Passive membrane

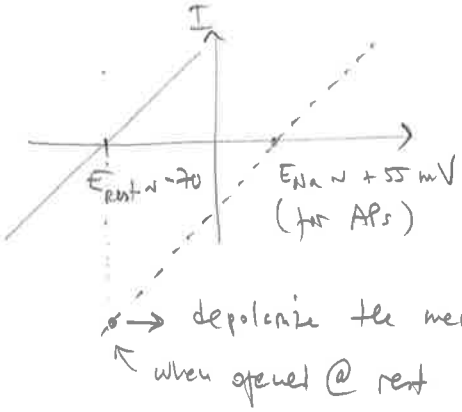
From last lecture:

Biophysics behind membrane potential:

1) Membrane : in vs. out
   insulator / capacitor
2) Ionic pumps : $[ion]_{in} \neq [ion]_{out}$
3) Selective ion-channels

} Reversal potentials : $E_{K^+}, E_{Na^+}, \dots$

When conductances are "ohmic" : $I = g \cdot V$: (passive properties)



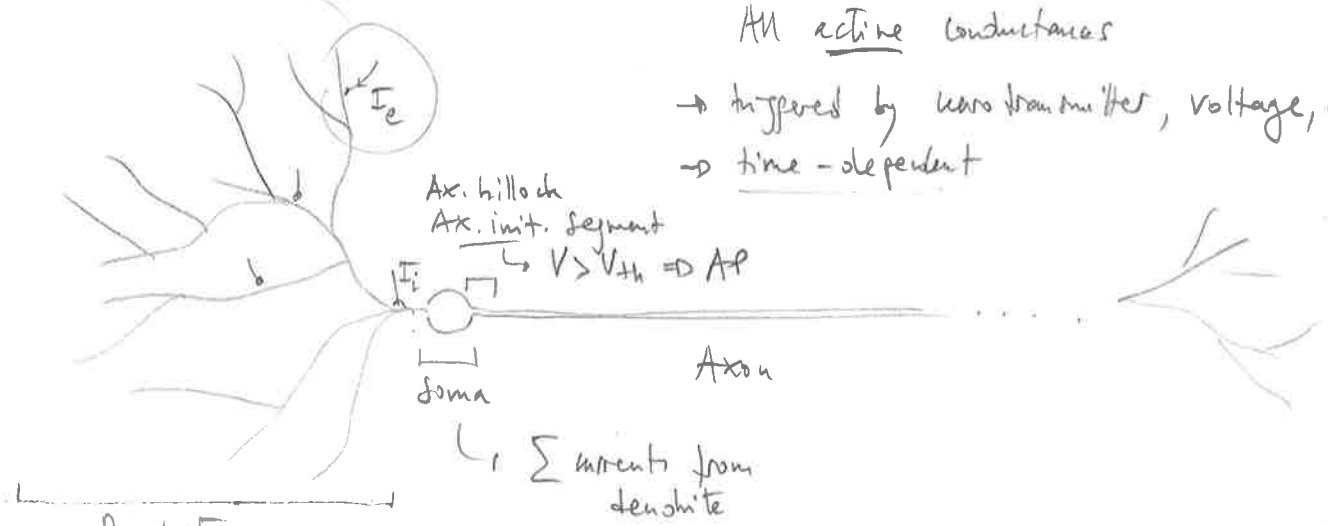
→ depolarize the membrane
↖ when opened @ rest

Different channel types:

- AMPA / NMDA : $E_{Rev} \simeq 0$ mV
  mixed cation
  Ketamine = Antagonist
  } excitatory
- GABA A : $E_{Rev} \simeq -65$ mV
  Chloride Cl^-
- GABA B : $E_{Rev} \simeq -90$ mV
  Potassium K^+
  } inhibitory
- Action potential :
  $E_{Na} \simeq 55$ mV $E_k \simeq -90$ mV

first: consider synapse as generating external current I_S

All active conductances
→ triggered by neurotransmitter, voltage, ...
→ time-dependent



Today : passive (up to external current)

But : - dendritic non-linearities / computations
- back propagating AP

Today: reduce complexity to capture essence of computations
- active conductances
- morphology

