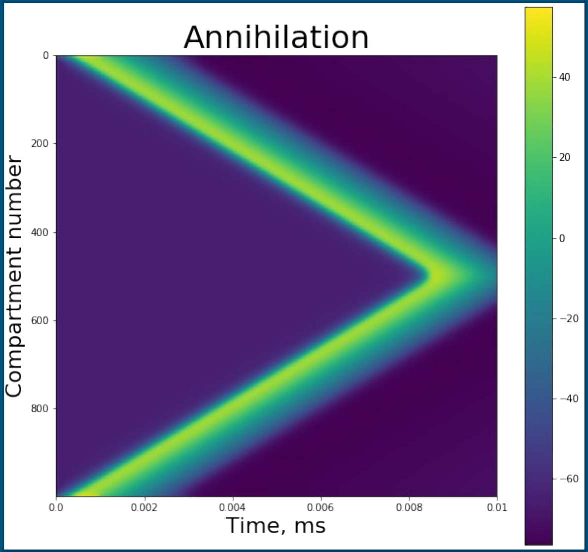


Action Potential Propagation Velocity - Numerically

Annihilation of Two Action Potentials

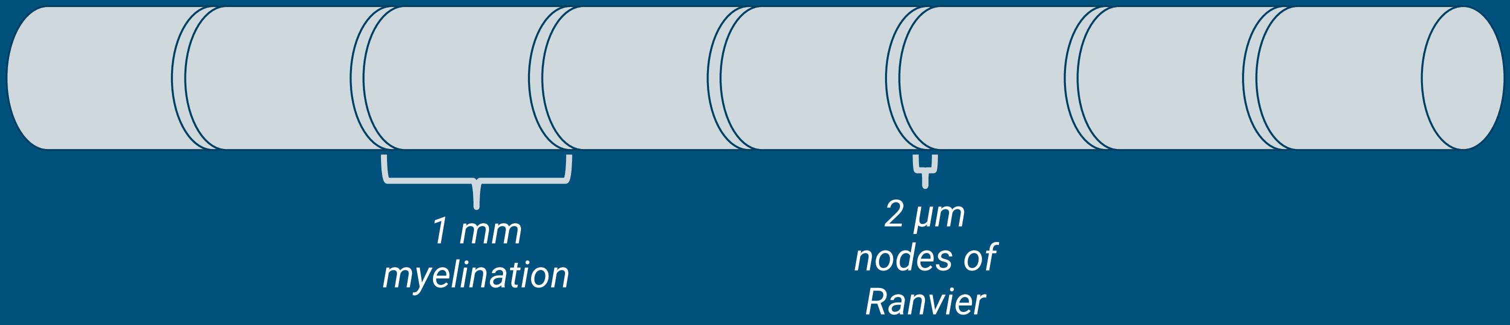






Annihilation of Two Action Potentials

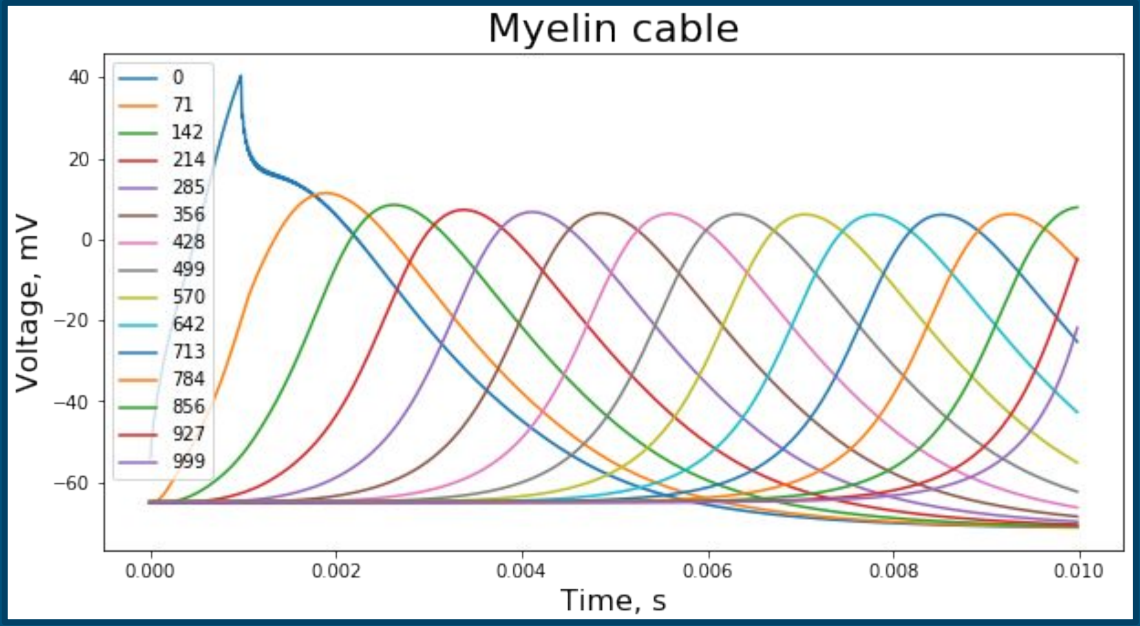
Myelinated Axons

