

THEORETICAL NEUROSCIENCE I

Lecture 7: Modeling morphology

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1 Motivation

Neurons with long and narrow processes cannot be treated as a single electronic compartment, as the membrane potential can vary considerably over the cell surface.

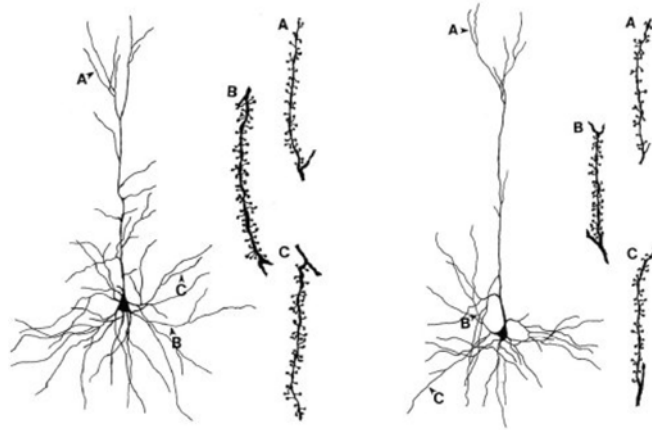


Figure 1: Apical dendrites of pyramidal neurons with dendritic spines (enlarged). [1]

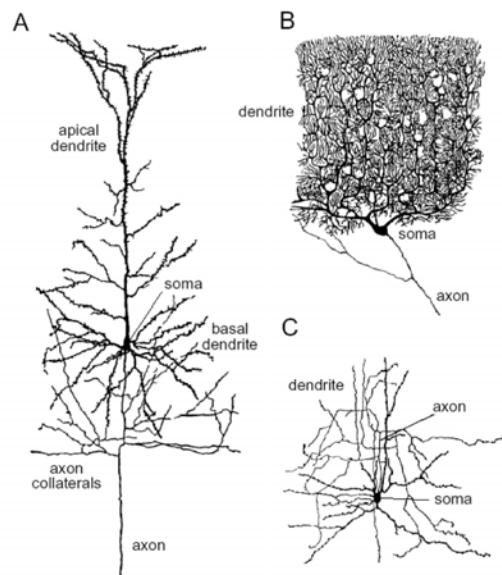


Figure 2: A Pyramidal cell. B Purkinje cell. C Stellate cell [2]

Conduction delay and attenuation

Comparing a single event (AP, EPSP) at distant sites (dendrite, soma) typically shows a delayed and attenuated conduction.

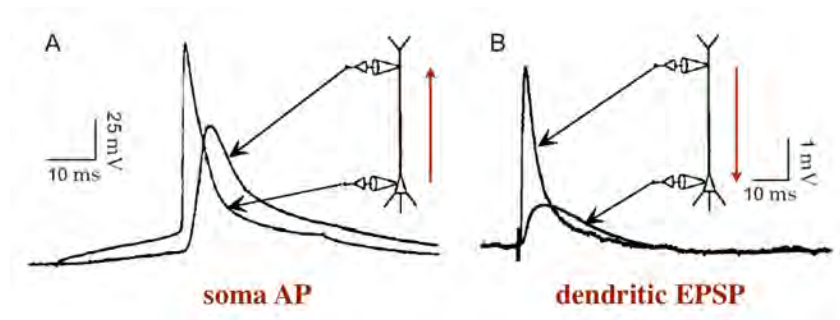


Figure 3: Soma AP vs. Dendritic EPSP. [3]

- Proximal synapses produce shorter, larger EPSPs.
- Multiple such EPSPs must coincide exactly in order to produce a cumulative effect.

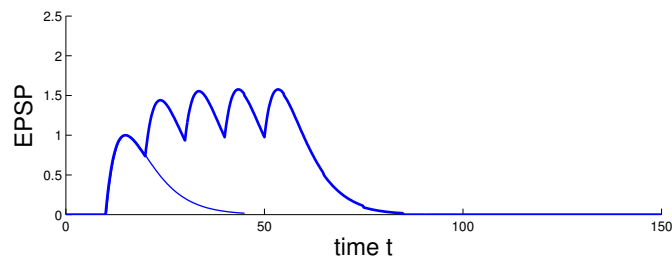


Figure 4: Multiple EPSPs.

- Distal synapses produce longer, smaller EPSPs.
- Multiple such EPSPs need not coincide exactly to produce a cumulative effect.

- Collective effect of multiple EPSPs is highly sensitive to time course!

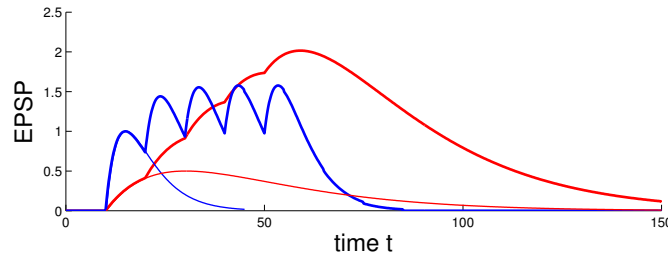


Figure 5: Collective effect of EPSPs.

Summary introduction

- We wish to consider the functional consequences of neuron morphology, in particular of complex dendritic trees with ‘passive’ membranes.
- Conduction along ‘passive’ dendrites typically delays and attenuates an electric signal (e.g., PSP, AP).
- This matters, because electric delays, attenuation, summation and cancellation of PSPs determines exactly when a neuron reaches threshold and fires.
- It matters further because electric delays and attenuation of APs determines the postsynaptic potential at synaptic spines, which in turn governs synaptic plasticity (e.g., NMDA).

2. Cable theory

The effects of passive conduction are most pronounced for long and narrow dendritic branches, which may be treated like a ‘cable’.

The typical problem of “cable theory” (Wilfrid Rall, 1977) is to determine the distribution of voltage $V(x, t)$ along the length of the cable x and over time t , given a current input $I_0(t)$ at one end or another.

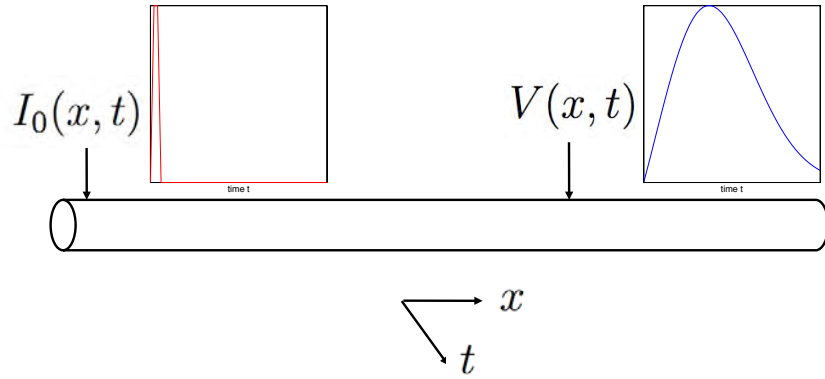


Figure 6: Cable diagram.

Longitudinal resistance

Longitudinal resistance R_L of a cylindrical segment of length Δx and cross-section πa^2

$$R_L = \frac{r_L \Delta x}{\pi a^2}$$

where r_L is the specific resistance in $[\Omega \text{ mm}]$.

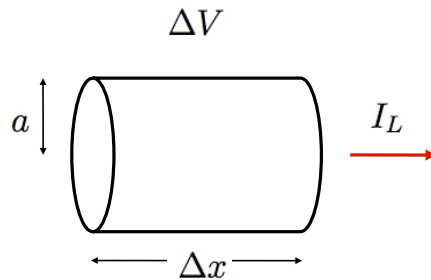


Figure 7: Longitudinal resistance.

