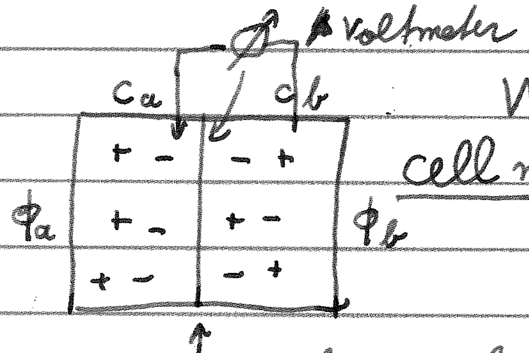
# Electophysiology

~1800 : muscle contraction induced by electrical potentials / batteries (Leyden Jars) where are the batteries, wires, ...

~1890



W. Nernst: cell membranes

ma membrane only permits water & ± ions

$c_{a,b}$ salt conc.

$\phi_{a,b}$ potentials $\quad \overset{+\text{ion}}{\mu^+} = \underset{\text{enth}}{e\phi} + \underset{\text{ent}}{k_B T \ln c}$ Gibbs

~~$\mu^0$~~

$\mu_a^+ = \mu_b^+$ equilibrium ~~pot~~ conditn

$$\underbrace{\phi_a - \phi_b} = \frac{k_B T}{e} \ln(c_b/c_a)$$

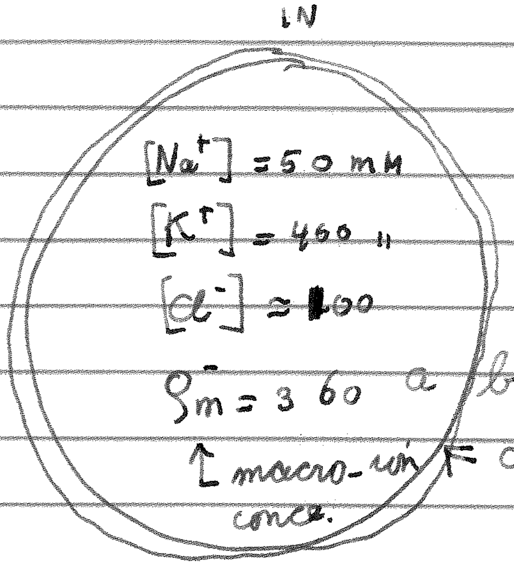
$$\boxed{V_{eq} = \frac{k_B T}{e} \ln c_b/c_a}$$ "equilibrium potential"

~25 mV universal potential scale

# Human Cell

$\Pi_{IN} = \Pi_{OUT}$

**Neuron**

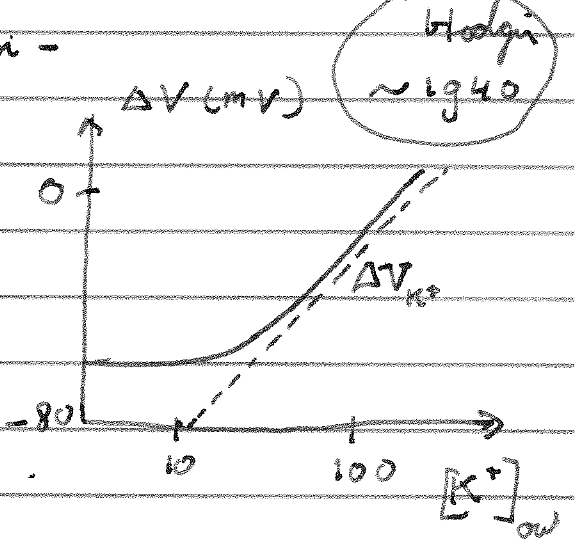


$[Na^+] = 50$ mM
$[K^+] = 460$ "
$[Cl^-] \approx$ [illegible]00
$\rho_m^- = 360$
↑ macro-ion conc.