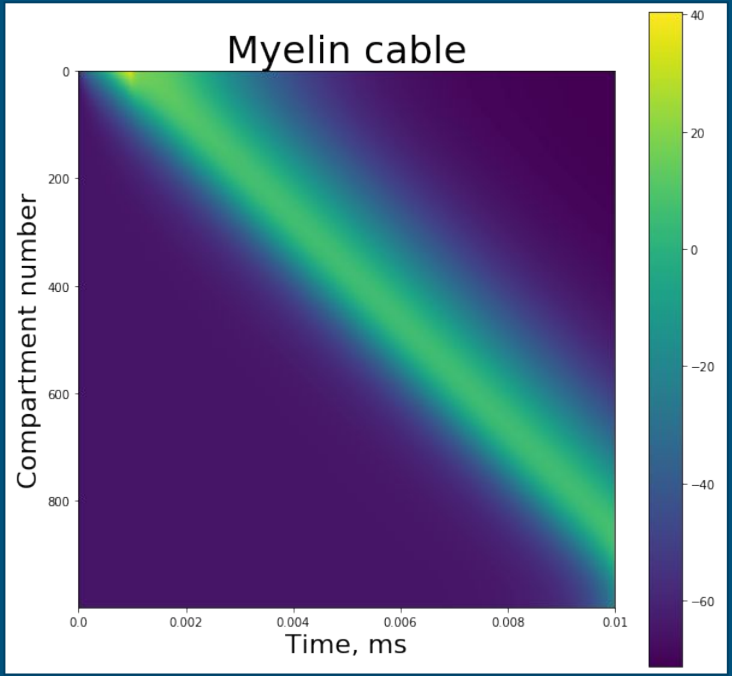


Impact of myelin:

- Increases resistance r_m by a factor of 5,000
- Decreases capacitance c_m by 50

Myelinated Axons





Branching Cable

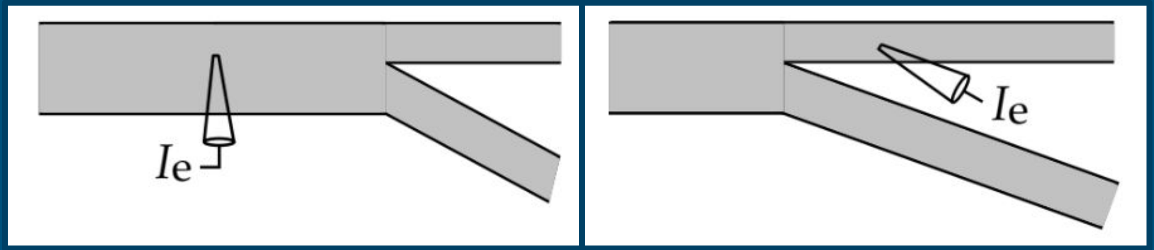
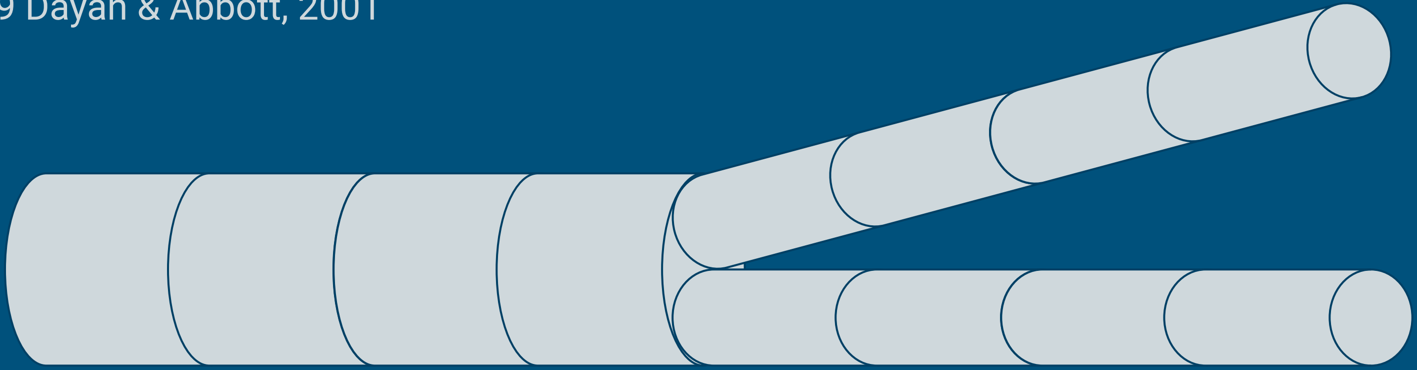