Longitudinal current and voltage drop

Longitudinal current I_L and voltage drop ΔV

$$\Delta V = -R_L I_L = -\frac{r_L \Delta x}{\pi a^2} I_L \quad \Leftrightarrow \quad I_L = -\frac{\pi a^2}{r_L} \frac{\Delta V}{\Delta x}$$

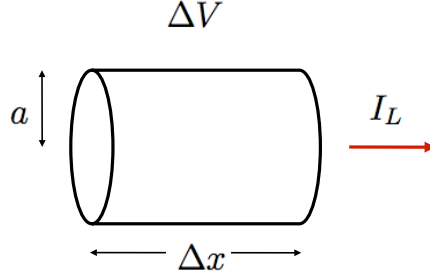


Figure 8: Longitudinal resistance.

The *minus sign* is because, by convention, ΔV is positive when voltage increases with x , and I_x is positive towards positive x .

In the limit $\Delta x \rightarrow 0$, this becomes

$$I_L = -\frac{\pi a^2}{r_L} \frac{\partial V}{\partial x}$$

Radial resistance

Membrane resistance R_m of a cylindrical segment of length Δx and circumference $2\pi a$

$$R_m = \frac{r_m}{2\pi a \Delta x}$$

where r_m is the specific resistance in $[\Omega \text{ mm}^2]$.

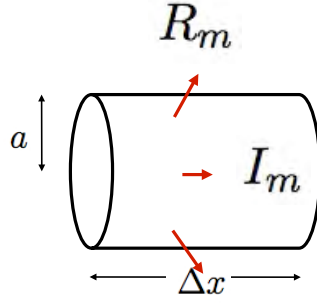


Figure 9: Radial current.

Radial current

For a passive cable, r_m is constant and Ohm's Law relates the voltage V and the membrane current i_m

$$V = I_m R_m \qquad V = 2\pi a \Delta x i_m \frac{r_m}{2\pi a \Delta x} = i_m r_m$$

where I_m is the absolute current (in $[A]$) and i_m is the specific current (in $[A\,mm^{-2}]$).

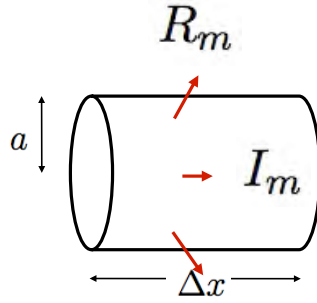


Figure 10: Radial current.

Membrane capacitance

After considering all flows into and out of the segment, any net current charges the capacitance C_m (membrane area $2\pi a \Delta x$):

$$I_{net} = C_m \frac{\partial V}{\partial t} \qquad C_m = 2\pi a \Delta x c_m$$

where c_m is the specific capacitance in $[F\ mm^{-2}]$

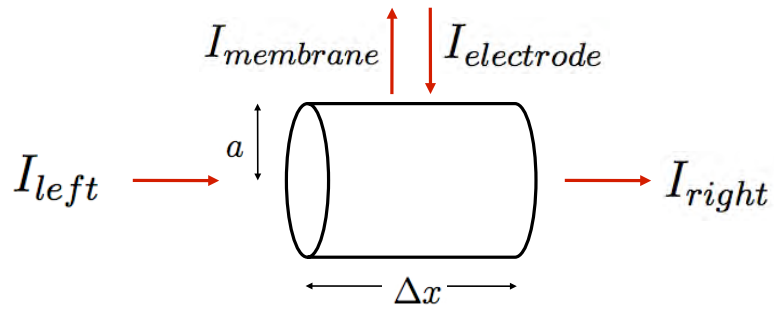


Figure 11: Cable components.

2 Cable Equation

Cable equation I

There are four possible contributions to such a net current:

- through surface of cylinder
- longitudinally through left face
- longitudinally through right face
- through an electrode

$$I_{net} = I_{left} - I_{right} - I_{membrane} + I_{electrode}$$

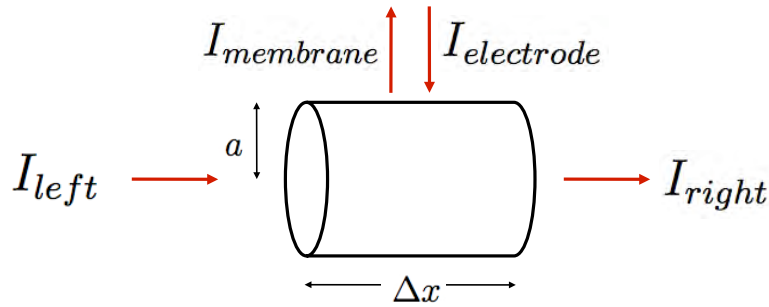


Figure 12: Cable equation components.

Cable equation II

Relate each current term to $V(x, t)$:

$$I_{net} = I_{left} - I_{right} - I_{membrane} + I_{electrode}$$

$$2\pi a \Delta x c_m \frac{\partial V}{\partial t} = - \left(\frac{\pi a^2}{r_L} \frac{\partial V}{\partial x} \right) \Big|_l + \left(\frac{\pi a^2}{r_L} \frac{\partial V}{\partial x} \right) \Big|_r - 2\pi a \Delta x (i_m - i_e)$$

$$r_m c_m \frac{\partial V}{\partial t} = \frac{a r_m}{2 r_L} \frac{1}{\Delta x} \left[\left(\frac{\partial V}{\partial x} \right) \Big|_r - \left(\frac{\partial V}{\partial x} \right) \Big|_l \right] - r_m i_m + r_m i_e$$

$$\tau_m \frac{\partial V}{\partial t} = \lambda_m^2 \frac{1}{\Delta x} \left[\left(\frac{\partial V}{\partial x} \right) \Big|_r - \left(\frac{\partial V}{\partial x} \right) \Big|_l \right] - V + r_m i_e$$

time constant $\tau_m = c_m r_m$

length constant $\lambda_m = \sqrt{\frac{a r_m}{2 r_L}}$

Cable equation III

$$\tau_m \frac{\partial V}{\partial t} = \lambda_m^2 \frac{1}{\Delta x} \left[\left(\frac{\partial V}{\partial x} \right) \Big|_r - \left(\frac{\partial V}{\partial x} \right) \Big|_l \right] - V + r_m i_e$$

$$\Delta x \rightarrow 0$$

$$\tau_m \frac{\partial V}{\partial t} = \lambda_m^2 \frac{\partial^2 V}{\partial x^2} - V + r_m i_e$$

This partial differential equation is the **cable equation**. It describes how currents entering, leaving, and flowing along the dendrite change the membrane potential. Typically, the CE is solved for certain boundary conditions (see next section).

Electrotonic length

A typical value of the *length constant* or *electrotonic length* λ_m is 1 mm ($r_m = 1 \text{ M}\Omega \text{ mm}^2$, $r_L = 1 \text{ k}\Omega \text{ mm}$, $a = 2 \mu\text{m}$.)

$$\lambda_m = \sqrt{\frac{a r_m}{2 r_L}} \approx 1 \text{ mm}$$

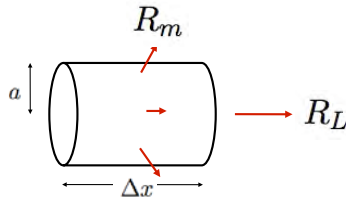


Figure 13: Electronic length.

