Introduction to Neural Computation

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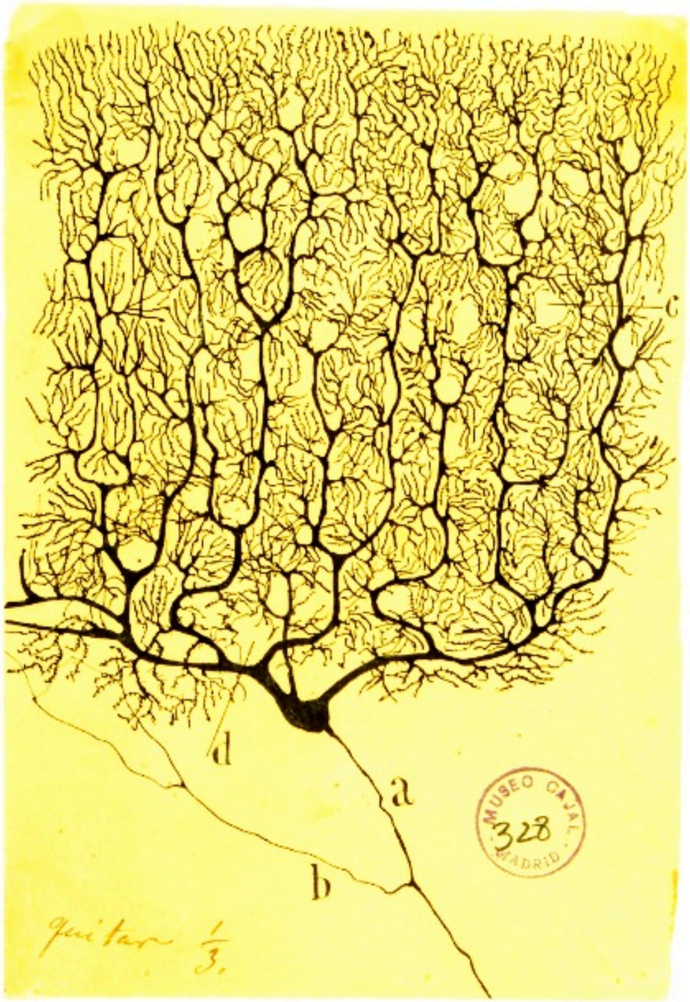
MIT BCS 9.40 — 2018

Lecture 6

Signal propagation in dendrites and axons

- So far we have considered a very simple model of neurons – a model representing the soma of the neuron.
- We did this because in most vertebrate neurons, the region that initiates action potentials is at the soma.
- This is usually where the 'decision' is made in a neuron whether to spike or not.

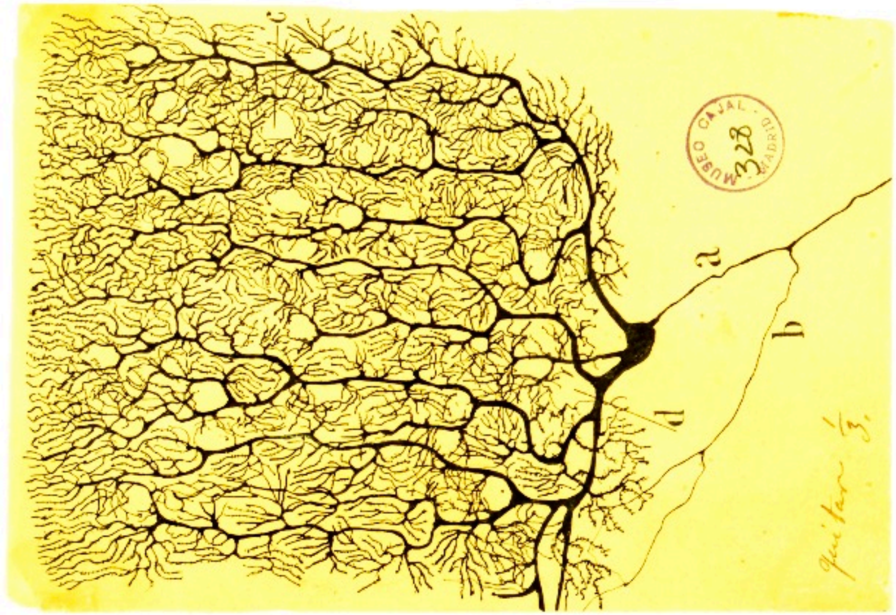


Ramon y Cajal

Signal propagation in dendrites and axons

- Relatively few inputs to a neuron are made onto the soma.
- Inputs arrive onto the dendrites – which are thin branching processes that radiate from the soma.
- Many synapses form onto the dendrite at some distance from the soma (as much as 1-2 mm away)

Ramon y Cajal



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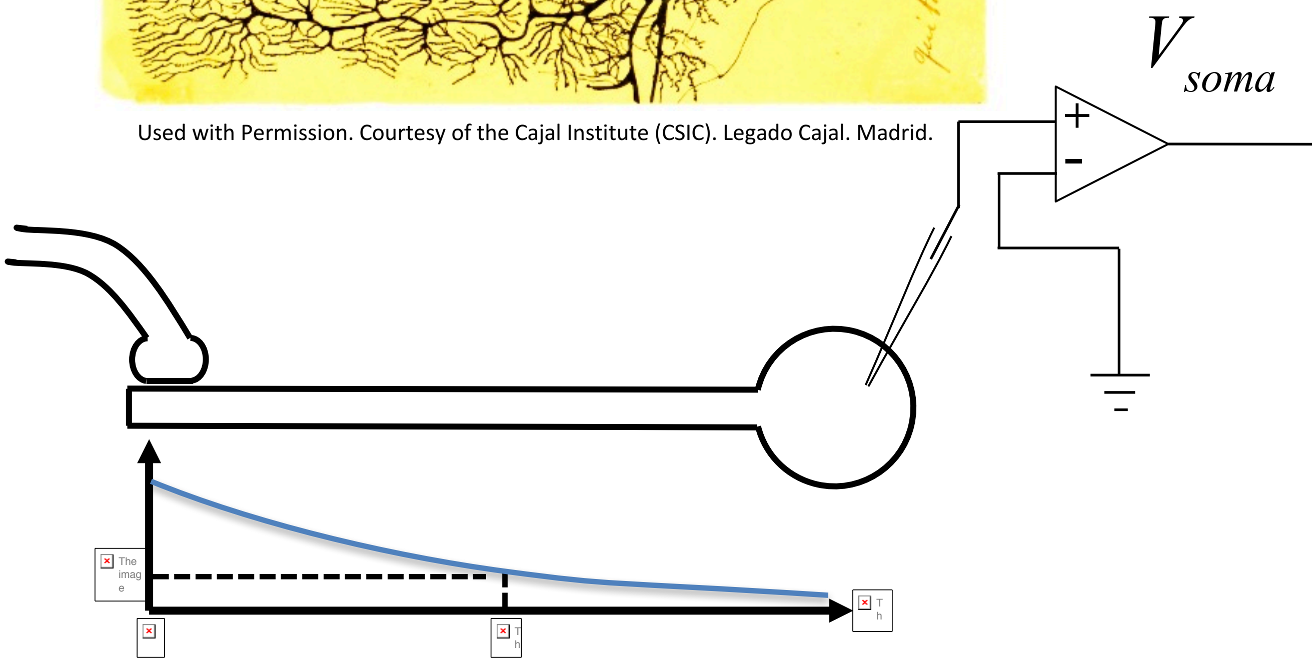
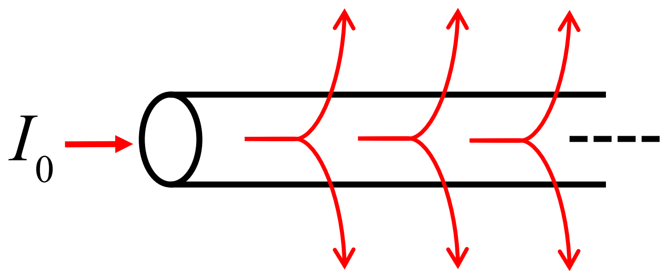
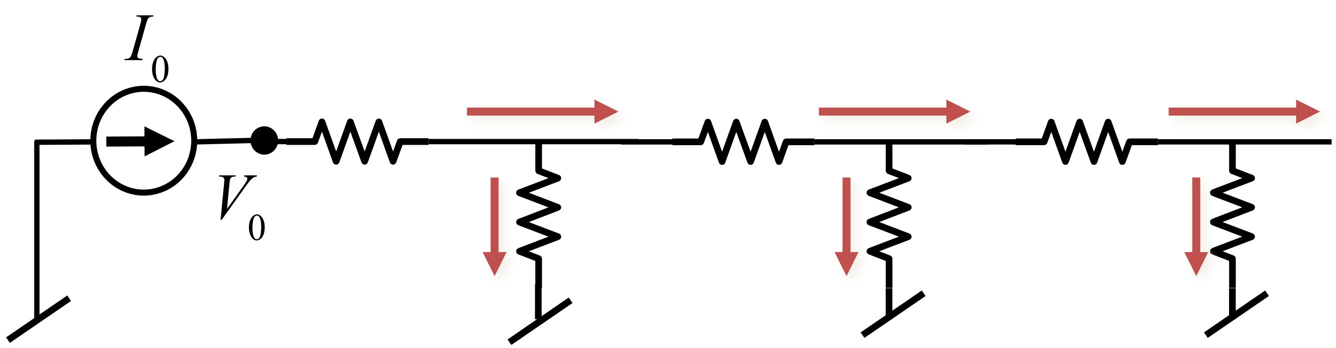


How does a pulse of synaptic current affect the membrane potential at the soma (and elsewhere in the dendrite)?

