A QUANTITATIVE DESCRIPTION OF MEMBRANE CURRENT AND ITS APPLICATION TO CONDUCTION AND EXCITATION IN NERVE

By A. L. HODGKIN AND A. F. HUXLEY

From the Physiological Laboratory, University of Cambridge

(Received 10 March 1952)
Neurons – Fundamental units of computation
Resting Membrane Potential

- Difference in voltage between the interior and exterior of a neuron

- Three main players
  - Salty fluids on either side of the membrane
  - The membrane itself
  - Proteins that span the membrane
**Typical Ionic Concentrations**

**(a) Potassium ions (K⁺).** K⁺ are more concentrated in the cytosol and have a tendency to move out of the cell, leaving behind trapped anions. Membrane potential becomes more negative.

**(b) Sodium ions (Na⁺).** Na⁺ are much more concentrated outside the cell than inside and tend to enter the cell. As Na⁺ ions enter, they neutralize some excess negative charge in the cytosol, and membrane potential becomes more positive.

**(c) Chloride ions (Cl⁻).** Cl⁻ usually crosses the membrane together with a permeable cation (normally K⁺). As Cl⁻ enters a cell, it tends to make the membrane potential more negative.

---

Copyright © 2009 Pearson Education, Inc.
Movements of ions - Diffusion

Na⁺ cation
Cl⁻ anion

Membrane impermeable to the ions
Movements of ions – Electric Field

\[ \text{Na}^+ \text{ cation} \]
\[ \text{Cl}^- \text{ anion} \]

(a) No current

(b) Electrical current
Establishing equilibrium

Diffusion causes Potassium ions to move from region of higher concentration (intracellular side) to a region of lower concentration (extracellular side)

A net accumulation of positive charge on the outside and negative charge on the inside retards movement of $K^+$

An equilibrium is established such that there is no movement of ions and there is a charge difference

Neuroscience, Bear et al. 3rd edition
Reversal potential

**Nernst Equation**

\[ E_{\text{ion}} = \frac{RT}{zF} \ln \left( \frac{[\text{ion}_{\text{out}}]}{[\text{ion}_{\text{in}}]} \right) \]

\([\text{ion}_{\text{in}}], [\text{ion}_{\text{out}}]\) are ionic concentration inside and outside the cell

\(T\) is temperature (Kelvins)

\(R\) is gas constant

\(z\) is the valence of the ion

\(F\) is Faraday’s constant: it is the magnitude of electric charge per mole of electrons

Reversal potential at 25°C

\(E_{\text{NA}} = 55\text{mV}\)

\(E_K = -77\text{ mV}\)

\(E_{\text{CL}} = -61\text{ mV}\)
Resting membrane potential

- Goldman Hodgkin and Katz equation

\[ E_{Na,K,Cl} = \frac{RT}{F} \ln \left( \frac{P_K[K_{out}] + P_{Na}[Na_{out}] + P_{Cl}[Cl_{in}]}{P_K[K_{in}] + P_{Na}[Na_{in}] + P_{Cl}[Cl_{out}]} \right) \]

Typical resting membrane potential

\[ V_{rest} = -65 \text{ mV} \]
Some terminology

- **Depolarization**
  - Change in cell’s membrane potential making the inside of the cell more positive (or less negative) with respect to the cell’s outside

- **Hyper-polarization**
  - Change in cell’s membrane potential making the inside of the cell more negative (or less positive) with respect to the cell’s outside

- **Inward current (example due to Na\(^+\) ions)**
  - Flowing into the cell (considered negative)

- **Outward current (example due to K\(^+\) ions)**
  - Flowing out of the cell (considered positive)

- **Action potential, Spike**
  - An “all or nothing” event during which the membrane potential rapidly rises and for a brief moment \(V_{\text{inside}} - V_{\text{outside}}\) is positive
Action Potential

Potassium Channels are opened

$E_{Na}$

$0 \ mV$

$E_K$
Action Potential

Sodium Channels are opened
Action Potential

$E_{Na}$

0 mV

-65 mV

$E_{K}$

Close Na Channels

Open K Channels

Open Sodium Channels
Action Potential

(a) An action potential

- Overshoot
- Rising phase
- Falling phase
- Voltage threshold
- Resting potential
- Undershoot

Membrane potential (mV)

