Propagation of Voltage in a Neuron

The Cable Equation

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Overview

1. Motivation
2. Neuronal Cable Equation
3. Passive Membrane
4. Bi-stable Ion Channels

How Do Neurons Communicate?

Within one cell

- Electrochemical signals
- Membrane Potential: $\Delta V_m = V_i - V_e$
- Ions: charge-carriers
- Ion Channels in Membrane

Between cells

- Neurotransmitters

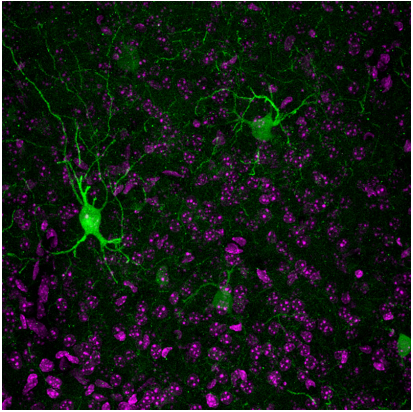


Figure: Mouse neurons, 40X. Bosch Institute Advanced Microscopy Facility, The University of Sydney

Action Potentials

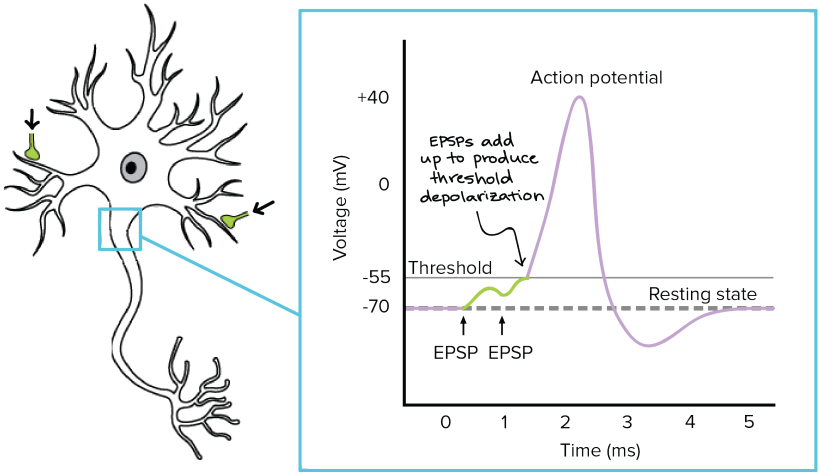


Figure: Changes in axonal membrane voltage due to an action potential. Image from Khan Academy

Hodgkin-Huxley's Neuronal Cable Model (1952)

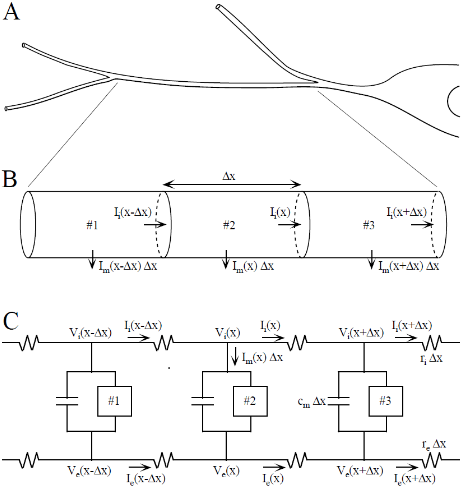


Figure: Differential membrane patches as circuit. Image from jh.edu/motn

Cable Equation

$$\frac{\partial v(x,t)}{\partial t} - \frac{\partial^2 v(x,t)}{\partial x^2} - f(v(x,t)) = J_{ext}(x,t)$$

$\partial_t v(x,t)$ represents capacitive current across membrane

$\partial_{xx} v(x,t)$ represents current coming in from the adjacent segments

$f(v(x,t))$ represents ionic currents across the membrane

$J_{ext}(x,t)$ represents applied current

Passive Membrane

Linear Cable Equation with Impulse Current Injection:

$$\frac{\partial v(x,t)}{\partial t} - \frac{\partial^2 v(x,t)}{\partial x^2} + v(x,t) = \delta(t - t_0)\delta(x - x_0)$$

$$x \in (-\infty, \infty)$$

$$t \in (0, \infty)$$

Boundary Conditions:

$$\lim_{x \to \pm\infty} v(x,t) = 0$$

Green's Function for Linear Infinite Cable Equation

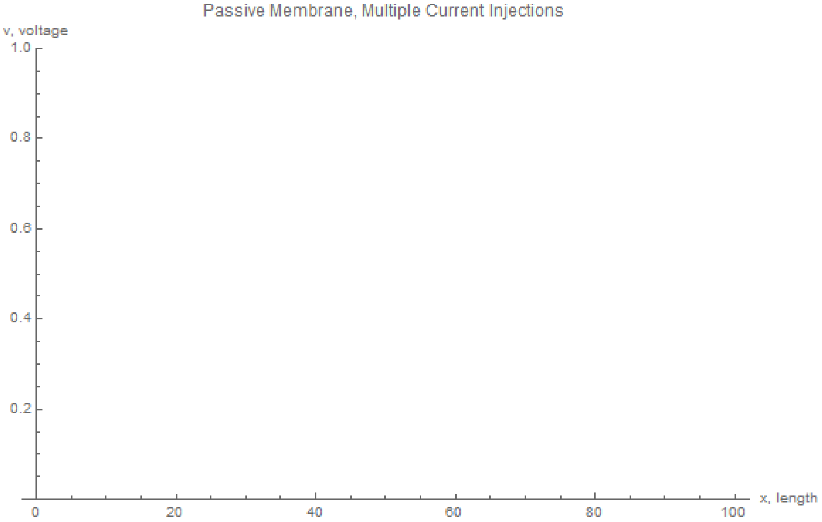
Fourier transform $\rightarrow$ 2 ODE's $\rightarrow$ Inverse Fourier transform

$$G_\infty(x - x_0, t - t_0) = \frac{\mathcal{H}(x - x_0, t - t_0)}{\sqrt{4\pi(t - t_0)}} e^{-(t-t_0) - \frac{(x-x_0)^2}{4(t-t_0)}}$$

Fundamental Solution for Arbitrary Forcing Term, $J_{ext}(x, t)$:

$$\hat{v}(x, t) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} G_\infty(x - x_0, t - t_0) J_{ext}(x_0, t_0) dx_0 dt_0$$

Multiple Current Injections: $(x^*, t^*, A^*) = (1, 0.3, 0.3), (10, 1.1, 1), (30, 0, 0.5)$



Numerical Solutions

- Finite Difference Method
- Plugging approximations for the partial derivatives into the original PDE gives:

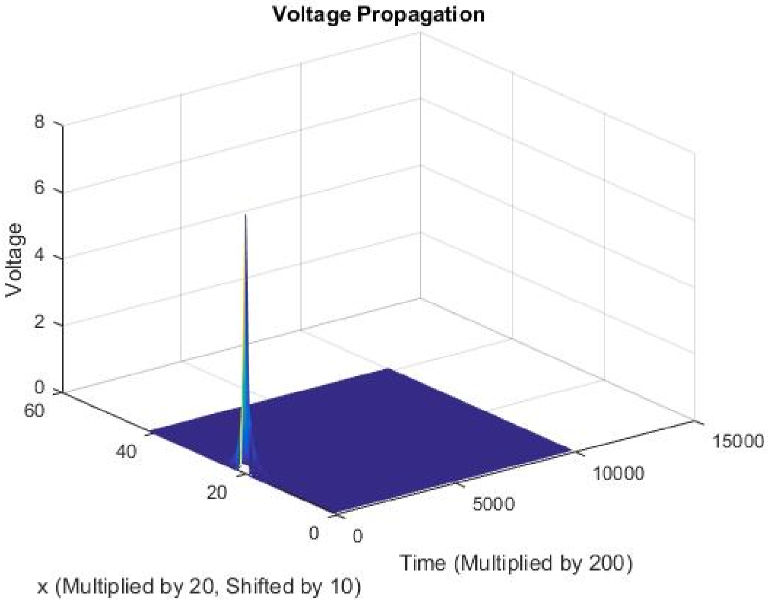
$$\frac{v_i^{j+1} - v_i^j}{\Delta t} = \frac{v_{i+1}^j - 2v_i^j + v_{i-1}^j}{(\Delta x)^2} - v_i^j + J_{ext}(x,t)$$

- Solving for the unknown term:

$$v_i^{j+1} = \frac{\Delta t}{(\Delta x)^2}(v_{i+1}^j + v_{i-1}^j) + (1 - \frac{\Delta t(2 + (\Delta x)^2)}{(\Delta x)^2})v_i^j + \Delta t * J_{ext}(x,t)$$

- Stability

Numerical Solutions Results



Bi-stable Ion Channels

Cable Equation: $\frac{\partial v(x,t)}{\partial t} = \frac{\partial^2 v(x,t)}{\partial x^2} + f(v(x,t))$

