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Oct. 8, 2004

Oct. 4, 2005

- Skills development points: need to sign log sheet

- name / email
  Q's name / email
  ~~tutorial~~
  review session: Friday 2-3, here

~~- homework~~

- reading: now on the web ... /courses

- homework: assigned ~~Fri.~~ Tue $\boxed{\text{20\% of grace}}$ on website
  due Fri

- Class: 11-1 w/ 10 minute break around 12. please ask lots of questions

- main textbook: "theor. neuro," dayan + abbott

- prerequisites: math math math, physics ← $V = IR = Q/C$, $V = \int E \cdot dl$
  ~~ODE's~~, Calculus (ODE's), linear algebra, probability theory

  ODE's, integrals, derivatives

  (see also website)

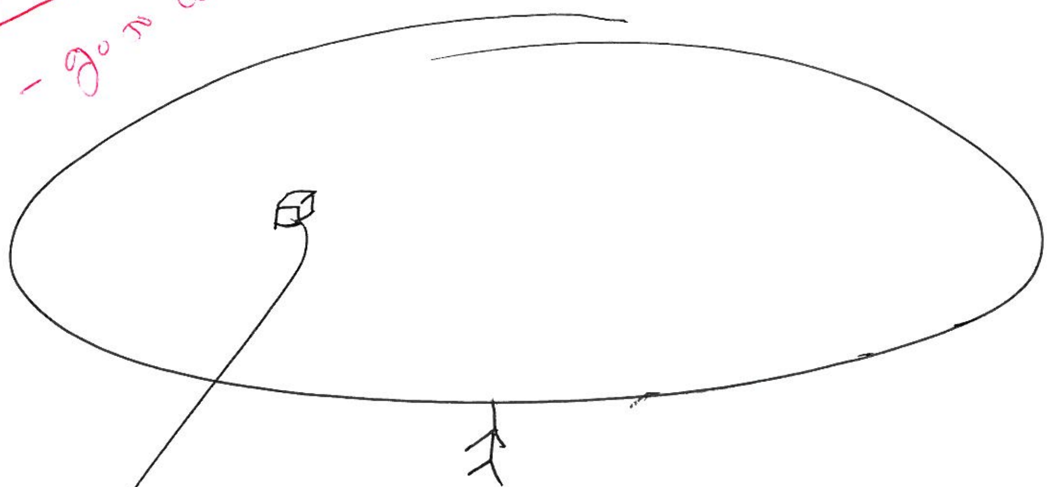
  ... ~zoubin/course05 ... look for "cribsheets"

next: outline

Now on slides

- go to course outline

2



mm^3 ($\approx 3\cdot10^{-5}$ oz)

50 thousand neurons

~5000 connections/neuron

⇒ 250 million connections

4 km axons

whole brain (human)

2 Kg

10^{11} neurons

$5\cdot10^{14}$ conn

8~~0~~ million km of axons

(10~~0~~ times to moon & back)

mm^2

1 million transistors

~? 2 connections / transistor

2 m of wires

whole cpu

1 billion transis

2 km of wire

(not enough to reach to top of reasonable size mountain)

Input neurons : $\sim 10^6$

outputs neurons : $\sim 10^6$

the brain mainly talks to itself!!! ← 80-90% of connections local

Outline of course

1. building blocks: single neurons / axons / dendrites / synapses Lat
2. language of neurons: neural coding Maneesh Sahani, Liam Paninski
3. what we know about networks of neurons + how they compute (very little) me
4. learning at network & behavioral level Peter Dayan

~~Final exam 2 1/2 hours?~~ (ask Peter)

~~What you will learn~~

~~- comput~~

What you will learn:

