(A) 10/12/04

Other ~~currents~~ ions

Ca^{2+} ← appears to do everything

$\Bigg\Downarrow$ $I_{Ca} \neq g_{Ca}(V - \mathcal{E}_{Ca})$,

because $[Ca^{2+}]_{in} \sim 10^{-4}-10^{-8}$, out $\sim 1-2$

1-2 mM

lots of Ca receptors inside cell

but, can still write gating as $\boxed{m^3 h\, I_{Ca}(V)}$

Other channels ← 100's

differ by: activation ← transient: inactivation; persistent: no inactivation

inactivation

~~type~~ type of ion (reversal potential)

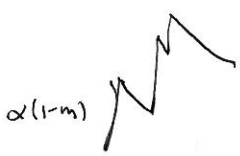
some depart from the classic $x^{l_1} y^{l_2}(V - \mathcal{E})$ scenario

~~eg~~ classic: K-Ca (A-currents)

$$I_{K-Ca} = m([Ca^{++}])\, \bar{g}_{K-Ca}(V - \mathcal{E}_K)$$ ← hyperpolarize cell

$m([Ca^{++}], V)$ ← can have it's own dynam

$$\dot{m} = \alpha(1-m)\sum_i \delta(t-t_i) - \frac{m}{\tau_{off}}$$



~~H-C~~

H (hyperpolarization) ~~→~~ current: Na^+ current activated by hyperpolarization – leads to ~~repetitiv~~ repetitive firing.

main take-home

drop first time through, but add

$$I_x = \bar{g} \underbrace{m^k h^l}_{e.g.} \cancel{f(v)} \; I_x(v)$$

← due to channels w/ a particular ~~resistance~~ resistance

$I_x(v)$: $V - E_x$ ← typical

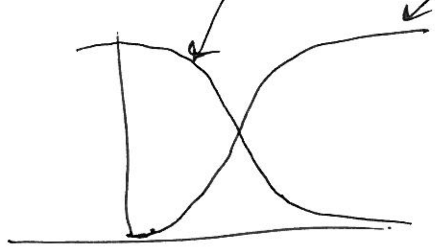
GHK ← more generally (see hwk)

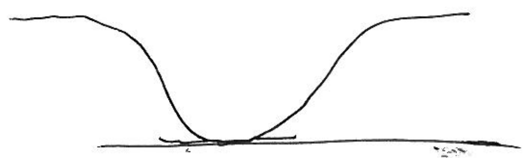
m, h obey channel dynamics

$$\tau_m(v)\, \dot{m} = m_\infty(v) - m$$

$$\tau_h(v)\, \dot{h} = h_\infty(v) - h$$

important params: $\tau(v)$, $m_\infty(v)$, $h_\infty(v)$





← can even get a cell to fire in this regime

(C)

Why so many channels?

Prob. (spike) = F (history of inputs)

↑

channels + their kinetics determine F !!!

~~press~~

Oct. 12, 2004

HH summary

1. Neuron consists of cell membrane that contains pumps + channels.

2. Pumps maintain concentration gradients.

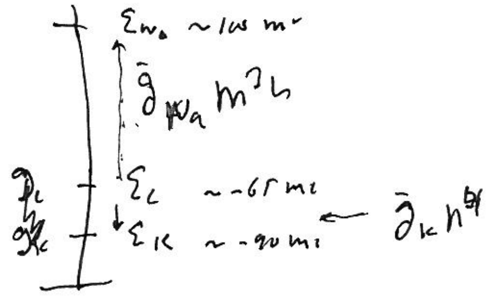
3. Channels allow current to flow in and out.

4. Master equation: $C\frac{dV}{dt} = -I + I_{injected}$ (experimenter or synapses)
   I ← outward current.

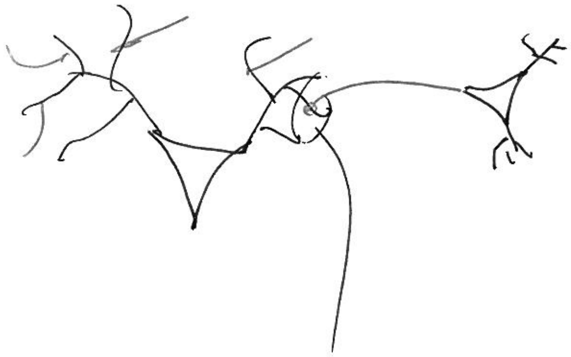
5. Current flows through channels; trick is to find $I(V)$ so we can solve ODE.

