Theoretical & computational Neuroscience:
Programming the Brain

(BM 6140)

2-credit

What are the underlying assumptions ?

Assumptions

- Ion channel = Cell ???

  For realistic cell, increase in surface area causes decrease in input resistance

- Even after this compensation, entire cell is not at same potential

  How do we modify the equivalent circuit ?

Neurons are not point objects !

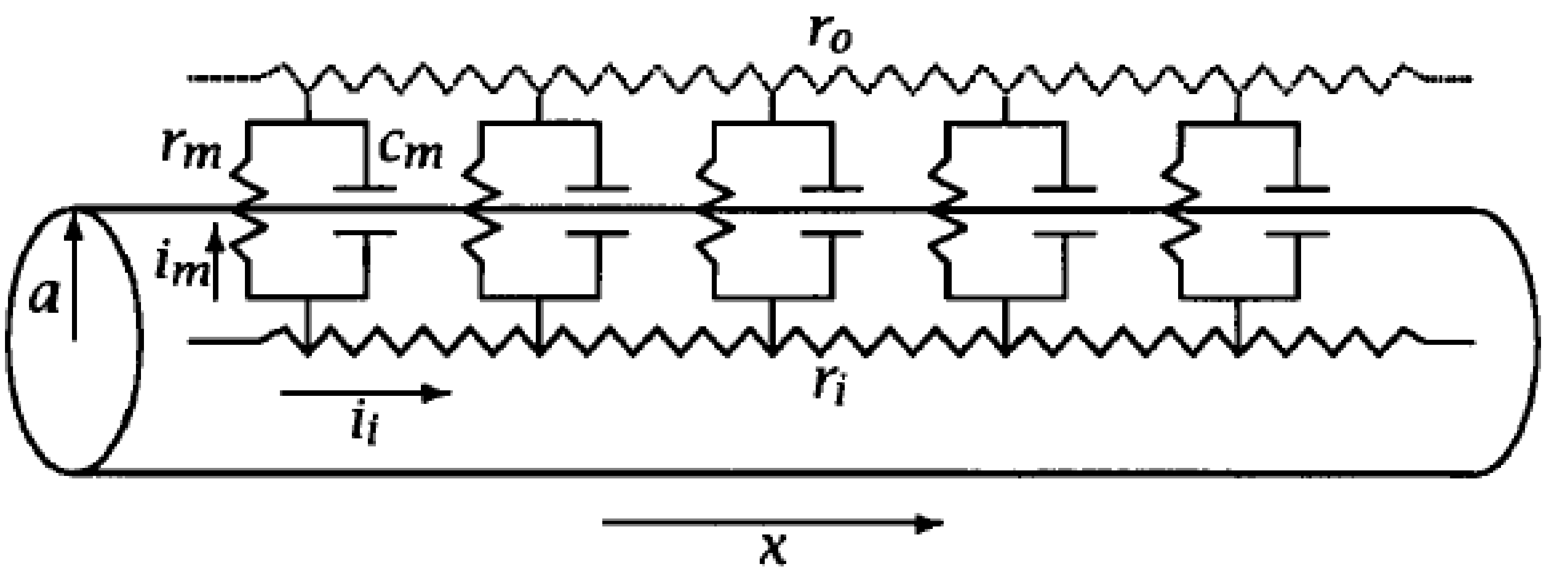
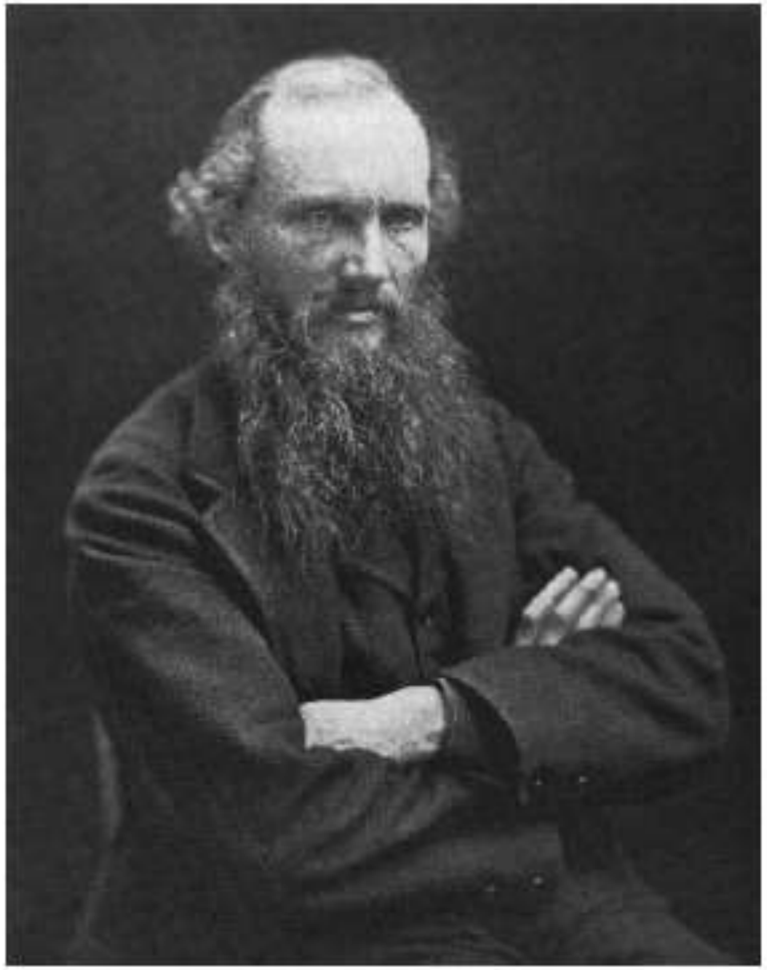


Figure 4.6 Diagram for current flow in a uniform cylinder such as an axon or segment of dendrite.

Johnston & Wu, Foundations of Cellular Neurophysiology

Cable theory

- Lord Kelvin (William Thomson)
- Originally developed for the transatlantic telegraph cable laying project



Lord Kelvin
(William Thomson)
1824-1907

Spatially extended cell

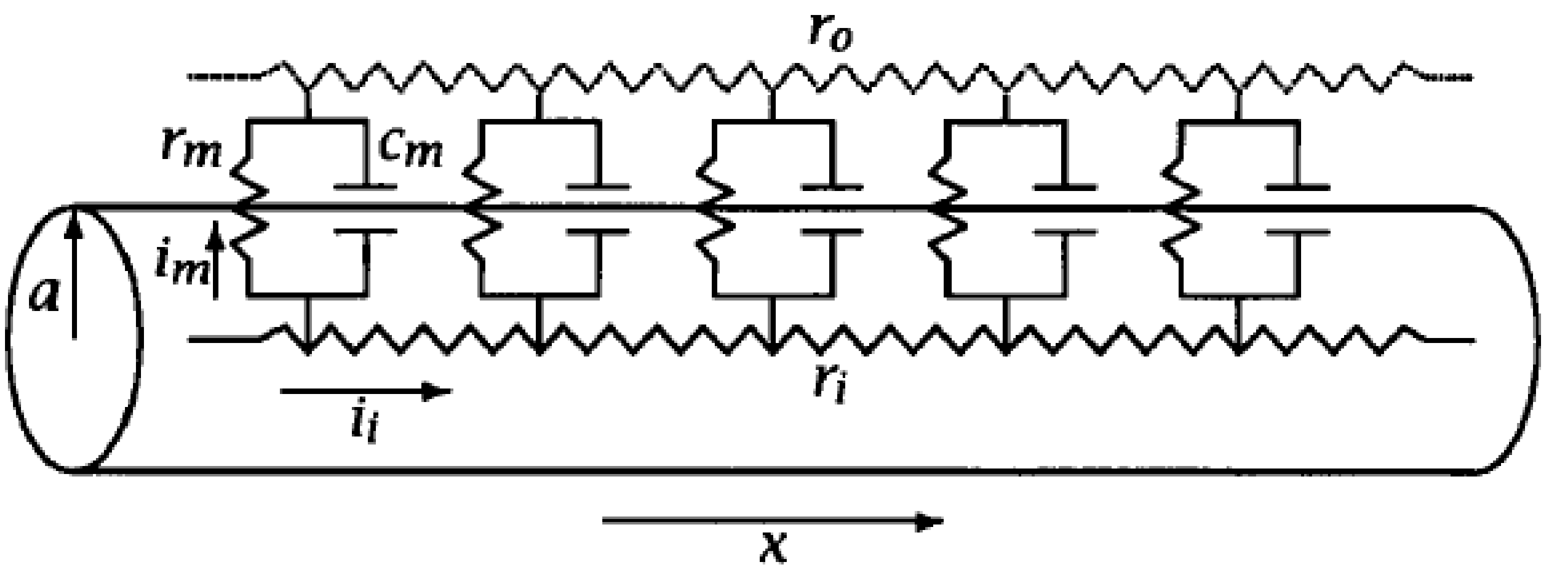
Assume extracellular medium is isopotential

