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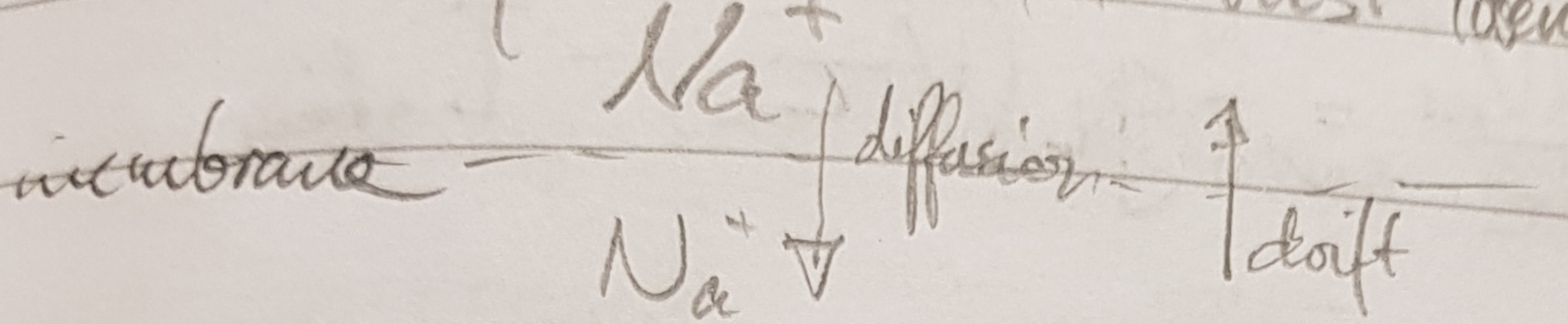
Where are we?

Reverse potential (Nernst potential)



eq:

$$\Delta V = E_{Na} = \frac{RT}{Z_{Na}F} \ln \frac{[Na^+]_{out}}{[Na^+]_{in}}$$

Typical

$$E_{Na} \simeq 50 \text{ mV}$$
$$E_{K} \simeq -75 \text{ mV}$$
$$E_{Cl} \simeq -60 \text{ mV}$$
$$E_{Ca} \simeq 120 \text{ mV}$$