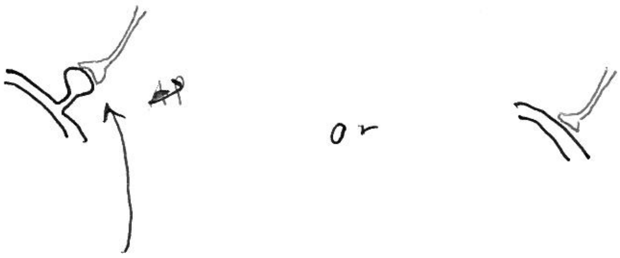
6. $I = \sum_{\text{chan}=x} I_x(V)$. Linear approximation yields

$$I = g_L(V-E_L) + \bar g_{Na} m^3 h (V-E_{Na}) + \bar g_K \cancel{(V-E_K)}\, n^3 (V-E_K)$$



7. Hidden assumptions:
   0. Linear
   1. Voltage is the same everywhere in cell ~~(drop this)~~ (often not true)
   2. Concentrations don't change enough to change the reversal potentials. (good approx. usually)
      except for Ca^{++}





AP causes channels to open

exCIT. $E \sim 0$ mV mixed cation

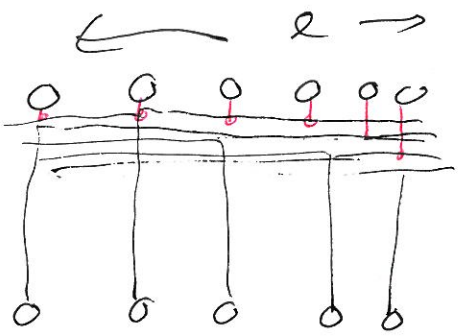
inh. $E \sim -75$ mV Cl^-

~~Constant voltage model no good in~~ dendrites?

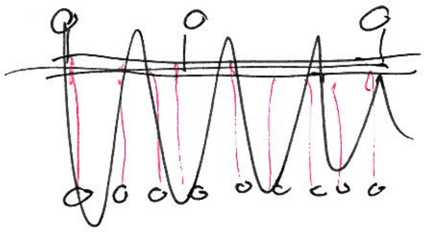
- want to ~~study~~ understand how voltage in dendrites affects voltage in soma.

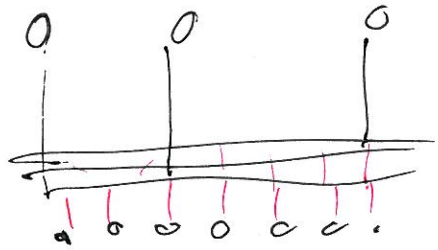
Why dendrites?

- increase surface area of cells
- wiring length

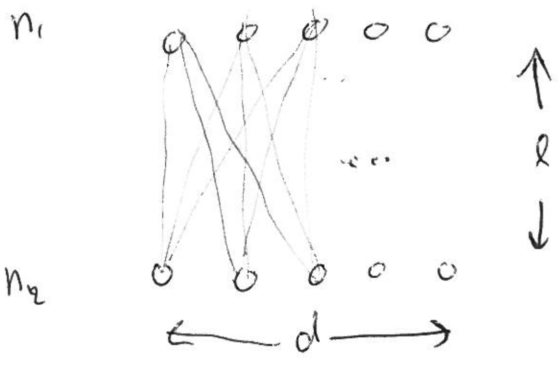


$N\ell$ = total wire length



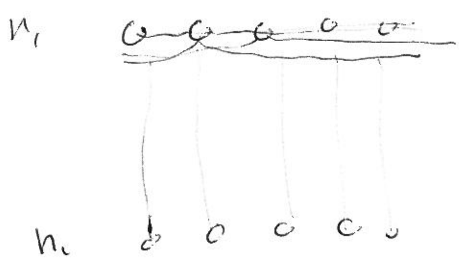


Mitya Chklovskii



somewhere between these two

all-all : $n_1 n_2 \cdot [\ell, \sqrt{\ell^2+d^2}]$

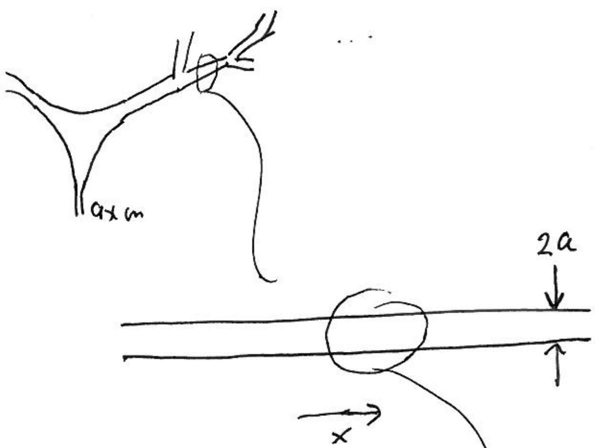


$n_1 d + n_2 \ell$ ← much smaller!!!

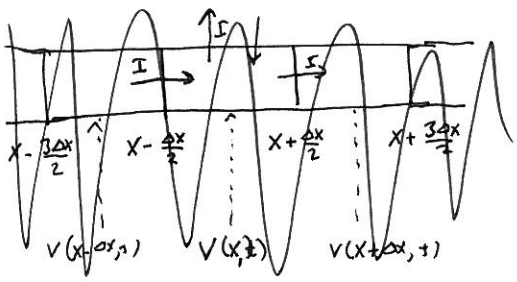
$\sim(n_1+n_2)\ell$

Dendrites [start w/ picture]

- Constant Voltage approx no good!