$$\frac{\partial V_m(x,t)}{\partial x} = -r_i i_i.$$

$$\frac{\partial i_i}{\partial x} = -i_m.$$

$$\frac{\partial^2 V_m}{\partial x^2} = -r_i \frac{\partial i_i}{\partial x} = r_i i_m.$$

$$\frac{1}{r_i}\frac{\partial^2 V_m}{\partial x^2} = c_m \frac{\partial V_m}{\partial t} + \frac{V_m}{r_m}.$$



$$i_m = i_C + i_{\text{ionic}} = c_m \frac{\partial V_m}{\partial t} + \frac{V_m}{r_m}$$

Johnston & Wu, Foundations of Cellular Neurophysiology

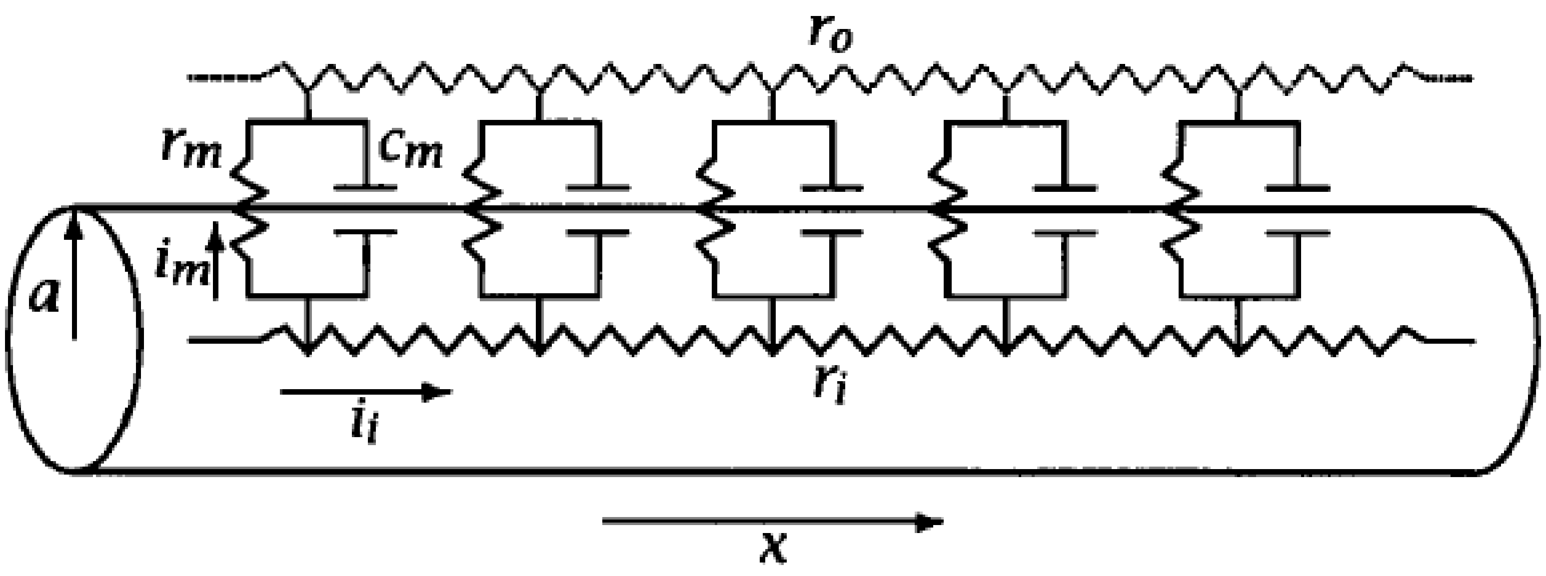
Spatially extended cell

$$\frac{1}{r_i}\frac{\partial^2 V_m}{\partial x^2} = c_m\frac{\partial V_m}{\partial t} + \frac{V_m}{r_m}.$$

$$\lambda^2\frac{\partial^2 V_m}{\partial x^2} = \tau_m\frac{\partial V_m}{\partial t} + V_m,$$

where

$$\lambda = \sqrt{\frac{r_m}{r_i}} = \sqrt{\frac{aR_m}{2R_i}}.$$



Note the conversion between r and R

Johnston & Wu, Foundations of Cellular Neurophysiology

Solutions of the cable equation : assuming Infinite cable

A general solution to the cable equation is

$$V_m(T,X) = \frac{r_i I_0 \lambda}{4}\left[e^{-X}\operatorname{erfc}\left(\frac{X}{2\sqrt{T}} - \sqrt{T}\right) - e^{X}\operatorname{erfc}\left(\frac{X}{2\sqrt{T}} + \sqrt{T}\right)\right],$$

X,T are distance and time normalized by space and time constants

$$\operatorname{erfc}(x) = 1 - \operatorname{erf}(x) = 1 - \frac{2}{\sqrt{\pi}}\int_0^x e^{-y^2}\,dy = \frac{2}{\sqrt{\pi}}\int_x^\infty e^{-y^2}\,dy,$$

where $\operatorname{erf}(0) = 0$, $\operatorname{erf}(\infty) = 1$, and $\operatorname{erf}(-x) = -\operatorname{erf}(x)$.

Johnston & Wu, Foundations of Cellular Neurophysiology

Why are we looking at cable properties ?

Neuronal inputs come in at the dendrite.