For segments of length $\Delta x = \lambda_m$, longitudinal and membrane resistance of are equal:

$$R_L = \frac{r_L \lambda_m}{\pi a^2} = \sqrt{\frac{r_L r_m}{2\pi^2 a^3}} \qquad R_m = \frac{r_m}{2\pi a \lambda_m} = \sqrt{\frac{r_L r_m}{2\pi^2 a^3}}$$

Summary cable equation

- The space- and time-dependent voltage along a passive cable is governed by a partial differential equation (PDE), the cable equation:

$$\tau_m \frac{\partial V}{\partial t} = \lambda_m^2 \frac{\partial^2 V}{\partial x^2} - V + r_m i_e$$

- The time-constant $\tau_m = r_m c_m$ describes voltage attenuation over time.
- The length-constant $\lambda_m = \sqrt{\frac{a r_m}{2 r_L}}$ describes voltage attenuation over space.
- The time-derivative term $\frac{\partial V}{\partial t}$ relates to charging of the membrane capacitance.
- The second space-derivative term $\frac{\partial^2 V}{\partial x^2}$ relates to accumulation of longitudinal currents.

3 Linear cable theory

Linear cable theory assumes a passive membrane governed by

$$V = r_m i_m$$

and by the cable equation

$$\tau_m \frac{\partial V}{\partial t} = \lambda_m^2 \frac{\partial^2 V}{\partial x^2} - V + r_m i_e,$$

where $\tau_m = r_m c_m$ and $\lambda_m^2 = \frac{a r_m}{2r_L}$.

Next, we consider analytical solutions of the CE for special cases (boundary conditions).

a) Infinite cable with constant local current

Steady-state potential for a current spike at $x = 0$:

$$\frac{\partial V}{\partial t} = 0, \quad i_e = i_0 \delta(x) \quad \Rightarrow \quad 0 = \lambda_m^2 \frac{\partial^2 V}{\partial x^2} - V$$

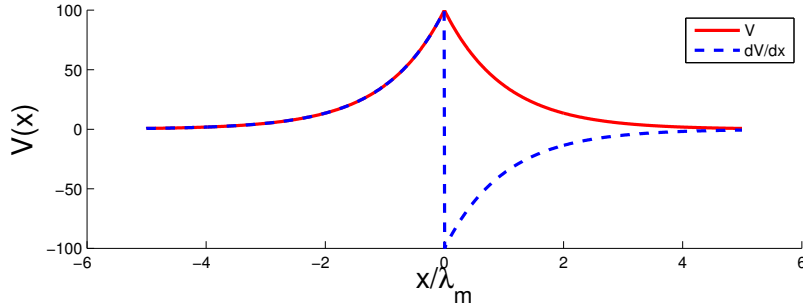


Figure 14: Infinite cable with constant local current.

$$V = V_0 \exp\left(-\left|\frac{x}{\lambda_m}\right|\right), \quad \frac{\partial V}{\partial x} = \text{sign}(x) V_0 \exp\left(-\left|\frac{x}{\lambda_m}\right|\right)$$

b) Infinite cable with linear voltage profile

$$\frac{\partial^2 V}{\partial x^2} = 0, \quad i_e = 0 \quad \Rightarrow \quad \tau_m \frac{\partial V}{\partial t} = -V$$

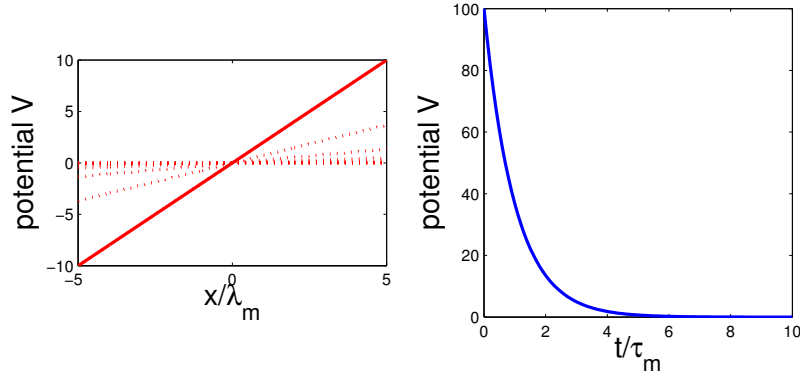


Figure 15: Infinite cable with linear voltage profile.

$$V_0(x) = \alpha_1 x + \alpha_0, \quad V = V_0(x) \exp\left(-\frac{t}{\tau_m}\right)$$

c) Infinite cable with multiple constant local currents

As mentioned, the steady-state potential evoked by a single current spike at $x = 0$ is

$$V = I_e R_\lambda \exp\left(-\left|\frac{x}{\lambda_m}\right|\right)$$

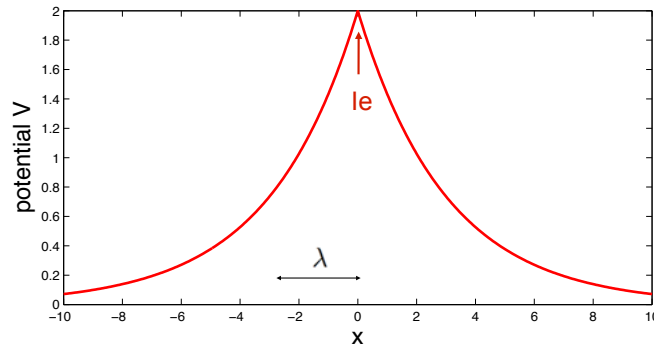


Figure 16: Infinite cable with multiple constant local currents.

If current is injected at multiple points, the resulting steady-state potential will be the sum of the potentials evoked by each injection alone. This is because the CE is linear!

$$\lambda_m^2 \frac{\partial^2 V_{1,2,3}(x)}{\partial x^2} = V_{1,2,3}(x) - r_m I_{1,2,3}(x)$$

$$I_{sum}(x) = I_1(x) + I_2(x) + I_3(x)$$

$$\Leftrightarrow$$

$$V_{sum} = V_1(x) + V_2(x) + V_3(x) \qquad \lambda_m^2 \frac{\partial^2 V_{sum}}{\partial x^2} = V_{sum} - r_m I_{sum}$$

Steady-state solution for constant input currents at three points.

$$V_{sum} = V_1(x) + V_2(x) + V_3(x)$$

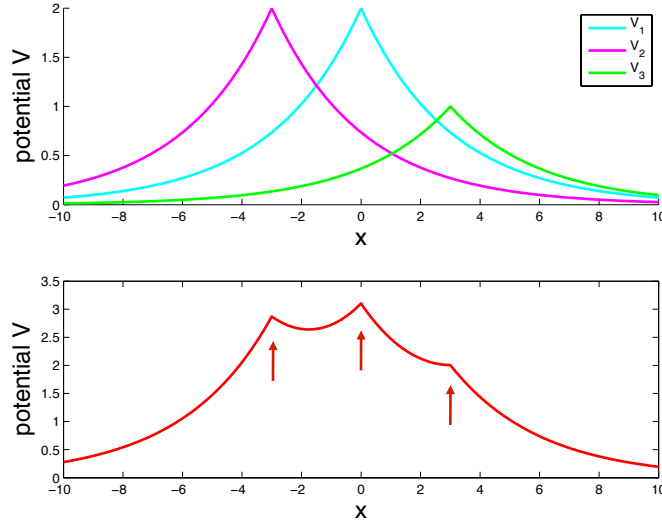


Figure 17: Steady-state solution for constant input currents at three points.