out

$[Na^+] = 440$ mM
$[K^+] = 20$ "
$[Cl^-] = 560$ mM

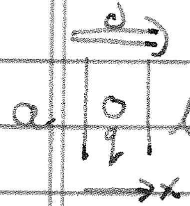
RNA, DNA, protein -



$\Delta V_{Na} = 56$ mV
$\Delta V_{K^+} = -77$ mV

what is "right" equil pot

$$\Delta V_{K^+} = \frac{k_B T}{e} \ln \frac{[K^+_{out}]}{[K^+_{in}]}$$



Only Na, K current

## ~~Membra~~Electrochemical Current

DIFFUSION DRIFT

$$J = -D\left\{\frac{dc}{dx} + \frac{q}{kT}\frac{d\phi(x)}{dx}c\right\}$$ flux ion

↑ $-E_{membran}$

mobility $= \frac{D}{kT}$

D : membrane diffusion

q : charge

C(x) concentr profile

$C(x) \propto \exp -\beta q \phi$
$J = 0$

[illegible]EC

rewrite

$$J = -D\, e^{-\beta q \phi} \frac{d}{dx}\left[c\, e^{+\beta q \phi}\right]$$

electrical flux

$$I^{+}_{\substack{Na\\K}} = -e\, D_{\substack{Na\\K}}\, e^{-\beta e \phi} \frac{d}{dx}\left[c_{\substack{N\\K}}\, e^{\beta e \phi}\right]$$

$$I^{+}_{Na} + I^{+}_{K} = 0$$

Why? Charge Neutrality

no endless accumulat + charge

$$0 = -\cancel{e}\,\cancel{e^{-\beta e \phi}} \frac{d}{dx}\left\{\left(D_N c_N + D_k c_K\right) e^{\beta e \phi}\right\}$$

Integrate across membrane

$$\left(D_N c_N^a + D_k c_k^a\right) e^{\beta e \phi_a} + \left(D_N c_N^b + D_k c_k^b\right) e^{\beta e \phi_b} = 0$$

Solve for $\Delta V = \phi_a - \phi_b$ ~~membrane~~

P

$D_{cl}[Cl^-]^a$

$$\boxed{\Delta V = -\left(\frac{k_B T}{e}\right) \ln\left\{\frac{D_{Na}\, c_{Na}^{b} + D_K\, c_K^{b} + \cdots}{D_{Na}\, c_{Na}^{a} + D_K\, c_K^{a} + \cdots}\right\}}$$

$D_{cl}[Cl^-]^b$

20 mev

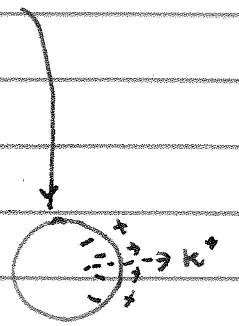
Goldman - Hodgkins - Katz Equation

"REST POTENTIAL"

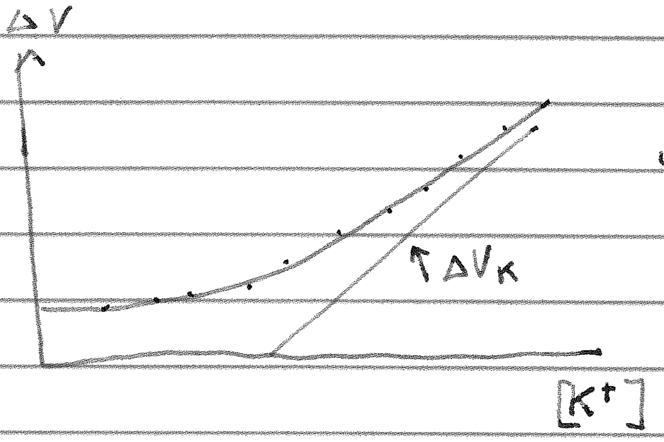
1) "Rest Potential" ~ -60 mV or so most cells

2) $D_{Na} \gg D_K$ $\Delta V \sim \Delta V^{eq}_{Na}$

$D_{Na} \ll D_K$ $\Delta V \sim \Delta V^{eq}_{K}$



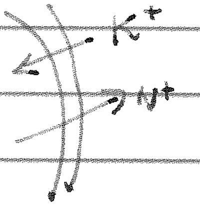
3) $D_K / D_N \sim 19$ ~~$\Delta V \sim -60\,mV$~~