Time (ms)
Action Potential

(a) Resting membrane potential

Extracellular fluid

\[ \text{K}^+ \text{ leak channel} \]

\[ \text{K}^+ \]

\[ \text{Voltage-gated Na}^+ \text{ channel} \]

\[ \text{Voltage-gated K}^+ \text{ channel} \]

Cytoplasm

\[ \text{K}^+ \]

40

0

-65

\[ E_{Na} \]

\[ P_K > P_{Na} \]

\[ E_K \]

(b) Rising phase

\[ \text{K}^+ \]

\[ \text{Na}^+ \]

40

0

-65

\[ E_{Na} \]

\[ P_{Na} \gg P_K \]

\[ E_K \]
Action Potential

(c) Falling phase

(d) Recovery

Neuroscience, Bear et al. 3rd edition
Membrane Current and Conductance

- Net movements of ion will cause ionic current $I_{ion}$

- The number of ion channels open will be proportional to an electrical conductance ($g_k$, $g_{Na}$; inverse of resistance)

- Ionic current will flow only as long as membrane potential $V_m$ is not equal to reversal potential $E_{ion}$

$$I_{ion} = g_{ion} (V_m - E_{ion})$$
Refractory Period

![Diagram showing the refractory period with absolute and relative periods, action potential, Na⁺, and K⁺ ions.](From web)
Electrical Circuit of a Patch of Neuron

[Notes borrowed from Araneda]
Passive properties of a Neuron

Capacitor

\[ C = \frac{Q}{V} \quad \text{Coulomb/Volt or Farads (F)} \]

\[ C = \varepsilon_0 \frac{A}{d} \quad \varepsilon_0 \text{ electrostatic permittivity} \]

\[ \uparrow_A = \uparrow_C \quad \uparrow_d = \downarrow_C \]

[Notes borrowed from Araneda]
Passive properties of a Neuron

Resistance

\[ R = \frac{V}{I} \quad \text{Ohms (}\Omega) \]

\[ R = \rho \frac{l}{A} \quad \rho \quad \text{resistivity} \]

\[ \uparrow l = \uparrow R \quad \uparrow A = \downarrow R \]

For the same current, a larger \( R \) produces larger \( V \)

[Notes borrowed from Araneda]
Passive properties of a Neuron

![Diagram of a neuron showing ionic and capacitive membrane currents](image)

**Equation:**

\[ I_m = I_i + I_c \]

[Notes borrowed from Araneda]
Electrical Circuits with R and C elements

Effects of passing current on circuits containing R and C

[Notes borrowed from Araneda]
Electrical Structure of Small Passive Neuron

Many Small RC circuits

Since the cell is so small we can assume same membrane potential everywhere (isopotential)

A battery to account for resting membrane potential

Resistor mimics ion channel

[Koch, 1999]
Membrane Patch Equation

\[ I_{inj} = C \frac{dV_m(t)}{dt} + \frac{V_m(t)}{R} \]

Show that the solution is:

\[ V_m(t) = V_\infty (1 - e^{-t/\tau}) \]

at \( t = 0 \) \( V = 0 \)

\( \tau = RC \)

\( V_\infty = I_{inj}R \)
RC Circuit

For a rising exponential

\[ V = V_0 \times (1-e^{-t/RC}) \]
Current is carried through the membrane either by charging the membrane capacitor or by movement of ions through the resistances in parallel with the capacitor.
Currents

\[ I = C_M \frac{dV}{dt} + I_i, \]

**Total current = Capacitive current + Ionic current**

\[ I_i = I_{Na} + I_{K} + I_l. \]

**Ionic current = Sodium-Current + Pottasium-Current + Leakage Current (Cl\textsuperscript{-} and other ions)**
Ionic currents

\[ I_{Na} = g_{Na} (E - E_{Na}), \]
\[ I_{K} = g_{K} (E - E_{K}), \]
\[ I_{l} = g_{l} (E - E_{l}), \]

\(E_{Na}, E_{k}\) and \(E_{l}\) are equilibrium or reversal potential for respective ion species
\(g_{Na}, g_{k}\) and \(g_{l}\) are ionic conductances

Notice
\[
\begin{align*}
E_{ion-type} &< E & I_{ion-type} \text{ is positive} \\
E_{ion-type} &> E & I_{ion-type} \text{ is negative}
\end{align*}
\]

Larger \(E - E_{ion}\) the larger the current due to that ionic species
Squid Axon Experiments
Voltage Clamp Technique

1. One internal electrode measures membrane potential ($V_m$) and is connected to the voltage clamp amplifier.

2. Voltage clamp amplifier compares membrane potential to the desired (command) potential.

3. When $V_m$ is different from the command potential, the clamp amplifier injects current into the axon through a second electrode. This feedback arrangement causes the membrane potential to become the same as the command potential.