d) Infinite cable with transient local current

We now consider an infinite cable with a transient and local input current. Specifically, for an instantaneous current pulse

$$i_e = I_e \tau_m \delta(x) \delta(t)$$

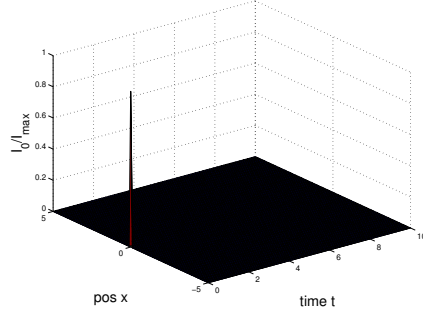


Figure 18: Infinite cable with transient local current.

the CE

$$\tau_m \frac{\partial V}{\partial t} = \lambda_m^2 \frac{\partial^2 V}{\partial x^2} - V + r_m i_e$$

has the solution

$$V(x, t) = \frac{I_e R_\lambda}{\sqrt{4\pi \lambda_m^2 t / \tau_m}} \exp\left(-\frac{\tau_m x^2}{4\lambda_m^2 t}\right) \exp\left(-\frac{t}{\tau_m}\right)$$

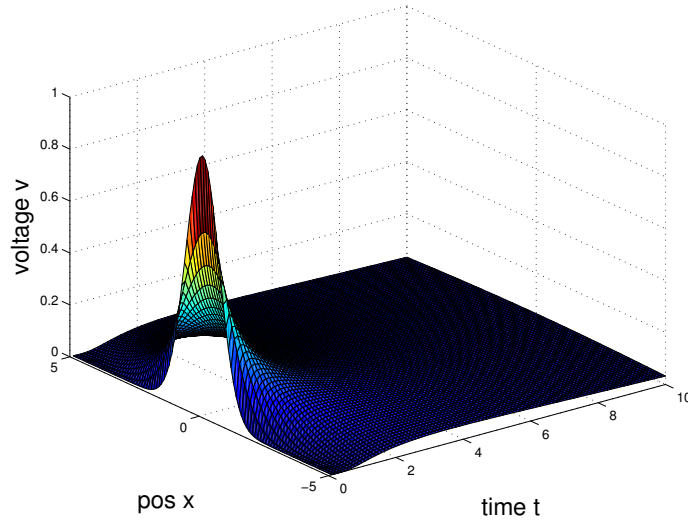


Figure 19: Infinite cable with transient local current solution.

$$V(x, t) = \frac{I_e R_\lambda}{\sqrt{4\pi \lambda_m^2 t / \tau_m}} \exp\left(-\frac{\tau_m x^2}{4\lambda_m^2 t}\right) \exp\left(-\frac{t}{\tau_m}\right)$$

can be rewritten as

$$V(x, t) = \frac{A(t)}{\sqrt{2\pi \sigma^2(t)}} \exp\left(-\frac{x^2}{2\sigma^2(t)}\right)$$

which reveals a Gaussian profile with time-dependent area $A(t)$ and standard deviation $\sigma(t)$:

$$A(t) = I_e R_\lambda \exp\left(-\frac{t}{\tau_m}\right), \quad \sigma(t) = \lambda_m \sqrt{\frac{2t}{\tau_m}}$$

$$A(t) = I_e R_\lambda \exp\left(-\frac{t}{\tau_m}\right), \quad \sigma(t) = \lambda_m \sqrt{\frac{2t}{\tau_m}}$$

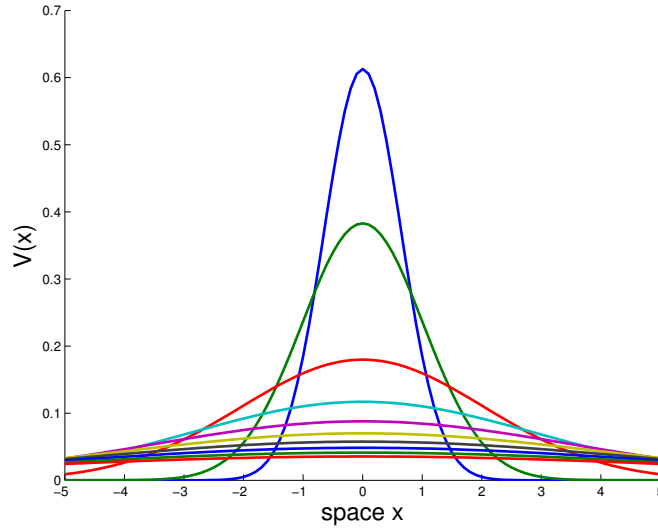


Figure 20: Gaussian profile with time-dependent area $A(t)$ and standard deviation $\sigma(t)$.

At each time t , a different location x reaches its peak potential $V_{peak}(x, t)$:

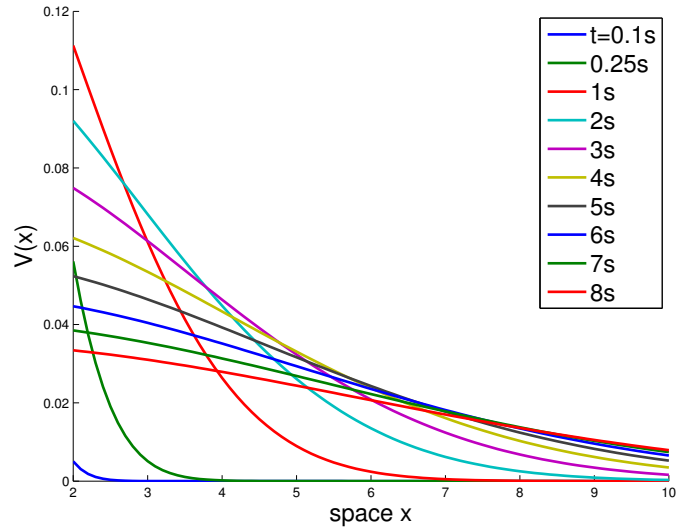


Figure 21: At each time t , a different location x .

Colors represent different times t !

Each location x reaches its peak potential $V_{peak}(x, t)$ at a different time t :

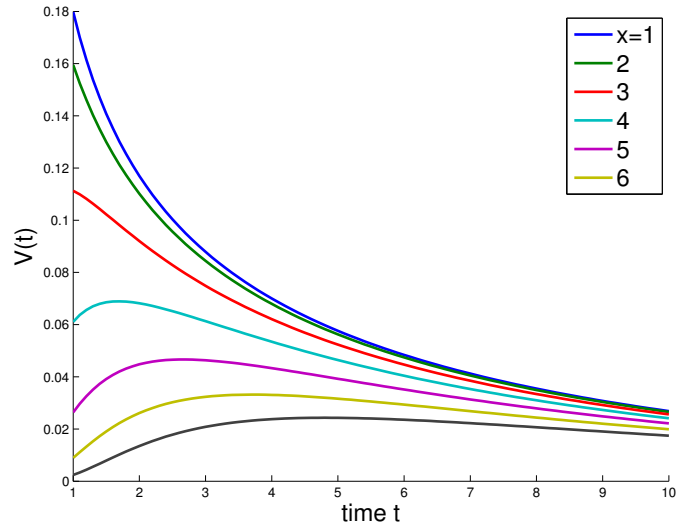


Figure 22: Each location x reaches its peak potential $V_{peak}(x, t)$ at a different time t .