" on the money "

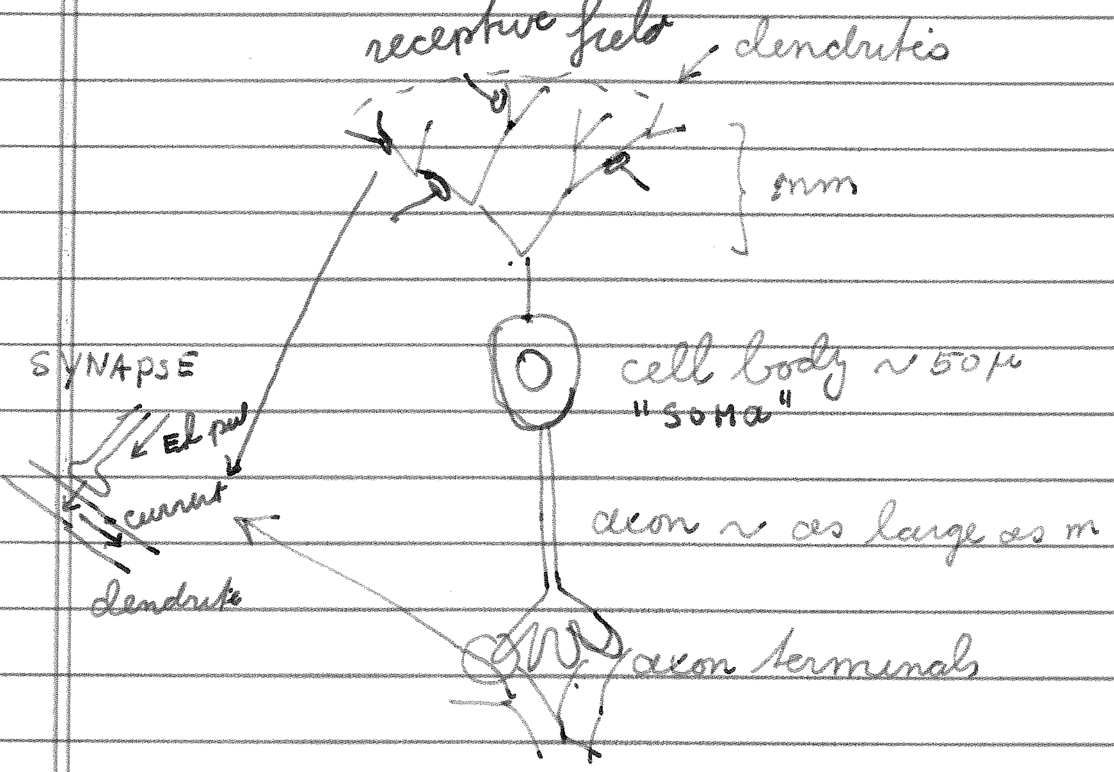
4) How can a equilibrium pot depend on D?
: dynamic. <u>Not</u> equilibrium

need $Na^+$ pump, $K^+$ pump, consume ATP.



5) ~~Voltage sensitive ion channels~~

# Neurons

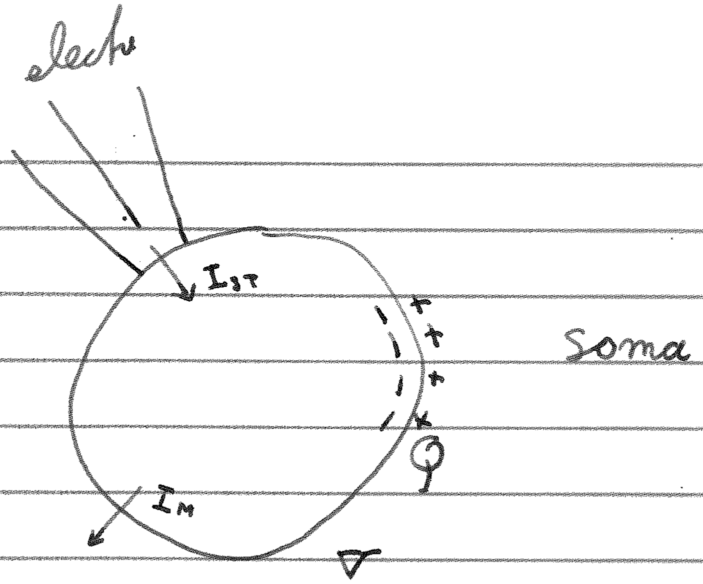


* transport electrical signals ~ meter
  time scale: fraction of sec. Computer

* sensors light, touch, heat, .....