But the integration happens (at least was thought so until recently) at soma

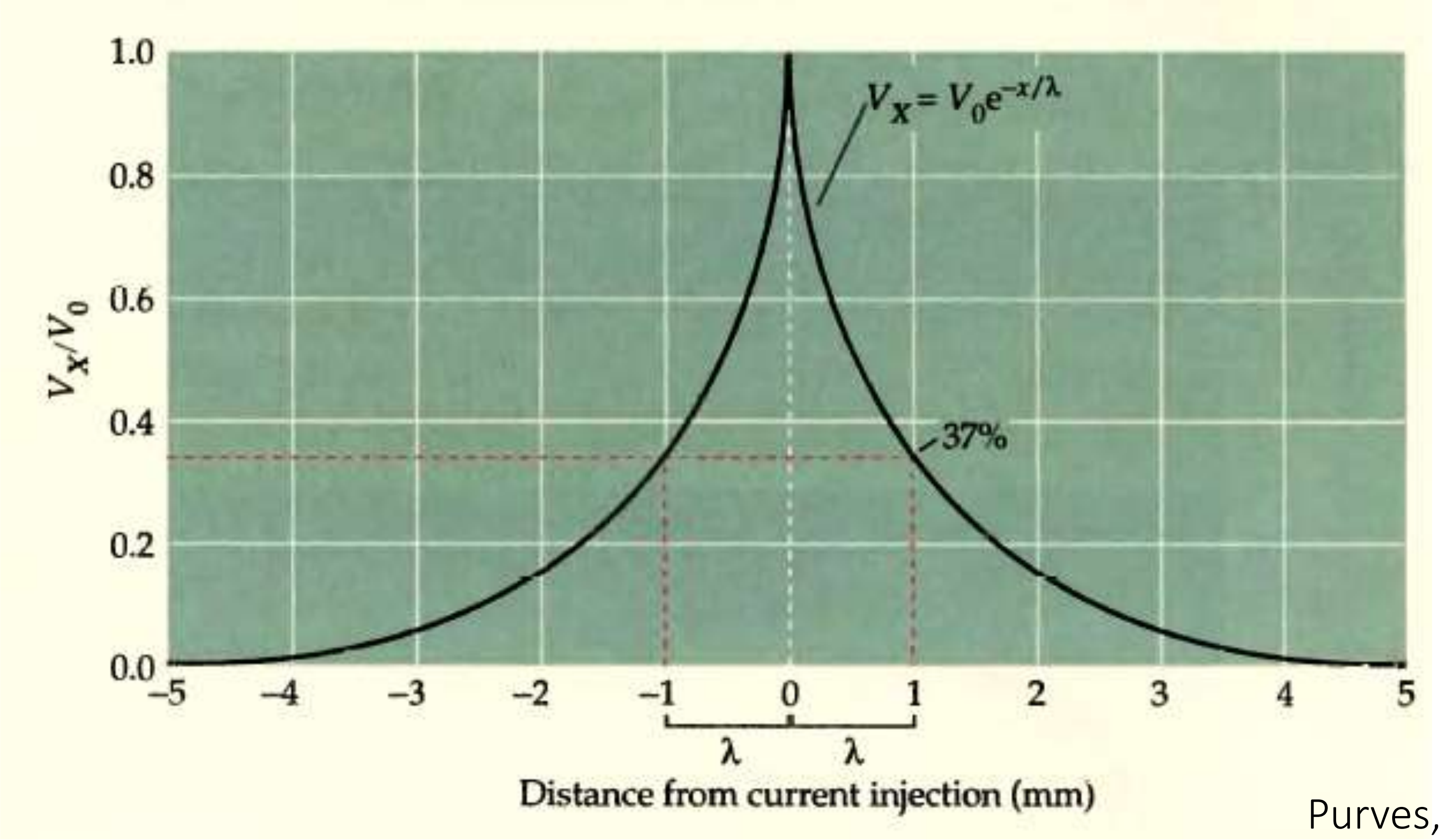
Cable properties are critical to understanding computational properties of a neuron

Insights from infinite cable theory solutions

$V_m(\infty, X)$: $Steady\ state\ Voltages\ at\ different\ points = ?$

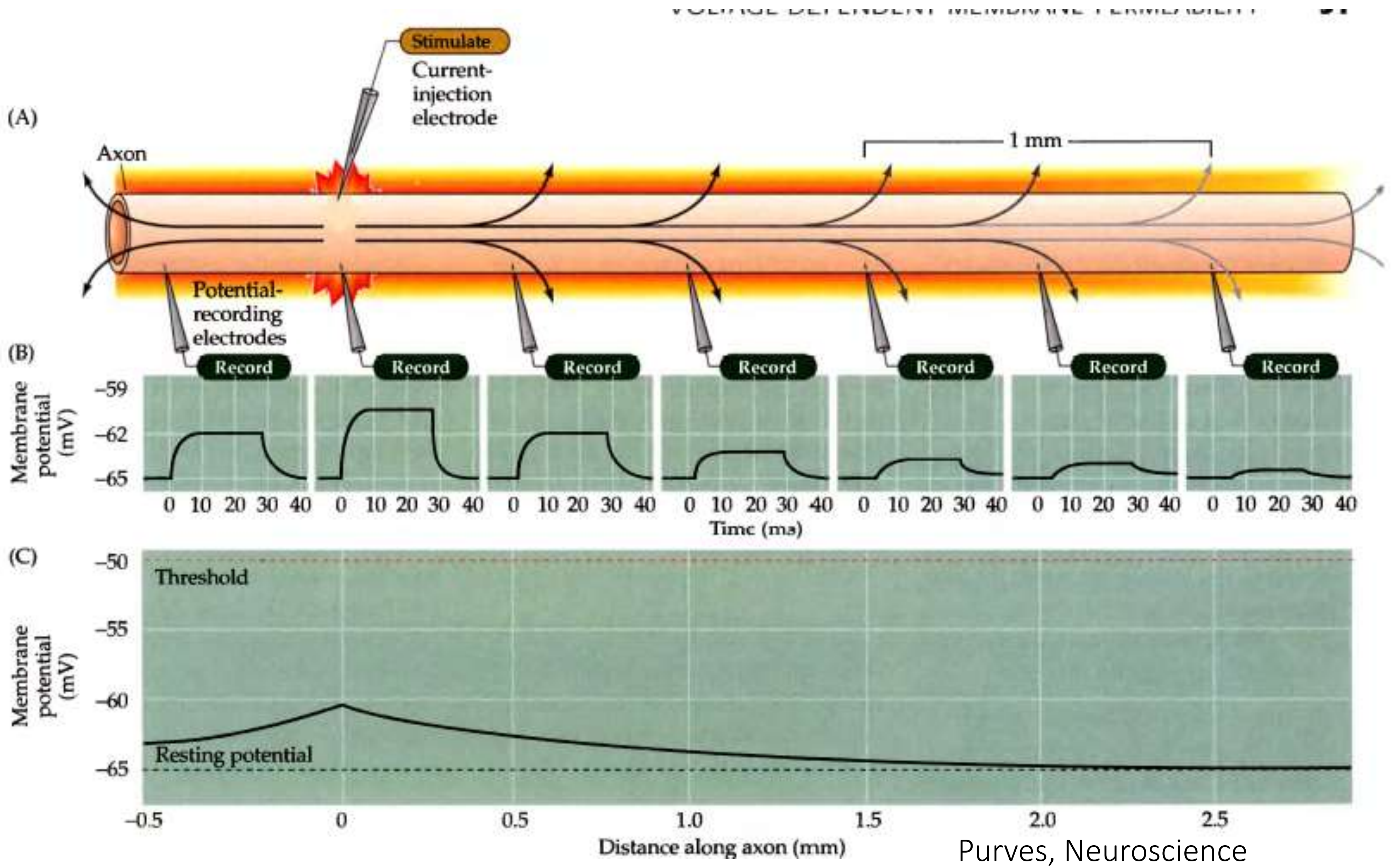
Insights from infinite cable theory solutions

