

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

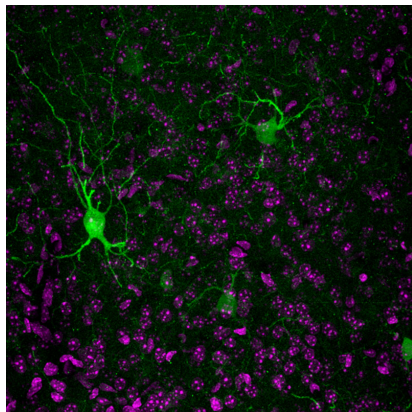


Figure: Mouse neurons, 40X. Bosch Institute Advanced Microscopy Facility, The University of Sydney

Action Potentials

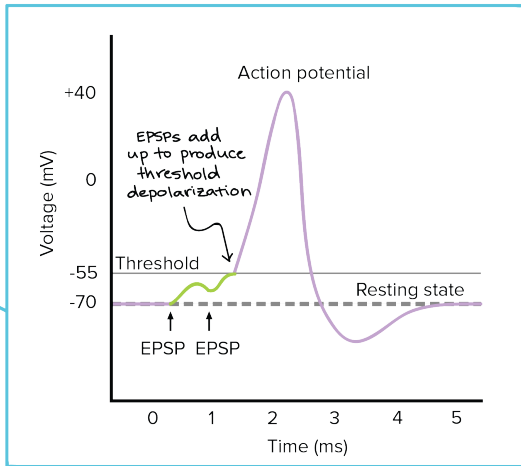
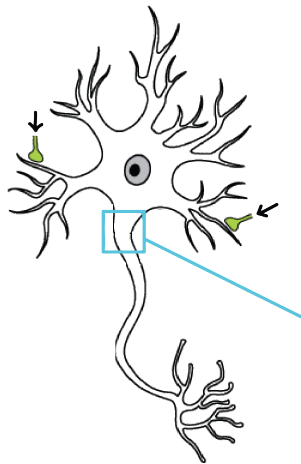
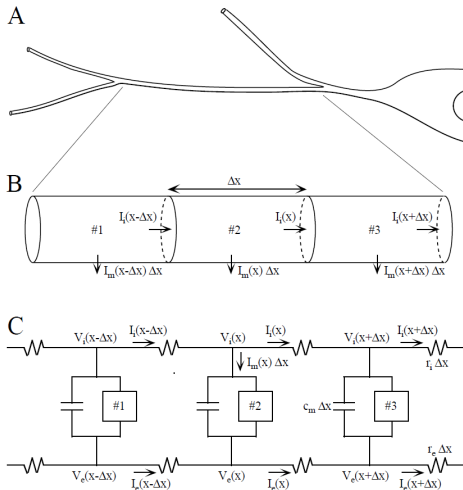


Figure: Changes in axonal membrane voltage due to an action potential.
Image from Khan Academy

Hodgkin-Huxley's Neuronal Cable Model (1952)



- ▶ 1-D & Ohmic assumption
- ▶ Intracellular current
- ▶ Extracellular current
- ▶ Membrane current
- ▶ Membrane as capacitor
- ▶ Ion channels as conductances
- ▶ Length Constant:

$$\lambda = \sqrt{\frac{r_m}{r_i + r_e}}$$
- ▶ Time Constant: $r_m C_m$

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

Cable Equation

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

$\partial_t v(x, t)$ 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

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

Passive Membrane

Linear Cable Equation with Impulse Current Injection:

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

$$x \in (-\infty, \infty), \quad t \in (0, \infty), \quad x_0 = 0, \quad t_0 = 0$$

Boundary Conditions:

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

Green's Function for Linear Infinite Cable Equation

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

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

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

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

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

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:

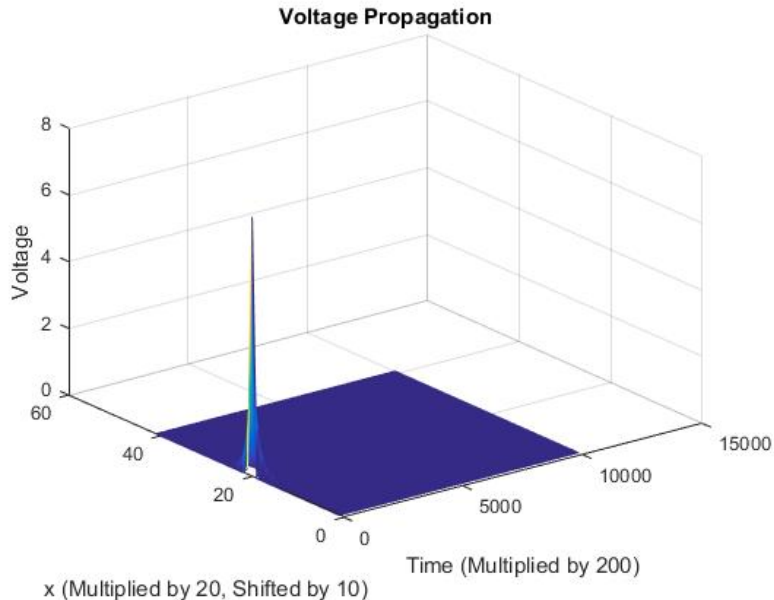
$$\frac{v_i^{j+1} - v_i^j}{\Delta t} = \frac{v_{i+1}^j - 2v_i^j + v_{i-1}^j}{(\Delta x)^2} - v_i^j + J_{\text{ext}}(x, t)$$