* memory, computation, ...

## Dynamics



Capacitor $C = Q/V$

specific capacitance

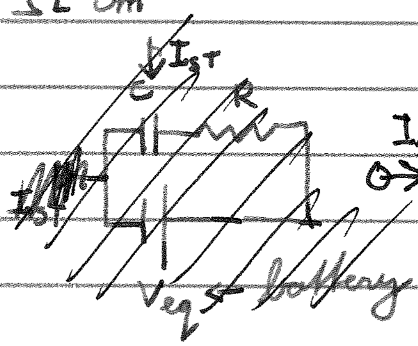
$C = \epsilon \, Area/d \qquad C_m \sim 1 \mu F/cm^2$

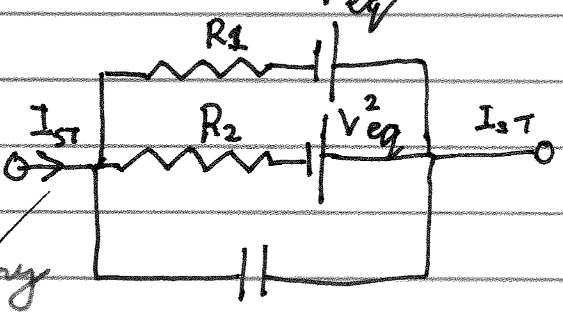
$$\mathcal{E} = \frac{1}{2} C V^2 = \frac{1}{2} C_m \times A_{cell} \times (100 mV)^2$$
$$\approx 10^{-11} J \approx 10^{10} k_B T$$

Resistor $R_M = \rho_m / A$

$\rho_m \approx 10^3 - 10^4 \Omega cm^2$

## Equivalent Circuit





$\frac{dQ}{dt}$

stimulus

$$C \frac{dV}{dt} = \underbrace{\sum_i \frac{1}{R_i} (V_{eq}^i - V)}_{I_m^{(i)} \text{ membrane current ion } i} + I_{ST} \quad 10^{-9}$$

$V_{eq}^i$ = Equilibrium Potential of ion i

$R_i$ = membrane resistance of ion i

Rewrite

$$\mathcal{G} \equiv \sum_i \frac{1}{R_i}$$ conductance

$$C\frac{dV}{dt} = \frac{1}{R}(V^R - V) + I_{ST}$$

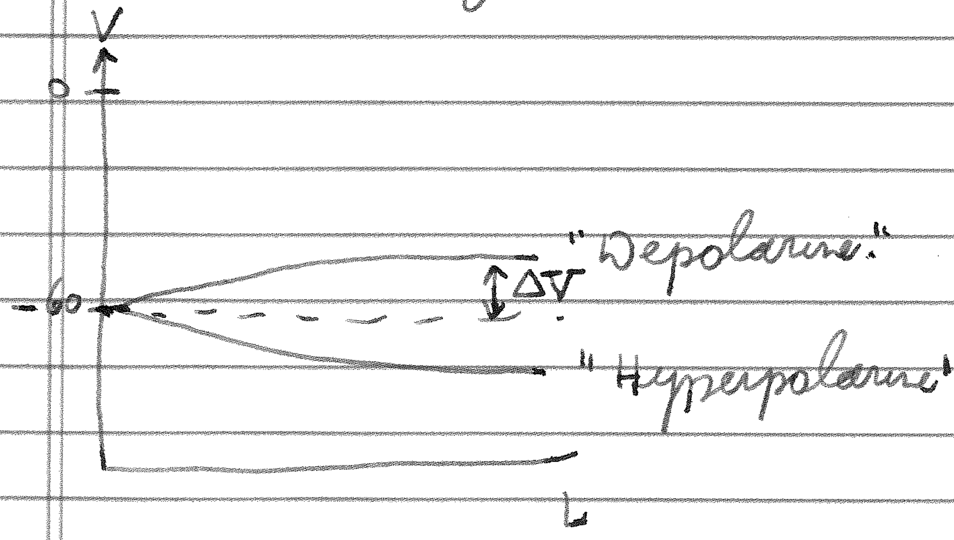
$$V^R \equiv \frac{1}{\mathcal{G}}\sum_i g_i V_{eq}^i$$ ← Rest potential