$$V_m(\infty, X) = \frac{r_i I \lambda}{2} e^{\frac{-x}{\lambda}}$$



Purves, Neuroscience

Passive propagation of neuron



Purves, Neuroscience

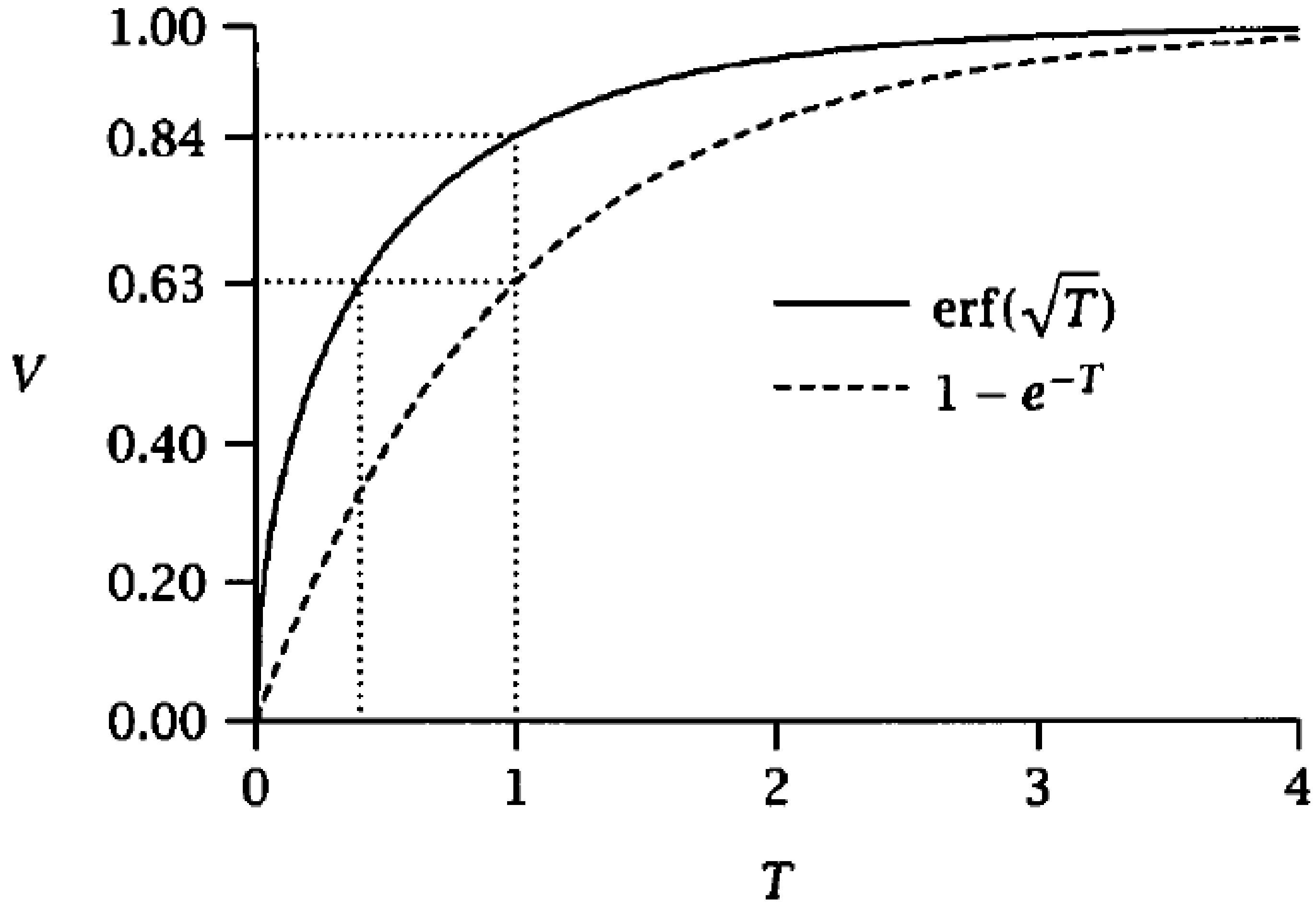
Insights from infinite cable theory solutions

$V_m(T, 0) = ?$

Insights from infinite cable theory solutions

$$V_m(T,0) = \frac{r_i I \lambda}{2} \operatorname{erfc}\left(\sqrt{\frac{t}{\tau}}\right)$$

Even with finite cable length it can be shown that charging is faster than in an isopotential sphere



AP decays faster than a synaptic potential

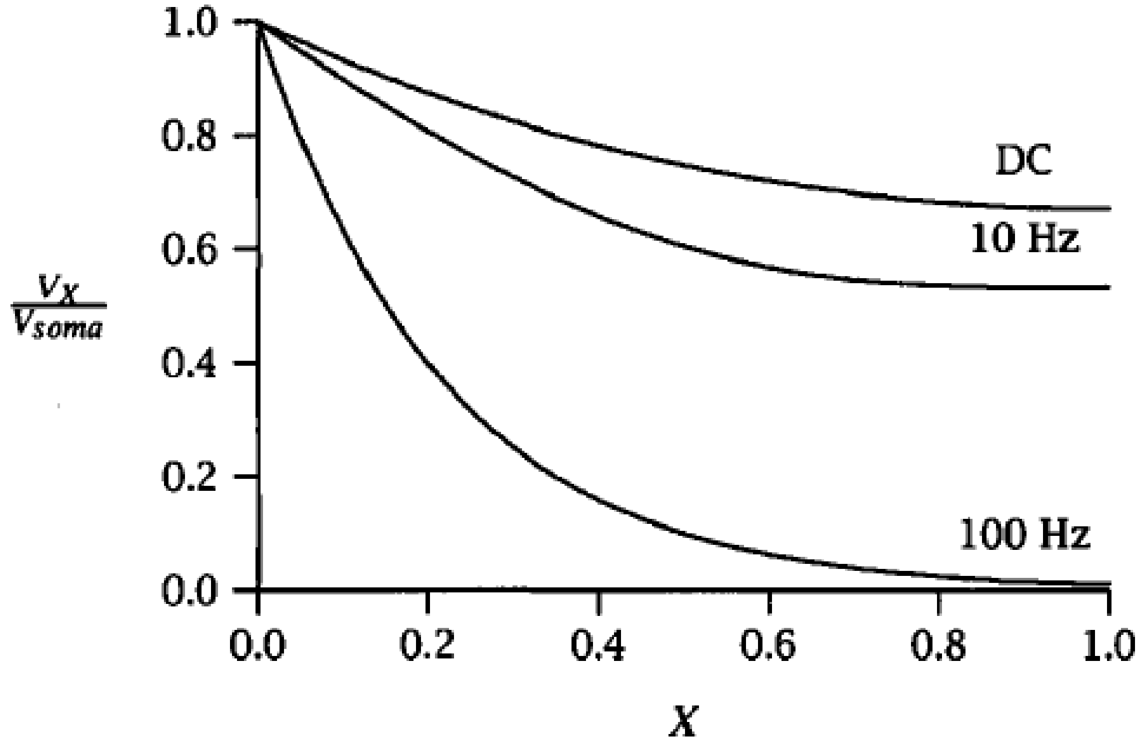


Figure 4.18 Voltage attenuation along a finite-length cable ($L = 1$) for current injections (DC to 100 Hz) at $X = 0$ (i.e., soma) ($R_m = 50,000\ \Omega\text{-cm}^2$).

Insights from infinite cable theory solutions

$$What\ is\ this\ quantity\ \frac{V_m(\infty,0)}{I}\ ?$$

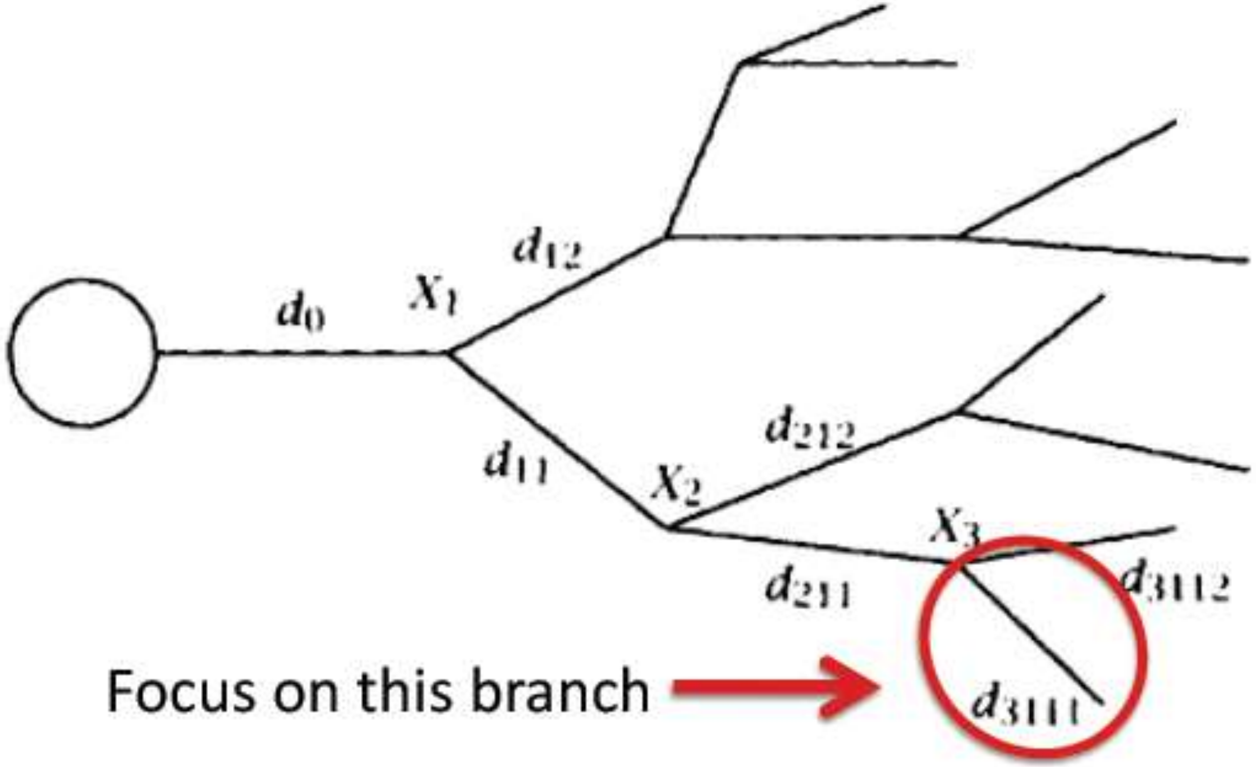
Insights from infinite cable theory solutions