- computational aspects
  - ~~single neurons~~
  - ~~networks (a little)~~

Exp. clam ⇓ make up exam

main skill ⇓ solve them

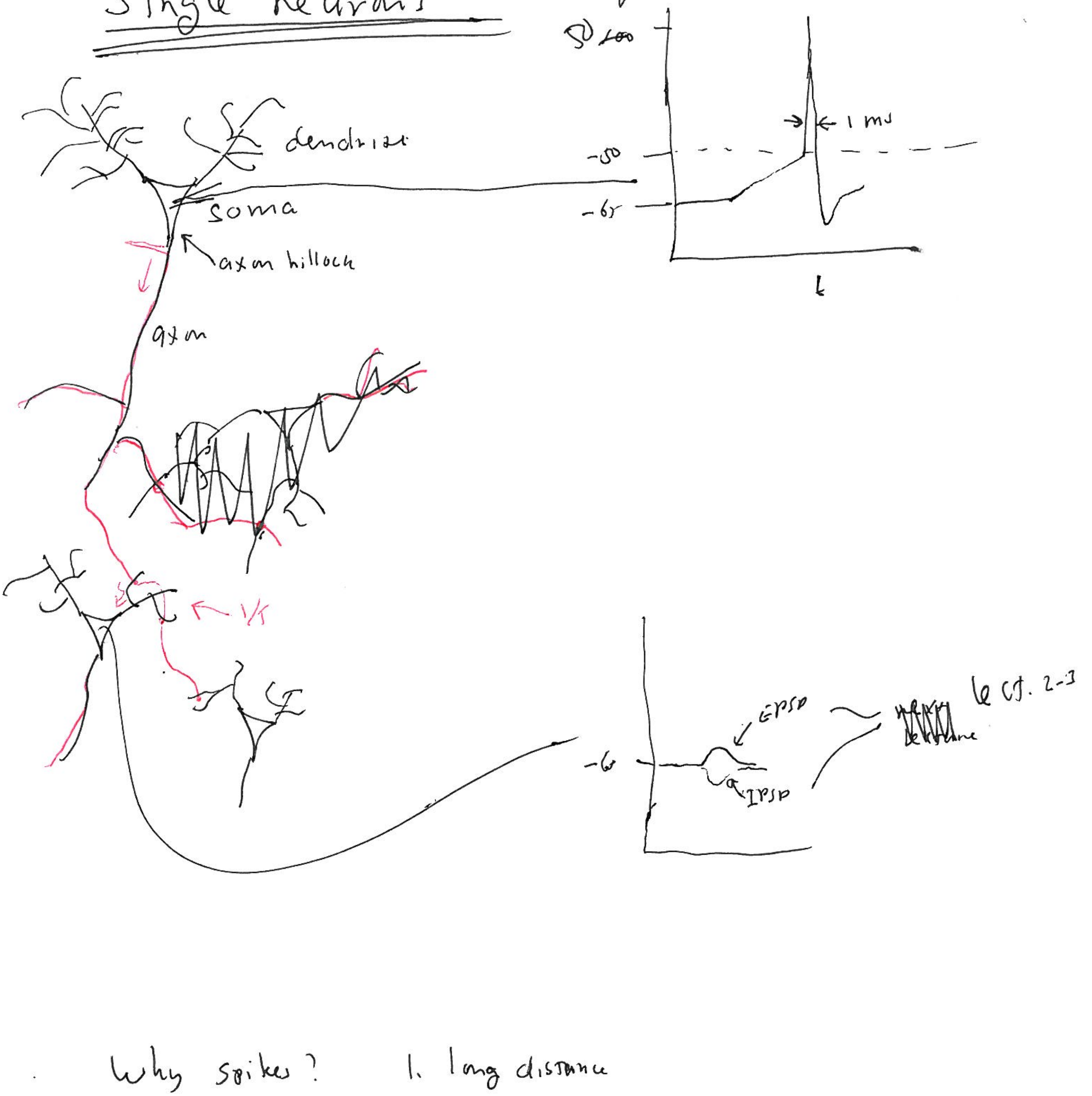
What you won't learn:

- ~~experiment~~
- anatomy.
- experimental facts.