Goal: Expression for $V = V(x,t)$ (x: space, t: time) — non-equilibrium

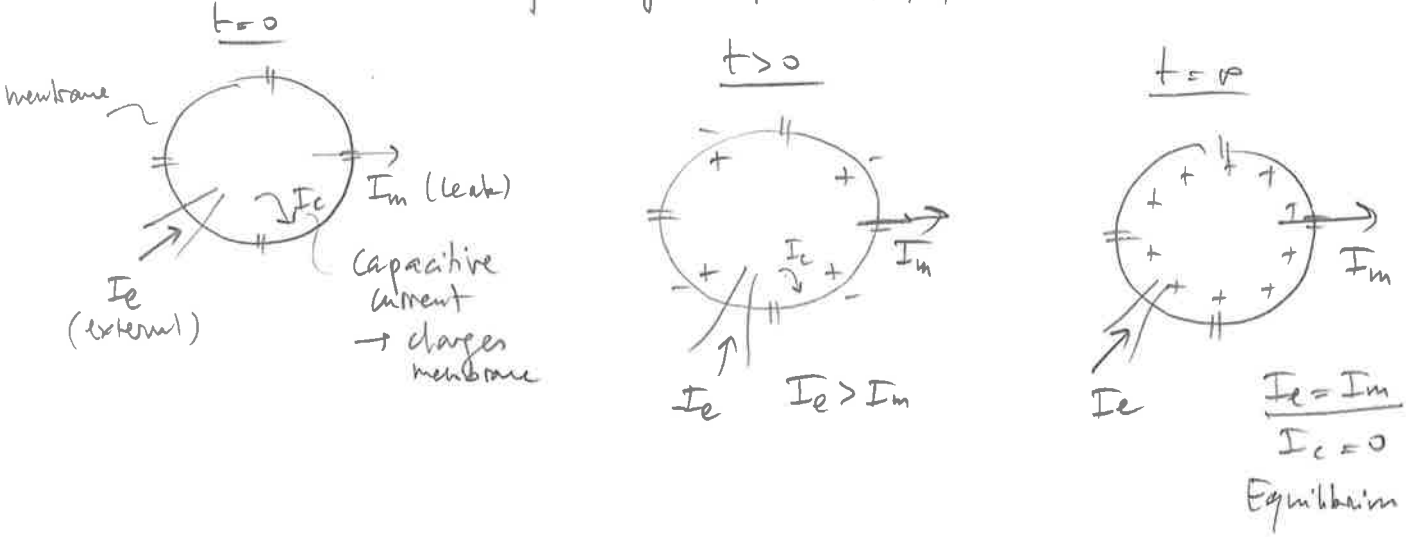
3 steps:
1) Single-compartment models: $V = V(t)$
2) Cable-Equation $V = V(x,t)$ → analytical solutions
3) Multi-compartment models $V = V(x,t)$ → numerical solut.

Tradeoff: realism vs. complexity / contradictility for population models

Problem: not clear what is relevant!

① Single compartment models

- $V = V(t)$ ↪ **isopotential**: holds locally (better models later)
- for simplicity: consider $[in] = [out] \Rightarrow V_{rest} = 0$ } Equivalent to using $U = V - E_{rest}$
  Nothing changes for $V_{rest} \neq 0$



Note: for derivation of Nernst Eq.:

$I_e = 0$, $I_c = I_m$

To derive $V(t)$

$$C = \frac{Q}{V} \quad CV = Q \xrightarrow{\frac{d}{dt}} C\frac{dV}{dt} = \frac{dQ}{dt} = I$$

$$I_e - I_m = I_c$$

$$I_e - g_m \cdot V(t) = C_m \cdot \frac{d}{dt} V(t)$$

$$R_m C_m \cdot \frac{d}{dt} V(t) = R_m \cdot I_e - V(t) \qquad R_m = \frac{1}{g_m}$$

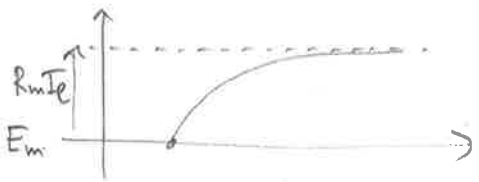
$$\tau_m \frac{dV}{dt} = R_m \cdot I_e - V(t) \quad \text{or} \quad \tau_m \frac{dV}{dt} = R_m I_e - (V - E_m)$$

$\tau_m = R_m \cdot C_m$ membrane time-constant

R_m: membr. resistance; C_m: membr. capacitance

"input resistance"

(i) $\frac{dV}{dt} = 0$ (steady state) $\Rightarrow V_\infty = R_m \cdot I_e + E_m$