Want to know $V(x,t)$.



← need giant picture!!

$$C = c_m A$$

$$R_L = \frac{r_L \Delta x}{\pi a^2} \qquad r_L \sim 1\,k\Omega\text{-mm}$$

$$R_m = \frac{r_m}{A} \qquad r_m \sim 1\,M\Omega\text{-mm}^2$$

$$R_\lambda = \frac{r_m}{2\pi a \lambda}$$

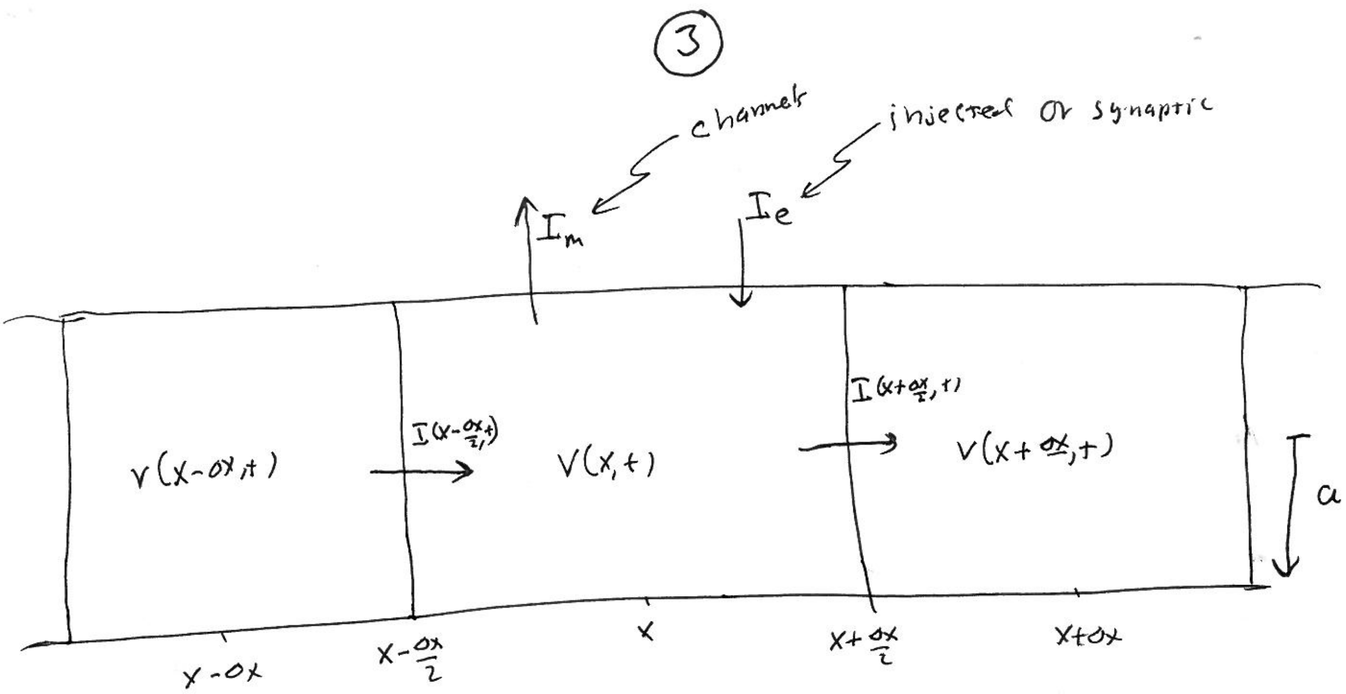
$$I = -\frac{\Delta x}{R_L}\frac{\partial V}{\partial x} = -\frac{\pi a^2}{r_L}\frac{\partial V}{\partial x}$$

$$I_m = i_m A = i_m 2\pi a \Delta x$$

$$I_e = i_e A = i_e 2\pi a \Delta x$$

$$\lambda^2 = \frac{r_m a}{2 r_L} \sim \frac{10^6}{2 \cdot 10^3}\frac{\Omega\text{-mm}^2}{\Omega\text{-mm}} a = 500\, a(mm) = \lambda(mm) \qquad \lambda_{mm} = \sqrt{5 \cdot 10^5\, a(mm)}$$

③



channels

injected (or synaptic)

$$C \frac{\partial V(x,t)}{\partial t} = I(x-\tfrac{\Delta x}{2}, t) - I(x+\tfrac{\Delta x}{2}, t) - I_m + I_e$$

specific membrane capacitance $\sim 10 \frac{nF}{mm^2}$

$$C = 2\pi a \Delta x \boxed{c_m}$$

$$I(x-\tfrac{\Delta x}{2}, t) = \frac{-V(x,t) + V(x-\Delta x, t)}{R} = -\frac{\Delta x}{R} \frac{\partial V(x-\frac{\Delta x}{2}, t)}{\partial x}$$

intracellular resistivity ~ 1-3 kΩ·mm

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

$$\Rightarrow I(x-\tfrac{\Delta x}{2}, t) = -\frac{\pi a^2}{r_L} \frac{\partial V(x-\frac{\Delta x}{2}, t)}{\partial x}$$