④

drop

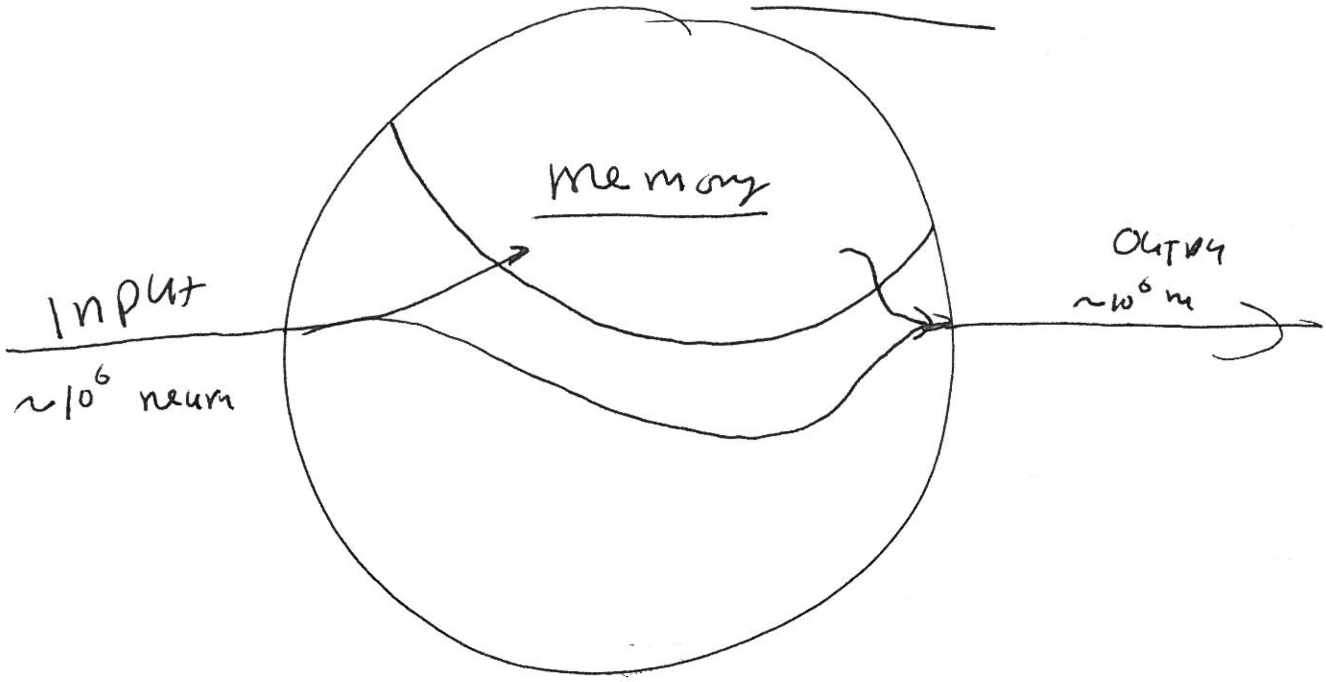
Single neurons



Why spikes? 1. long distance
2. other reasons

~~rewrite + simple in~~

Brain 10^{11} neurons



How does this thing work?

- what we ~~know~~ think.
  1. brain is divided into different areas which do different things. (we know) (~~show slide~~)
  2. processing is done by neurons (we think)
  3. learning/memory involves adjusting synaptic strength (we think)

  ~~4. Just a lot of little facts.~~
- Have to do experiments.
- Can control input
- Can measure outs
- Can record from neurons (~~10 at most~~, 100 at most, ~~typically 1~~ typically 1)

Models one might build

$$X_i(t+\delta t) = \begin{cases} 1 & V_i^{(t)} > \theta \quad \text{(spike)} \\ 0 & \cancel{\text{oth}}\ V_i \leq \theta \quad \text{(no spike)} \end{cases}$$

$$V_i^{(t)} = \sum_j W_{ij} X_j(t)$$

- if one chooses W's correctly, you will get a function brain

problem: most of what the brain does we don't know how to do

$$\cancel{\frac{d}{dt} W_{ij} = f(X_i, X}$$

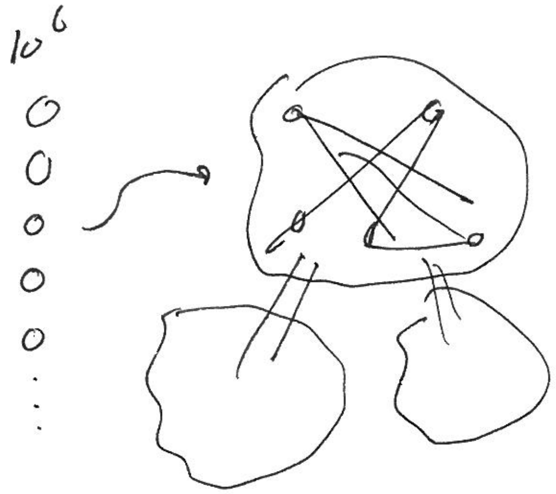
$$W_{ij}(t+dt) = \eta f(X_i, X_j)$$

- If you choose f correctly, you'll get a function brain.