4. The current flowing back into the axon, and thus across its membrane, can be measured here.

Voltage clamp technique for studying membrane currents of a squid axon.
Hodgkin Huxley Experiments

Voltage Clamping
**Voltage Clamp**

Potential inside the membrane

**Membrane voltage**
- 0 mV
- 20 mV
- 40 mV
- 60 mV
- 80 mV
- 100 mV

**Time [ms]**
- 0 ms
- 1 ms
- 2 ms
- 3 ms
- 4 ms
- 5 ms

- 85 mV step (voltage clamp)
- Resting potential -65 mV

Measured trans-membrane current

**Membrane current**
- 0 mA/cm²
- 1 mA/cm²
- 2 mA/cm²
- 3 mA/cm²

- Capacitive current
- Delayed outward current
- Transient inward current

**Time [ms]**
- 0 ms
- 1 ms
- 2 ms
- 3 ms
- 4 ms
- 5 ms
Measuring individual ionic currents

A  Voltages in axon [mV]

- $V_L = -54.4 \text{ mV}$
- $V_r = -65 \text{ mV}$
- $V_{Na} = 50 \text{ mV}$
- $V_{K} = -77 \text{ mV}$
- $V_m = -9 \text{ mV}$

Depolarization = 56 mV (Voltage clamp)

$V_m - V_{K} = 68 \text{ mV}$

$V_m - V_{Na} = -59 \text{ mV}$

$V_m - V_L = 45 \text{ mV}$

B  $i_m [\text{mA/cm}^2]$

Total membrane current

$ i_m = i_{Na} + i_{K} + (i_C + i_L) $

Capacitive current

Delayed outward current

Transient inward current
Voltage Clamp

Inward current become smaller as Clamp voltage gets close to Na Reversal Potential (+55mV) and flips sign for larger depolarizations.

Outward current is monotonic as you move away from K reversal Potential (-77mV)

\[ E_{ion} = \frac{RT}{zF} \ln \left( \frac{[ion_{out}]}{[ion_{in}]} \right) \]
Voltage Clamp (continued …)

![Graph showing voltage clamp currents](image)

-9 mV

-65 mV

10% Na

$I_K$

$I_K + I_{Na}$

100% Na

$I_{Na}$

0 1 2 3 4 5
Measuring individual ionic currents

- Selective measurement of the K ion flow alone is possible by utilizing a voltage clamp step corresponding to the Na Nernst potential.

![Graphs showing potassium, sodium, and capacitive and leakage currents](image-url)
Pharmacological agents

Lips and tongue tinges, hands feel numb and trouble making movements
Tetrodotoxin (TTX) – blocks voltage-gated Na channels
Pharmacological agents

Scorpion toxin blocks voltage-gated K channels

Another popular blocker is tetraethylammonium (TEA)
One of the most important contributions of Hodgkin and Huxley was their detailed discussion of membrane kinetics.

The model was not formulated from fundamental principles but rather from theoretical insights and curve fitting.
Dynamics of K Conductance (3)

How do K conductance change with V?
- Becomes more rapid at higher depolarization

Does K conductance ever return back to baseline?
- No!
K conductance

Depolarization to 25 mV

Repolarization back to Resting potential

Inflexion of the curve
What’s the best fit?

\[ 1 - \exp\left(-\frac{t}{\tau}\right) \]

\[ (1 - \exp\left(-\frac{t}{\tau}\right))^2 \]

\[ (1 - \exp\left(-\frac{t}{\tau}\right))^3 \]

\[ (1 - \exp\left(-\frac{t}{\tau}\right))^4 \]
Why $n^4$?

\[ g_K = \bar{g}_K n^4, \]
Dynamics of $K$ conductance (1)

- Hodgkin-Huxley assumed that there is only one variable that determines the dynamics of potassium conductance

\[ g_K = \bar{g}_K n^4, \]