Colors represent different locations x !

e) Local peak potential V_{peak}

To determine the time t_{max} , at which location x reaches its local peak potential V_{max} , we set $\frac{\partial V}{\partial t} = 0$:

$$\frac{\partial V(x, t)}{\partial t} \propto \left[-\frac{1}{\tau_m} - \frac{\sigma'(t)}{\sigma(t)} + \frac{\sigma'(t) x^2}{\sigma^3(t)} \right] V(x, t) \stackrel{!}{=} 0$$

$$\sigma = \lambda_m \sqrt{\frac{2t}{\tau_m}}, \quad \sigma' = \lambda_m \sqrt{\frac{1}{2t\tau_m}}$$

$$\frac{\partial V(x, t)}{\partial t} \propto \left[-\frac{1}{\tau_m} - \frac{1}{2t} + \frac{\tau_m x^2}{4\lambda_m^2 t^2} \right] V(x, t) \stackrel{!}{=} 0$$

$$\frac{4t^2}{\tau_m^2} + 2\frac{t}{\tau_m} - \frac{x^2}{\lambda_m^2} \stackrel{!}{=} 0 \quad \Rightarrow \quad \frac{2t}{\tau_m} \stackrel{!}{=} \sqrt{\left(\frac{x}{\lambda_m}\right)^2 + 1} - 1 \quad \Rightarrow \quad \frac{2t}{\tau_m} \stackrel{!}{\approx} \frac{x}{\lambda_m}$$

Solving for $t = t_{max}$ reveals the “conduction velocity” v_{cond}

$$t_{max} \approx \frac{x \tau_m}{2 \lambda_m} \quad \Rightarrow \quad v_{cond} \equiv \frac{x}{t_{max}} \approx 2 \frac{\lambda_m}{\tau_m}$$

Normalized voltage

Normalization to local maximum – $V(x, t)/V_{max}(x)$ – illustrates the conduction velocity v_{cond} :

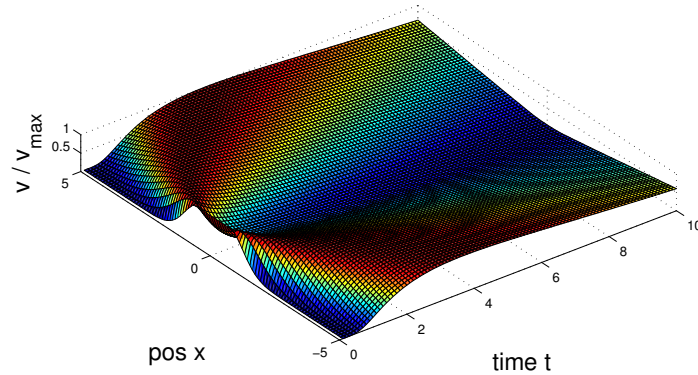


Figure 23: Normalization to local maximum – $V(x, t)/V_{max}(x)$ – illustrates the conduction velocity v_{cond} .

Summary linear cable theory

- Analytical solutions of CE for certain special cases.
- Constant, local input current \rightarrow exponential attenuation over space.
- Multiple constant, local input currents \rightarrow multiple exponential attenuations.
- Transient, local input current \rightarrow Gaussian attenuation over space, exponential attenuation over time.
- Local peak voltage propagates with

$$v_{cond} = 2^{\lambda_m/\tau_m}$$

- Analytical solution for electric delays, attenuation, summation and cancellation of current pulses!

4 Branching points (advanced)

To model complex dendritic trees, we must consider not only cylindrical dendrites, but also dendrites with increasing width and dendrites with branching points.

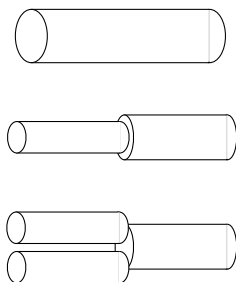


Figure 24: Dendritic trees.

To illustrate the effect of branching, we consider a T-junction of 3 semi-infinite cables, with radii a_1 , a_2 , a_3 . We measure distance x outward from the junction and inject a current into branch 2 at distance x_e .

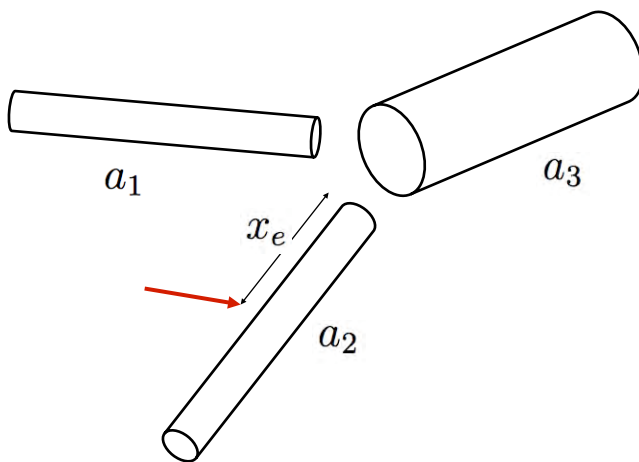


Figure 25: Dendritic trees.

The static current into branch 2 evokes the following steady-state

voltages in branches 1, 2, and 3:

$$v_1(x) = I_e R_{\lambda_1} p_1 \exp\left(-\frac{x}{\lambda_1} - \frac{x_e}{\lambda_2}\right)$$

$$v_2(x) = I_e R_{\lambda_2} \left[(p_2 - 1) \exp\left(-\frac{x}{\lambda_2} - \frac{x_e}{\lambda_2}\right) + \exp\left(-\frac{|x_e - x|}{\lambda_2}\right) \right]$$

$$v_3(x) = I_e R_{\lambda_3} p_3 \exp\left(-\frac{x}{\lambda_3} - \frac{x_e}{\lambda_2}\right)$$

Exponential attenuation within branches is governed by length constants λ_i (“electrotonic length”). Transmission between branches is governed by input resistances R_{λ_i} and coupling factors p_i .

thick \rightarrow thin

thin \rightarrow thick

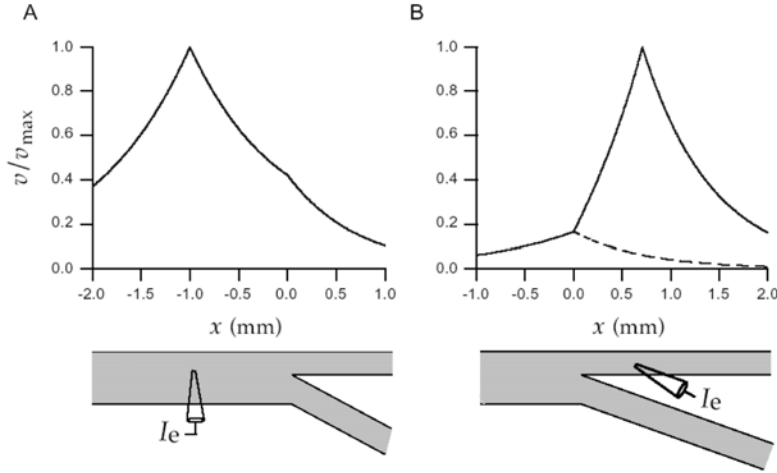


Figure 26: Comparison of branches [4]

Branch thickness

Length constants and input resistances depend on branch thickness:

$$\lambda_i = \sqrt{\frac{a_i r_m}{2 r_L}}$$

$$R_{\lambda_i} = \frac{r_L \lambda_i}{\pi a_i^2}$$

This dependence is even more pronounced for coupling factors:

$$p_i = \frac{a_i^{3/2}}{a_1^{3/2} + a_2^{3/2} + a_3^{3/2}}$$

The Rall model

Rall (1957, 1977) has suggested a method for applying linear cable theory to responses of real neurons. It allows us to compute the effect of the soma potential of synaptic input currents on the distal dendrite. In Rall's model the entire dendritic region between soma and synapse is replaced by single equivalent cable.