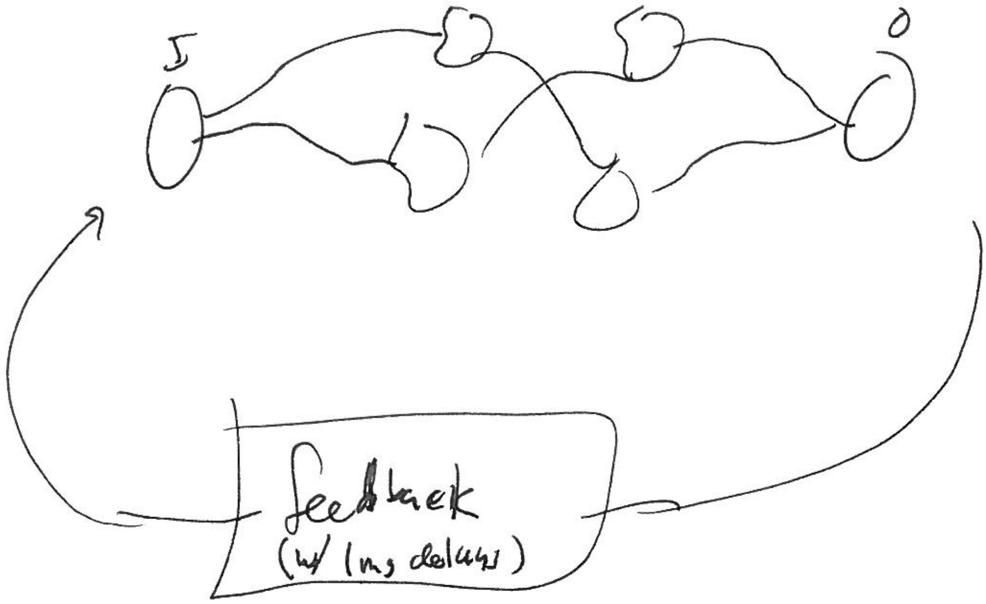
problem: ~~so far success has been limited.~~

<u>credit</u> <u>assignment</u>

10^{11} 10^{32} possible weights.



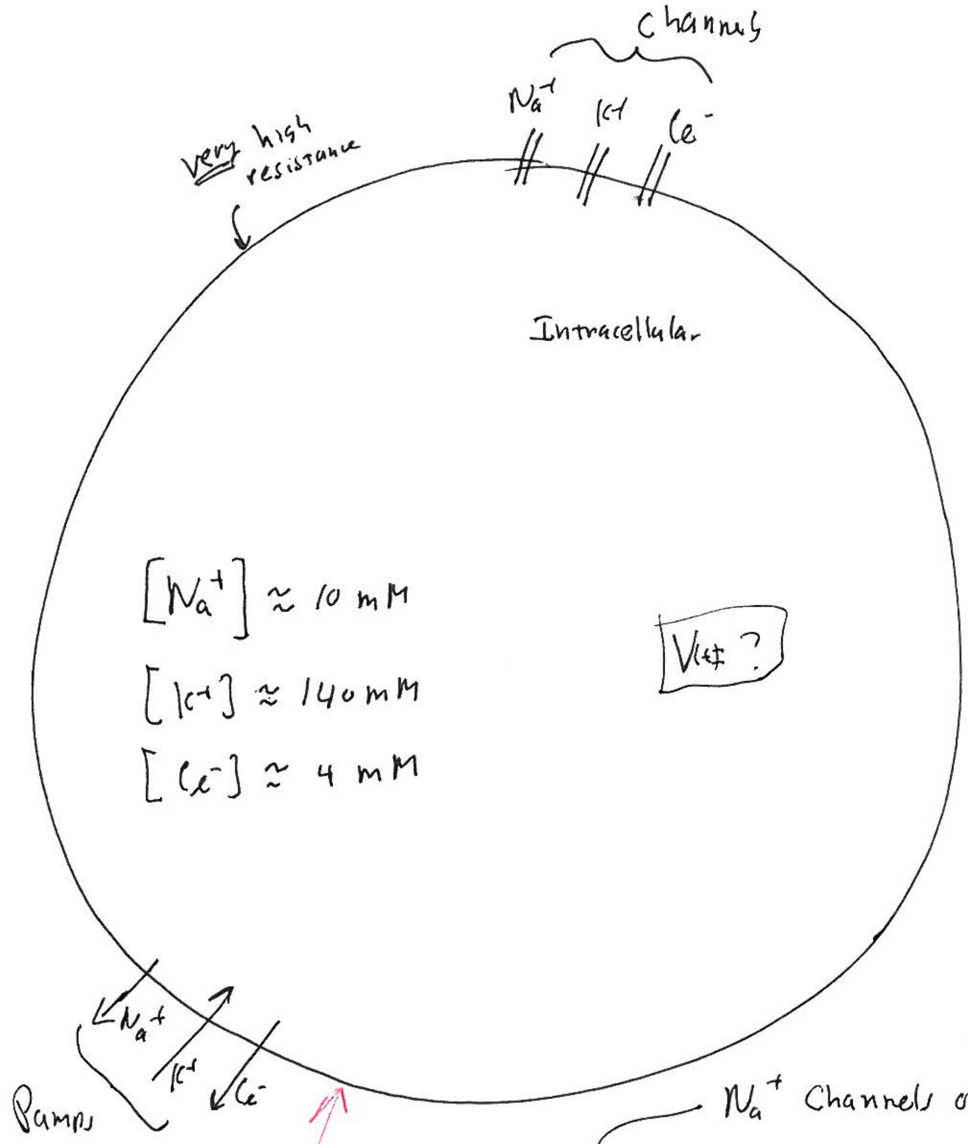
10^6



- credit assignment problem!