- Two stable states of membrane: active and inactive
  - Heaviside step nonlinearity:
    $$f(v) = -v + H(v-\theta) = -v + \begin{cases} 0, & v < \theta \\ 1, & v > \theta \end{cases}$$
- Goals:
  - Seek solutions of the form $v(x,t) = V(\xi) = V(x - ct)$
  - Understand how impulse current propagates through neural membrane

Traveling Wave Solutions

- Boundary conditions:
  - $V(\xi)$ approaches a homogeneous solution as $\xi \to \pm\infty$
  - $\frac{dV(\xi)}{d\xi}$ is bounded as $\xi \to \pm\infty$
  - $V(\xi)$ is continuous and smooth at $\xi = 0$

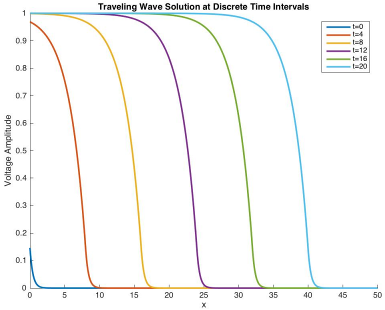


Figure: Traveling front solutions

- Solutions:

$$V_1(\xi) = \frac{-c+\sqrt{c^2+4}}{2\sqrt{c^2+4}} e^{-\frac{1}{2}(c+\sqrt{c^2+4})\xi}, \quad \xi \in (0,\infty)$$

$$V_2(\xi) = \frac{-c-\sqrt{c^2+4}}{2\sqrt{c^2+4}} e^{\frac{1}{2}(-c+\sqrt{c^2+4})\xi} + 1, \quad \xi \in (-\infty,0)$$

Animation of Traveling Front Solution

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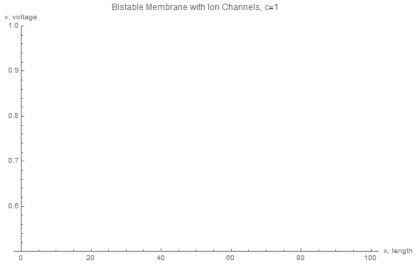


Speed of Traveling Wave

- Threshold condition: $V(0) = \theta \Rightarrow$ $c = \sqrt{\frac{-(2\theta-1)^2}{\theta^2-\theta}}$
- c represents speed of traveling wave front
- $0 < \theta < 1$
- High cell activity for $\theta \to 0$ and $\theta \to 1$

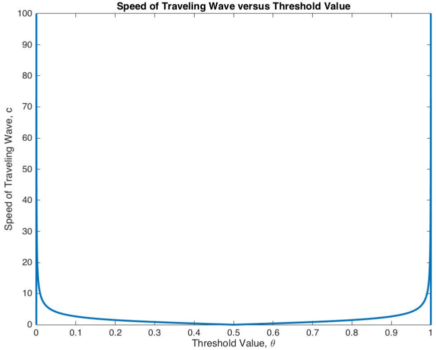
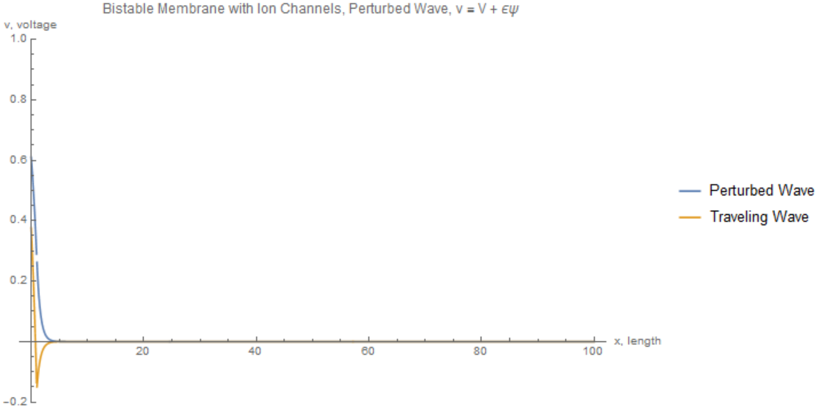


Figure: Threshold Value versus Speed

Stability of Traveling Wave

- Perturbation: $v(x,t) = V(\xi) + \epsilon\psi(\xi,t)$
  - v(x,t) still must satisfy the cable equation: $\frac{\partial v}{\partial t} = \frac{\partial^2 v}{\partial x^2} - v + H(v-\theta)$
- What happens to $\psi(\xi,t)$ as $t \to \infty$?
- Plug $v = V + \epsilon\psi$ into cable equation $\Rightarrow$ Linearize $\Rightarrow$ extract PDE governing $\psi(\xi,t)$: $\frac{\partial \psi}{\partial t} = c\frac{\partial^2 \psi}{\partial \xi^2} + \frac{\partial \psi}{\partial \xi} - (1 - \delta(V-\theta))\psi$
- Separation of variables:
  - $\lambda < 0$ case: $\rightarrow \psi(\xi,t) = S(\xi)e^{\lambda t}$
  - $\lambda = 0$ case: no time dependence $\Rightarrow$ perturbation propagates as traveling front solution