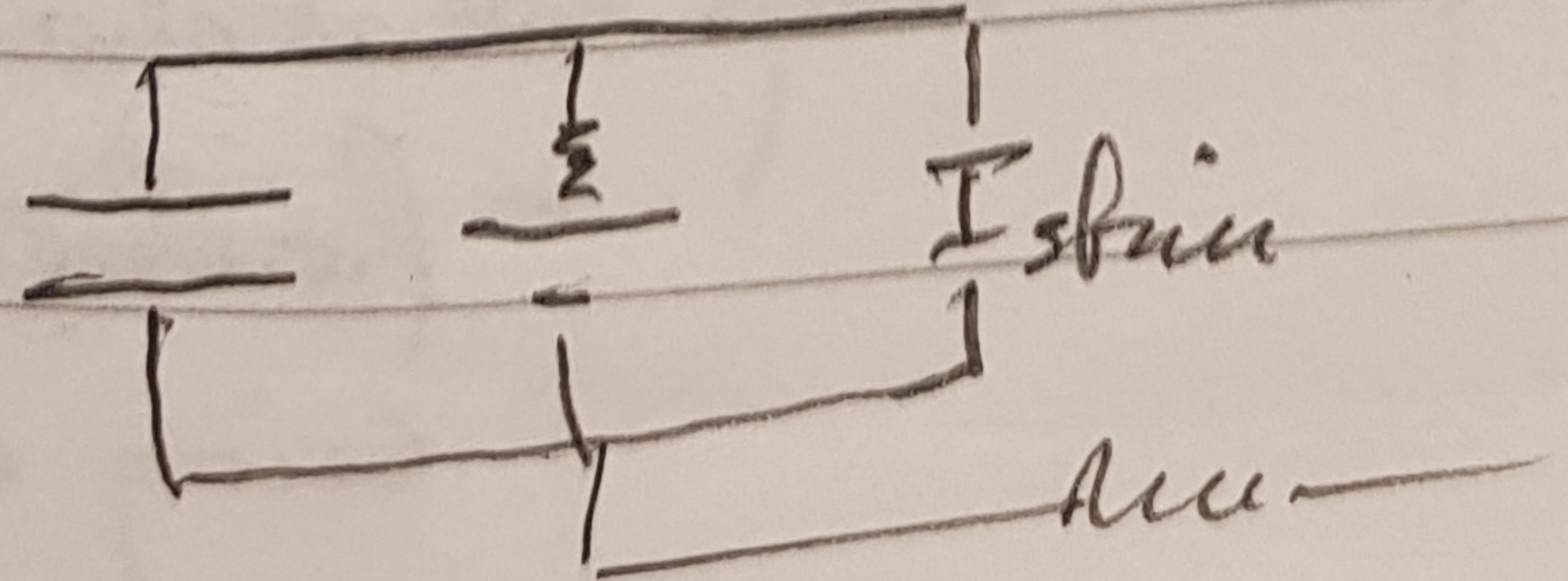
Pumps use energy to set up gradients

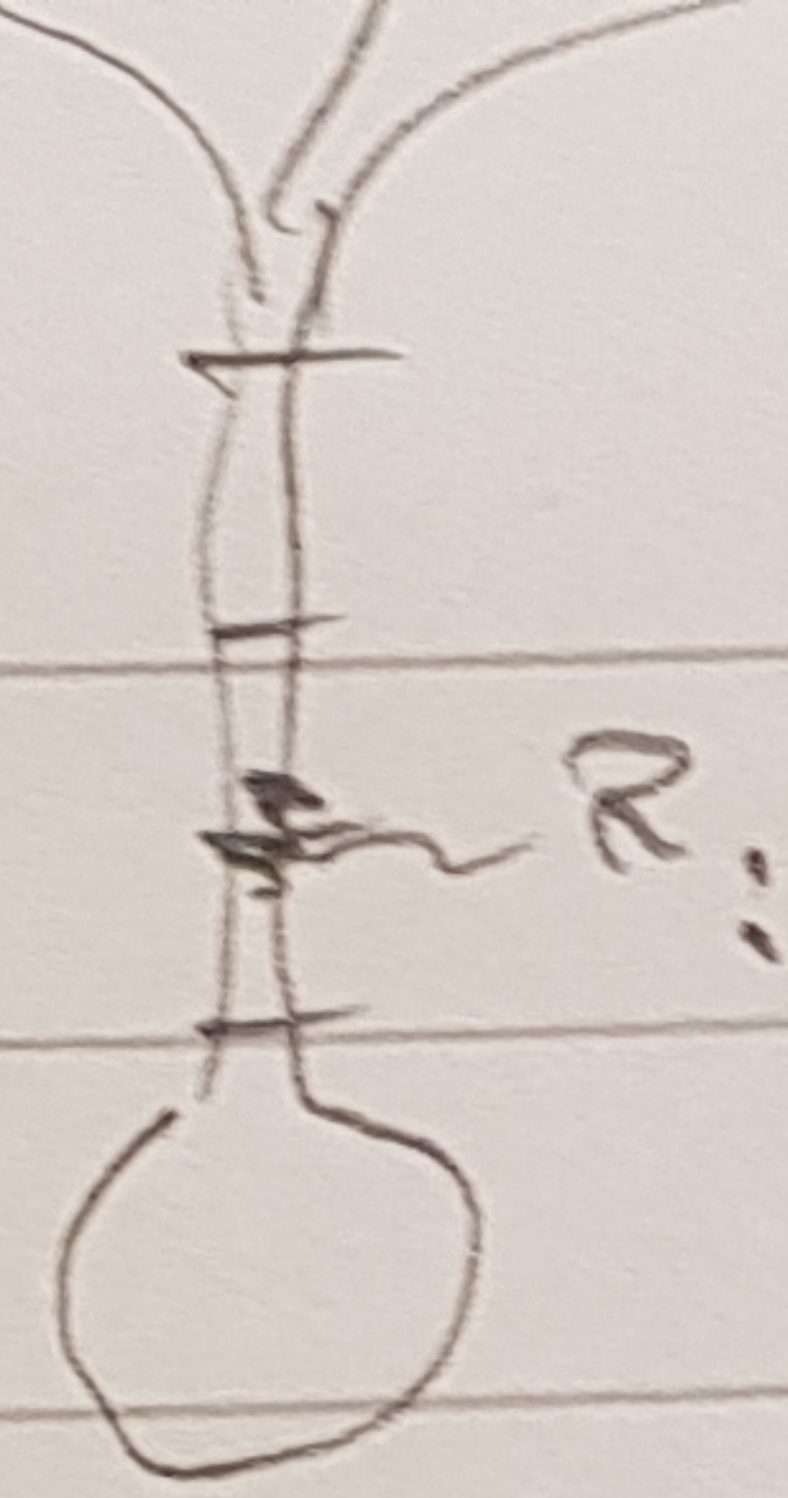
Passive model:

Group all passive leakages & pumps into one current $I_{pas} = g_L (V - E_L)$ Quasi-Ohmic approximation

$\uparrow$ resting potential $= \Sigma E_i \ldots$ $\sim -80 - -60$ mV

RC-model





: Add up elements => cable equation

$$C_m \frac{dV_m}{dt} = -g_L(V-E_L) - I_{stim}$$

H.1 H.2 Hodkin-Huxley model

Equivalent circuit of single-compartment HH-model

* membrane current

$$\underbrace{C_m \frac{dV_m}{dt} = -\bar{g}_L(V-E_L)}_{\text{passive}} \underbrace{- I_{Na} - I_K - I_{stim}}_{\text{active}}$$

Time and voltage dependent:

$$I_{Na} = g_{Na}(V,t)(V-E_{Na})$$

$$I_K = g_K(V,t)(V-E_K)$$

conductances can be written

$$g_x(V,t) = \underbrace{\bar{g}_x}_{\text{conductance of fully open channels}} \underbrace{P_x(V,t)}_{\text{Probability that channel is open = fraction of channels being open}}$$

H.3 Potassium channel

How to determine $g_K(V,t)$?

* manipulate conditions so that I_K is the only current.

* control V → set $V = V_h$ (holding potential)

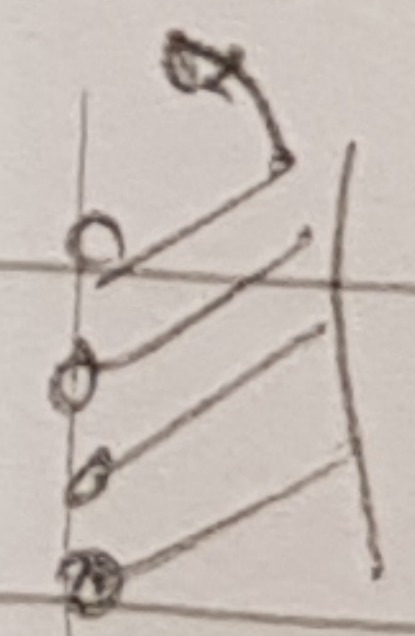
* Measure $I_K(V_h,t)$

$$\Rightarrow g(V_h,t) = \frac{I_K(V_h,t)}{(V_h - E_K)}$$

*observation: Conductance increases with time and settles in a steady state (ss) $g_{K\infty}(V_h,t)$

- ss depends on V_h
- time to reach ss depends on V_h

× Fit conceptual model to curves



↳ - each channel is controlled by 4 gating particles (n)