(5)

What makes a neuron spike?



Extracellular

$[Na^+] \approx 145$ mM

$[K^+] \approx 5$ mM

$[Cl^-] \approx 110$ mM

$V = 0$

Very few ions needed to change voltage - so concentration doesn't change much

$\frac{6 \cdot 10^{23} \, [\;] \cdot 10^{-3}}{10^3 \, cm^3} \cdot \frac{4}{3}\pi (10^{-}$

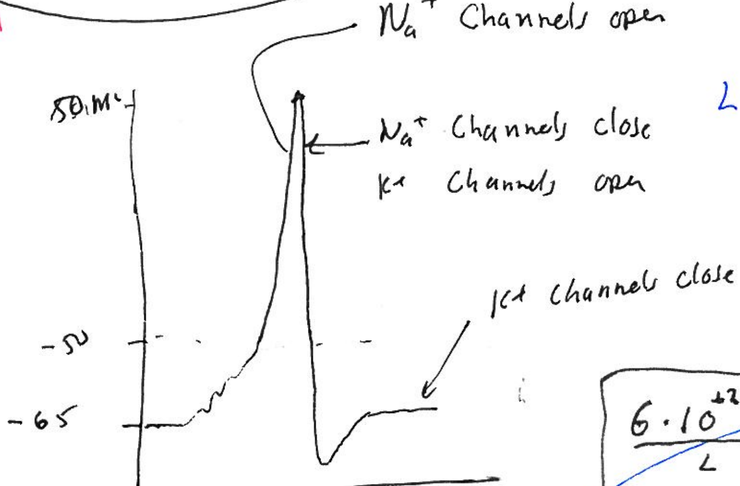
$L \rightarrow 10^3 cm^3$

$= 6 \cdot 10^{23-3-3-9} \frac{4}{3}\pi$

$= 8\pi \cdot 10^{8}$

$V = \frac{N \cdot 1.6 \cdot 10^{-19}}{C\Omega} \Omega = \frac{N \cdot 1.6 \cdot 10^{-}}{10^{-2}}$

mM $\times 10^{8}$ $= N \cdot 1.6 \cdot$



Key point: Current is a function of voltage

Can we find $v(t)$? given external current?

$N = 10^6 \Rightarrow 1.6$ mV

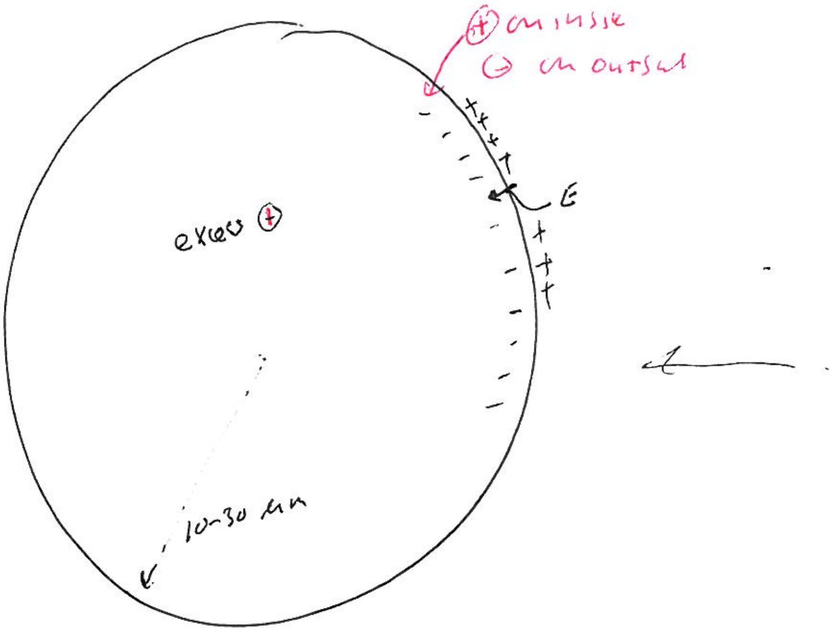
$\frac{6 \cdot 10^{+23} \cdot 10^{-3}}{L} \cdot \frac{10^{-3} \, dm^3}{cm^3} \cdot 10^{-3} \cdot 10^{-3}$