④

$$I\left(x-\frac{\Delta x}{2},t\right)-I\left(x+\frac{\Delta x}{2},t\right)$$

$$=-\frac{\pi}{r_L}a^2\left[\left.\frac{\partial v}{\partial x}\right|_{x-\frac{\Delta x}{2}}-\left.\frac{\partial v}{\partial x}\right|_{x+\frac{\Delta x}{2}}\right]$$

$$=+\frac{\pi}{r_L}a^2\Delta x\,\frac{\partial^2 v}{\partial x^2}$$

$$I_m=2\pi a\Delta x\, i_m$$

$$I_a=2\pi a\Delta x\, i_e$$

$$2\pi a\Delta x\, C_m\frac{\partial v}{\partial t}=\frac{\pi}{r_L}a^2\Delta x\frac{\partial^2 v}{\partial x^2}-2\pi a\Delta x\left(i_m-i_e\right)$$

$$\Rightarrow\quad C_m\frac{\partial v}{\partial t}=\frac{a}{2r_L}\frac{\partial^2 v}{\partial x^2}-\left(i_m-i_e\right)$$

Check units: $r_L C_m \sim \frac{RLC}{L^2}\sim\frac{RC}{L}\sim\frac{t}{L}$

$$i_m\sim\frac{I}{L^2}$$

$$\frac{t}{L}\frac{\partial v}{\partial t}\sim\frac{V}{L}\sim\frac{V}{L}-\frac{I}{L^2}R_L$$

$$\sim\frac{V}{L}-\frac{IR}{L}\qquad \underline{\underline{OK}}$$

5

I) Passive properties: linear cable equation.

2 meanings

remember: $I = \bar{g}_L (V - \mathcal{E}_L) = \dfrac{V - \mathcal{E}_L}{\bar{R}_L}$

$= 2\pi a \Delta x \, i_m$

$\Rightarrow i_m = \dfrac{I}{2\pi a \Delta x} = \dfrac{V - \mathcal{E}_L}{2\pi a \Delta x \bar{R}_L}$

$\bar{R}_L = \dfrac{\cancel{2\pi a \Delta x}\, \boxed{r_m}}{2\pi a \Delta x}$ ← specific membrane resistance ~ 1 MΩ mm²

$\Rightarrow i_m = \dfrac{V - \mathcal{E}_L}{r_m}$

$v \equiv V - \mathcal{E}_L$

$\Rightarrow c_m \dfrac{\partial v}{\partial t} = \dfrac{a}{2 r_L} \dfrac{\partial^2 v}{\partial x^2} - \dfrac{v}{r_m} + i_e$

$r_m c_m = \dfrac{\bar{R}_L}{A} C A = \bar{R}_L C = \tau_m$ ~5-10 ms

$\Rightarrow \tau_m \dfrac{\partial v}{\partial t} = \underbrace{\dfrac{r_m a}{2 r_L}}_{\lambda^2} \dfrac{\partial^2 v}{\partial t^2} - v + r_m i_e$

$$\boxed{\lambda \equiv \sqrt{\dfrac{r_m a}{2 r_L}}}$$

⑥

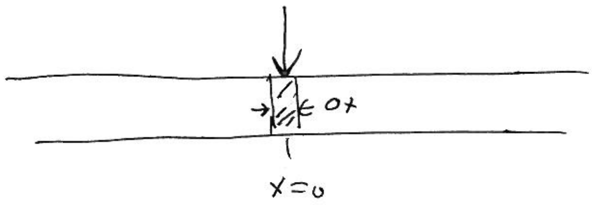
$$\boxed{\tau_m \frac{\partial v}{\partial t} = \lambda^2 \frac{\partial^2 v}{\partial x^2} - v + r_m i_e}$$

<u>linear</u> <u>cable</u> <u>equation</u>

1) Steady state : $\frac{\partial v}{\partial t} = 0$

$$\lambda^2 \frac{\partial^2 v}{\partial x^2} = v - r_m i_e$$

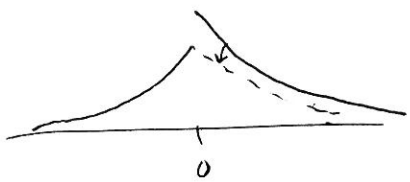
$$i_e = \frac{I_e}{2\pi a \Delta x}$$



$x \neq 0$: $\lambda^2 \frac{\partial^2 v}{\partial x^2} = v \Rightarrow V = A e^{x/\lambda} + B e^{-x/\lambda}$

$$V(x>0) = A e^{-x/\lambda}$$

$$V(x<0) = B e^{x/\lambda}$$



$$\frac{\partial v}{\partial x} \sim \times (A-B) \Rightarrow A = B$$

~~v(x≠0)~~ $v = A e^{-\frac{|x|}{\lambda}}$

$$\cancel{\frac{\partial v}{\partial x} = \frac{A}{\lambda} \left\{ \begin{array}{ll} e^{-\frac{x}{\lambda}} & x<0 \\ -e^{\frac{x}{\lambda}} & \end{array} \right.}$$

$$\frac{\partial v}{\partial x} = \frac{A}{\lambda} e^{-\frac{|x|}{\lambda}} \begin{cases} 1 & x<0 \\ -1 & x>0 \end{cases}$$