Figure 6.9 Dayan & Abbott, 2001

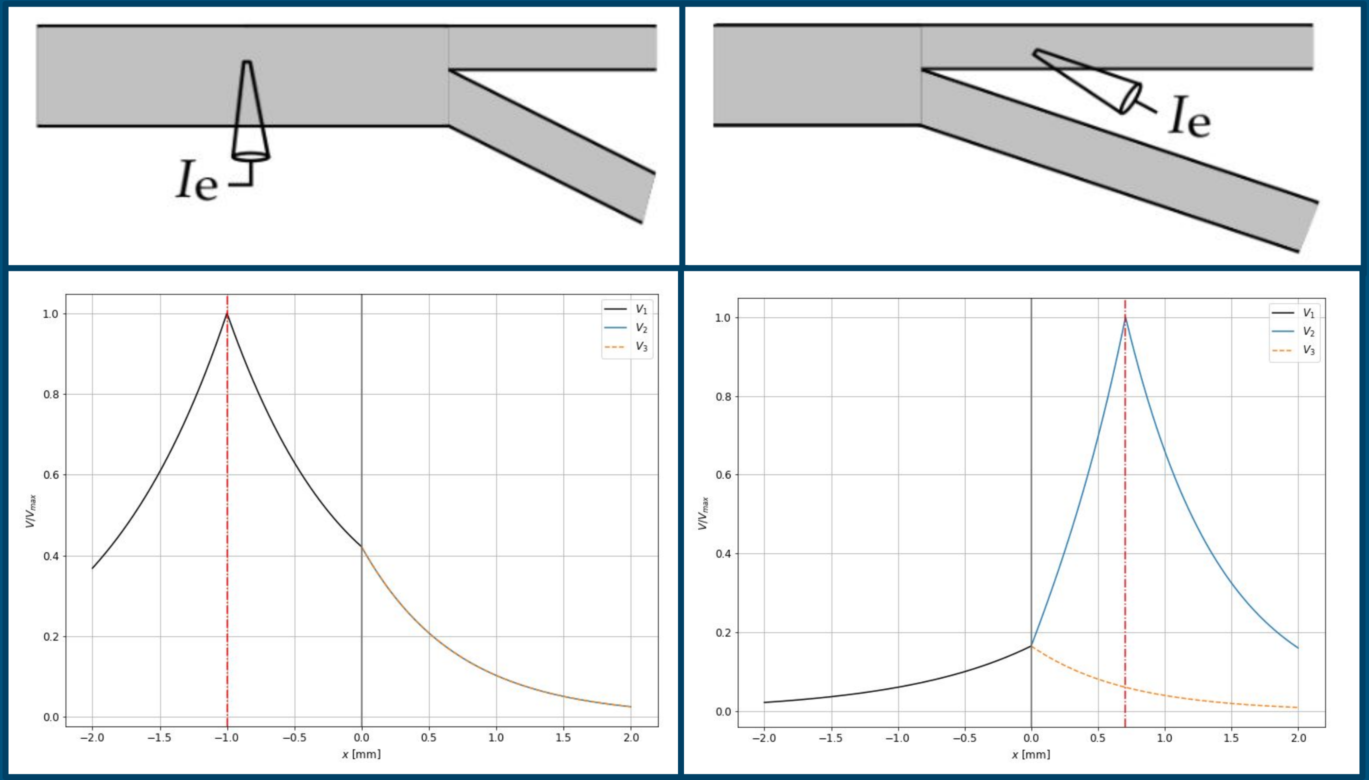


Branching Cable

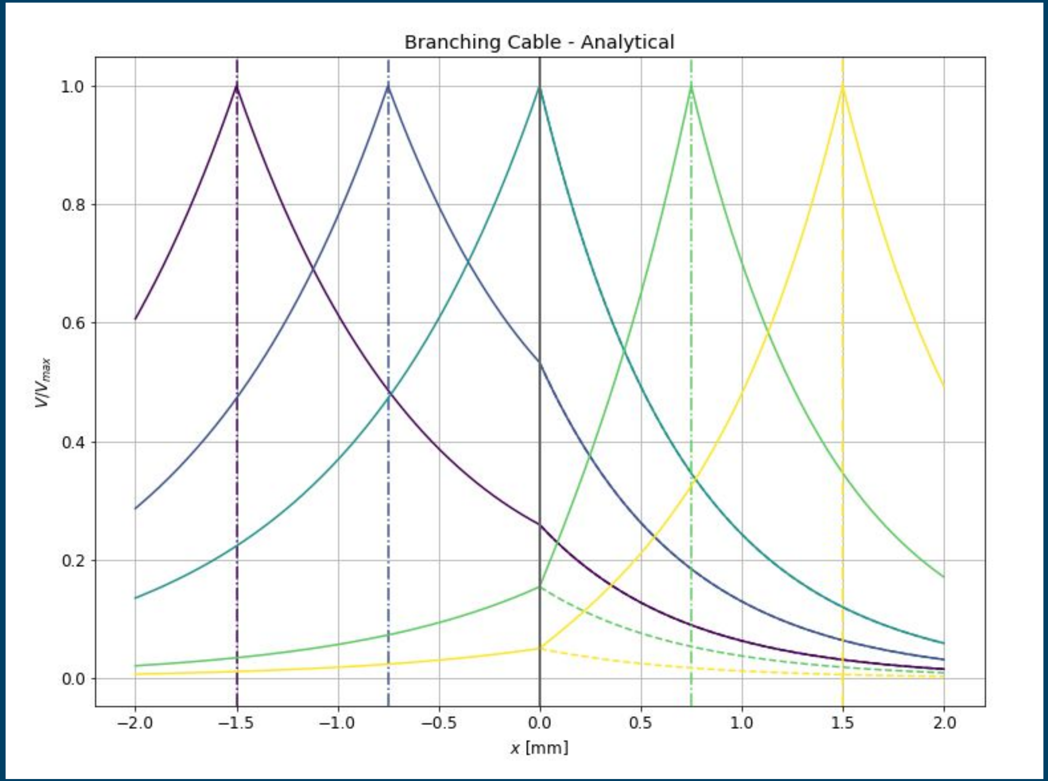
$$\begin{cases} v_1(x) = p_1 I_e R_{\lambda_1} exp(\frac{-x_1}{\lambda_1} - \frac{y}{\lambda_2}) \\ v_2(x) = \frac{I_e R_{\lambda_2}}{2}[exp(\frac{-|y-x_2|}{\lambda_2}) + (2p_2 - 1)exp(\frac{-(y+x_2)}{\lambda_2})] \\ v_3(x) = p_3 I_e R_{\lambda_3} exp(\frac{-x_3}{\lambda_3} - \frac{y}{\lambda_2}) \end{cases}$$

$$p_i = \frac{a_i^{3/2}}{a_1^{3/2}+a_2^{3/2}+a_3^{3/2}} \quad \lambda_i = \sqrt{\frac{a_i r_m}{2r_L}} \quad R_{\lambda_i} = \frac{r_L \lambda_i}{\pi a_i^2}$$

Figure 6.9 Dayan & Abbott, 2001



Branching Cable - Analytical



Branching Cable - Analytical

Questions?