A dendrite is like a leaky garden hose



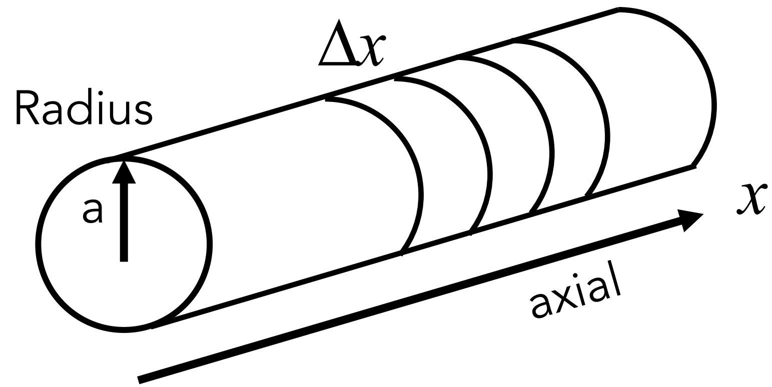
- Current is like water flow
- Voltage is like pressure

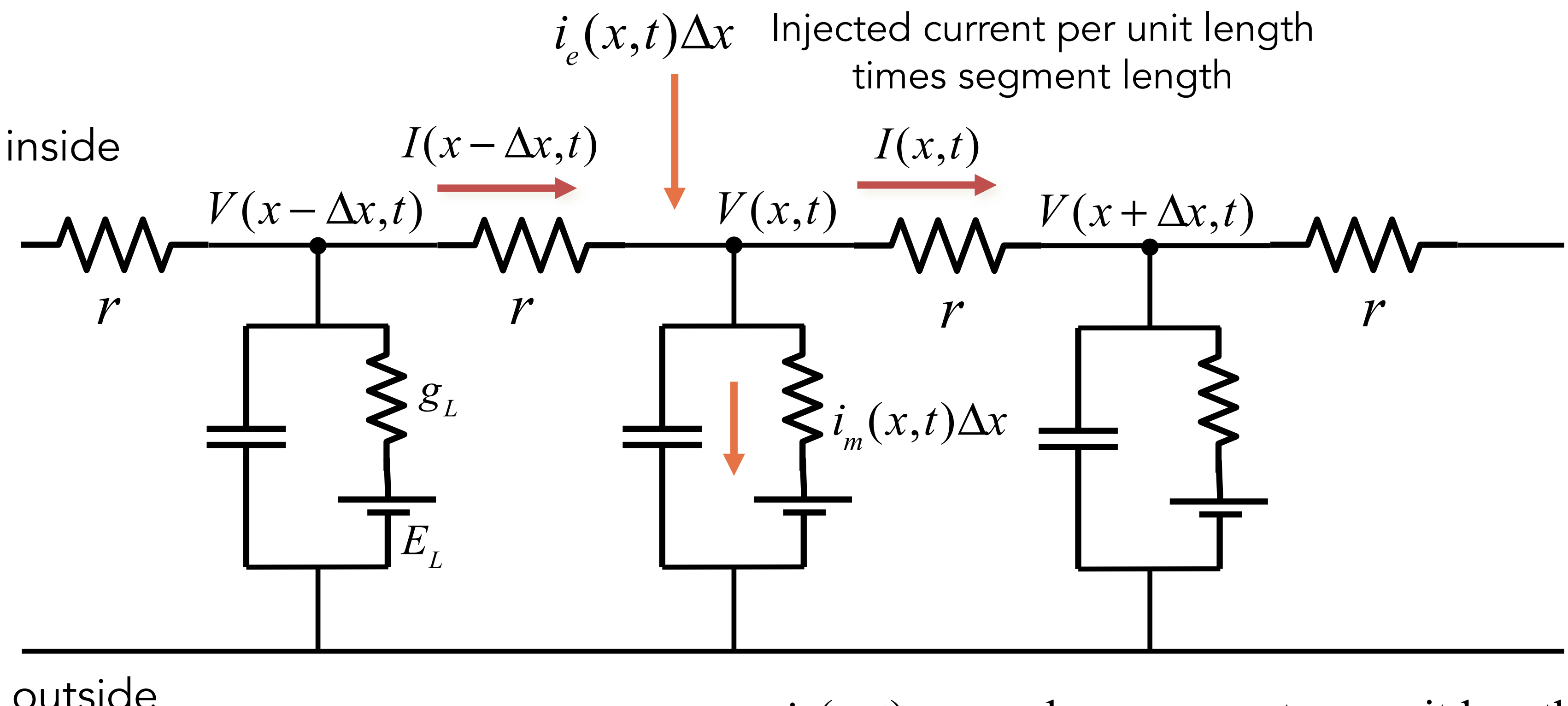


Learning objectives for Lecture 6

- To be able to draw the ‘circuit diagram’ of a dendrite
- Be able to plot the voltage in a dendrite as a function of distance for leaky and non-leaky dendrite, and understand the concept of a length constant
- Know how length constant depends on dendritic radius
- Understand the concept of electrotonic length
- Be able to draw the circuit diagram a two-compartment model

Finite element analysis

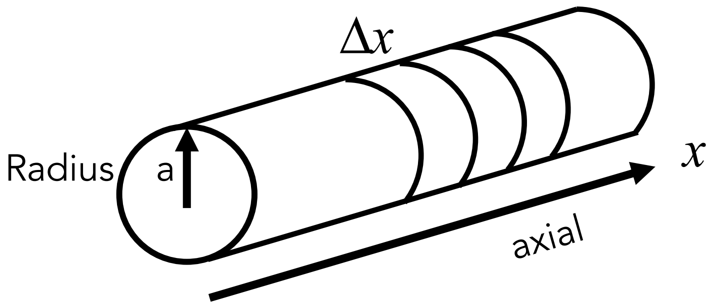




$i_m(x,t) =$ membrane current per unit length

Extracellular resistance is small compared to intracellular.

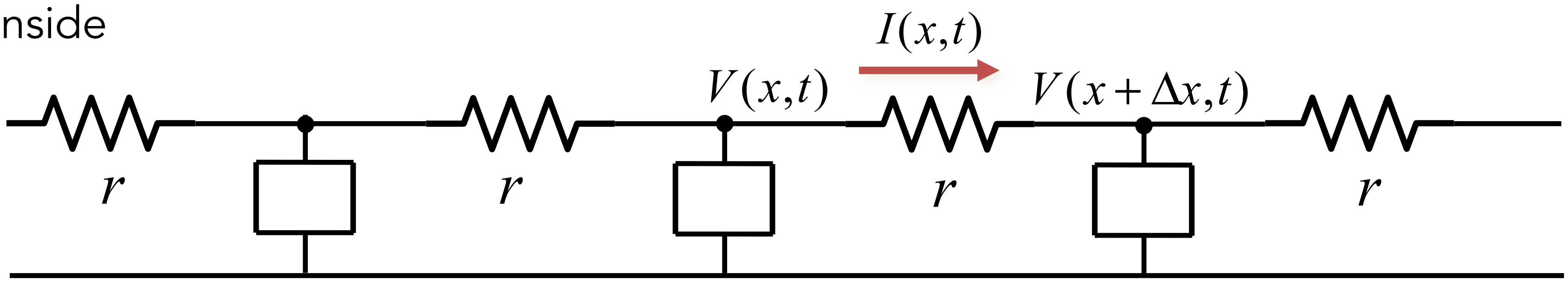
The cable equation



Let's write down the relation between V(x,t) and I(x,t)

Ohm's Law $\Delta V = I\,R$

inside



outside

$$-\frac{\partial V}{\partial x} = R_a\, I(x,t)$$

$$R_a = \frac{r}{\Delta x} = \text{axial resistance per unit length}$$

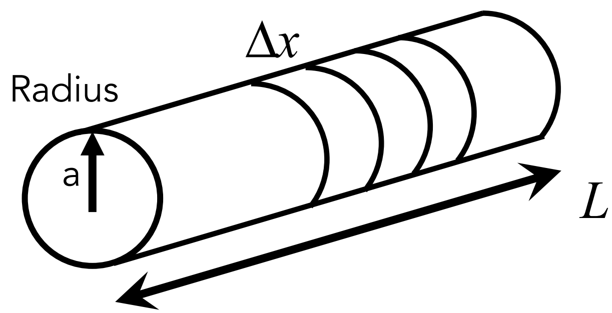
$$V(x,t) - V(x+\Delta x,t) = r\, I(x,t)$$

$$\frac{1}{\Delta x}\left[V(x,t) - V(x+\Delta x,t)\right] = \frac{r}{\Delta x} I(x,t)$$

This is just the definition of a derivative!