$$\frac{V_m(\infty,0)}{I} = Input\ resistance = \frac{r_i\lambda}{2} = \frac{\sqrt{r_m r_i}}{2} = \frac{\sqrt{\frac{R_m R_i}{2}}}{2\pi a^{\left(\frac{3}{2}\right)}}$$

Rall's law

Take an arbitrary dendritic tree

Represent the soma as an isopotential sphere



As an semi-infinite cylinder, its input resistance as an independent cable is:

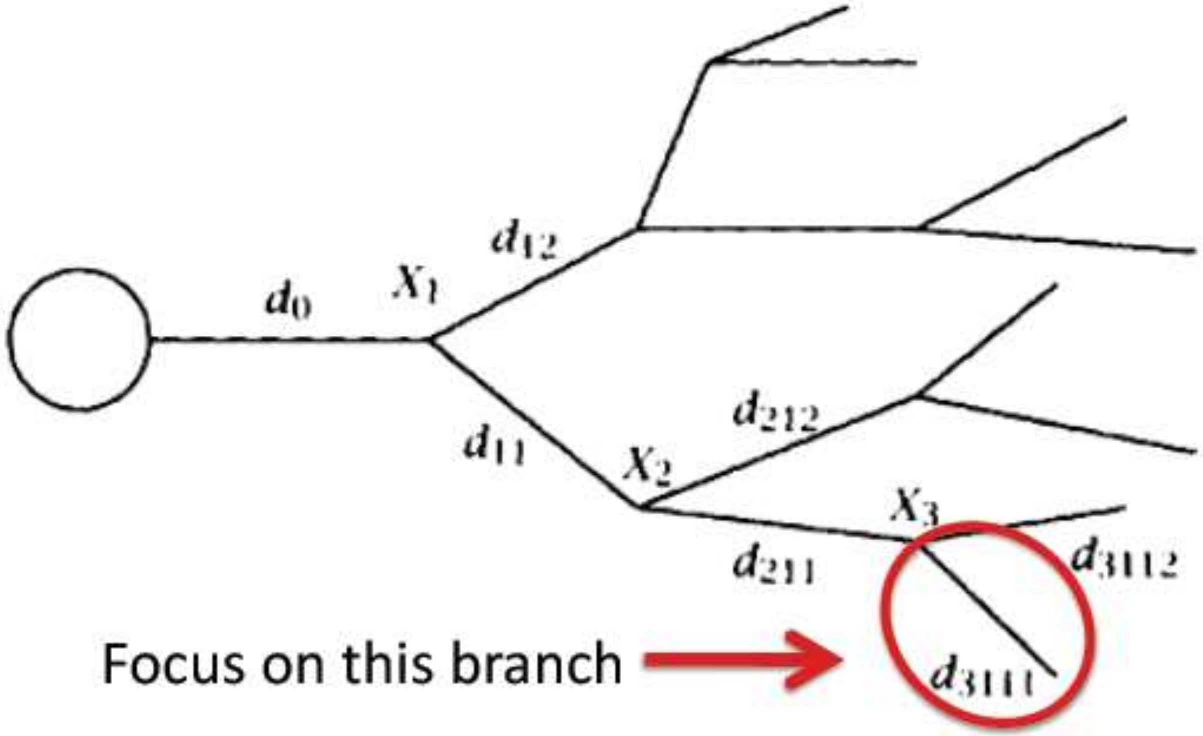
$$R_{in}(3111) = \frac{2\sqrt{R_m R_i}}{\pi d_{3111}^{3/2}}$$

Johnston, Wu, Foundation of Cellular Neuroscience
Slide : Courtesy : Dr. Rishikesh Narayanan

Johnston and Wu Book

Rall's law

Conductances in parallel sum up



Focus on this branch

Input conductance for branch 3111: $G_{in}(3111) = \frac{\pi d_{3111}^{3/2}}{2\sqrt{R_m R_i}} = K d_{3111}^{3/2}$

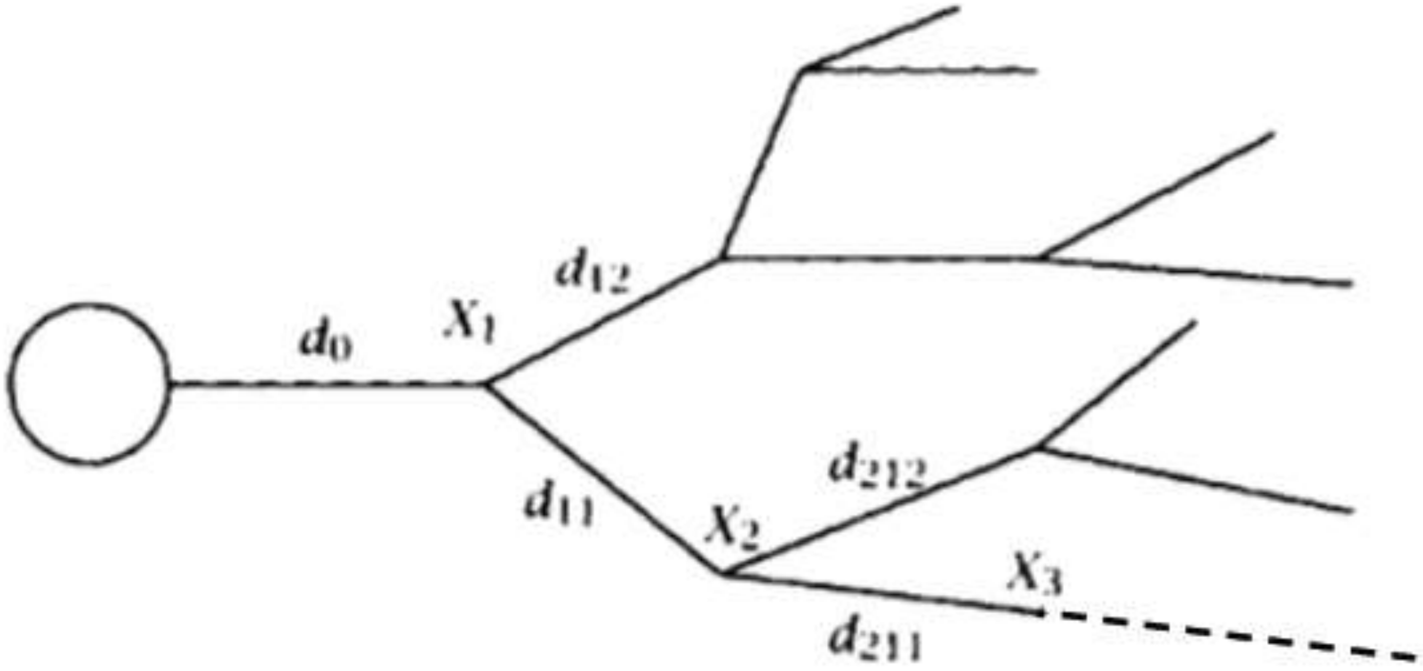
At node X_3: $G_{in}(X_3) = G_{in}(3111) + G_{in}(3112) = K\left(d_{3111}^{3/2} + d_{3112}^{3/2}\right)$

Johnston, Wu, Foundation of Cellular Neuroscience
Slide : Courtesy : Dr. Rishikesh Narayanan

Johnston and Wu Book

Rall's law

If branch point X_3 were absent...