$\cdot \frac{10^{-3} \, mm^3}{mm} = 6 \cdot 10^{-3+23-3-3-9}$

$= 6 \cdot 10^{5}$

(6)

Key point: Current as a function of voltage



5 nm

$E \propto Q \qquad V = \int^{\varepsilon} E \cdot dl = {}^{\varepsilon} E \cdot l \Rightarrow E = \frac{V}{\varepsilon l}$

$V \propto \frac{Q}{\varepsilon l}$

$\boxed{V \equiv \frac{Q}{C}}$ capacitance $= 100 \frac{\mu F}{cm^2} = 10 \frac{nF}{mm^2}$

× area

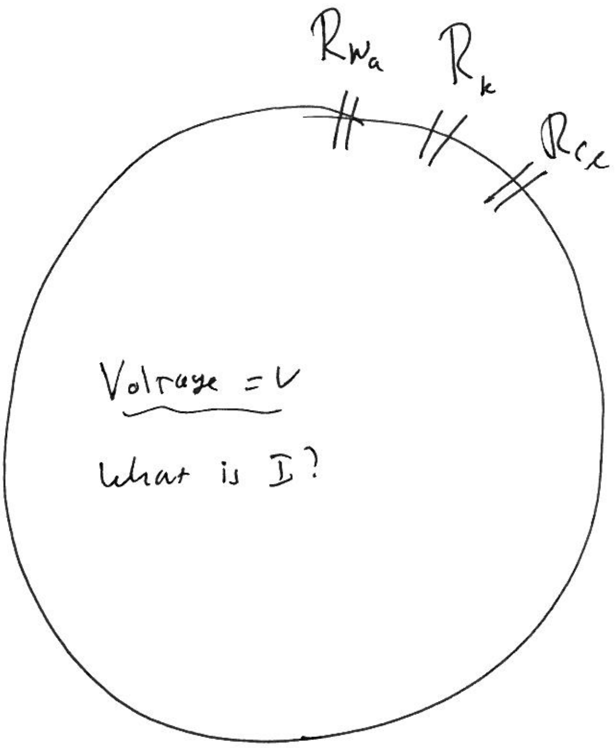
$\frac{dV}{dt} = \frac{1}{C}\frac{dQ}{dt} = -\frac{I(t)}{C}$ goal: find $I(t)$!!!

Convention

[Find I vs. V, so we can solve the differential equation]

Passive properties

R independent of voltage



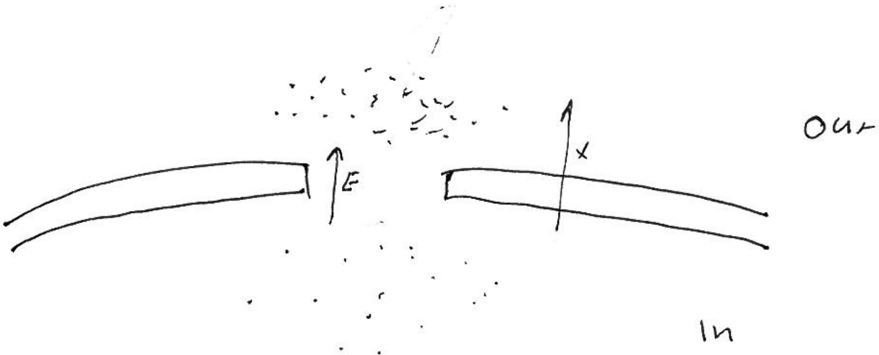
Assume: pumps keep concentrations fixed, influx doesn't change concentration

Guess #1

$$I = +\frac{V}{R_A} + \frac{V}{R_K} + \frac{V}{R_{Cl}}$$

Wrong!!!

Concentration gradients



$J_{inward} \propto q[C]\frac{\partial V}{\partial x} - D\frac{\partial [C]}{\partial x}$

A trick: how big a voltage drop would you need to reduce current flow to zero?
ΔV = voltage drop, then current associated w/ difference in densities is $\frac{\Delta V}{R}$