Note that current flow to the right produces a negative gradient

The cable equation

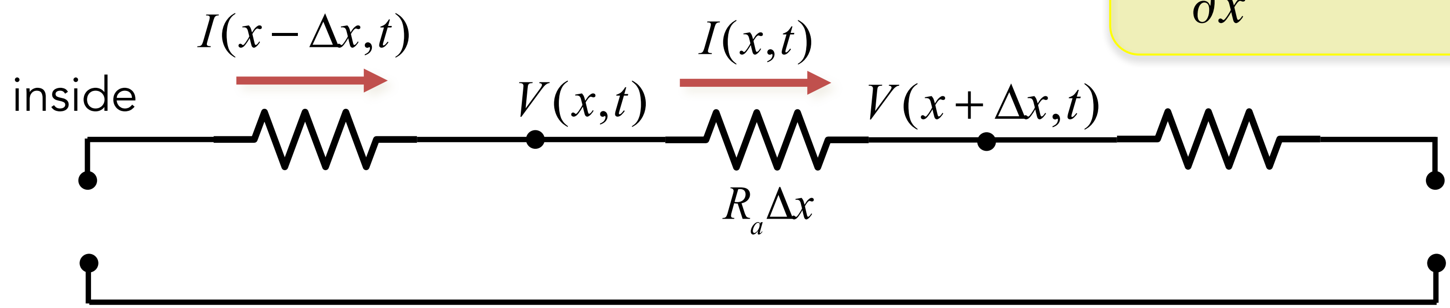


Consider the special case of a length L

And no membrane currents …

and steady state

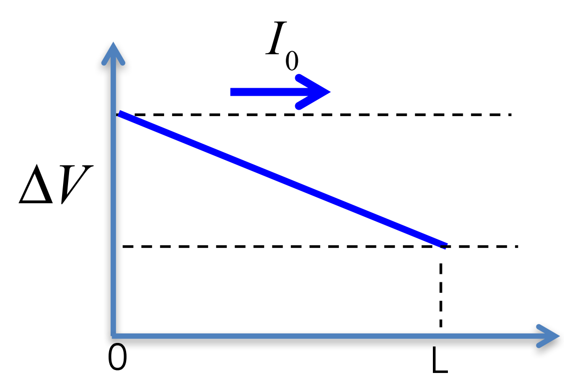
$$-\frac{\partial V}{\partial x} = R_a\, I(x,t)$$



$$I(x,t) = I(x-\Delta x,t) \;= I_0$$

$$\frac{\partial V}{\partial x} = -R_a\, I_0$$

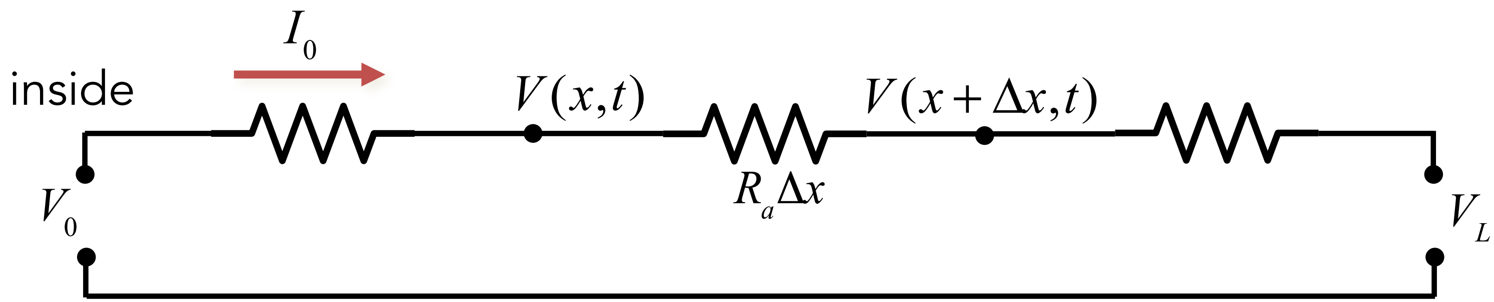
If there are no membrane conductances then:
Membrane potential changes linearly!



$$\Delta V = R\ I_0$$

$$R = R_a L$$

Boundary conditions

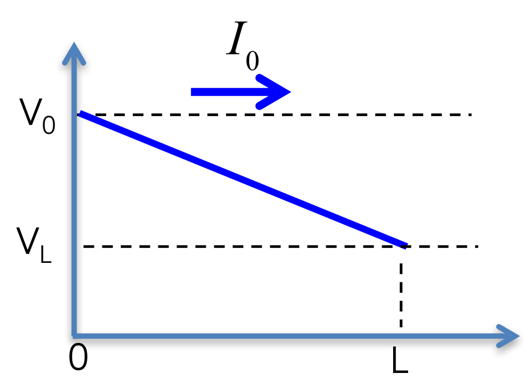


$$-\frac{\partial V}{\partial x} = R_a I_0$$

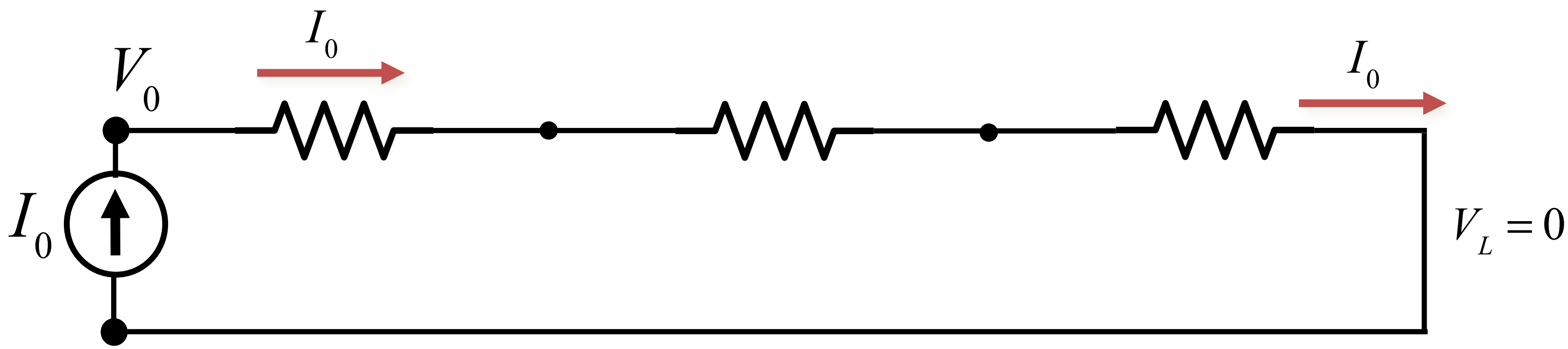
In order to solve this equation, we need to specify two unknowns (boundary conditions):

Integrate over x: $V(x) = V_0 - R_a I_0 x$ $\qquad V_L = V_0 - R_a I_0 L$

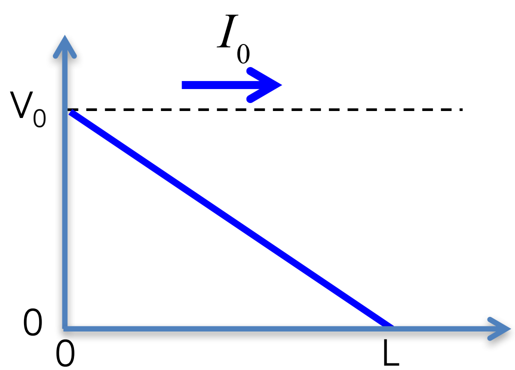
If you know any two of these quantities (V_0 ,V_L , I_0), you can calculate the third.



Boundary conditions



'open end'

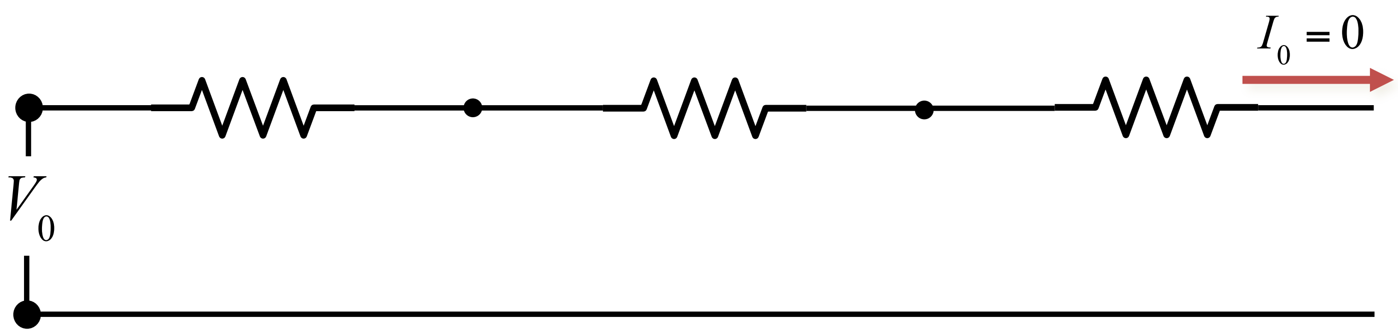


$$V_L = V_0 - R_a I_0 L = 0$$

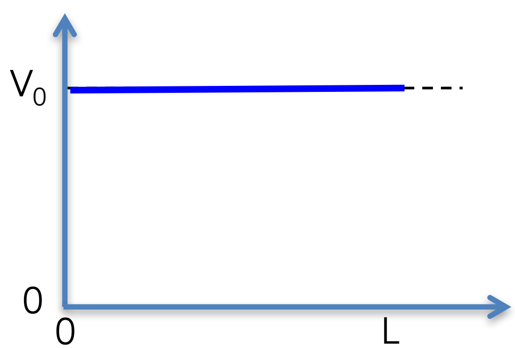
$$V_o = R_{in} I_0 \qquad R_{in} = R_a L$$

Input impedance

Boundary conditions



'closed end'