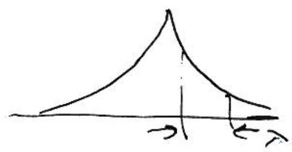
$$\frac{\lambda^2\left[\frac{\partial v}{\partial x}\Big|_{x+\frac{\Delta x}{2}} - \frac{\partial v}{\partial x}\Big|_{x-\frac{\Delta x}{2}}\right]}{\Delta x} = -r_m i_e$$

$$= -\lambda^2 \frac{2A}{\lambda}\frac{1}{\Delta x} = -\frac{2\lambda A}{\Delta x} = -\frac{r_m I}{2\pi a\, \Delta x}$$

$\boxed{R_\lambda = \frac{r_L \lambda}{\pi a^2}}$ = resistance across one length constant.

$$A = \frac{1}{2} I \frac{r_m}{2\pi a \lambda} = \frac{I R_\lambda}{2}$$

$$V(x) = \frac{I R_\lambda}{2} e^{-\frac{|x|}{\lambda}}$$



$$\lambda^2 = \frac{r_m a}{2 r_L} \propto \frac{10^6\, \Omega\, mm^2\, a}{2\cdot 2\cdot 10^3\, \Omega\, mm} = 250\, a(mm)$$

$$= 250\cdot 10^{-3}\, a(\mu m)$$

~~λ units~~

$$\lambda = \frac{\sqrt{a(\mu m)}}{2}\,(mm) = 500\sqrt{a(\mu m)}$$

~~$a = 1\,\mu m \Rightarrow \lambda$~~ $a = 1\,\mu m \Rightarrow \lambda = 500\,\mu m = 0.5\,mm$

$$\tau_m \frac{\partial v}{\partial x} = \lambda^2 \frac{\partial^2 v}{\partial x^2} - v + i_e e^{i\omega t}\delta(x)$$

$$v \sim e^{i(kx-\omega t)} \Rightarrow -i\omega\tau = -\lambda^2 k^2 - 1$$

$$k = \pm\sqrt{-\frac{(1+i\omega\tau)}{\lambda^2}} = \pm i\frac{\sqrt{1+i\omega\tau_m}}{\lambda}, \quad v \sim e^{-\frac{\sqrt{1+i\omega\tau_m}}{\lambda}x}$$

$i_e \to \frac{I_e}{2\pi a}\delta(x)$

$r_m i_e = \underbrace{\frac{r_m}{2\pi a}\frac{1}{\lambda R_\lambda}}\, R_\lambda I_e \lambda\delta(x)$

$\frac{r_m}{2\pi a}\frac{1}{\lambda}\frac{\pi a^2}{r_L\lambda}$

$= \frac{r_m a}{2 r_L}\frac{1}{\lambda^2} = 1$

$\Rightarrow \lambda^2 \frac{\partial^2 u}{\partial x^2} = u - R_\lambda I_e \lambda \delta(x)$

→ sol'n is easy

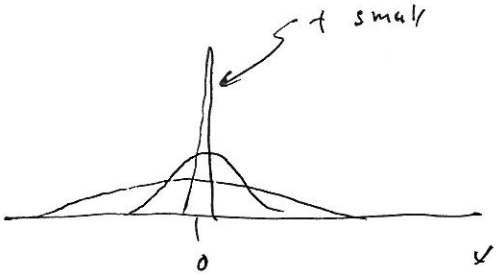
→ superposition principle!!!

- FT approach

next: branching

$$r_m i_e = I_e R_\lambda \tau_m \lambda\, \delta(x)\,\delta(t)$$

$$\Rightarrow \quad v(x,t) = \frac{I_e R_\lambda}{\sqrt{4\pi t/\tau_m}} \exp\left[-\frac{\tau_m x^2}{4\lambda^2 t}\right] \exp\left[-\frac{t}{\tau_m}\right] \Theta(t)$$



$$\tau_m \frac{\partial u}{\partial t} = \lambda^2 \frac{\partial^2 u}{\partial x^2} - u + I_e R_\lambda \lambda\,\delta(x)\,\tau_m\,\delta(t)$$