- each gate either open or closed
- for channel to be open all gates must be open => $p \sim n^4$

$$I_K = \bar{g}_K \cdot n^4 (V - E_K)$$

Dynamics of gating particles

$$C \underset{\beta_n}{\overset{\alpha_n}{\rightleftharpoons}} O$$

$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n$$

Alternative form:

$$\frac{dn}{dt} = \Big(\underbrace{\frac{\alpha_n}{\alpha_n+\beta_n}}_{n_\infty} - n\Big)\underbrace{(\alpha_n+\beta_n)}_{1/\tau_n}$$

$$\frac{dn}{dt} = \frac{n_\infty - n}{\tau_n}$$

n approaches n_∞ with time constant τ_n

Best curve fitting with $n = 4$

Beracche & Roux 2001 Nature model of K^+ channel embedded in cell membrane

Summary of K^+ channel

$$I_K = \bar{g}_K n^4 (V_m - E_K)$$

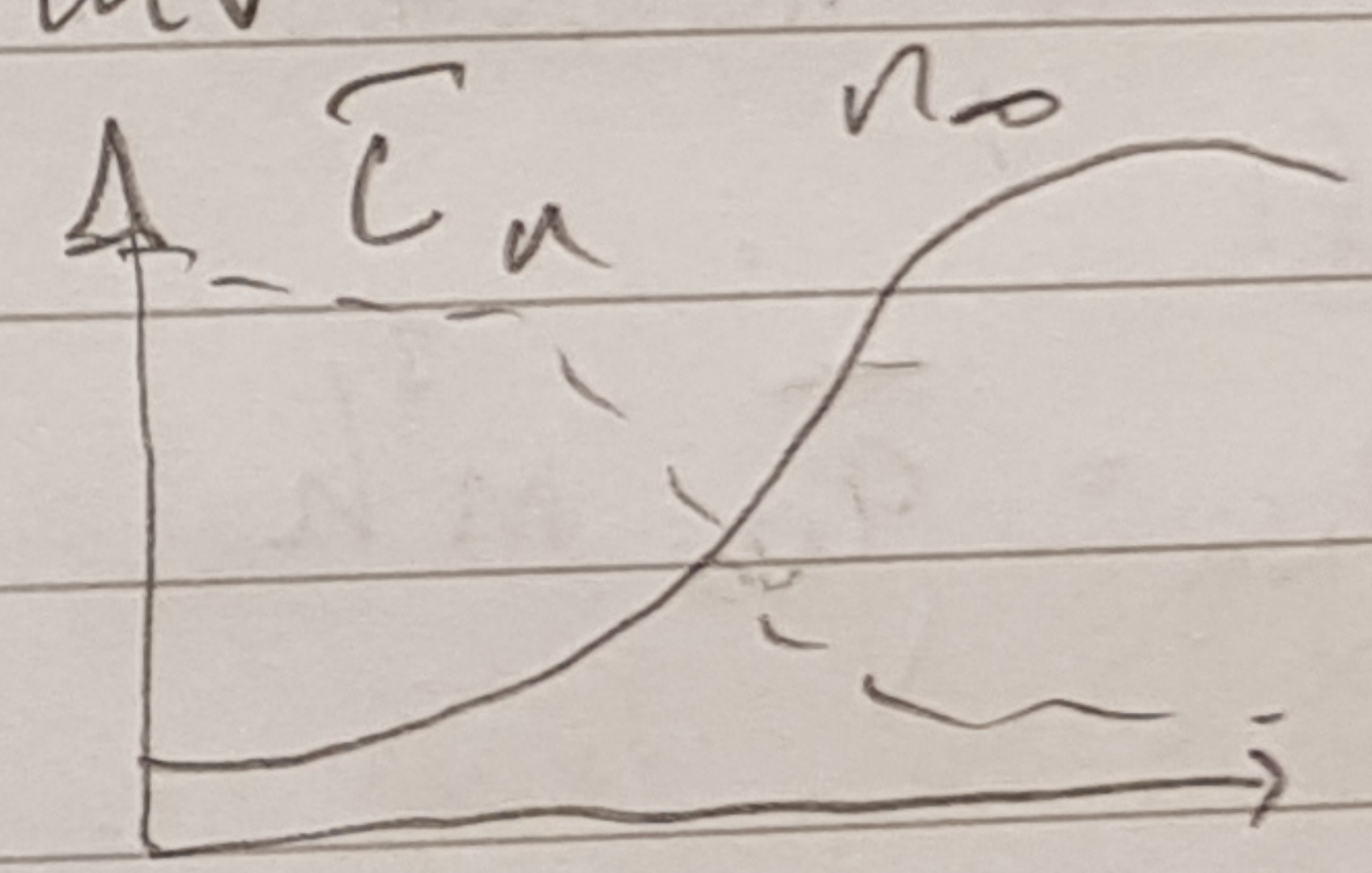
$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n$$