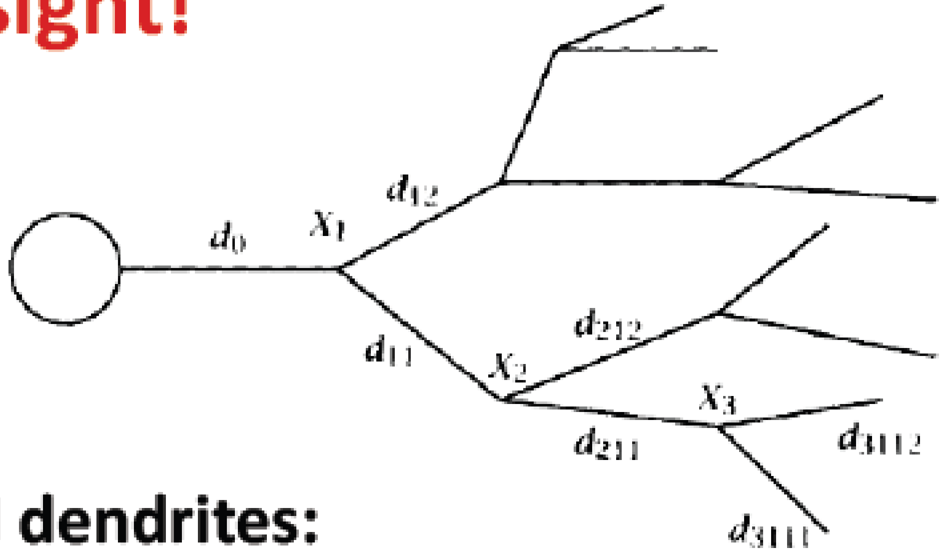
If 3111 and 3112 were not present, the input conductance at X_3 (detaching the cable 211 at the point would make it a semi-infinite cable) would have been:

$$G_{in}(X_3) = G_{in}(211) = Kd_{211}^{3/2}$$

Johnston, Wu, Foundation of Cellular Neuroscience
Slide : Courtesy : Dr. Rishikesh Narayanan

Rall's law

Rall's insight!



Without branch:

$$G_{in}(X_3) = G_{in}(211) = Kd_{211}^{3/2}$$

With branch and the two additional dendrites:

$$G_{in}(X_3) = G_{in}(3111) + G_{in}(3112) = K\left(d_{3111}^{3/2} + d_{3112}^{3/2}\right)$$

IF: $d_{211}^{3/2} = \left(d_{3111}^{3/2} + d_{3112}^{3/2}\right)$ these two quantities will be equal!

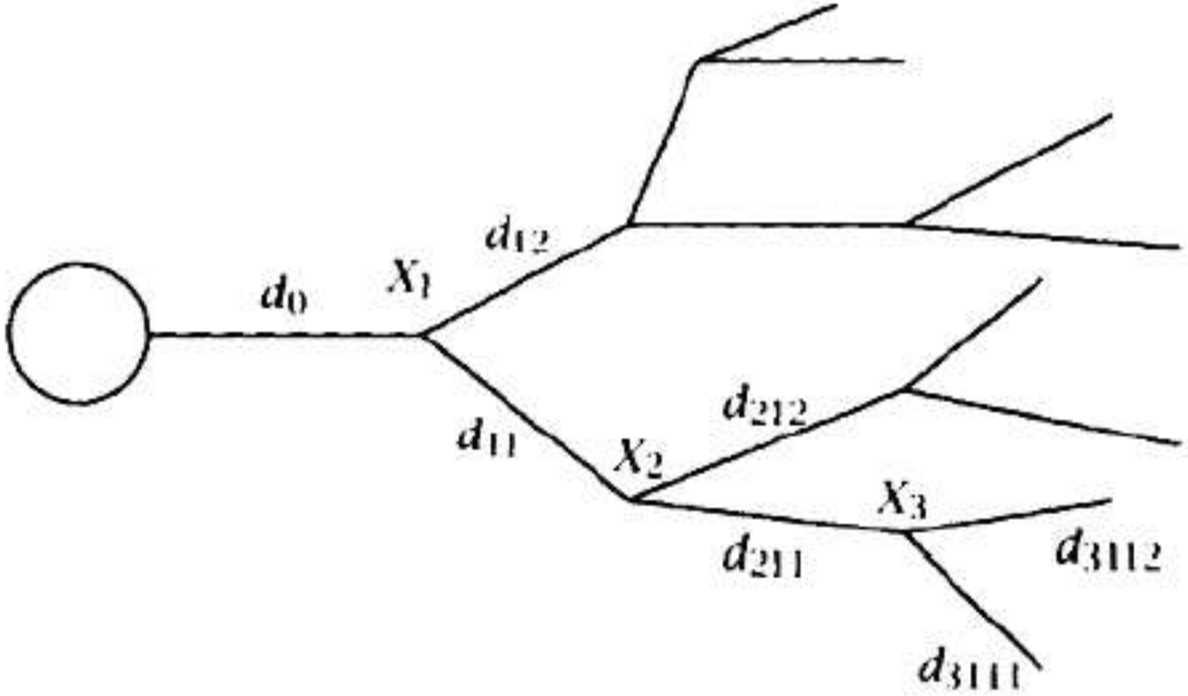
Johnston, Wu, Foundation of Cellular Neuroscience
Slide : Courtesy : Dr. Rishikesh Narayanan

Then, having the branch point X_3 with branches 3111 and 3112 is equivalent to extending branch 211 to infinity.

Rall’s law

Ball-and-stick model

Initial tree:



After applying equivalence at all branch points:

Johnston and Wu Book

Johnston, Wu, Foundation of Cellular Neuroscience
Slide : Courtesy : Dr. Rishikesh Narayanan

Caution : Assumptions

- Passive propagation
- Extracellular medium is isopotential
- All terminal dendrites are semi infinite
- Same result holds for finite dendrites too provided all dendrites terminate at same depth (in electrotonic units - λ)

Proof for Ralls law in nature

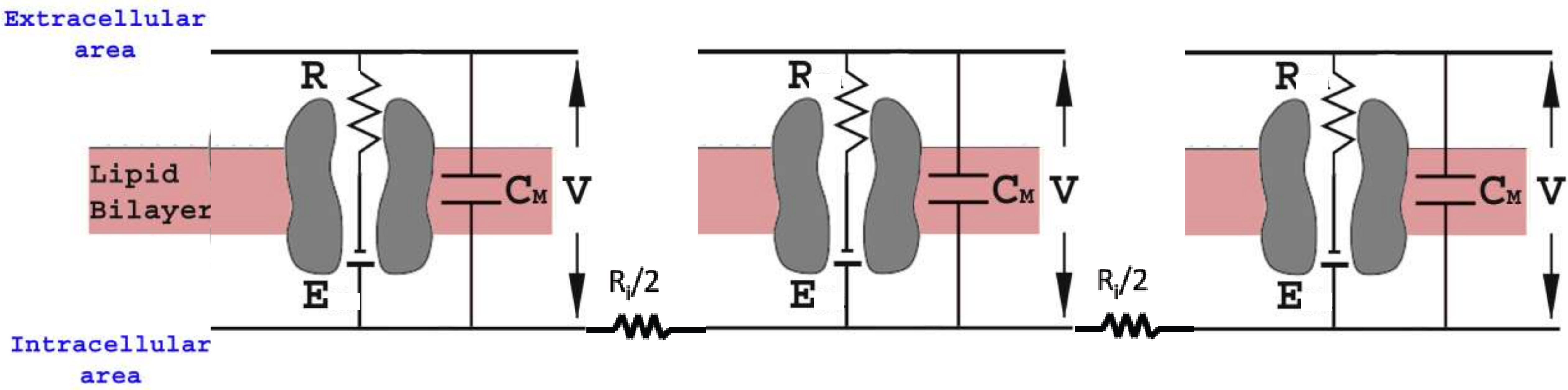
PASSIVE CABLE PROPERTIES AND MORPHOLOGICAL CORRELATES OF NEURONES IN THE LATERAL GENICULATE NUCLEUS OF THE CAT