$V_\infty \uparrow$ if $R_m \uparrow$ (less leak)
$I_e \uparrow$ (more input)

Consequence:

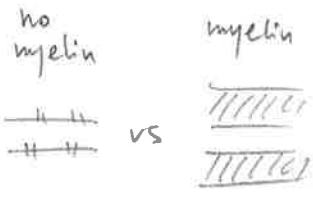
(a)

$R_{small} > R_{large}$

$V_\infty^{small} > V_\infty^{large}$

bec.: $R_m = \frac{\tau_m}{\text{Area}}$

(b)

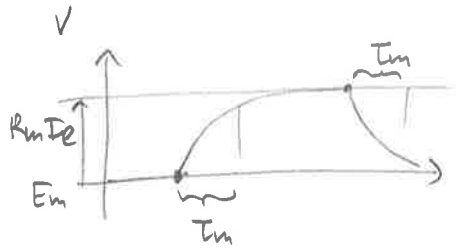


$\Rightarrow$ smaller I_e needed in myelinated axon for same Voltage change.

(ii) time-dependence : general solution :

$$V(t) = E_m + R_m I_e + (V(0) - E_m - R_m I_e)\, e^{-t/\tau_m}$$

or simply $U(t) = U_\infty + (U(0) - U_\infty)\, e^{-t/\tau_m}$ for $U = V - E_m$



τ_m = memory of cell ~ 10–100 ms

Neuron forgets after τ_m (without addition of mechanisms...)

→ longer memory requires other mechanisms

ex: change in synapses / reverberation

Consequences :

(a) if $V_1(t)$ is solution for $I_{e,1}$ & $V_2(t)$ for $I_{e,2}$

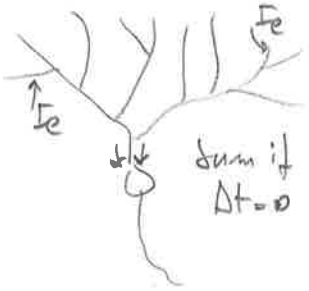
⇒ $V_1(t) + V_2(t)$ is solution for $I_{e,1} + I_{e,2}$

↑ linear equation

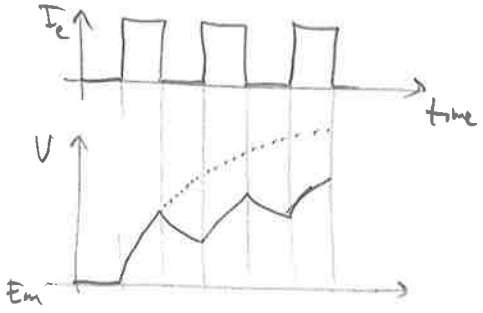
Example $I_e \to k \cdot I_e \Rightarrow V_\infty \to k \cdot V_\infty$

i.e.: simultaneous inputs sum linearly

Spatial summation



(b) sequential inputs sum if $\Delta t < \tau_m$



Temporal summation

Quite tricky ...

→ very different from computers...

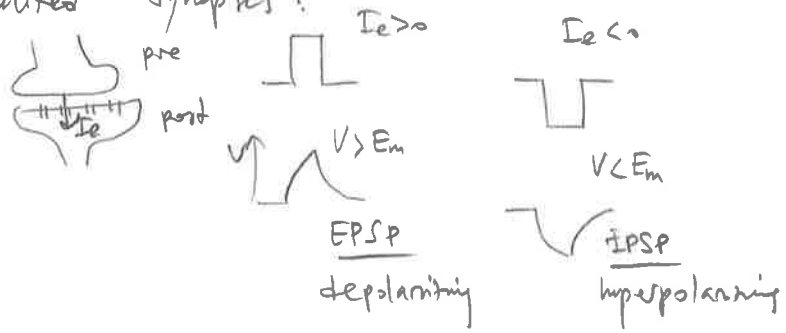
"Integrate & fire" neuron

(b*) constant input : Assume $V \to V_{reset}$ after AP (triggered @ V_{th})

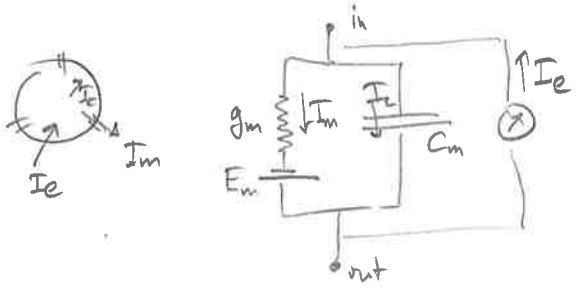
$$r_{isi} = \frac{1}{t_{isi}} \simeq \left[\frac{E_m - V_{th} + R_m I_e}{\tau_m \cdot (V_{th} - V_{reset})} \right]_+$$