SKIP

also: $I \propto q[C]E - D\frac{d(c)}{dx}$

$E \downarrow \frac{V}{x}$

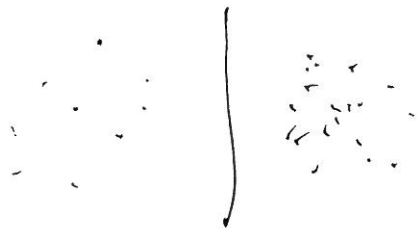
next page

$I \propto \cancel{q()V}$

$()[C]V - D\frac{d(c)}{dx}$ 1st order ODE

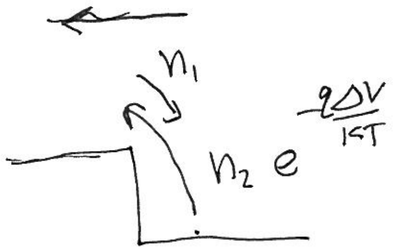
2) $I = I(V)$; nonlinear, HWK

Another cheap trick:



n_1, v_1 $\quad$ n_2, v_2 $\qquad$ $V_1 > V_2$

$q > 0$

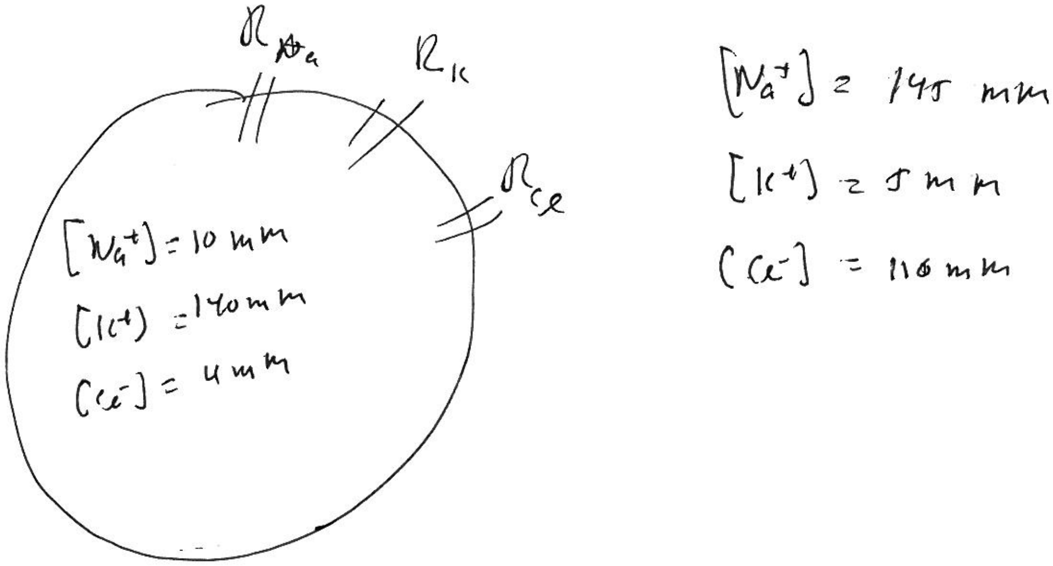


$$n_1 = n_2 e^{-\frac{q\Delta V}{kT}}$$

$$\log \frac{n_1}{n_2} = -\frac{q\Delta V}{kT}$$

$$\Delta V = \frac{kT}{q} \log \frac{n_2}{n_1} \equiv \mathcal{E}$$

$$I = \frac{\Delta V}{R}$$



$$\underline{I} = +\frac{(V - \mathcal{E}_{Na})}{R_{Na}} + \frac{(V - \mathcal{E}_K)}{R_K} + \frac{(V - \mathcal{E}_{Cl})}{R_{Cl}}$$

but really nonlinear

$$= +\bar{g}_{Na}(V - \mathcal{E}_{Na}) + \bar{g}_K(V - \mathcal{E}_K) + \bar{g}_{Cl}(V - \mathcal{E}_{Cl})$$

$$= +\underbrace{(\bar{g}_{Na} + \bar{g}_K + \bar{g}_{Cl})}_{g_L} V - \underbrace{(\bar{g}_{Na}\mathcal{E}_{Na} + \bar{g}_K\mathcal{E}_K + \bar{g}_{Cl}\mathcal{E}_{Cl})}_{g_L \mathcal{E}_L}$$

$$= +g_L(V - \cancel{V_L}\,\mathcal{E}_L)$$

$$\mathcal{E}_{Na} = \frac{KT}{q} \log \frac{145}{10} \simeq 100 \text{ mV}$$

$$\mathcal{E}_{K} = \frac{KT}{q} \log \frac{5}{140} \simeq -90 \text{ mV}$$

$$\mathcal{E}_{Cl} = -\frac{KT}{q} \log \frac{110}{4} \simeq -70 \text{ mV}$$

$$C \frac{dV}{dt} = -g_L (V - \mathcal{E}_L)$$

$$\frac{C}{g_L} \sim \text{time} \equiv \tau \simeq 5\text{-}20 \text{ ms}$$

$$\tau \frac{dV}{dt} = -(V - \mathcal{E}_L)$$

solve ~~the la~~ the long way: math

$$\tau \dot{x} = -x$$

$$\tau e^{-t/\tau} \frac{d}{dt} e^{+t/\tau} x = 0$$

$$\frac{d}{dt}\left[e^{t/\tau} x\right] = 0$$

$$e^{t/\tau} x(t) = x(0)$$

$$x(t) = x(0) e^{-t/\tau}$$

repeat w/ I_{stim}

1) $V(0) = V_0$

2) add $I(t)$ term

$$\Rightarrow V - \mathcal{E}_L = (V_0 - \mathcal{E}_L) e^{-t/\tau} + \int_0^t dt' \, e^{-\frac{t-t'}{\tau}} (V(t') - \mathcal{E}_L)$$