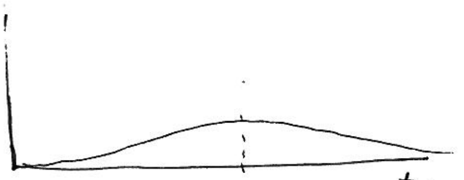
$$\int_{-\infty}^{\infty} dx \int_{-\infty}^{\infty} dt \,[\quad] \quad \text{(both sides)}$$

$$\Rightarrow \int_{-\infty}^{\infty} dx \int_{-\infty}^{\infty} dt\, u = \int_{-\infty}^{\infty} dx \int_{-\infty}^{\infty} dt\, I_e R_\lambda \lambda\,\delta(x)\,\tau_m\,\delta(t)$$

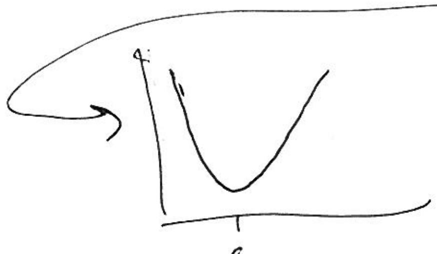
$$= I_e R_\lambda \lambda \tau_m$$

$$= \int_0^{\infty} \frac{I_e R_\lambda}{\sqrt{4\pi t/\tau_m}} \sqrt{4\pi\lambda^2 t/\tau_m}\; e^{-t/\tau_m}\, dt = I_e R_\lambda \lambda \int_0^{\infty} dt\, e^{-t/\tau_m} =$$

OK



$$s \equiv t/\tau_m \qquad v(x,s) \sim \exp\left[-\left(\frac{\overset{\equiv\rho}{x^2/4\lambda^2}}{s} + s + \frac{1}{2}\log s\right)\right]$$



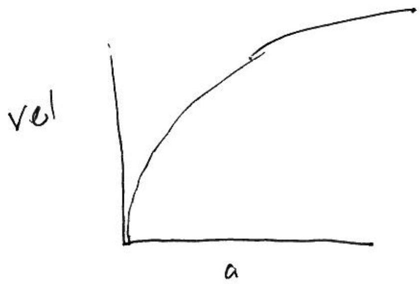
$$\frac{d}{ds}\left(\frac{\rho}{s} + s + \log s\right) = -\frac{\rho}{s^2} + 1 + \frac{1}{2s} = 0$$

$$\Rightarrow s^2 + \frac{s}{2} - \rho = 0 \Rightarrow \cancel{s = \frac{-1 \pm \sqrt{1+4\rho}}{2} \to \sqrt{\rho + 1/4} - \frac{1}{2} \to \sqrt{\rho}}$$

$$s = \frac{1}{4}\left[\sqrt{16\rho + 1} - 1\right]$$

$$t_0 = \tau_m \sqrt{\rho} = \tau_m \frac{X}{2\lambda}$$

$$\text{"Vel"} = \frac{X}{t_0} = \frac{2\lambda}{\tau_m} \sim \sqrt{a}$$

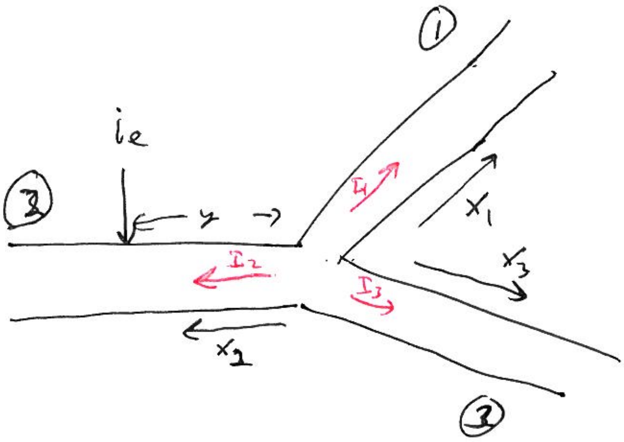


$$\text{max: } \exp\left[-\left(\sqrt{\rho+\tfrac{1}{4}} + \log\left[\sqrt{\rho+\tfrac{1}{4}} - \tfrac{1}{2}\right]\right)\right]$$

$$\sim \exp\left[-\frac{X}{2\lambda}\right]$$

next: pg. 13

Branching



1 $V_1(x_1) = A_1 e^{-\frac{x_1}{\lambda_1}}$

3 $V_2(x_2) = A_3 e^{-\frac{x_3}{\lambda_3}}$

2 $V_3(x_3) = \frac{I_e R_{\lambda_2}}{2} \left[e^{-\frac{|y-x|}{\lambda_2}} + A_2 e^{-\frac{x_2}{\lambda_2}} \right]$

B.C. $V_1(0) = V_2(0) = V_3(0)$

$I_1(0) + I_2(0) + I_3(0) = 0$

$\uparrow$

$-a_1^2 \frac{\partial V_1}{\partial x_1} - a_2^2 \frac{\partial V_2}{\partial x_2} - a_3^2 \frac{\partial V_3}{\partial x_3} = 0$