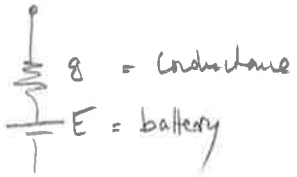
current → rate of AP

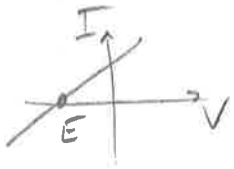
(c) "idealized" synapses:



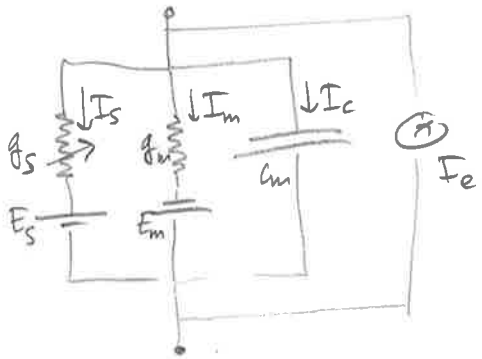
(iii) Equivalent electrical circuits for the above:







Add synapse



$$I_c + I_m + I_s = I_e$$

$$C_m \cdot \frac{dV}{dt} + g_m \cdot (V - E_m) + g_s (V - E_s) = I_e$$

$\frac{dV}{dt} = 0 \Rightarrow$

$$V_\infty = \frac{g_m \cdot E_m + g_s E_s + I_e}{g_m + g_s}$$

Note: for $g_s \gg g_m$

$$V_\infty = E_s + \frac{I_e}{g_s}$$

effect of I_e is reduced
→ shunting inhibition

(iv) Last lecture: few ions need to move in + out to achieve E_{rest}.

But what if $V = V(t) \neq E_{rest}$ most of the time?

- Leak currents: $\sum_{time} I_{Leak} \simeq 0$; Balance of exc. & inh. when no AP.

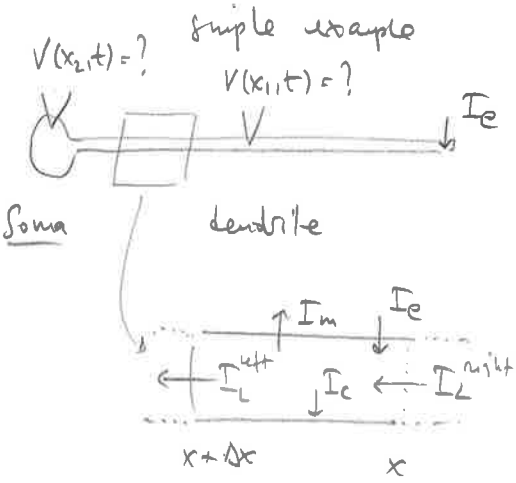
- Synaptic currents: $\sum_{time} |I_S| > 0$ → depletes concentration gradients

⇒ need pumps (need Energy)

(2) Cable Equation

Goal: $V = V(x,t)$ ← longitudinal loc.

e.g.:

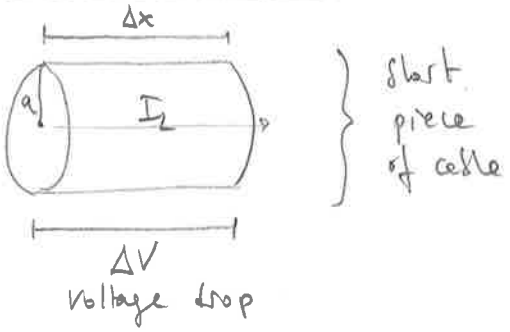


Have expressions for I_m, I_c (see before)

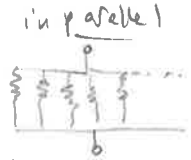
→ need expression for I_L = ?

Longitudinal current

(i) Longitudinal current : I_L = ?



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

- r_L = constant, property of intracellular medium
- $\frac{1}{\text{Area}}$: see.  =  in parallel

$$\frac{1}{R_{tot}} = \sum \frac{1}{R} \Rightarrow R_{tot} = \frac{R}{N}$$

- Δx: see. 