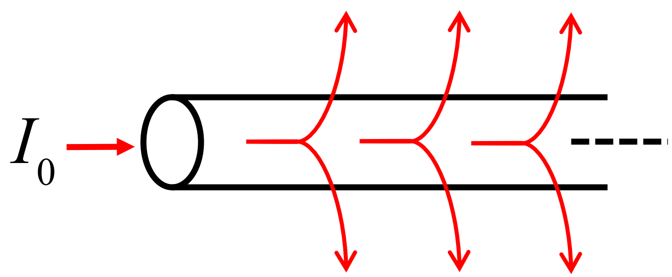


$$V_L = V_0 - R_a I_0 L = V_0$$

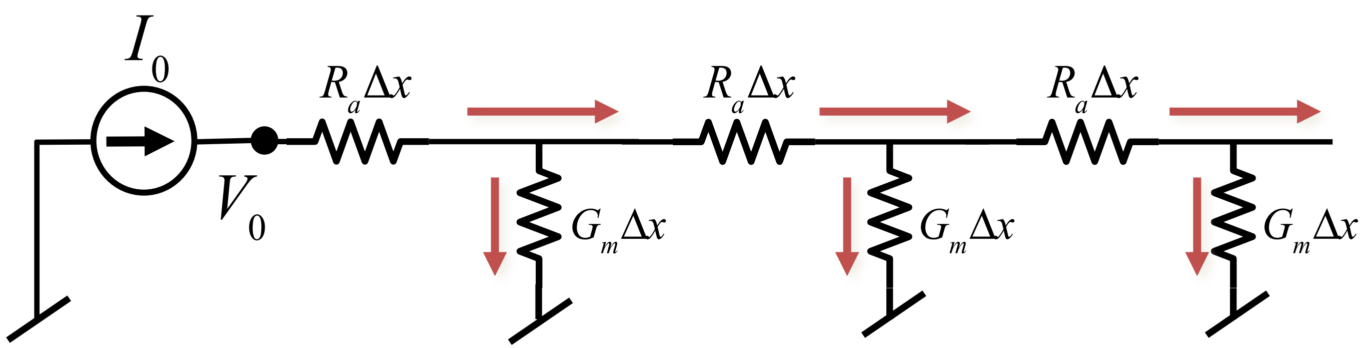
$$R_{in} = \frac{V_o}{I_0} = \infty$$

Cable with membrane conductance

Leaky garden-hose analogy

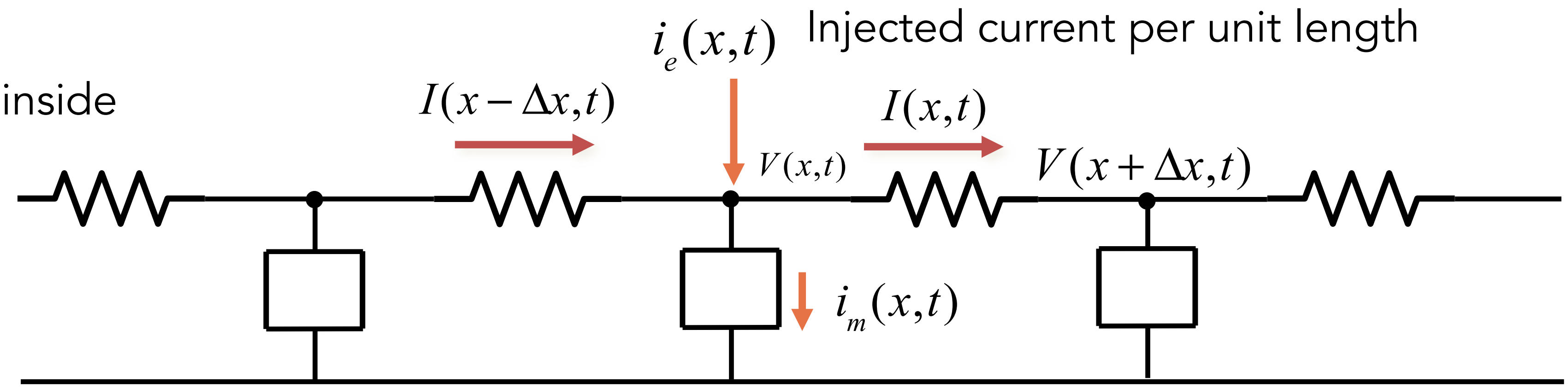


- Current is like water flow
- Voltage is like pressure



A leaky dendrite acts like a series of voltage dividers.

Deriving the cable equation



Kirchoff's law: sum of all currents out of each node must equal zero.

$$i_m(x,t)\,\Delta x \;-\; i_e(x,t)\,\Delta x \;+\; I(x,t) \;-\; I(x-\Delta x,t) \;=\; 0$$

Length of element

Membrane current per unit length

$$i_m(x,t)-i_e(x,t)=-\frac{1}{\Delta x}\left[I(x,t)-I(x-\Delta x,t)\right]$$

$$i_m - i_e = -\frac{\partial I}{\partial x}(x,t)$$

Substitute

But remember that:

$$\frac{\partial V}{\partial x} = -R_a\, I(x,t)$$

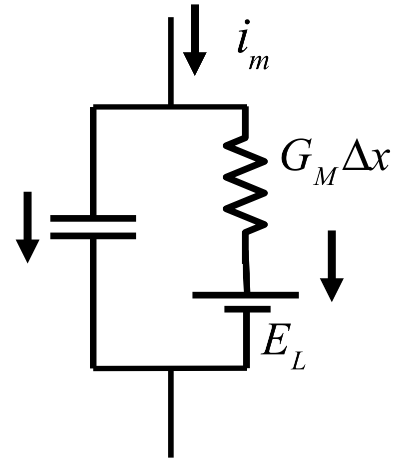
Assuming R_a is constant

$$\frac{\partial^2 V}{\partial x^2} = -R_a \frac{\partial I}{\partial x}(x,t)$$

Deriving the cable equation

$$\frac{1}{R_a}\frac{\partial^2 V}{\partial x^2}(x,t) = i_m - i_e$$

This we know!!



Each element in our cable is just like our model neuron!

So, the total membrane current in our element of length Δx is:

$$i_m(x,t)\,\Delta x = C_m\,\Delta x\frac{dV}{dt}(x,t) + G_m\,\Delta x\,(V - E_L)$$

Capacitance per unit length

Membrane ionic conductance per unit length

Plug this expression for $i_m(x,t)$ into the equation at top…

Deriving the cable equation

E_L is just a constant offset, so we ignore it

$$\frac{1}{R_a}\frac{\partial^2 V}{\partial x^2}(x,t) = C_m \frac{dV}{dt}(x,t) + G_m(V - E_L) - i_e(x,t)$$

Divide both sides by G_m to get the cable equation!

$$\lambda^2 \frac{\partial^2 V}{\partial x^2}(x,t) = \tau_m \frac{\partial V}{\partial t}(x,t) + V(x,t) - \frac{1}{G_m} i_e(x,t)$$

where

$$\lambda = \left(\frac{1}{G_m R_a}\right)^{1/2}$$

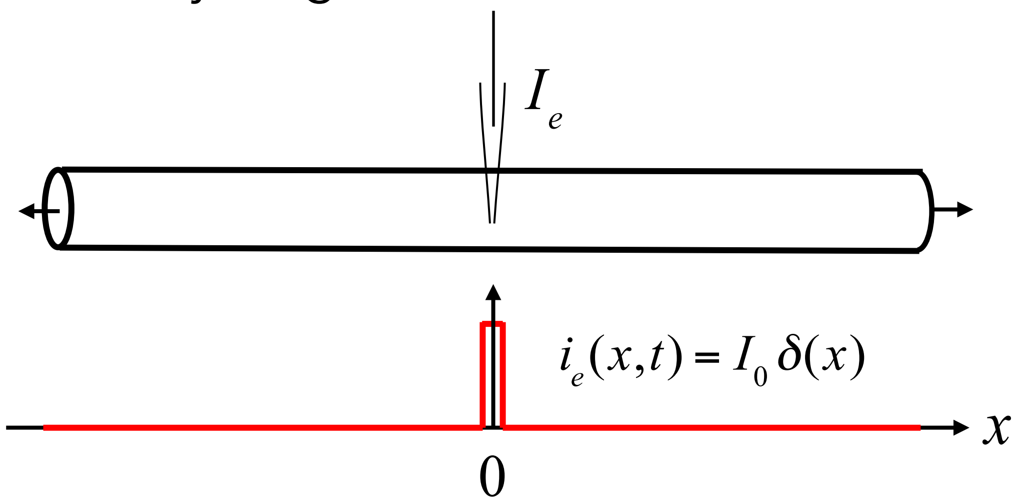
Steady state space constant (length, mm)

$$\tau_m = \frac{C_m}{G_m}$$

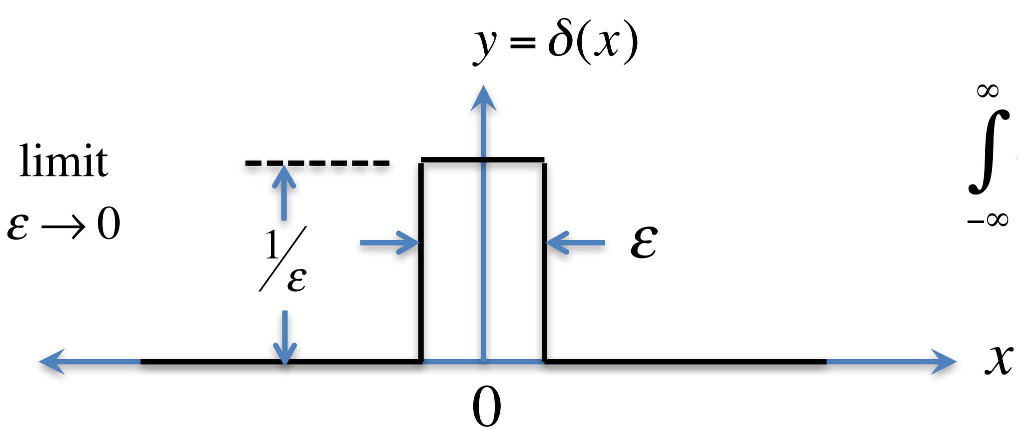
Membrane time constant (sec)

An example

Let's solve the cable equation for a simple case. What is the steady state response to a constant current at a point in the middle of an infinitely long cable?