- \( g_K \) is a constant

- What does \( n^4 \) represent?
  - That $K$ ions cross membrane only when four particles occupy a certain region of the membrane
Dynamics of K conductance (1)

www.bem.fi/book/04/04.htm
Dynamics of K Conductance (2)

\[ \frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n, \]

- \( \alpha_n \) represents transfer from outside to inside
- \( \beta_n \) represents transfer from inside to outside

The solution of this first order ODE that satisfies the boundary condition \( n = n_0 \) at \( t = 0 \) is:

\[ n = n_\infty - (n_\infty - n_0) \exp\left(\frac{-t}{\tau_n}\right) \]

\[ n_\infty = \frac{\alpha_n}{\alpha_n + \beta_n} \]

\[ n_0 = \frac{\alpha_0}{\alpha_0 + \beta_0} \]

\[ \tau_n = \frac{1}{\frac{\alpha_n + \beta_n}{\tau_n}} \]
Dynamics of K Conductance (3)

Fig. 3. Rise of potassium conductance associated with different depolarizations. The circles are experimental points obtained on axon 17, temperature 6–7°C, using observations in sea water and choline sea water (see Hodgkin & Huxley, 1952a). The smooth curves were drawn from eqn. (11) with $g_{K0}=0.24$ m.mho/cm² and other parameters as shown in Table 1. The time scale applies to all records. The ordinate scale is the same in the upper ten curves (A to J) and is increased fourfold in the lower two curves (K and L). The number on each curve gives the depolarization in mV.

$$g_K = \bar{g}_K n^4,$$

$$n = n_\infty - (n_\infty - n_0) \exp \left( \frac{-t}{\tau_n} \right)$$

$$g_K = \left\{ (g_{K\infty})^{\frac{1}{4}} - [(g_{K\infty})^{\frac{1}{4}} - (g_{K0})^{\frac{1}{4}}] \exp \left( -t/\tau_n \right) \right\}^4,$$
Rate constants $\alpha_n, \beta_n(6)$

$$\alpha_n = 0.01 (V + 10) \left/ \left[ \exp \left( \frac{V + 10}{10} \right) - 1 \right] \right.,$$

$$\beta_n = 0.125 \exp (V/80),$$
How does Na conductance change with V?

Becomes more rapid at higher depolarization

Does Na conductance ever return back to baseline?

Yes!

Are the rising and falling portions of the curves similar?

No!
Hodgkin-Huxley assumed that there are two variables that determine the dynamics of sodium conductance:

\[ g_{Na} = m^3 h \bar{g}_{Na}, \]

- \( g_{Na} \) is a constant
- \( m \) represents the proportion of activating molecules on the inside
- \( h \) represents the proportion of inactivating molecules on the outside

**What does \( m^3 h \) represent?**
- That sodium conductance is proportional to the number of sites on the inside of the membrane which are occupied simultaneously by three activating molecules (\( m^3 \)) and not blocked by an inactivating molecule (\( m^3 h \)).
Dynamics of Na Conductance (1)

www.bem.fi/book/04/04.htm
Dynamics of Na Conductance (2)

- The two variables obey the following first order differential equation

\[ \frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m, \]

\[ \frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h, \]

- \( \alpha_m \) or \( \beta_h \) represents of transfer from outside to inside

- \( \beta_m \) or \( \alpha_h \) represents of transfer from inside to outside
Dynamics of Na Conductance (3)

- Solving the first order differential equation

\[ m = m_\infty - (m_\infty - m_0) \exp \left( -t/\tau_m \right), \quad h = h_\infty - (h_\infty - h_0) \exp \left( -t/\tau_h \right), \]

\[ m_\infty = \alpha_m/(\alpha_m + \beta_m) \quad h_\infty = \alpha_h/(\alpha_h + \beta_h) \]

\[ \tau_m = 1/(\alpha_m + \beta_m), \quad \tau_h = 1/(\alpha_h + \beta_h). \]