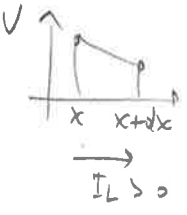
$R_{tot} = N \cdot R$ in series

Ohm's law: $\Delta V = R_L \cdot I_L$

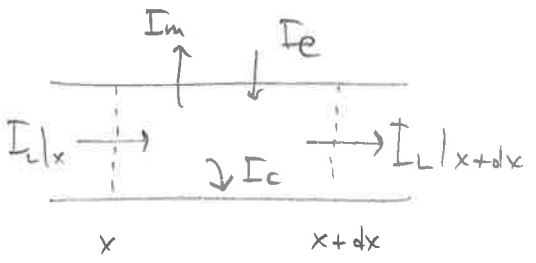
$$= \frac{r_L}{\pi a^2} \cdot \Delta x \cdot I_L$$

$$\Rightarrow_{\Delta x \to 0} \quad \boxed{\frac{dV}{dx}(x) = -\frac{r_L}{\pi a^2} \cdot I_L(x)}$$

by def: $\Delta V < 0$ for pos. current from $x \to dx + x$



(ii) Charge conservation



In essence:

$$I_L(x+dx) = I_L(x) - I_m + I_e - I_c$$

$$\sim \frac{\partial V}{\partial x}\Big|_{x+dx} \qquad \sim \frac{\partial V}{\partial x}\Big|_x \qquad \sim \frac{\partial}{\partial t} V$$

$$\sim \frac{\partial}{\partial x^2} V \qquad \sim g_m \cdot (V - E_R)$$

To derive cable Eq. use

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

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

$\Rightarrow$ current densities = current / Area

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

$$I_c = 2\pi a \, \Delta x \, c_m \cdot \frac{\partial V}{\partial t}$$

$$\Rightarrow \boxed{c_m \cdot \frac{\partial V}{\partial t} = \frac{1}{2a r_L} \cdot \frac{\partial}{\partial x}\left(a^2 \frac{\partial V}{\partial x}\right) - i_m + i_e}$$

$C_m = c_m \cdot$ Area

$R_m = \frac{r_m}{\text{Area}}$

Note:
- a need not be const., i.e. $a = a(x)$
- i_m could be very complicated: $i_m \sim \sum_i g_i (V - E_i)$
- in general: no analytic solution
- but: countless simple cases where solutions exist (in general: simulate, i.e. numerical solutions)

$g_i = g_i(V)$
or $g_i = g_i$(Neurotransm.)
...

(a) Assume:
- a = const
- $i_m = \frac{V - E_R}{r_m}$
- define $v = V - E_R$

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

Define: $\tau_m = r_m \cdot c_m$ & $\lambda = \sqrt{\frac{a r_m}{2 r_L}}$

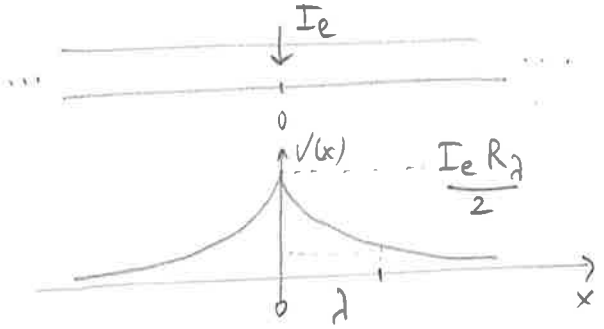
τ_m: time constant

λ: length constant "electrotonic length"

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

Solutions for simple cases:

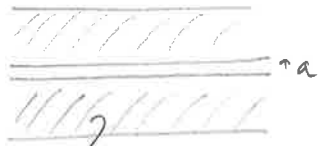
(6) Infinite cable, constant I_e (not time-varying)
final steady state solution $V = V(x)$ for $t \to \infty$



for $\frac{\partial V}{\partial t} = 0$ $\quad V_m(x) = \frac{I_e R_\lambda}{2} e^{-\frac{|x|}{\lambda}}$

Consequences:
- if I_e injected @ $x=0$ in dendrite (e.g. through synapse)
  - ⇒ $V(x)$ decays exponentially with distance
  - ⇒ $V(x)$ reduced to $\frac{1}{e}$ @ $x = \lambda$ compared to $V(x=0)$
- dendrites have effective length close to λ (or in that order of magnitude)
  - ⇒ strong attenuation of $V(x)$ from distal dendrites to soma
- increase λ ?
  - $r_m \uparrow$ less leak current I_m
  - $r_L \downarrow$ less intracellular resistance
  - $a \uparrow$ larger cable

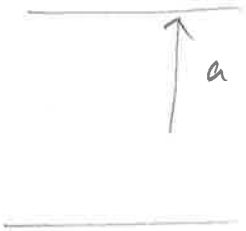
e.g. Axons



myelin $r_m \downarrow \Rightarrow \lambda \uparrow$

e.g. white matter in mammals

vs.