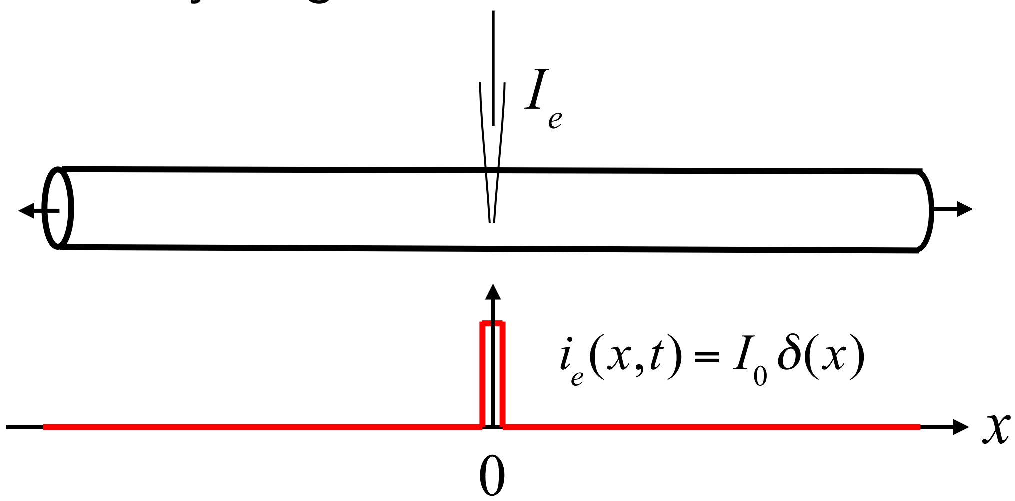
$\delta(x)$ - Dirac delta function



$$\int_{-\infty}^{\infty} \delta(x)\,dx = \varepsilon\left(\frac{1}{\varepsilon}\right) = 1$$

An example

Let's solve the cable equation for a simple case. What is the steady state response to a constant current at a point in the middle of an infinitely long cable?



$\delta(x)$ - Dirac delta function

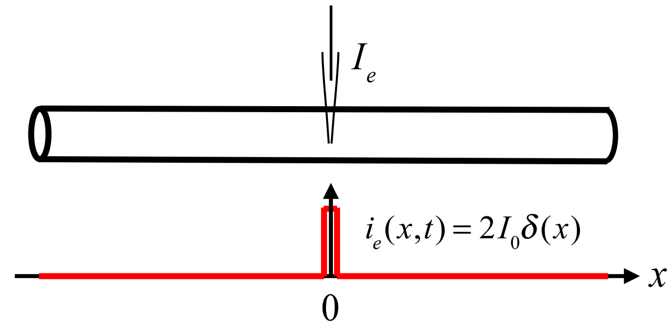
$$\int \delta(x)dx \equiv 1$$

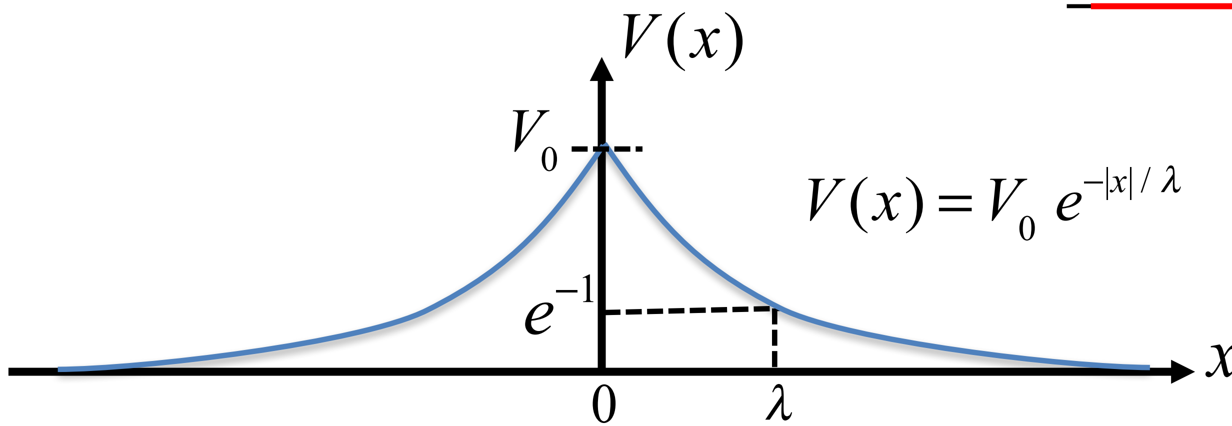
$$\lambda^2 \frac{\partial^2 V}{\partial x^2}(x,t) = \cancelto{0}{\tau_m \frac{\partial V}{\partial t}(x,t)} + V\left(x,t\right) - \frac{1}{G_m} i_e(x,t)$$

$$\lambda^2 \frac{\partial^2 V}{\partial x^2}(x) = V(x) - \frac{1}{G_m} 2I_0\delta(x)$$

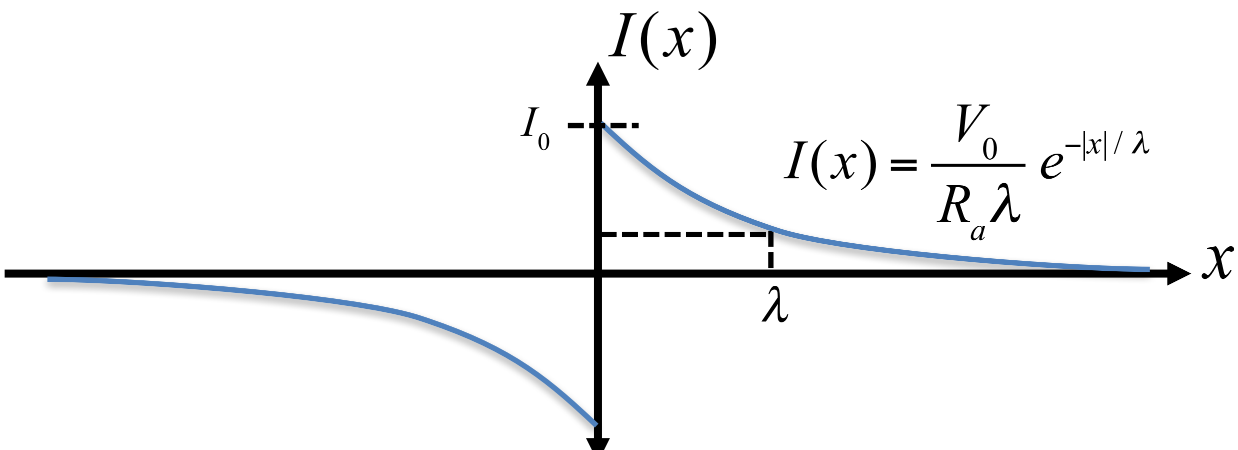
An example

$$\lambda^2 \frac{\partial^2 V}{\partial x^2}(x) = V(x) - \frac{1}{G_m} 2 I_0 \delta(x)$$





$$V(x) = V_0\, e^{-|x|/\lambda}$$



$$I(x) = \frac{V_0}{R_a \lambda}\, e^{-|x|/\lambda}$$

$$\frac{\partial V}{\partial x}(x) = -R_a I(x)$$

$$I(x) = -\frac{1}{R_a}\frac{\partial V}{\partial x}$$

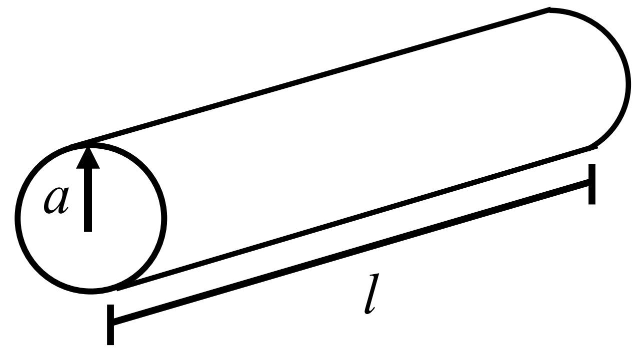
$$I(x) = -\frac{1}{R_a}\left(-\frac{V_0}{\lambda}\right) e^{-|x|/\lambda}$$

A closer look at the space constant

G_m is membrane conductance per unit length

$$\lambda = \left(\frac{1}{G_m R_a} \right)^{1/2}$$

- Total membrane conductance G :



$$G_{tot} = \underbrace{2\pi a l}_{\text{total area}} \, g_L$$

conductance per unit area (S/mm^2)