1) $V_\infty = V^R + I_{ST}R$ change rest potential by current injection

2) $V(t) = V_\infty + (V(0) - V_\infty)\exp^{-t/\tau}$

$\tau = RC = \rho_m C_m = 10^3 \times 10^{-6} = 10^{-3}$ sec

Shortest time for electrical cell activity

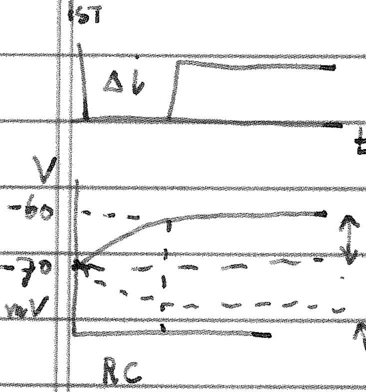


Neurons: hyperpolarize: OK

$$V(t) = V_\infty + C \exp^{-t/RC}$$

$$\tau = RC = \frac{\rho_m C_m \cancel{A}}{\cancel{A}} = 10^{8} \times 10^{4} \times 10^{-6} \sim \underline{\underline{\text{m sec}}}$$

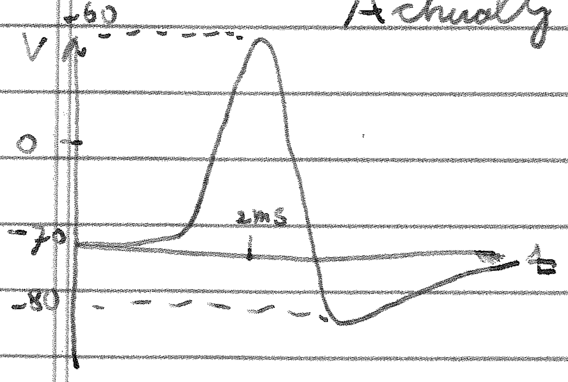
## * Dynamical Time Scale Neurons



$\updownarrow I_{ST} R = \Delta V$ "~~current~~ depolarizes"

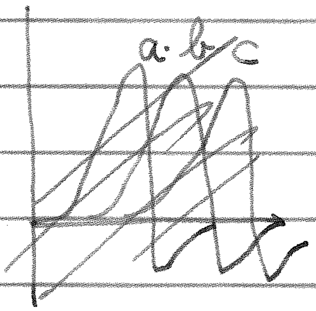
↑ hyperpol.

Actually $\Delta V \gtrsim 10$ mV

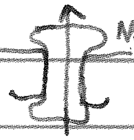


60 mV $\sim V_{eq}^{Na}$

-80 mV $\sim V_{eq}^{K}$



* depolarization : triggers $\overset{\text{rapid}}{\text{opening}}$ $Na^+$ $\Delta V \rightarrow \Delta V_{eq}^{Na}$