BY STEWART A. BLOOMFIELD, JAMES E. HAMOS AND S. MURRAY SHERMAN

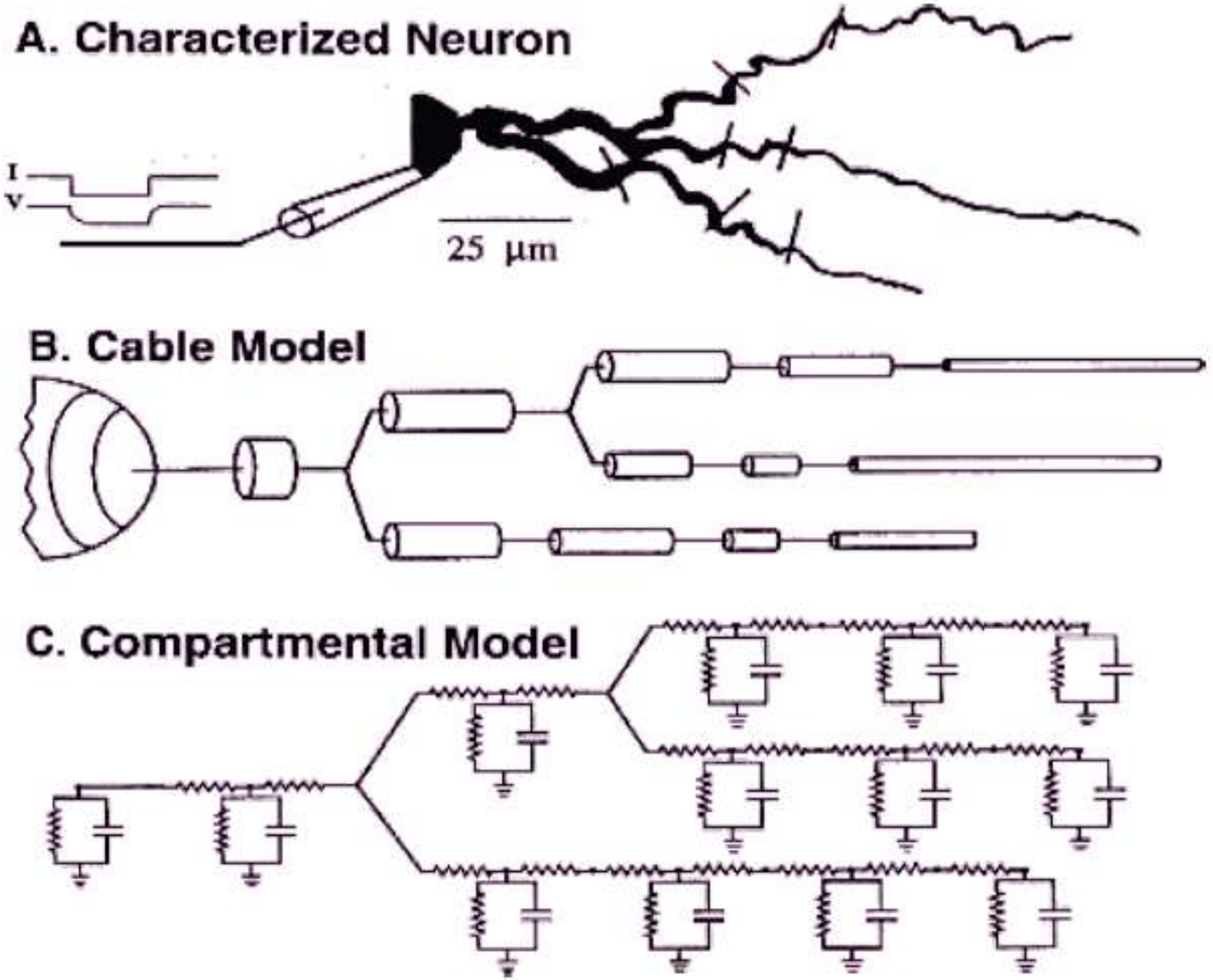
2. Analysis of HRP-labelled geniculate neurones showed that the dendritic branching pattern of these cells adheres closely to the $\frac{3}{2}$ power rule. That is, at each branch point, the diameter of the parent branch raised to the $\frac{3}{2}$ power equals the sum of the diameters of the daughter dendrites after each is raised to the $\frac{3}{2}$ power. Furthermore, preliminary data indicate that the dendritic terminations emanating from each primary dendrite occur at the same electrotonic distance from the soma. These observations suggest that both X and Y cells meet the geometric constraints necessary for reduction of their dendritic arbors into equivalent cylinders.