α_n & β_n fitted to data:

$$\alpha_n = 0{,}01 \cdot \frac{V_m + 55}{1 - e^{-(V+55)/10}}$$

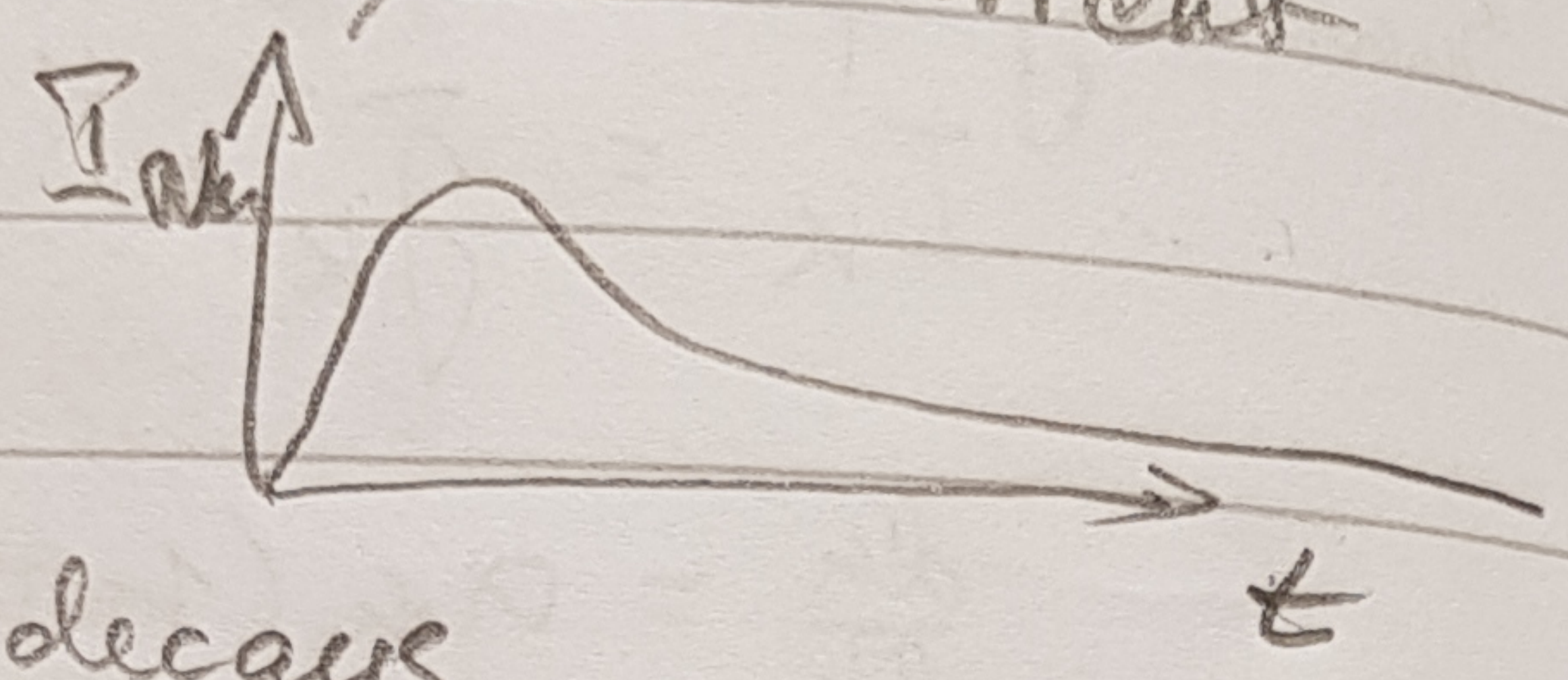
$$\beta_n = 0{,}125 \cdot e^{(V_m+65)/80}$$