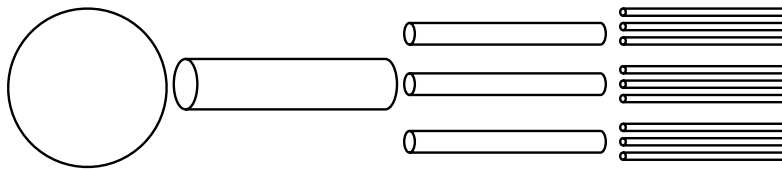


Figure 27: Rall model.

Radius a and length L of the equivalent dendrite are chosen to match the properties of the actual dendritic tree:

- (i) Surface area $2\pi L a$ is set equal to surface area of full dendritic tree.
- (ii) Electrotonic length L/λ is set equal to total electrotonic length of tree segments $\sum_i \frac{L_i}{\lambda_i}$

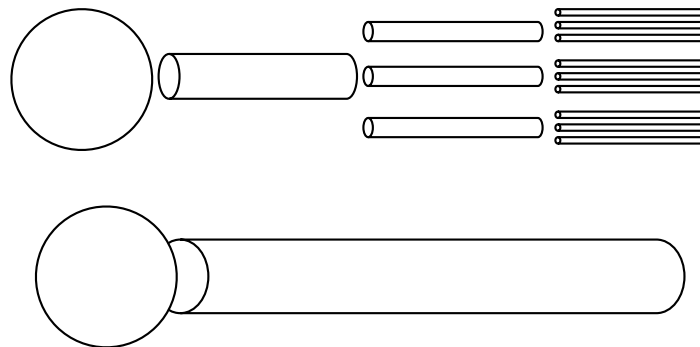


Figure 28: Rall model components.

The Rall model is exact when

$$a_1^{3/2} = a_2^{3/2} + a_3^{3/2} \quad \Rightarrow \quad p_1 = p_2 + p_3 = \frac{1}{2}$$

Actual dendritic geometry conforms well to this rule.

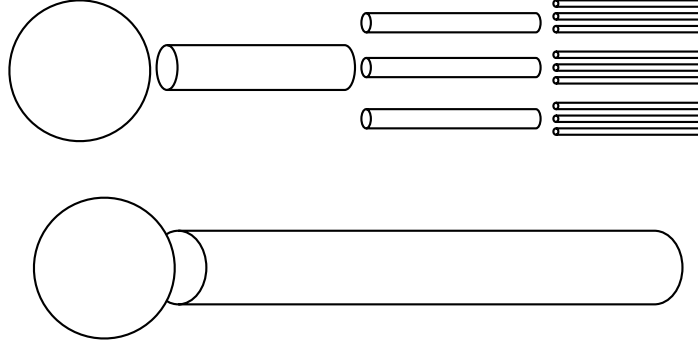


Figure 29: Rall model components.

Constant current to soma

The Rall model can be described in an intuitive way by *equivalent circuits*. Consider the case of a constant current being injected in the soma. The voltage measured at a distance x is given by an equivalent circuit with three resistances, R_{soma} (soma to ground), R_1 (soma to point x), and R_2 (point x to ground).

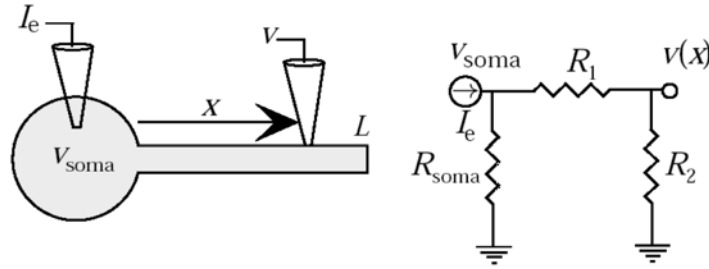


Figure 30: Soma current diagram. [5]

Constant current to dendrite

Similarly, consider the case of a constant current injected to the dendrite, with the soma potential clamped to V_{rest} . The current entering the soma is given by an equivalent circuit with two resistances R_3 and R_4 . (The soma resistance is irrelevant).

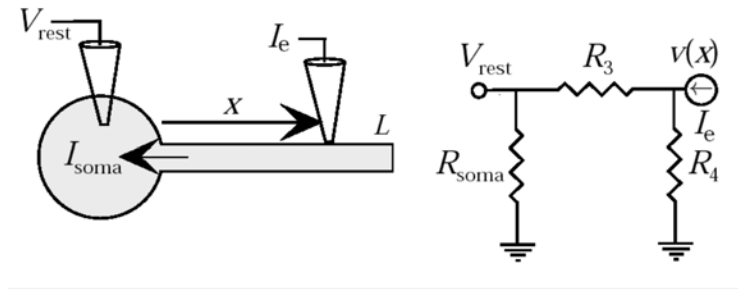


Figure 31: Constant current to dendrite. [5]

Voltage and current attenuation

The Rall model highlights a general result of linear cable theory (for constant current/voltage):

Inward attenuation of current equals outward attenuation of voltage.

Example: if a current is attenuated 10-fold as it propagates from given point on a dendrite to the soma, the soma voltage is also attenuated 10-fold as it propagates to the same point on the dendrite.

Summary branching points

- Cable theory applies also to more complex dendrites (varying diameters, branching points).
- Voltage attenuation is governed by length constants (electrotonic length).

- Current distribution between branches is governed by coupling factors (diameter^{3/2}).
- The Rall model replaces an entire dendritic tree with an equivalent dendrite (matching surface and electrotonic length).
- For steady-state currents and voltages, inward attenuation of current equals outward attenuation of voltage.

5 Morphoelectrotonic transform

The electric behaviour of dendrites with realistic morphology reconstructed from EM must be computed numerically. This is done by apportioning the continuous dendrite into discrete compartments, each assumed to be electronically compact and represented by a single $V(x, t)$. The number of compartments can range from one to several thousand, depending the desired accuracy.

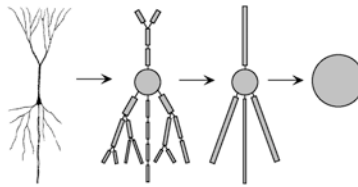


Figure 32: Morphoelectrotonic transform. [6]

World GDP, local PPP

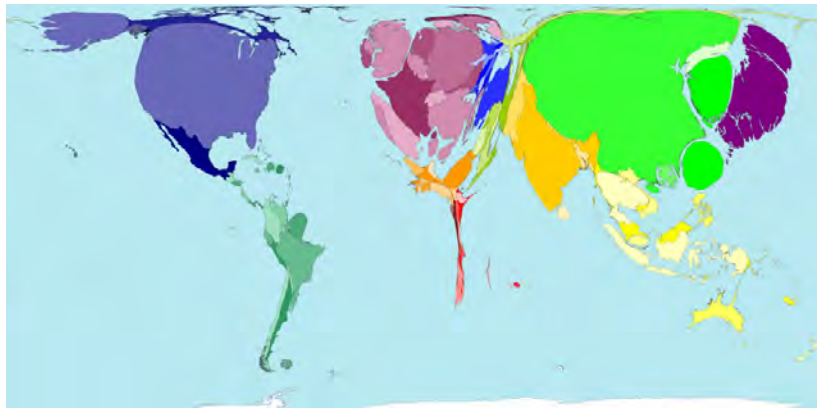


Figure 33: World GDP, local PPP. [7]

Logarithmic voltage attenuation

To visualise the results of such computations, the *morphoelectrotonic transform* can be helpful.

The MT distorts the anatomical shape of a neuron into an ‘electric shape’ that illustrates *additive* electrical properties.