Modeling and simulation : Getting around complicated assumptions

- Spilit cell into multiple isopotential cells connected by axial resistance

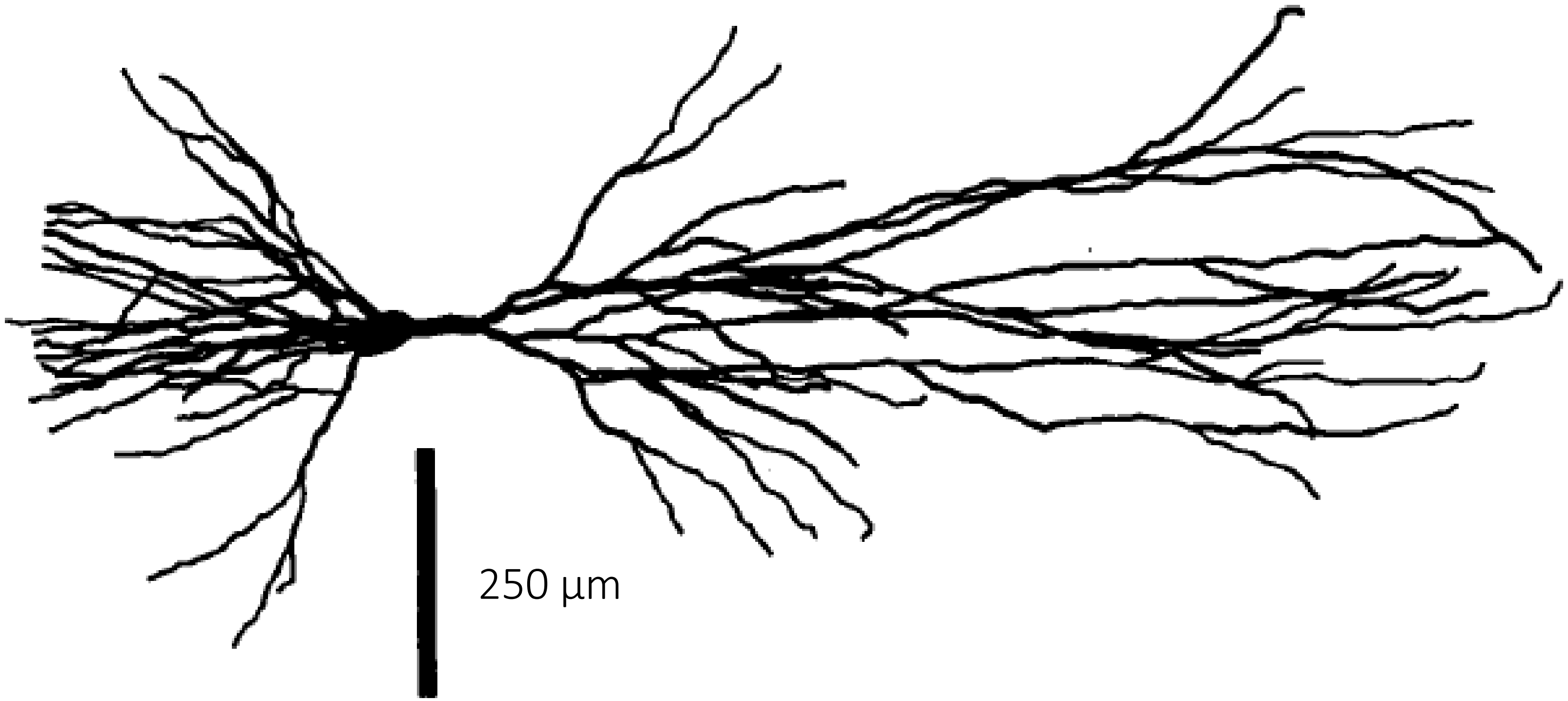


Modeling morphologica realistic neurons



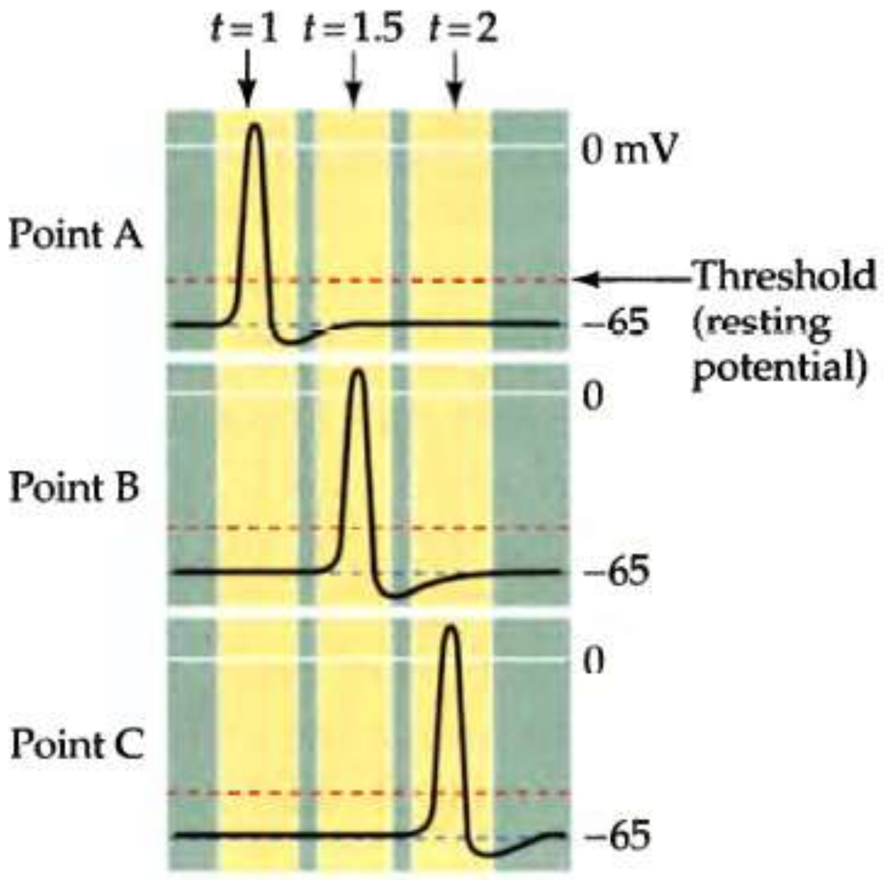
Bower and Beeman, Book of Genesis

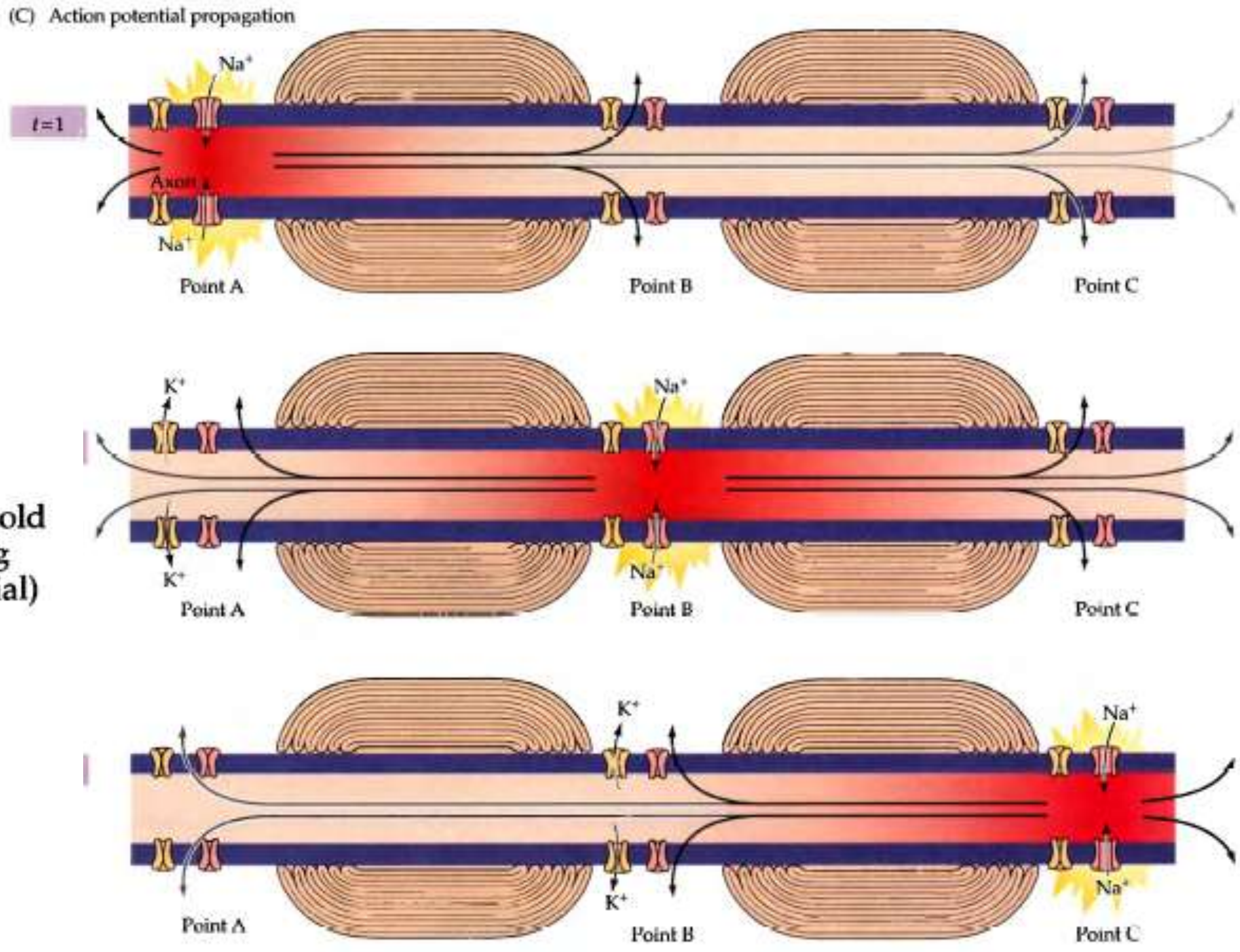
A rat hippocampal CA3 cell



Johnston & Wu, Foundations of Cellular Neurophysiology

AP propagation





Questions

How do you parcellate a long cable in to segments ? How do you choose length of segment ? λ

Hhow does myelination affect ??? Lambda = root (rm / ri)… increased space constant hence lower loss along cable

Thank you !

Emergence of the AP (Qualitative)

- At Rest
- *K^+ channel moderate conductance, Na^+ channel very low conductance, at around resting membrane potentials*
- *So what will be the resting membrane potential be like? (Take a guess)*

- Depolarisation
- *Deposit some charge inside*
- *What happens if K^+ channel is the only active conductance?*
- *What happens if Na^+ channel is also active albeit with low conductance?*

- At highly depolarized states ?