- At \( t=0 \); \( m = m_0, h = h_0 \)
**Dynamics of Na Conductance (4)**

- HH noted that in resting state, sodium conductance is negligible, so we can neglect $m_0$, and inactivation in nearly complete if $V < -30\text{mV}$ and $h_\alpha$ can also be neglected

$$g_{Na} = g_{Na}' [1 - \exp \left(-\frac{t}{\tau_m}\right)]^3 \exp \left(-\frac{t}{\tau_h}\right),$$

where

$$g_{Na}' = \tilde{g}_{Na} m_\infty^3 h_0$$

is the value of sodium conductance if $h$ remained in its resting level $h_0$
Fig. 6. Changes of sodium conductance associated with different depolarizations. The circles are experimental estimates of sodium conductance obtained on axon 17, temperature 6–7° C (cf. Fig. 3). The smooth curves are theoretical curves with parameters shown in Table 2; A to H drawn from eqn. 19, I to L from 14, 17, 18 with $\tilde{g}_{Na} = 70 \cdot 7$ m.mho/cm². The ordinate scales on the right are given in m.mho/cm². The numbers on the left show the depolarization in mV. The time scale applies to all curves.

$$g_{Na} = g'_{Na} \left[ 1 - \exp \left( -t/\tau_m \right) \right]^3 \exp \left( -t/\tau_h \right),$$
Rate constants $\alpha_m, \beta_m(6)$

\[
\alpha_m = 0.1 \left( V + 25 \right) / \left( \exp \frac{V + 25}{10} - 1 \right),
\]

\[
\beta_m = 4 \exp \left( V / 18 \right),
\]
How does activation variable m change with V?
Rate constants $\alpha_h, \beta_h(8)$

\[
\alpha_h = 0.07 \exp\left(\frac{V}{20}\right), \\
\beta_h = \frac{1}{\left(\exp\left(\frac{V + 30}{10}\right) + 1\right)}.
\]
How does activation variable $h$ change with $V$?
Putting pieces together – HH model

\[ I = C_M \frac{dV}{dt} + g_K n^4 (V - V_K) + g_{Na} m^3 h (V - V_{Na}) + g_i (V - V_i), \]

where

\[ \frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n, \]
\[ \frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m, \]
\[ \frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h, \]

\[ \alpha_n = 0.01 \frac{V + 10}{\exp \left( \frac{V + 10}{10} \right) - 1}, \]
\[ \beta_n = 0.125 \exp \left( \frac{V}{80} \right), \]
\[ \alpha_m = 0.1 \frac{V + 25}{\exp \left( \frac{V + 25}{10} \right) - 1}, \]
\[ \beta_m = 4 \exp \left( \frac{V}{18} \right), \]
\[ \alpha_h = 0.07 \exp \left( \frac{V}{20} \right), \]
\[ \beta_h = 1 \frac{1}{\exp \left( \frac{V + 30}{10} \right) + 1}. \]
Time courses of HH variables

Membrane potential, mV

10 μA/cm² current stim.

HH variables

Milliseconds

Conductance, mS/cm²

Current, mA/cm²

Milliseconds

m, n, h

I_Cap, I_Leak, I_K, I_Na
Refractory Period
HH model - Summary

- Models a patch of membrane
- Assumes isopotential i.e. the membrane potential is constant across the patch
- The number of channels is large enough that individual gating events are averaged out and the Na and K currents are smooth population currents
- The channels are not arranged in anyway which allows local interaction among small number of channels
Reducing HH models

- State variables of HH eqns: \([V, m, n, h]\)
- Most reduction rely on two simplifications
  - Time constants are very different
  - \(m\) changes so fast compared to \(n\) and \(h\) that you don’t need a ODE to describe it (removes one ODE)
  - \(n+h\) is almost a constant; so we can eliminate one more variable
  - Now the reduced HH will have state variable \([V, w]\); \(V\) – fast variable (membrane potential) and \(w\) – slow variable (potassium activation)
Reducing HH models (2)

Original

$$C \dot{V} = I - g_K n^4 (V - E_K) - g_{Na} m^3 h (V - E_{Na}) - g_L (V - E_L)$$

Reduced

$$C \dot{V} = I - g_K n^4 (V - E_K) - g_{Na} m^\infty (V) (0.89 - 1.1n) (V - E_{Na}) - g_L (V - E_L)$$
Reducing HH models (3)
Linear Cable Equation
**Action Potential Propagation**

Transmembrane current across unit length of the axon

\[ i_m = \frac{V_m - V_{rest}}{r_m} + c_m \frac{dV_m}{dt} \]

- \( i_m \) – Transmembrane current per unit length (A/cm)
- \( r_m \) – membrane resistance per unit length (Ω cm)
- \( c_m \) – membrane capacitance per unit length (F/cm)
Action Potential Propagation