$$[V_m] = mV$$

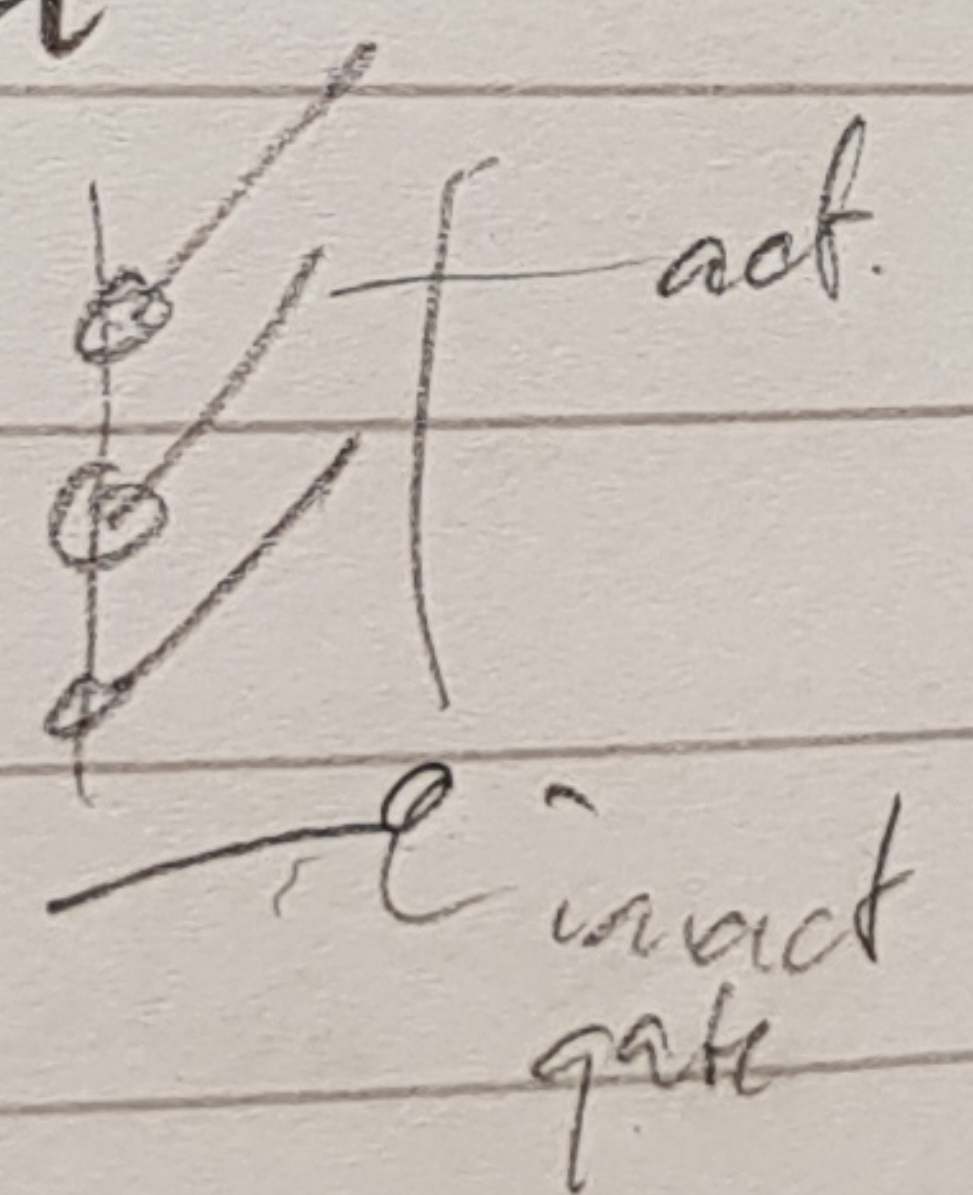


HH.4 Sodium conductance

- Unlike for potassium, Na^+ current is transient



- For a given V_h it peaks and it decays
- Something opens it and then something closes it
- HH introduced ~~an~~
  - an activation variable m (like n for K^+)
  - an inactivation — " — h