ion selective voltage sensitive channels

$\sim$ 1-2 ms : Na channels close

slow opening $K^+$ $\Delta V \rightarrow \Delta V_{eq}^{K^+}$

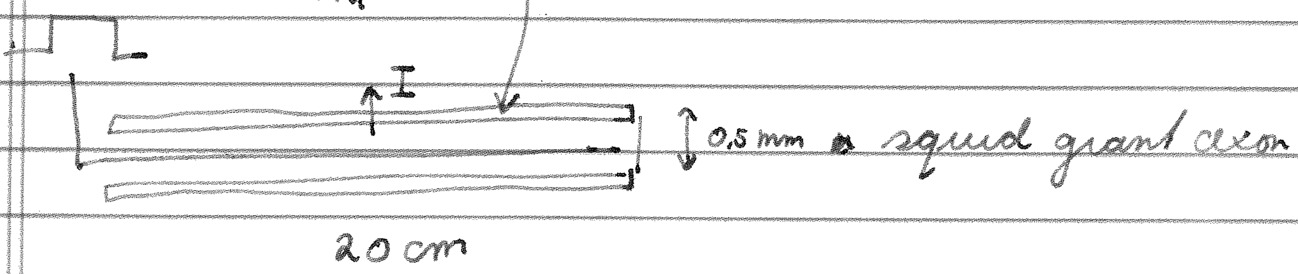
Hodgkin _ Huxley conductance ion channels ?? depends on V

" on time

$$c\frac{dV}{dt} = \sum \overset{?}{g_i}\,(V_{eq}^{\,i} - V)$$

||

$1/R_i$



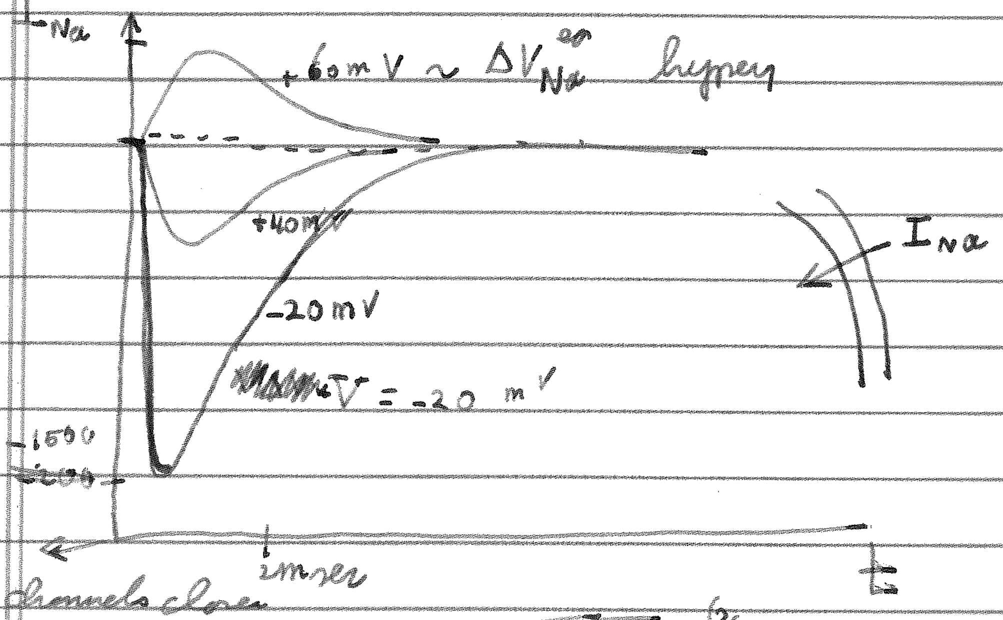
* insert electrode "space clamp" → V uniform