- Membrane conductance per unit length G_m :

$$G_m = \frac{G_{tot}}{l} = \underbrace{2\pi a}_{\text{circumference}} \, g_L$$

Units are S/mm

A closer look at the space constant

Axial resistance: the resistance along the inside of the dendrite

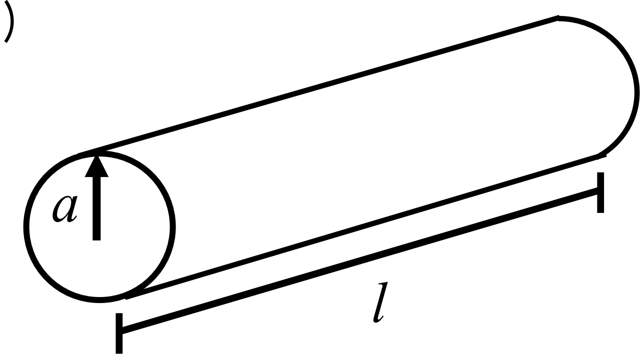
Total axial resistance along a dendrite of length l

$$R_{tot} = \frac{\rho_i l}{A} \quad \text{where}$$

$\rho_i =$ resistivity of the intracellular space (property of the medium $\sim 2000\ \Omega\ \text{mm}$)

A = cross sectional area = πa^2

$$\lambda = \left(\frac{1}{G_m R_a}\right)^{1/2}$$



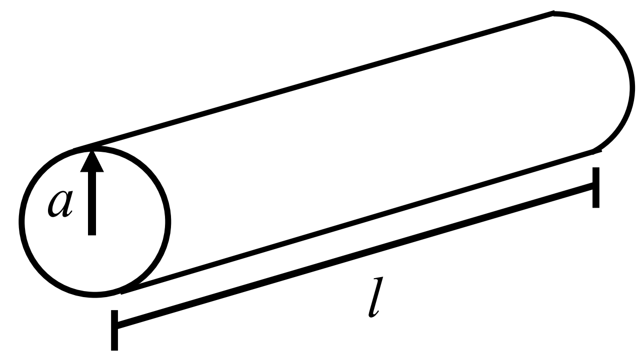
Axial resistance per unit length

$$R_a = \frac{R_{tot}}{l} = \frac{\rho_i}{A} = \frac{\rho_i}{\pi a^2} \quad (\Omega / \text{mm})$$

Steady-state space constant

$$\lambda = \left(\frac{1}{G_m R_a}\right)^{1/2} = \left(\frac{1}{S/\text{mm}\ \ \Omega/\text{mm}}\right)^{1/2} = \left(\text{mm}^2\right)^{1/2} = \text{mm}$$

Typical λ for a dendrite of a cortical pyramidal cell



$a = 2\mu\text{m} = 2\times10^{-3}\text{mm}$

First calculate membrane conductance

$$g_L = 5\times10^{-7}\,\text{S/mm}^2$$

$$G_m = 2\pi a g_L = 6\times10^{-9}\ \text{S/mm}$$

$$= 6\ \text{nS/mm}$$

Now we calculate axial resistance

$$R_a = \frac{\rho_i}{\pi a^2} = 160\ M\Omega\,/\,\text{mm}$$

$$\rho_i = 2000\ \ \Omega\ \text{mm}$$

Resistivity intracellular medium

$$\lambda = \left(\frac{1}{G_m R_a}\right)^{1/2} = \left(\frac{1}{6\,\text{nS/mm}\ \cdot 160\,\text{M}\Omega\text{/mm}}\right)^{1/2}$$

$$= \left(1\ \text{mm}^2\right)^{1/2}$$

$$\lambda \approx 1\,\text{mm}$$

Scaling with radius

$$\lambda = \left(\frac{1}{G_m R_a}\right)^{1/2} = \left[\frac{1}{2\pi a g_L}\frac{\pi a^2}{\rho_i}\right]^{1/2} = \left(\frac{a}{2\rho_i g_L}\right)^{1/2}$$

$$G_m = 2\pi a g_L$$

$$R_a = \frac{\rho_i}{\pi a^2}$$

$$\lambda \text{ scales as } \sqrt{\text{radius}}$$

Neurons need to send signals over a distance of a ~100 mm in the human brain.

What would *a* (radius) would have to be to get λ= 100 mm?

$$a = 20 \text{ mm!}$$

This would never work! This is why signals that must be sent over long distances in the brain are sent by propagating axon potentials.

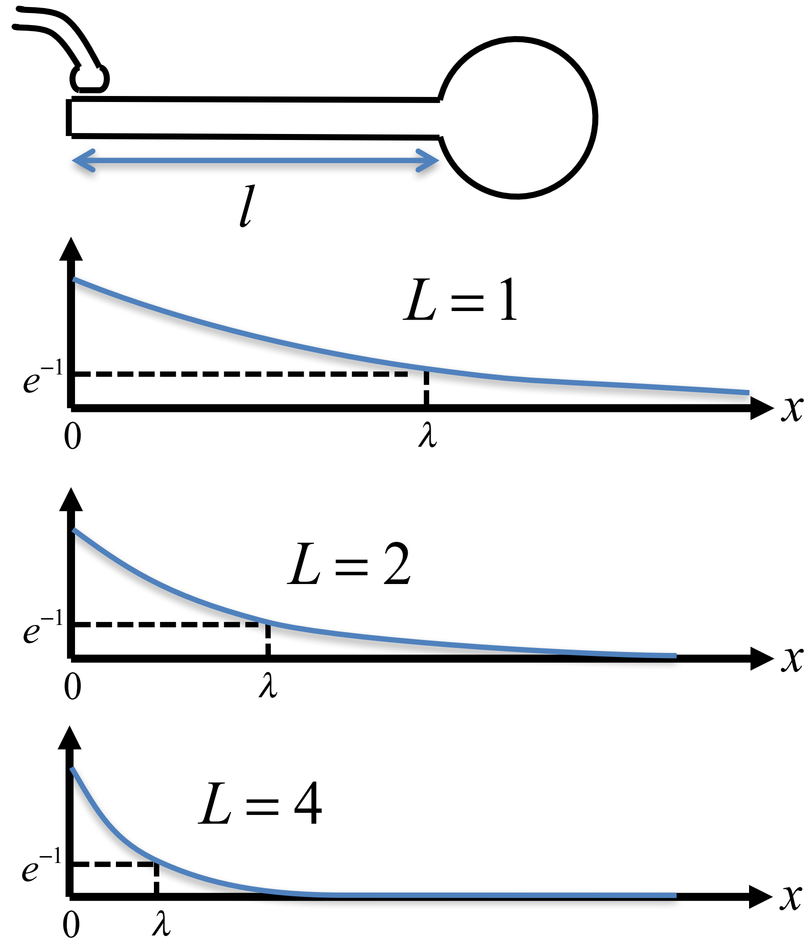
Electrotonic length

Electrotonic length is the physical length divided by the space constant.

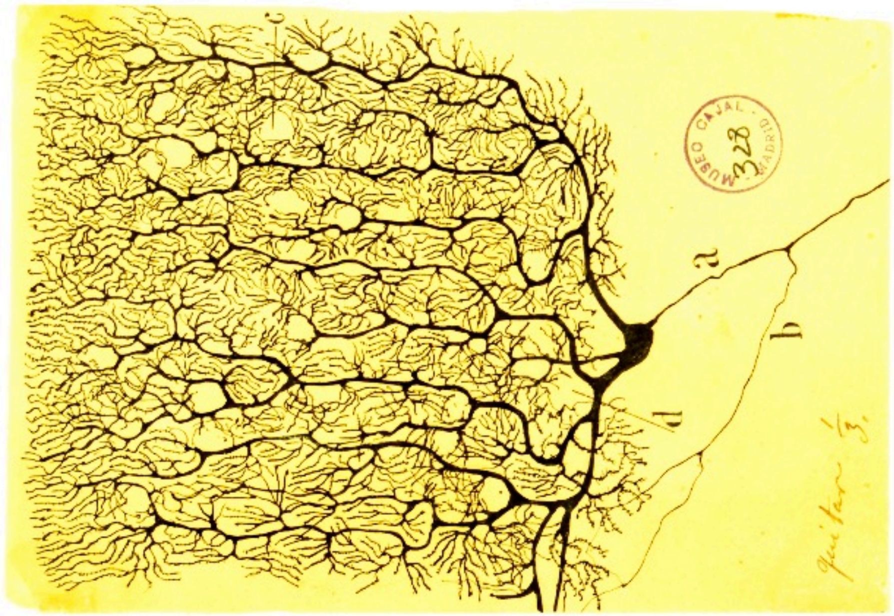
$$L = \frac{l}{\lambda}$$ unitless

The amount of current into the soma will scale as

$$e^{-L}$$



Multi-compartment model



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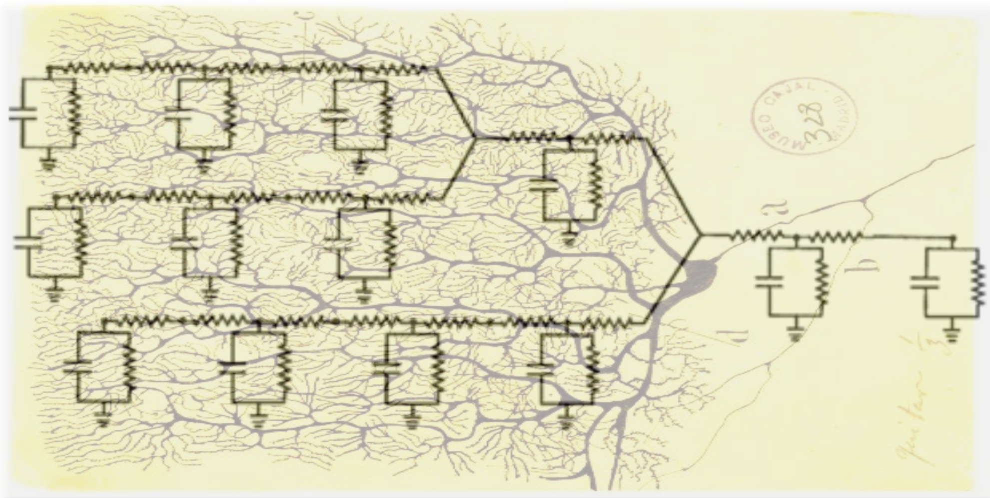