- model:

$$g_{Na} = \bar{g}_{Na}\, m^3 h$$

Summary:

$$I_{Na} = \bar{g}_{Na}\, m^3 h\,(V - E_{Na})$$

$$\frac{dm}{dt} = \alpha_m (1-m) - \beta_m m \qquad \alpha_m = 0{,}1\,\frac{V+40}{1-e^{-\frac{(V+40)}{10}}}$$

$$\beta_m = 4e^{-(V+65)/18}$$

$$\frac{dh}{dt} = \alpha_h (1-h) - \beta_h h \qquad \alpha_h = 0{,}07\, e^{-(V+65)/20}$$

$$\beta_h = \frac{1}{1+e^{-(V+35)/10}}$$

H.H5 Full HH model

$$c_m \frac{dV_m}{dt} = -\bar{g}_L (V-E_L) - g_K n^4 (V-E_K) - g_{Na} m^3 h (V-E_{Na}) - I_{stim}$$

$$\frac{dx}{dt} = \alpha_x (1-x) - \beta_x x \quad , x = n, m, h$$

Some parameters

$\bar{g}_{Na} = 120 \frac{mS}{cm^2}$ $\qquad c_m = 1\mu F/cm^2$

$\bar{g}_K = 36 \frac{mS}{cm^2}$ $\qquad E_{Na} = 50 mV$

$\bar{g}_L = 0{,}3 \frac{mS}{cm^2}$ $\qquad E_K = -77 mV$

$E_L = -54{,}4 mV$

HH6 HH-type models

- Many neuron types exist w/ different firing properties. Not all of them are well captured by I_{Na} & I_K in the HH model.
- Many types of ion channels (~150)
- Can use HH type formalism for most of them

$$I_x = \underbrace{\bar{g}_x}_{\text{open channel cond.}}\ \underbrace{m^a}_{\text{activ. gate}}\ \underbrace{h^b}_{\text{inactiv. gate}}\ (V - \underbrace{E_x}_{\text{reversal potential for ion through channel x!}})$$

HH7 Ca^{2+} channels

$[Na^+]$ & $[K^+]$ ~ 10-100 mM inside neurons

$[Ca^{2+}]$ ~ 100 nM — " —

lots of Na^+ & K^+ => currents do not affect concentrations

I_{Ca} can affect $[Ca^+]$ dramatically

Ca^{2+} used as signalling molecule

- → synaptic plasticity
- → biochemical reactions
- → Ca^{2+} gated ion channels
- → Ca^{2+} seen in Ca^{2+} imaging

Many Ca^{2+} channels exist

Ex: High-voltage-activated Ca^{2+} channels

Many neurons have this. Probably what we saw in experiment

Open during AP and then let some Ca^{2+} into the cell

Simplest model:

HH-type $I_{HVA} = \bar{g}_{HVA}\, s^2 (V - E_{Ca})$

└ 2 activation gates
0 inactiv. — "

$E_{Ca} \simeq 120\ mV$

Must also model $[Ca^{2+}]$. Simplistic model:

$$\frac{d[Ca^{2+}]}{dt} = -\alpha I_{Ca} - \frac{[Ca^{2+}] - [Ca^{2+}]_{basal}}{\tau_{Ca}}$$

(In fact there are internal stores of Ca^{2+} with dynamics)

α converts current to concentration change. We do not see all Ca^{2+} as free Ca^{2+} so α is some number taking this into account.