11

$$A_1 = A_3 = \frac{I_e \Omega_{\tau_2}}{2}\left[e^{-\frac{y}{\tau_2}} + A_2 \right]$$

$$\frac{A_1 a_1^2}{\tau_1} + \frac{A_2 a_3^2}{\tau_3} + \frac{I_e \Omega_{\tau_2}}{2}\frac{a_2^2}{\tau_2}\left[A_2 - e^{-\frac{y}{\tau_2}} \right]$$

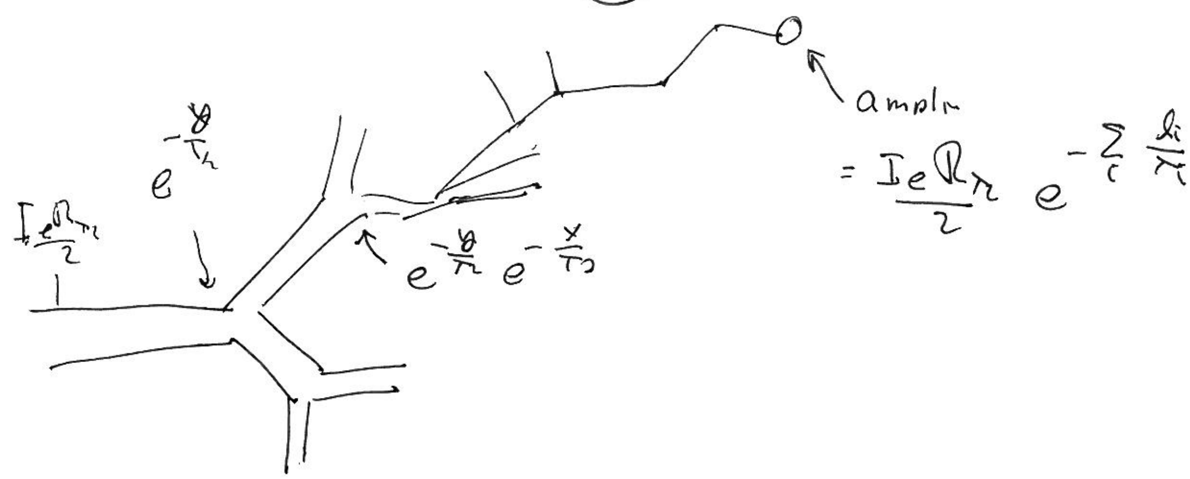
$A_2 = 0$? ($\Leftrightarrow$ no reflection)

$$A_1 = A_3 = \frac{I_e \Omega_{\tau_2}}{2} e^{-\frac{y}{\tau_2}}$$

$$\frac{I_e \Omega_{\tau_2}}{2} e^{-\frac{y}{\tau_2}} \left[\frac{a_1^2}{\tau_1} + \frac{a_3^2}{\tau_3} - \frac{a_2^2}{\tau_2} \right] = 0$$

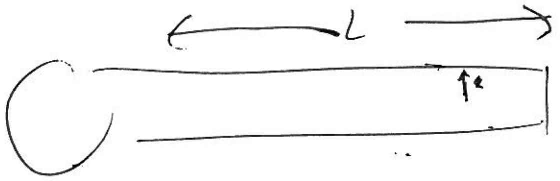
$$\lambda \sim \sqrt{a} \Rightarrow \boxed{a_2^{3/2} = a_1^{3/2} + a_3^{3/2}}$$

$3/2$ -law



$$\frac{L}{\lambda} = \left\langle \sum_i \frac{l_i}{\lambda_i} \right\rangle$$

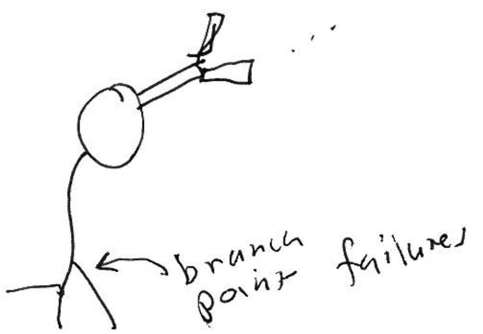
$$2\pi a L = \text{surface area} = \sum_{\text{all seg}} 2\pi l_i a_i$$



$\Rightarrow a$

$\Rightarrow \lambda$

In reality: multi-compartment models



$$\tau \frac{\partial V}{\partial t} = \lambda^2 \frac{\partial^2}{\partial x^2} - \bar{g}_L (V - \mathcal{E}_L) - \bar{g}_{Na} m^3 h (V - \mathcal{E}_{Na}) - \bar{g}_K n^4 (V - \mathcal{E}_K)$$

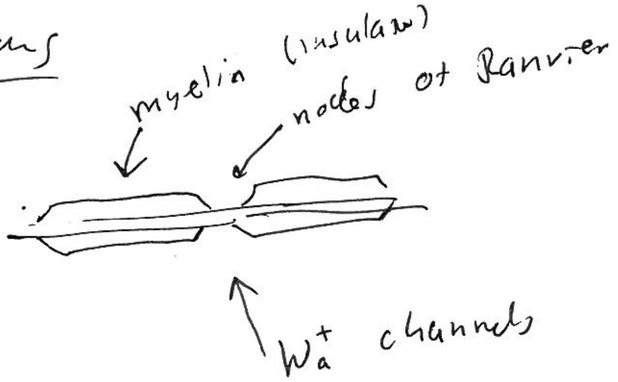
$\dot{m} =$

$\dot{h} =$

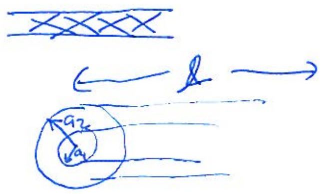
$\dot{n} =$

<u>very hard to solve</u> ← approx sol'n later!