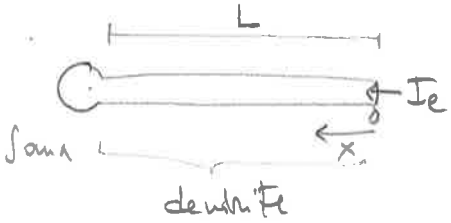


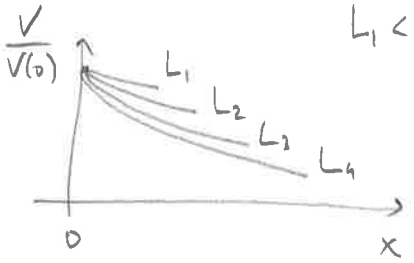
$a \uparrow \Rightarrow \lambda \uparrow$

e.g. squid giant axon $a = 1\,mm$

(invertebrates did not "invent" myelin...)

(c) Finite cable / dendrite



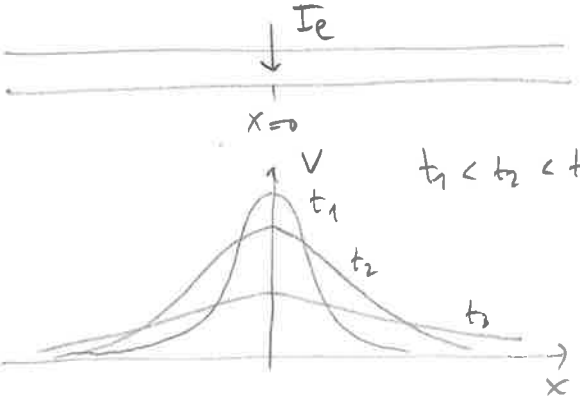


$L_1 < L_2 < L_3 < L_4$

$L \downarrow \Rightarrow$ closer to isopotential

(d) Infinite cable, pulse of input current $I_e = \delta(x) \cdot \delta(t)$

Find $V = V(x,t)$



$t_1 < t_2 < t_3$

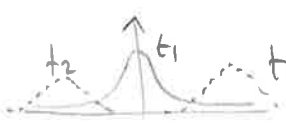
@ each time t:

$V(x,t)$ is a Gaussian in x

- width: $\sigma = \lambda \cdot \sqrt{\frac{t}{\tau_m}}$ (spatial scale; temporal scale)
- area: $\propto e^{-t/\tau_m}$

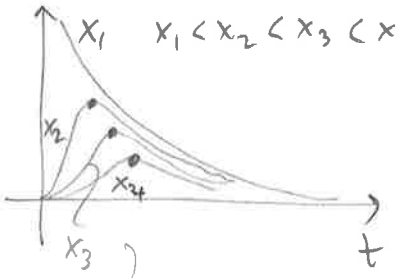
↳ decreases with time see some charge lost through im

Note: this is not a wave:



← not this!

But: plot V as fct of t for different x:



- time of max. V → changes with x
- width of peak → changes with x

⇓

can be used to infer "distance" of a synapse from EPSP in soma

"speed" of bump:

$$V_{bump} \cong 2 \cdot \frac{\lambda}{\tau_m}$$

- $\lambda \uparrow \rightarrow V$ goes far $\rightarrow V_{bump} \uparrow$
- $\tau_m \uparrow \rightarrow V$ changes slowly $\rightarrow V_{bump} \downarrow$

Also approximately holds for Action potentials: $V_{AP} \cong 0.25 - 100$ m/s

How to increase V_{bump}?

- $a \uparrow$ (giant axon)
- myelin ($r_m \uparrow$ & $c_m \downarrow$, but net effect $V_{bump} \uparrow$)

» with defs. for λ & τ_m: $V_{bump} = \sqrt{\frac{a}{2 \cdot r_m \cdot r_L}} \cdot \frac{1}{c_m}$