Transmembrane current across $\Delta x$ units of the axon

The total membrane resistance in a fiber of length $\Delta x$ is: $r_m/\Delta x$

The total membrane capacitance in a fiber of length $\Delta x$ is: $c_m\Delta x$
Action Potential Propagation

Plug membrane together: get linear cable

\[ V_m(x+\Delta x,t) = V_m(x,\Delta x,t) = r_m/\Delta x \]

\[ r_a \Delta x \]

\[ V_{rest} \]

\[ V_e = 0 \]

\[ \Delta x \]

RA - intracellular resistivity (Ωcm)

RM - specific membrane resistance (Ωcm²)

CM - specific membrane capacitance (F/cm²)

\[ r_a = \frac{4 R_a}{\pi d^2} \text{ Ω/cm} \]

\[ r_m = \frac{R_m}{\pi d} \text{ Ω · cm} \]

\[ c_m = C_m \cdot \pi d \text{ F/cm} \]
Action Potential Propagation

Plug membrane together: get linear cable

\[ V_m(x, t) = \text{V}_{\text{rest}} \]

Note: Constant \( V_e \) is an assumption
Action Potential Propagation

Plug membrane together: get linear cable

\[ V_m(x,t) - V_m(x+\Delta x,t) = r_a \cdot \Delta x \cdot i_i(x,t) \]

\[
\lim_{\Delta x \to 0} \frac{V_m(x,t) - V_m(x+\Delta x,t)}{\Delta x} = \frac{\partial V_m(x,t)}{\partial x} = -r_a \cdot I_i(x,t)
\]

Eqn 1
Action Potential Propagation

Plug membrane together: get linear cable

By applying Kirchhoff’s current law at node $x$

$$i_m(x,t)\Delta x + I_i(x,t) - I_i(x - \Delta x,t) = 0$$

$$\lim_{\Delta x \to 0} - \frac{\partial I_i}{\partial x}(x,t) = i_m(x,t)$$  \hspace{1cm} \text{Eqn 2}$$
Linear Cable Equation

Plug membrane together: get linear cable

\[ r_a \Delta x V_m(x-\Delta x,t) \]

\[ V_m(x,t) \rightarrow V_m(x+\Delta x,t) \]

\[ \lim_{\Delta x \to 0} \Delta x = 0 \]

\[ \frac{\partial V_m}{\partial x}(x,t) = -r_a \cdot I_i(x,t) \]

\[ \lim_{\Delta x \to 0} \Delta x = 0 \]

\[ -\frac{\partial I_i}{\partial x}(x,t) = i_m(x,t) \]

Substitute

\[ \frac{1}{r_a} \frac{\partial^2 V_m(x,t)}{\partial x^2}(x,t) = i_m(x,t) \]
Linear Cable Equation

Plug membrane together: get linear cable

If electrical nature of the membrane is constant, then

\[
\frac{1}{r_a} \frac{\partial^2 V_m(x,t)}{\partial x^2} = \frac{V_m(x,t) - V_{rest}}{r_m} + c_m \frac{\partial V_m(x,t)}{\partial t}
\]
Linear Cable Equation

Plug membrane together: get linear cable

Multiplying both sides by $r_m$ we get:

\[
\lambda^2 \frac{\partial^2 V_m(x,t)}{\partial x^2} = V_m(x,t) - V_{rest} + \tau_m \frac{\partial V_m(x,t)}{\partial t}
\]

\[
\lambda = \sqrt{\frac{r_m}{r_a}}
\]

\[
\tau_m = r_m c_m
\]

$\lambda$ – steady state space constant

$\tau$ - Membrane time constant
Space and Time constants

\[ \lambda = \sqrt{\frac{r_m}{r_i}} = \sqrt{\frac{R_m}{\frac{2\pi a}{\pi a^2}}} = \sqrt{\frac{R_m a}{2R_i}} \]

- Space constant increases with square root of the axon radius

\[ \tau_m = r_m c_m = \frac{R_m}{2\pi a} \cdot C_m 2\pi a = R_m C_m \]