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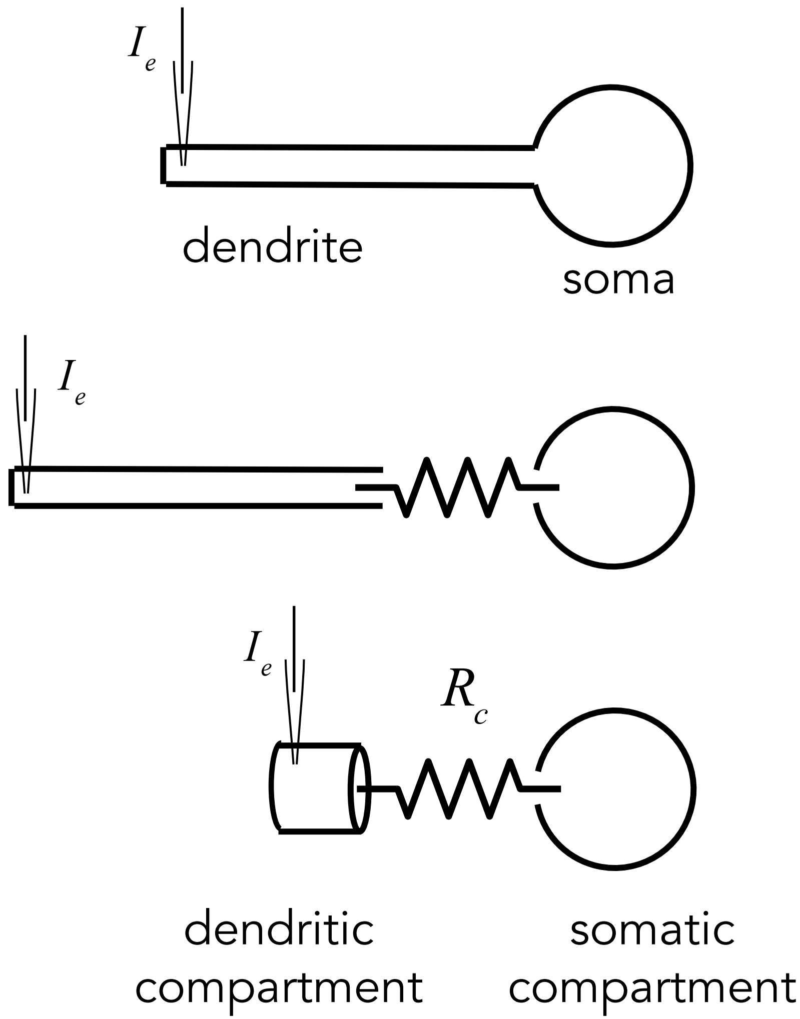
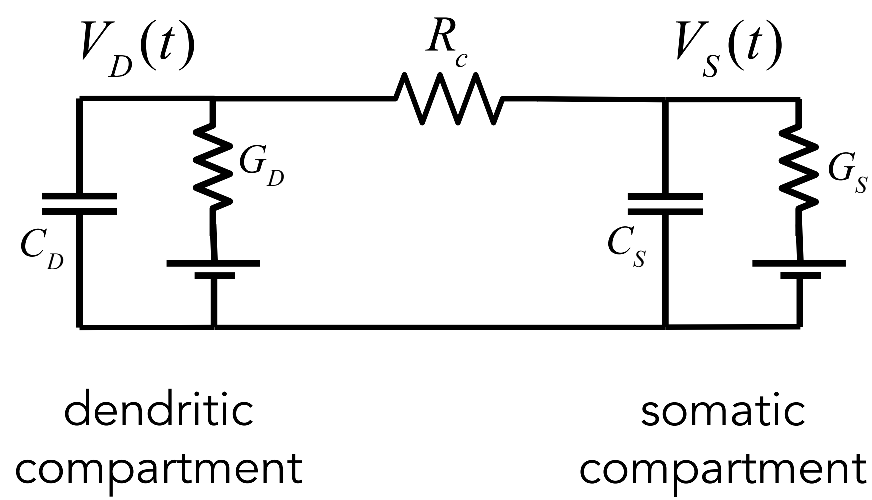
Two-compartment model





Learning objectives for Lecture 6

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- Be able to plot the voltage in a dendrite as a function of distance for leaky and non-leaky dendrite, and understand the concept of a length constant
- Know how length constant depends on dendritic radius
- Understand the concept of electrotonic length
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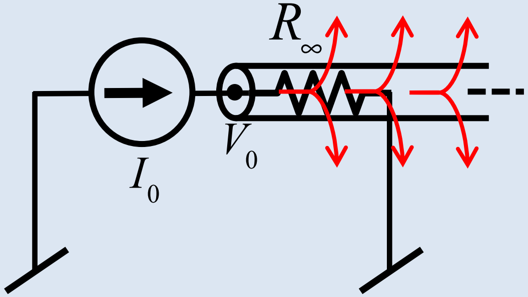
Extra Slides on Input impedance

How much voltage does it take to produce a given current into our dendrite? (How much pressure does it take to get a certain water flow?)

Obviously, a big hose has less resistance to flow. Ie. it takes less pressure



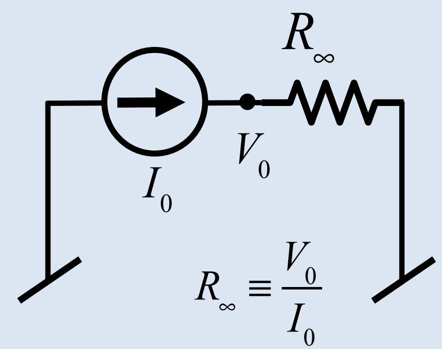
A small hose has more resistance and takes more pressure

This is called the 'input impedance' of the cable

$$R_\infty \equiv \frac{V_0}{I_0}$$

Input impedance

We can calculate the input impedance



We calculated earlier that the current along the cable is

$$I(x) = \frac{V_0}{R_a \lambda} e^{-|x|/\lambda}$$

If we evaluate the current at x=0, we get:

$$I(0) = \frac{V_0}{R_a \lambda} = I_0$$

Thus,

$$R_\infty = \frac{V_0}{I_0} = R_a \lambda$$

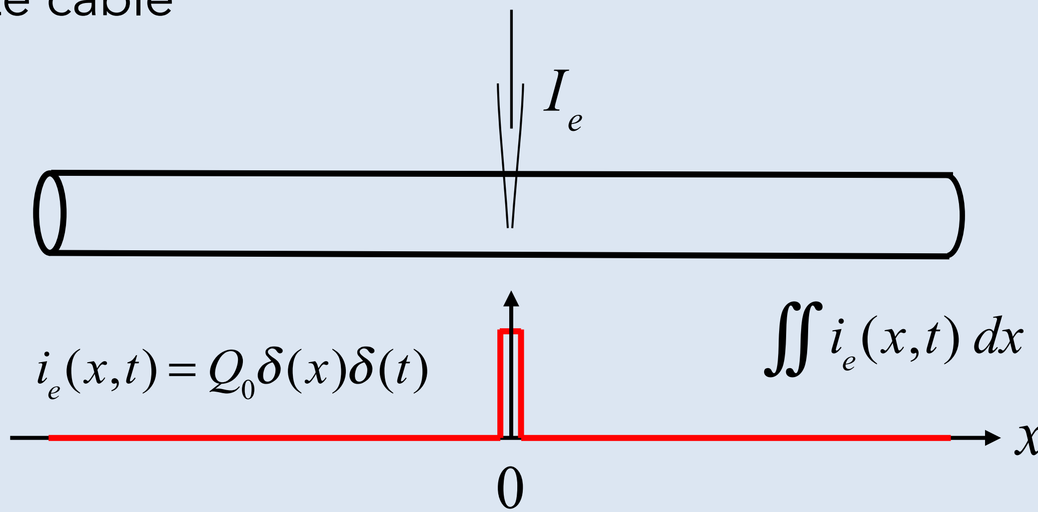
Thus the 'input impedance' of a cable is just the axial resistance of a length λ of the cable!