Animation of Perturbed Wave Solution



Numerical Solutions for Traveling Wave

- Finite Difference Method–Similar to Previous Numerical Solution
- Resultant Equation (solved for the unknown term):

$$v_i^{j+1} = \frac{\Delta t}{(\Delta x)^2}(v_{i+1}^j + v_{i-1}^j) + (1 - \frac{\Delta t(2 + (\Delta x)^2)}{(\Delta x)^2})v_i^j + \Delta t * H(v_i^j - \theta)$$

Results

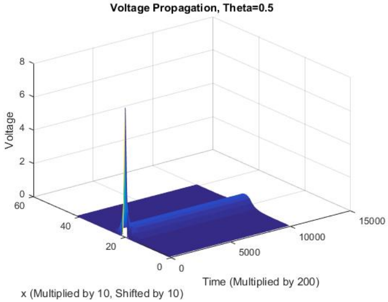


Figure: $\theta = 0.5$

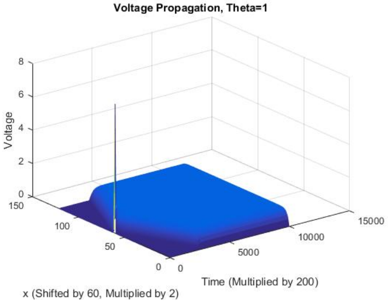


Figure: $\theta = 0.1$

- Numerically Solving for Speeds of the Waves
- Comparison with Analytic Results

Periodically Varying Threshold, Numerical Methods

- What is a periodically varying threshold?
- Governing Equation:

$$\frac{\partial v(x,t)}{\partial t} = \frac{\partial^2 v(x,t)}{\partial x^2} - v + H(v - \theta(1 + 0.5\cos(x))) + J_{ext}(x,t)$$

- Numerical Solution:

$$v_i^{j+1} = \frac{\Delta t}{(\Delta x)^2}(v_{i+1}^j + v_{i-1}^j) + (1 - \frac{\Delta t(2 + (\Delta x)^2)}{(\Delta x)^2})v_i^j$$

$$+\Delta t * H(v_i^j - \theta(1 + C\cos(x)))$$

Results

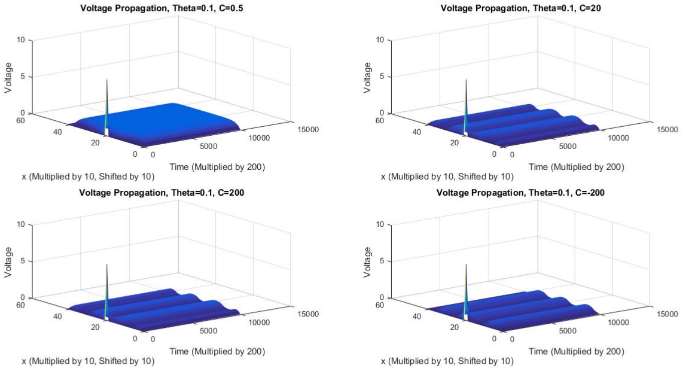


Figure: Varying C, $\theta = 0.1$

Conclusion: Comparison to full Hodgkin-Huxley Model

Three gating variables $x = m, n, h$, each satisfying ODE's:

$$C\frac{\partial v}{\partial t} = g_{\mathrm{Na}} m^3 h(v - E_{\mathrm{Na}}) + g_{\mathrm{K}} n^4(v - E_{\mathrm{K}}) + g_{\mathrm{L}}(v - E_{\mathrm{L}}) + J_{ext}$$

$$\frac{dx}{dt} = -\frac{1}{\tau_x(v)}\left[x - x_0(v)\right]$$

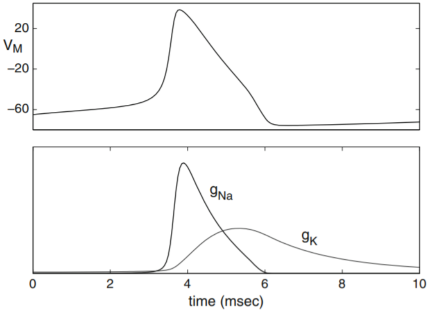


Figure: from Ermentrout & Terman, Math. Foundations of Neuroscience