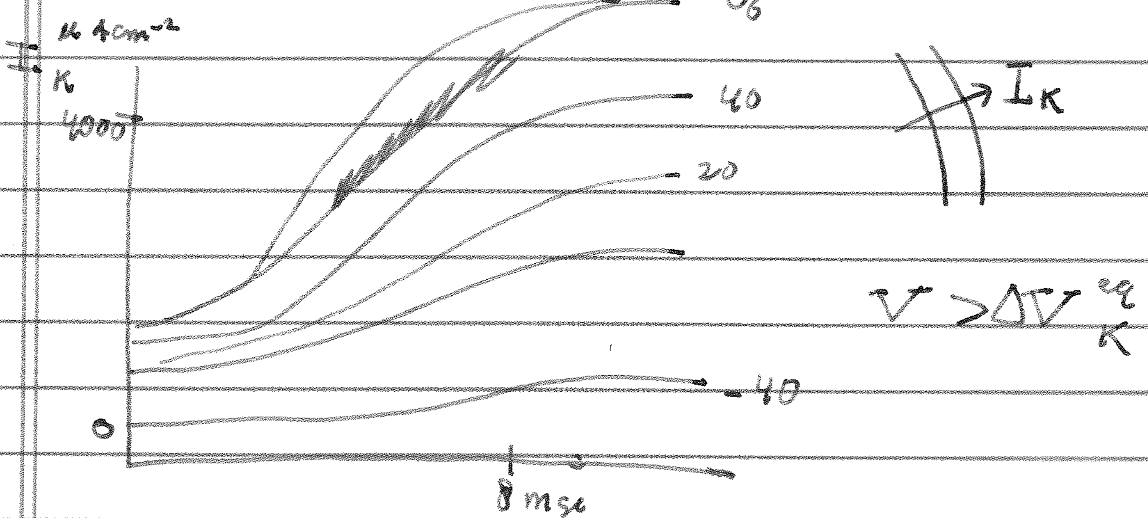
* "voltage clamp" conductance fluctuations feedback circuit keeps voltage fixed by injecting current ~~as~~ ⇒ measure I

* Measure $Na^+$ current, $K^+$ current seperately

↑ $Choline^+$ does not pass through

$\mu A\, cm^{-2}$ Voltage step $V$ depolarizing





## Theoretical Model for Ion channels

Channels: "2 state system(s)" ← complex of 2 state system

$$\begin{tikzcd} \text{open } A \arrow[d, shift left, "\alpha"] \\ \text{close } I \arrow[u, shift left, "\beta"] \end{tikzcd}$$

$$\frac{dA}{dt} = -\beta A + \alpha I \qquad \boxed{\tau = 1/_{\alpha+\beta}}$$

$$\frac{dI}{dt} = +\beta A - \alpha I$$

$$h = \frac{[A]}{[A]+[I]}$$

$$h(t) = (h_i - h_\infty) e^{-t/\tau} + h_\infty$$

$t \to \infty$ $A/I = \alpha/\beta$

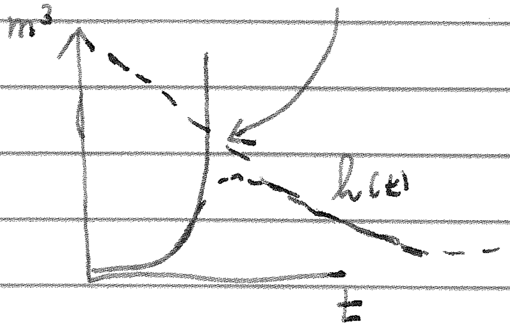
$h_\infty = \beta/\alpha+\beta$

Inactivation $h(t) = (h_i - h_\infty) e^{-t/\tau_h}$

~~Decay~~ Na: fast exponential

<u>Activation</u>: sigmoidal $\sim m^3$ : composed of three parts cooperative $\underline{\uparrow}$ $\underline{\uparrow}$ $\underline{E}$

$$m(t) = (m_i - m_\infty) e^{-t/\tau_m} + m_\infty$$



# channel/cm$^2$ ≈ 300 μm$^{-2}$

channel con 4 pS

$$I_{Na} \approx (V - V_{Na}) m^3 h \underbrace{N_{Na} \gamma_{Na}}_{g_{NA} = 120\ mS/cm^2}$$