For example, a suitable electrical quantity is *logarithmic voltage attenuation*:

$$\frac{v(x_1)}{v(x_3)} = \frac{v(x_1)}{v(x_2)} \cdot \frac{v(x_2)}{v(x_3)} \qquad \ln \frac{v(x_1)}{v(x_3)} = \ln \frac{v(x_1)}{v(x_2)} + \ln \frac{v(x_2)}{v(x_3)}$$

Log attenuation is additive!

Conduction delay

A second suitable quantity is the conduction delay for a voltage pulse.

$$\Delta t_{13} = \Delta t_{12} + \Delta t_{23} \qquad \Delta t_{ij} = t_i - t_j$$

The ‘delay’ can be defined, for example, for the centroid of the time-varying voltage:

$$t_i = \frac{\int t v(x_i, t) dt}{\int v(x_i, t) dt}$$

Conduction delays are additive!

Inward attenuation

Inward attenuation and delay of a peripheral constant current and voltage pulse. Note uniform electronic properties of apical and basal dendrites (cortical L5 pyramid).

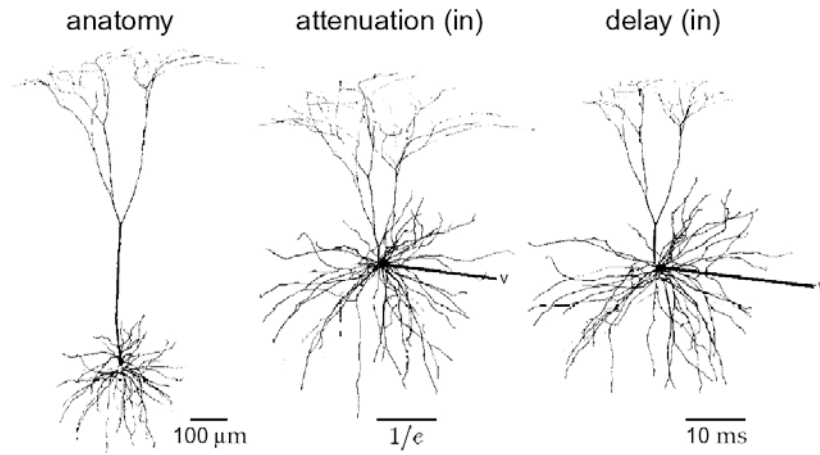


Figure 34: Anatomy, attenuation, delay [8]

Outward attenuation

Outward attenuation of alternating soma current. Slow signals penetrate much further than fast ones. Outward attenuation is smaller than inward attenuation (for most frequencies).

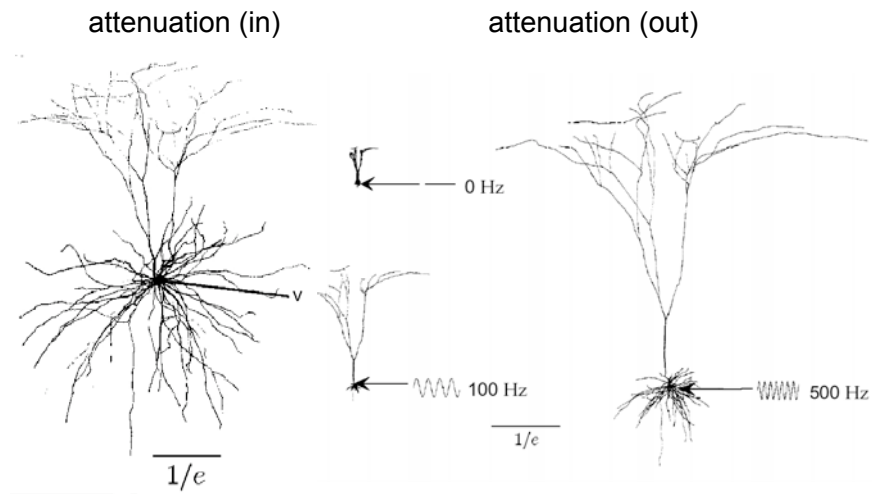


Figure 35: Left: Attenuation in. Right: Attenuation out [9]

Electric shape I

Outward attenuation of static current injected into the soma, for different cell types:

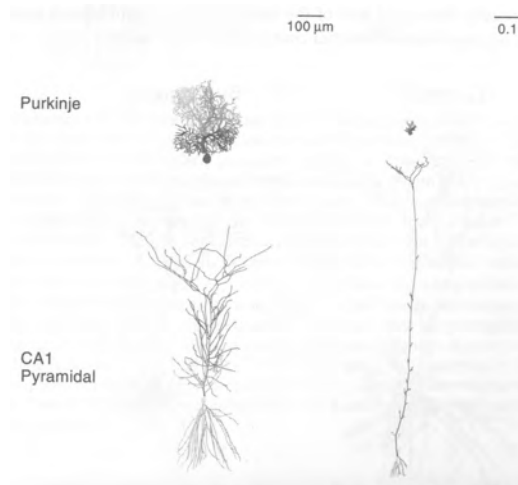


Figure 36: Electric shape I. [10]

Electric shape II

Outward attenuation of static current injected into the soma, for different cell types:

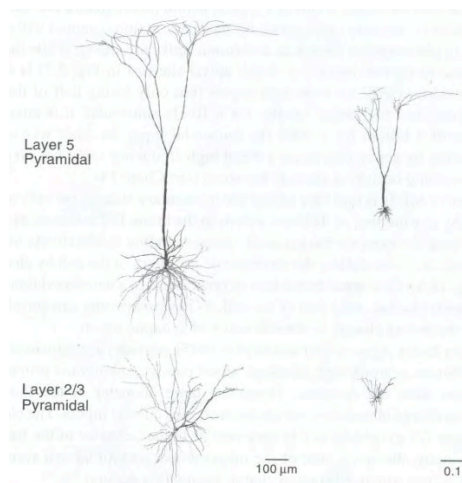


Figure 37: Electric shape II. [11]

Summary morphoelectronic transform

- Detailed numerical simulation of complex dendrites (reconstructed from EM) reveals the ‘electric shape’ of neurons.
- Outward attenuation depends on frequency. Slow signals (resting potential) penetrate much further than fast signals (action potentials).
- The ‘electric shape’ of a neuron can differ dramatically from its anatomical shape (compact Purkinje, elongated CA1 pyramid, isotropic L3 pyramid).

6 Myelinated axons (advanced)

Simulation of multi-compartment model with Hodgkin-Huxley conductances.

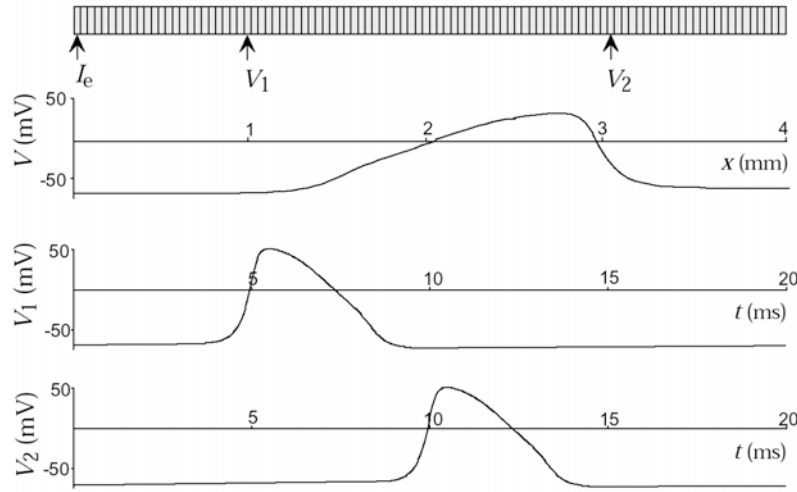


Figure 38: Simulation of multi-compartment model with Hodgkin-Huxley conductances. [12]

Scaling law for unmyelinated axons: $v \propto \sqrt{a}$

- Conduction velocities of unmyelinated axons range from 0.4 m/s to 10 m/s .
- Conduction velocity is proportional to the ratio between electrotonic length and membrane time constant:

$$v_{cond} \propto \frac{\lambda_m}{\tau_m} = \frac{\sqrt{a r_m / 2 r_l}}{r_m c_m} \propto \sqrt{a}$$

- The square root dependence on axon radius means that very thick axons are required to achieve high propagation speeds.
- The squid giant axon ($800 \mu\text{m}$) conducts 20-times faster than a typical (unmyelinated) mammalian axon ($2 \mu\text{m}$), but at the expense of 16000 times more tissue.