- ▶ Solving for the unknown term:

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

- ▶ Stability

Numerical Solutions Results



Bi-stable Ion Channels

- ▶ 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 $\xi \rightarrow \pm\infty$
 - ▶ $\frac{dV(\xi)}{d\xi}$ is bounded as $\xi \rightarrow \pm\infty$
 - ▶ $V(\xi)$ is continuous and smooth at $\xi = 0$

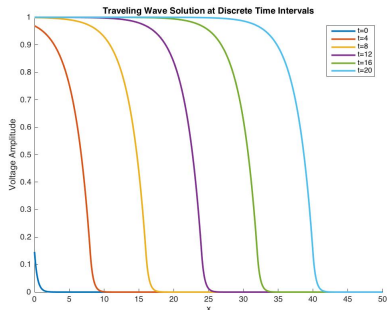


Figure: Traveling front solutions

- ▶ 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

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 $\theta \rightarrow 0$ and $\theta \rightarrow 1$

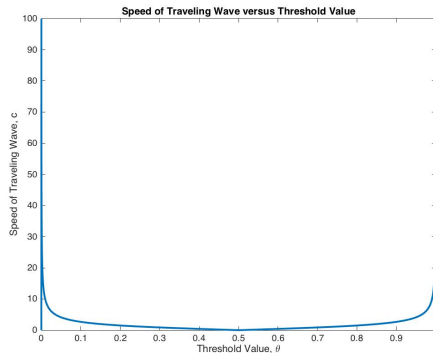


Figure: Threshold Value versus Speed

Stability of Traveling Wave

- ▶ Perturbation: $v(x, t) = V(\xi) + \epsilon\psi(\xi, t)$
- ▶ Goal: understand behavior of $\psi(\xi, t)$ as $t \rightarrow \infty$
- ▶ Perturbation satisfies cable equation:
$$\frac{\partial v}{\partial t} = \frac{\partial^2 v}{\partial x^2} - v + H(v - \theta)$$
- ▶ Linearize nonlinear terms, 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 $\rightarrow \psi(\xi, t) = S(\xi)e^{-f(t)}$

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):

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

Results

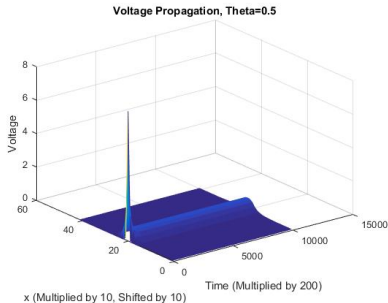


Figure: $\theta = 0.5$

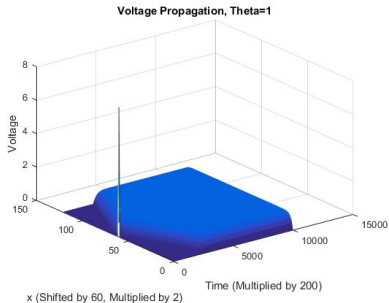


Figure: $\theta = 0.1$

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

Periodically Varying Threshold, Numerical Methods

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

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

- ▶ Numerical Solution:

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

Results

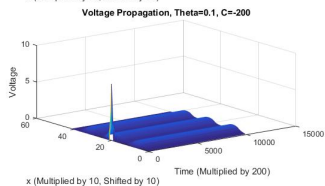
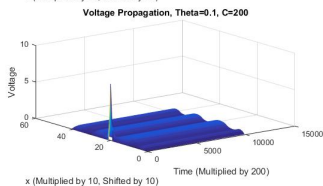
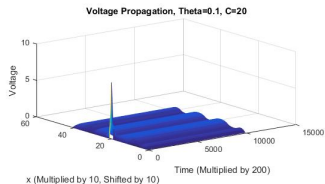
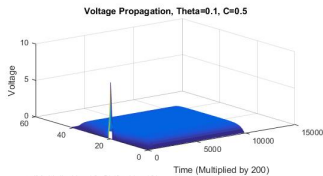


Figure: Varying C , $\theta = 0.1$

Conclusion: Comparison to full Hodgkin-Huxley Model

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

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

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

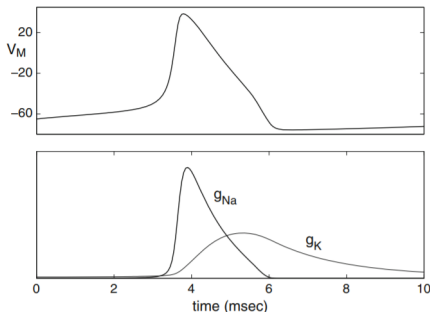


Figure: from Ermentrout & Terman, Math. Foundations of Neuroscience