Axons



$$C_m \frac{\partial V}{\partial t} = \frac{a}{2r_L}\frac{\partial^2 V}{\partial x^2}$$



$$V \propto \frac{Q}{l} \log \frac{a_2}{a_1}$$

$$\Rightarrow C \sim \frac{l}{\log \frac{a_2}{a_1}}$$

$\Big[\ a_2 = a_1 + \Delta \Rightarrow \log \frac{a_2}{a_1} = \log \frac{a_1+\Delta}{a_1} \approx \frac{\Delta}{a_1} \Rightarrow C \sim l a_1$

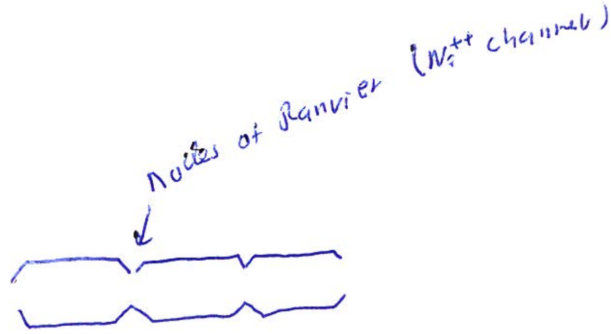
$$C_m \sim \frac{l}{\cancel{a} \log a_2/a_1} \frac{1}{2\pi a} \sim \frac{1}{a}$$

$$\Rightarrow \frac{\partial V}{\partial t} \propto \frac{a^2}{2r_L}\frac{\partial^2 V}{\partial x^2} \quad : \quad \tau \frac{\partial V}{\partial t} = \cancel{D \frac{\partial^2 V}{\partial x^2}}\ \tilde{\lambda}^2 \frac{\partial^2 V}{\partial x^2}$$

$\cancel{V \sim D}$

$\cancel{Vel \sim D^{1/2} \sim a}$

$Vel. \sim \tilde{\lambda} \sim a$



$$c_m r_m \frac{\partial v}{\partial t} = \frac{r_m a}{2 r_i} \frac{\partial^2 v}{\partial x^2}$$

$$\tau \frac{\partial v}{\partial t} = \lambda^2 \frac{\partial^2 v}{\partial x^2}$$

$$\Rightarrow \quad V(x,t) = \frac{e^{-\frac{x^2}{4\lambda^2 t/\tau}}}{\sqrt{4\pi t/\tau}}$$

Check: $\tau \partial_t V = V \left[\frac{x^2}{4\lambda^2 (t/\tau)^2} - \frac{1}{2} \frac{1}{t/\tau} \right]$

$$\partial_x V = V \left[\frac{-x}{2\lambda^2 (t/\tau)} \right]$$

$$\lambda^2 \partial_x^2 = V \left[\frac{x^2}{4\lambda^2 (t/\tau)^2} - \frac{1}{2\, t/\tau} \right] \quad \text{ok}$$

$$V \sim \exp\left[- \frac{x^2}{4\lambda^2\, t/\tau} - \frac{1}{2} \ln (t/\tau) \right]$$

a

$$\partial_{(t/\tau)} = 0 : \quad \frac{x^2}{4\lambda^2 (t/\tau)^2} - \frac{1}{2(t/\tau)} = 0$$

$$\frac{t}{\tau} = \frac{x^2}{2\lambda^2}$$

$$t = \frac{\tau x^2}{2\lambda^2} \sim L^2 \frac{\tau}{2\lambda^2}$$

$$\frac{\tau}{\lambda^2} = \frac{c_m r_m}{r_m a / 2 r_i} = 2 r_i \frac{c_m}{a}$$

$$c_m \sim \frac{1}{a} \Rightarrow \frac{\tau}{\lambda^2} \sim \frac{1}{a^2}$$

$$t \sim \frac{L^2}{a^2}$$

$$\text{Speed} = \frac{L}{t_L} = \frac{L}{L^2 T/4\lambda^2}$$

$$= \frac{2}{\ } \frac{\lambda^2}{LT}$$

$\lambda^2 \sim a^1$

$L \sim a$

$$\frac{\lambda^2}{\tau} = \frac{r_m a/2r_i}{c_m r_m} = \frac{a}{2 r_i c_m} \sim a^1$$

$$\text{Speed} \simeq \frac{a^1}{LT} \sim a$$