What can we say about the input conductance?

since $\lambda^2 = \dfrac{1}{G_m R_a}$ $\qquad R_\infty^{-1} = G_\infty = G_m \lambda$

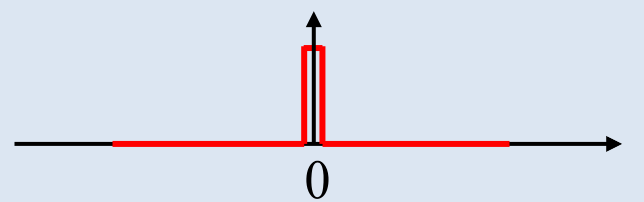
Extra Slides on Time Dependence

We can exactly solve the case of a brief pulse of current in an infinite cable



$$i_e(x,t) = Q_0\delta(x)\delta(t)$$

$$\iint i_e(x,t)\; dx\; dt = Q_0 = \text{total charge}$$



$$V(X,T) = \frac{Q_0}{C_\lambda}\frac{1}{\sqrt{4\pi T}}\, e^{-\frac{X^2}{4T}}\; e^{-T}$$

where $X = x/\lambda$ $T = t/\tau$

$$Q = CV$$

$$C_\lambda = 2\pi a c_m \lambda$$

Pulse of charge

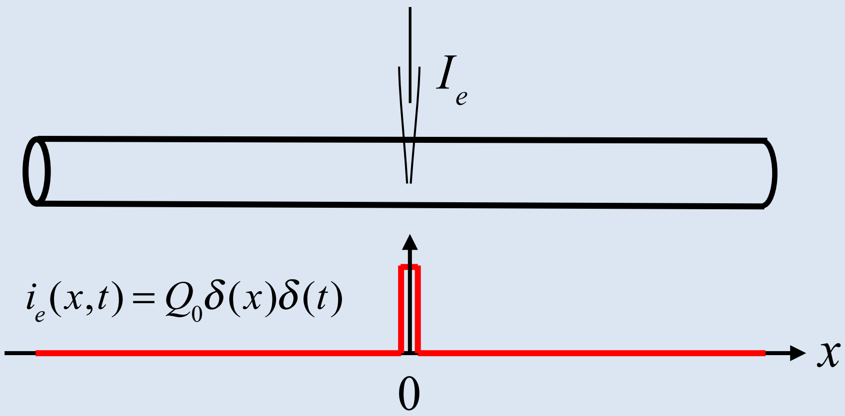


Figure removed due to copyright restrictions. See p. 39, Fig. 2.7A in Koch, Christof. *Biophysics of Computation: Information Processing in Single Neurons*. 1999, Oxford University Press.

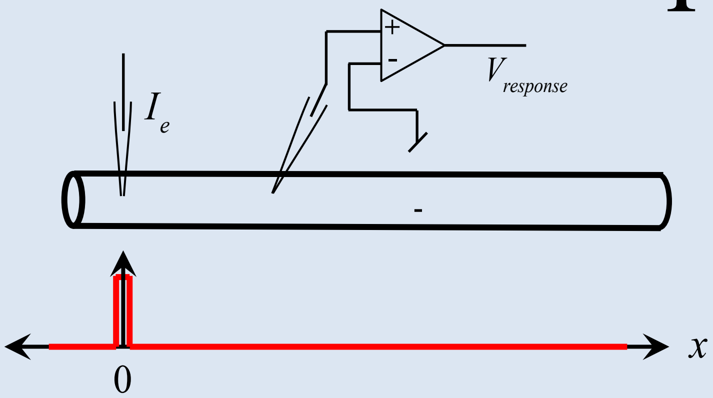
Looking at just the spatial dependence

$$V(X,T) \propto \frac{1}{\sqrt{4\pi T}}\, e^{-\frac{X^2}{4T}}$$

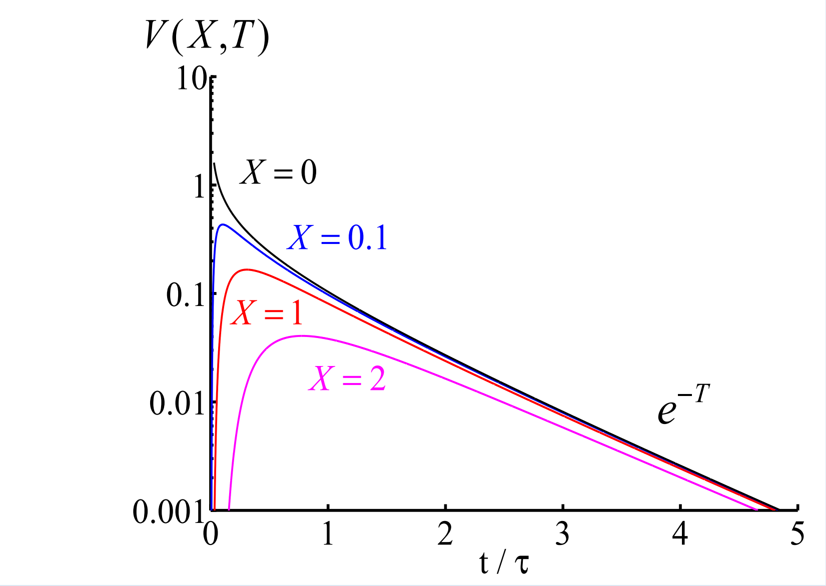
This is just a Gaussian profile.

Width increases as $\sigma = \sqrt{2T}$

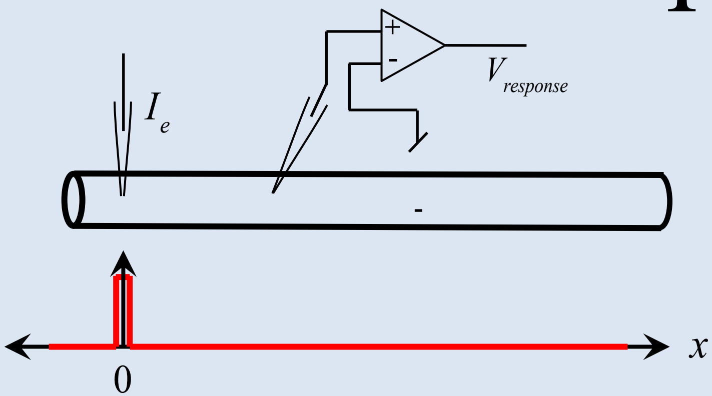
Propagation



$$V(X,T)=\frac{Q}{C_\lambda}\frac{1}{\sqrt{4\pi T}}\,e^{-\frac{X^2}{4T}}e^{-T}$$



Propagation

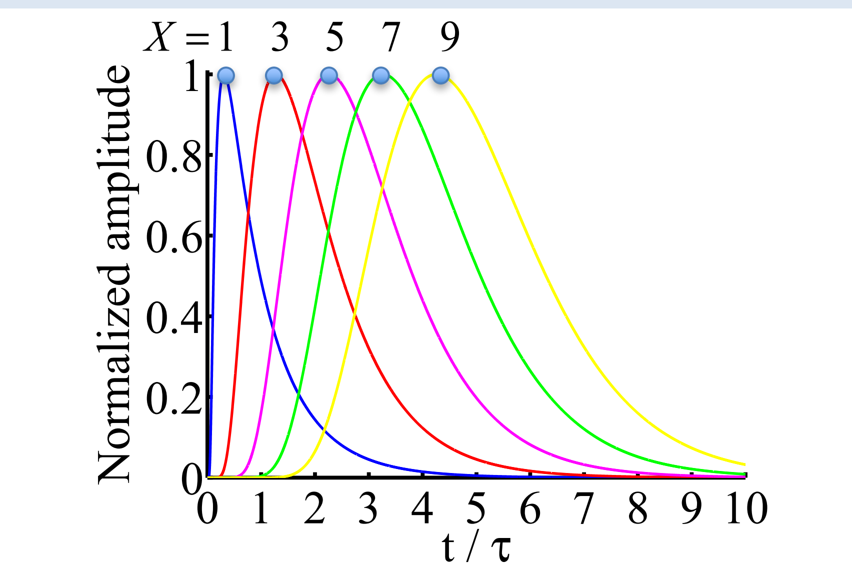


Find the peaks by calculating $\frac{\partial V}{\partial T}(X,T)$ and setting it to zero.

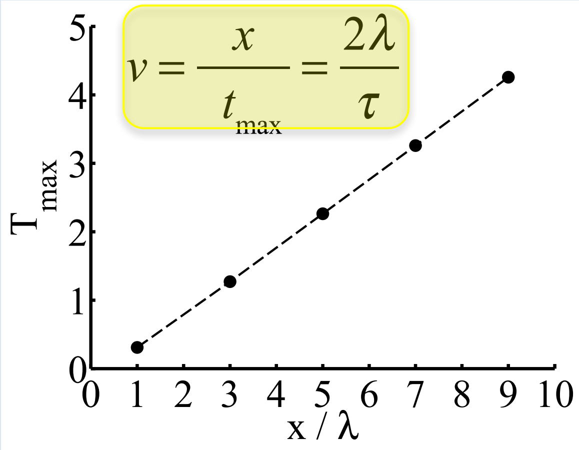
$$V(X,T) = \frac{Q}{C_\lambda}\frac{1}{\sqrt{4\pi T}}e^{-\frac{X^2}{4T}}e^{-T}$$

For any given X, you can solve for T_{max}.

$$T_{max} = \frac{1}{4}\left(\sqrt{1+4X^2}-1\right) \approx \frac{1}{2}X \qquad \frac{t_{max}}{\tau} \approx \frac{1}{2}\frac{x}{\lambda}$$



From this, we can calculate the velocity!



Dendritic filtering

As the voltage response propagates down a dendrite, it not only falls in amplitude, but it broadens in time.