- Time constant does not depend on axon size
Steady-State Solutions

Plug membrane together: get linear cable

\[ r_m \Delta x V_m(x, t) \]

\[ V_m(x, t) \]

\[ V_m(x + \Delta x, t) \]

\[ l_i(x, t) \]

\[ V_r \]

\[ V_{rest} \]

\[ r_a \Delta x V_m(x-\Delta x, t) \]

\[ \lambda^2 \frac{\partial^2 V_m(x, t)}{\partial x^2} = V_m(x, t) - V_{rest} + \tau_m \frac{\partial V_m(x, t)}{\partial t} \]

\[ \lambda = \sqrt{\frac{r_m}{r_a}} \]

\[ \tau_m = r_m c_m \]

\[ \lambda^2 \frac{d^2 V(x)}{dx^2} = V(x) \quad (V = V_m - V_{rest}) \]
Steady-State Solutions

Plug membrane together: get linear cable

\[ i_m(x,t) = \frac{V_m(x,t) - V_{\text{rest}}}{r_m} + c_m \frac{\partial V_m(x,t)}{\partial t} - I_{\text{inj}}(x,t) \]

\[ \frac{1}{r_a} \frac{\partial^2 V_m(x,t)}{\partial x^2} (x,t) = i_m(x,t) \]
Steady-State Solutions

Plug membrane together: get linear cable

\[
\frac{1}{r_a} \frac{\partial^2 V_m(x,t)}{\partial x^2} (x,t) = i_m(x,t)
\]

\[
\frac{1}{r_a} \frac{\partial^2 V_m(x,t)}{\partial x^2} (x,t) = \frac{V_m(x,t) - V_{\text{rest}}}{r_m} + c_m \frac{\partial V_m(x,t)}{\partial t} - I_{\text{inj}}(x,t)
\]
Steady-State Solutions

Plug membrane together: get linear cable

\[
\frac{1}{r_a} \frac{\partial^2 V_m(x,t)}{\partial x^2}(x,t) = \frac{V_m(x,t) - V_{\text{rest}}}{r_m} + c_m \frac{\partial V_m(x,t)}{\partial t} - I_{\text{inj}}(x,t)
\]

At steady state

\[
\lambda^2 \frac{d^2 V(x)}{dx^2} = V(x) - r_m I_{\text{inj}}(x,t) \quad (V = V_m - V_{\text{rest}})
\]
Steady-State Solutions

Plug membrane together: get linear cable

\[
\lambda^2 \frac{d^2 V(x)}{dx^2} = V(x) - r_m I_{\text{inj}}(x)
\]

A general solution to this ODE for constant current applied at \( x \)

\[
V(x) = A \exp(x / \lambda) + B \exp(-x / \lambda)
\]

A and B are constants will depend on the boundary conditions
Steady-State Solutions

Plug membrane together: get linear cable

\[ r_a \Delta x V_m(x-\Delta x, t) \]

\[ V_m(x, t) \]

\[ V_m(x+\Delta x, t) \]

For boundary-value solutions it is often convenient to use another pair of solutions to the second-order ordinary differential equation

\[ \lambda^2 \frac{d^2 V(x)}{dx^2} = V(x) - r_m I_{\text{inj}}(x) \]

\[ V(x) = A \exp(x/\lambda) + B \exp(-x/\lambda) \]

\[ V(x) = A \cosh(x/\lambda) + B \sinh(x/\lambda) \]

\[ \cosh(x) = \frac{\exp(x) + \exp(-x)}{2} \]

\[ \sinh(x) = \frac{\exp(x) - \exp(-x)}{2} \]
Case 1: Infinite Cable

\[ \lambda^2 \frac{d^2 V(x)}{dx^2} = V(x) - r_m I_{inj}(x) \]

\[ V(x) = A \exp(x/\lambda) + B \exp(-x/\lambda) \]

For the case in which the cable extends from \(-\infty\) to \(+\infty\) we require \(V(-\infty) = V(+\infty) = 0\). What should be values of \(A\) and \(B\) to obey this boundary conditions?