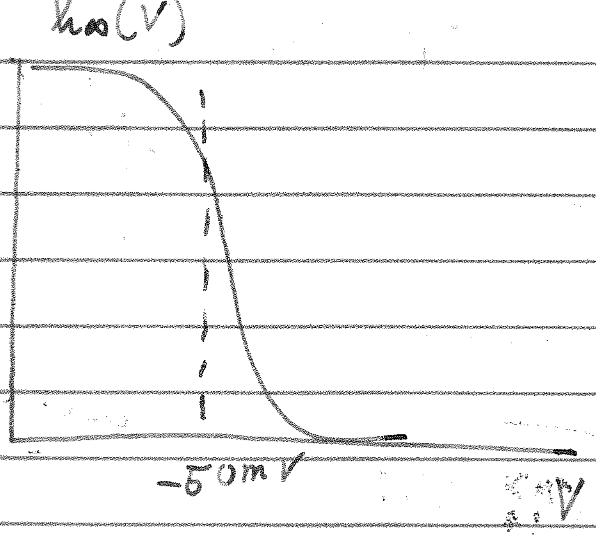
20 pS

$$I_K = \left(V - V_K^{eq}\right) n^4 \underbrace{N_K \gamma_K}_{g_K = 36\ mS/cm^2}$$ composed of 4 p cooperation

Time dependence

Voltage Depend

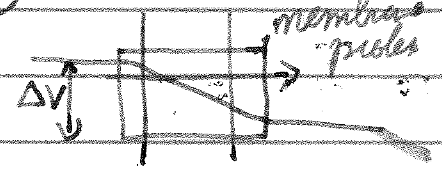
$\left.\begin{array}{l} m_\infty, h_\infty, n_\infty \\ \underbrace{\tau_m, \tau_h, \tau_n}_{\text{fit to } t \text{ dependence}} \end{array}\right\}$ vary $V$

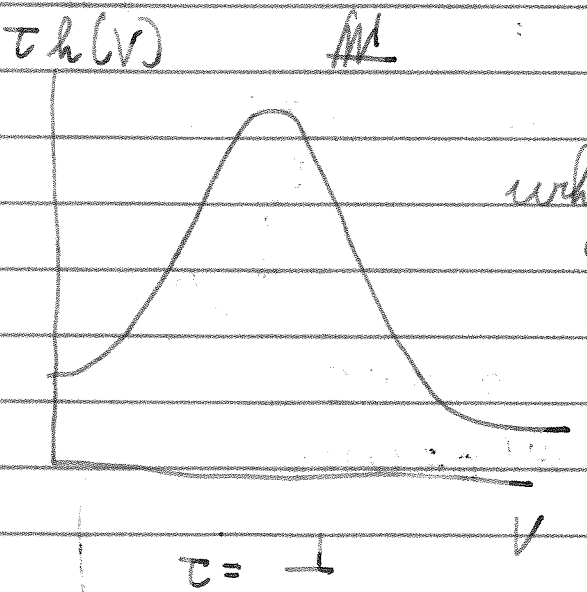


good fit $h_\infty = \frac{1}{1+e^{(V-V_0)/V_s}}$ ?

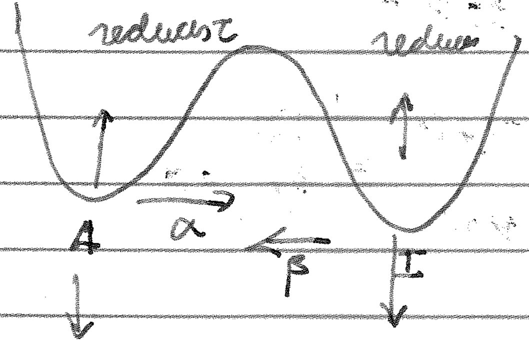
$P_{eq} = \frac{[I]}{[A]} = \exp - \beta(\Delta g + qV)$

$h_\infty = \frac{[A]}{[A]+[I]} = \frac{1}{1+\exp -\beta(\Delta g + qV)}$





why



$\tau = \frac{1}{\alpha + \beta}$ $\alpha = \alpha_0 \exp^{-\beta q V}$

$=$ $\beta = \beta_0 \exp^{+\beta q V}$

$$\boxed{\begin{aligned} C\frac{dV}{dt} = &-g_{Na}\, m^3 h\,(V - V_{Na}^{eq}) \\ &+ \\ &- g_K\, n^4\,(V - V_K) \\ &+ \\ &- g_L\,(V - V_L) \leftarrow \text{no t, v dependence} \\ &+ \\ &I_{ST} \end{aligned}}$$

H-H model

$$+ \boxed{\frac{1}{r_a}\frac{\partial^2 V}{\partial x^2}} \leftarrow \text{for axons}$$

"Soliton Solutions"