Myelinated axon

Many vertebrate axons are covered by an insulating layer of myelin, except at periodic gaps, called the nodes of Ranvier, where the membrane contains a high density of voltage-dependent channels. The myelin consists of many layers of glial membrane wrapped around the axon.

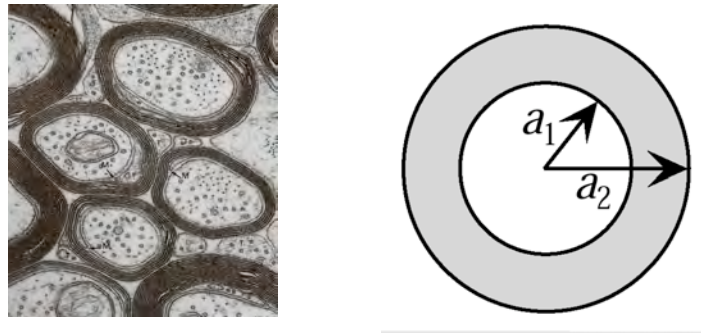


Figure 39: Left: Myelinated layers. Right: radius of the axon [13]

A myelinated axon can be modeled as a series of compartments, alternatingly with active membrane (Ranvier node) and with passive membrane with $r_m = \infty$ (myelinated segment).

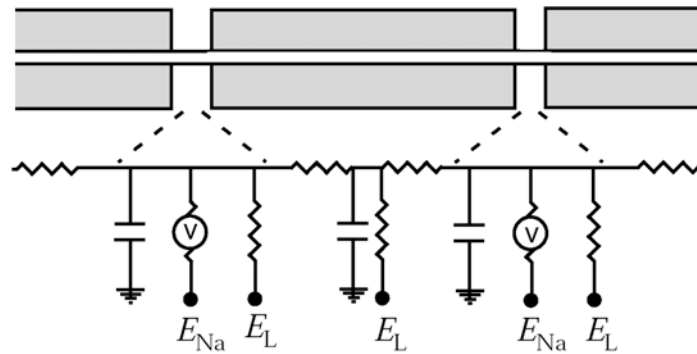


Figure 40: Myelinated axon electronic diagram. [14]

What follows focusses on myelin-covered segments. What is the membrane capacity c_m ? Conduction velocity? How does it scale with diameter?

Capacity of myelin-covered axon

To compute capacitance of a myelin-covered axon, we take the myelin to consist of a concentric arrangement of thin individual shells. Note that inverse capacitances add when arranged in series:

$$\frac{1}{C_i} = \frac{1}{2\pi c_m a_i L} \quad \frac{1}{C_m} = \sum_i \frac{1}{C_i} = \sum_i \frac{1}{2\pi c_m a_i L}$$

with specific capacitance c_m , length L , radius a , and individual thickness d_m .

Taking the limit $\Delta a \rightarrow 0$ and integrating gives

$$\frac{1}{C_m} = \frac{1}{2\pi c_m d_m L} \int_{a_1}^{a_2} \frac{da}{a} = \frac{1}{2\pi c_m d_m L} \ln \frac{a_2}{a_1}$$

Cable equation for $r_m = \infty$

We revisit the cable equation in the special case of infinite resistance and zero membrane current: $r_m \rightarrow \infty$, $i_m \rightarrow 0$

$$C_m \frac{\partial V}{\partial t} = \frac{\pi L a_1^2}{r_L} \frac{\partial^2 V}{\partial x^2}$$

or

$$\frac{\partial V}{\partial t} = D \frac{\partial^2 V}{\partial x^2}$$

with the ‘diffusion constant’

$$D = \frac{\pi L a_1^2}{C_m r_L} = \frac{\pi L a_1^2}{2\pi c_m d_m L r_L} \ln \frac{a_2}{a_1} = \frac{a_1^2}{2 c_m d_m r_L} \ln \frac{a_2}{a_1}$$

Diffusion constant and conduction velocity

The diffusion constant is proportional to the square of the conduction velocity:

$$v_{cond}^2 \propto D = \frac{1}{2 c_m d_m r_L} a_1^2 \ln \frac{a_2}{a_1}$$

For a given outer radius a_2 , the diffusion constant (and conduction velocity) is a non-monotonic function of inner radius a_1 :

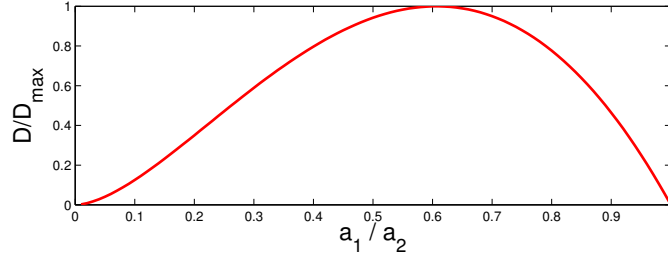


Figure 41: Diffusion constant and conduction velocity.

Optimal inner radius

For a given outer radius a_2 , the maximal values of D and v_{cond} are reached for

$$\begin{aligned}
 0 &\stackrel{!}{=} \frac{dD}{da_1} \propto 2a_1 \ln \frac{a_2}{a_1} - a_1^2 \frac{1}{a_1} = a_1 \left(2 \ln \frac{a_2}{a_1} - 1 \right) \\
 &\Rightarrow \\
 a_1 &= a_2 \exp(-1/2) \approx 0.6 a_2
 \end{aligned}$$

A fractional inner radius of ~ 0.6 is typical for myelinated axons!

Conduction velocities of myelinated axons reach up to 150 m/s .

Scaling law for myelinated axon: $v \propto a$

At the optimal inner radius a_1 , the propagation velocity becomes proportional to a_2

$$D \propto a_1^2 \ln \frac{a_2}{a_1} \quad a_1 = a_2 \exp(-1/2), \quad \ln \frac{a_2}{a_1} = \frac{1}{2}$$

$$D \propto a_2^2$$

The conduction velocity is proportional to axon radius a (not \sqrt{a} !)

$$v_{cond} \propto \sqrt{D} \propto a_2$$

Myelination increases velocity *and* ensures more favorable scaling law!

Summary axon conduction

- Unmyelinated axons can be modeled numerically as a series of compartments with active conductances.
- Unmyelinated axons conduct up to 10 m/s , velocity scaling with \sqrt{a} .
- Myelinated axons can be modeled as a series of compartments with, alternatingly, active and passive conductances.
- Myelination changes the physics of passive compartments, increasing c_m and reducing conductance $1/r_m$ to zero.
- Myelinated axons conduct up to 150 m/s , velocity scaling with a .
- In an optimal myelin sheath, inner diameter is 60% of outer diameter.

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