For \(x > 0\); \(A = 0\) and \(B = V_0\) (where \(V_0\) is the membrane voltage at the site of current injection)
Similarly for \(x < 0\); \(A = V_0\) and \(B = 0\)

\[ V(x) = V_0 \exp(-|x|/\lambda) \]
Case 2: Sealed End Cable

\[ \lambda^2 \frac{d^2 V(x)}{dx^2} = V(x) - r_m I_{\text{inj}}(x) \]

\[ V(x) = A \cosh(x / \lambda) + B \sinh(x / \lambda) \]

The idea for sealed end is that current should not flow across a boundary at length \( x = l \)

\[ \left. \frac{dV}{dx} \right|_{x=0} = -r_a I_{\text{inj}} \quad \text{At} \quad x = 0 \quad -r_a I_{\text{inj}} = \frac{B}{\lambda} \]

\[ \left. \frac{dV}{dx} \right|_{x=l} = 0 \quad \text{At} \quad x = l \quad 0 = A \sinh(l / \lambda) + B \cosh(l / \lambda) \]

\[ \frac{dV(x)}{dx} = \frac{A}{\lambda} \sinh(x / \lambda) + \frac{B}{\lambda} \cosh(x / \lambda) \]

\[ A = -B \coth(l / \lambda) \]

\[ A = r_a I_{\text{inj}} \lambda \coth(l / \lambda) \]
Case 2: Sealed End Cable

\[ \lambda^2 \frac{d^2V(x)}{dx^2} = V(x) - r_m I_{inj}(x) \]

\[ V(x) = A \cosh(x / \lambda) + B \sinh(x / \lambda) \]

*The idea for sealed end is that current should not flow across a boundary at length \( x = l \)*

\[ \frac{dV}{dx} \bigg|_{x=0} = -r_a I_{inj} \]

\[ \frac{dV}{dx} \bigg|_{x=l} = 0 \]

\[ B = -r_a I_{inj} \lambda \]

\[ A = r_a I_{inj} \lambda \coth(l / \lambda) \]

\[ V(x) = A \cosh(x / \lambda) + B \sinh(x / \lambda) \]

\[ V(x) = r_a I_{inj} \lambda [\coth(l / \lambda) \cosh(x / \lambda) - \sinh(x / \lambda)] \]

\[ V(x) = \frac{r_a I_{inj} \lambda}{\sinh(l / \lambda)} [\cosh(l / \lambda) \cosh(x / \lambda) - \sinh(l / \lambda) \sinh(x / \lambda)] \]
Case 2: Sealed End Cable

\[ \lambda^2 \frac{d^2V(x)}{dx^2} = V(x) - r_m I_{inj}(x) \]

\[ V(x) = A \cosh(x / \lambda) + B \sinh(-x / \lambda) \]

The idea for sealed end is that current should not flow across a boundary at length \( x = l \)

\[ \frac{dV}{dx} \bigg|_{x=0} = -r_a I_{inj} \]

\[ \frac{dV}{dx} \bigg|_{x=l} = 0 \]

\[ B = -r_a I_{inj} \lambda \]

\[ A = r_a I_{inj} \lambda \coth(l / \lambda) \]

\[ V(x) = A \cosh(x / \lambda) + B \sinh(-x / \lambda) \]

\[ V(x) = r_a I_{inj} \lambda [\coth(l / \lambda) \cosh(x / \lambda) - \sinh(x / \lambda)] \]

\[ V(x) = \frac{V_m(0) \cosh[(l - x) / \lambda]}{\cosh(l / \lambda)} \quad 0 \leq x \leq l \quad \text{sealed} \quad x = l \]

\[ V_m(0) = r_a I_{inj} \lambda \coth(l / \lambda) \]
Case 3: Killed End Cable

\[ \lambda^2 \frac{d^2 V(x)}{dx^2} = V(x) - r_m I_{inj}(x) \]

\[ V(x) = A \cosh(x / \lambda) + B \sinh(-x / \lambda) \]

The idea here is that one of the boundaries is clamped to resting membrane potential

\[ \frac{dV}{dx} \bigg|_{x=0} = -r_a I_{inj} \]

\[ V(l) = 0 \]

\[ V(x) = \frac{V_m(0) \sinh[(l - x) / \lambda]}{\sinh(l / \lambda)} \quad 0 \leq x \leq l \quad \text{killed end} \quad x = l \]

\[ V_m(0) = r_a I_{inj} \lambda \tanh(l / \lambda) \]
Cable Equation Solutions

![Graph showing the voltage distribution in a cable as a function of distance, with curves labeled for sealed end, infinite cable, and killed end.](image-url)
Propagation of AP along an axon
Saltatory Conduction
Saltatory conduction in myelinated axons

The Physiology of Excitable Cells. Cambridge: Cambridge Univ. Press, 1971