$$= \int_{-\infty}^{t} dt' \, e^{-\frac{(t-t')}{\tau}} (V(t') - \mathcal{E}_L)$$

$$= \int_0^{\infty} ds \, e^{-\frac{s}{\tau}} (V(t-s) - \mathcal{E}_L)$$

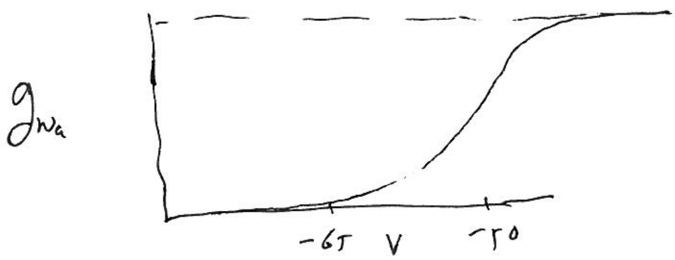
Discuss LIF! point out difficulty of ~~deal~~ dealing analytically w/ threshold

Active conductances

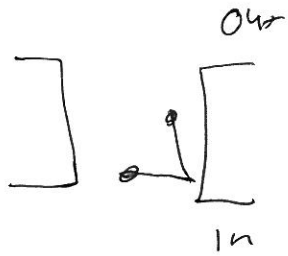
channels come in 2 types: active + passive

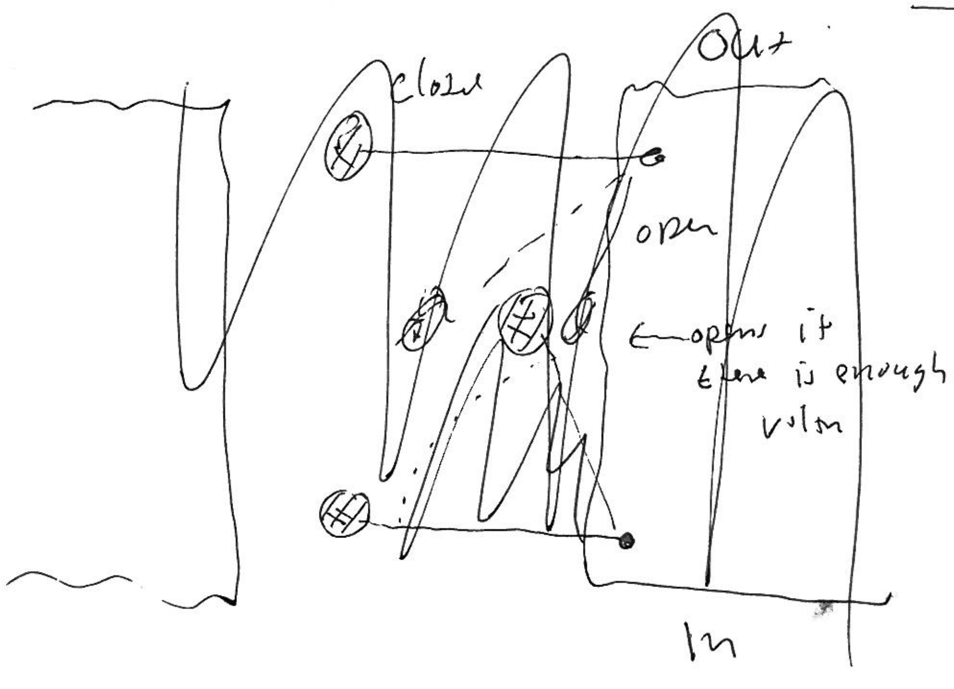
$$C \frac{dV}{dt} = -\bar{g}_L (V - E_L) - g_{Na}(V)(V - E_{Na}) - g_K(V)(V - E_K)$$

~100 mV



but life is more complicated!!!





- lots of channels!!

$m =$ ~~#~~ prob of ~~open~~ Na channel being open

$\alpha(v) =$ prob. of closed channel opening

$\beta(v)$ = " " open " closing

per unit time

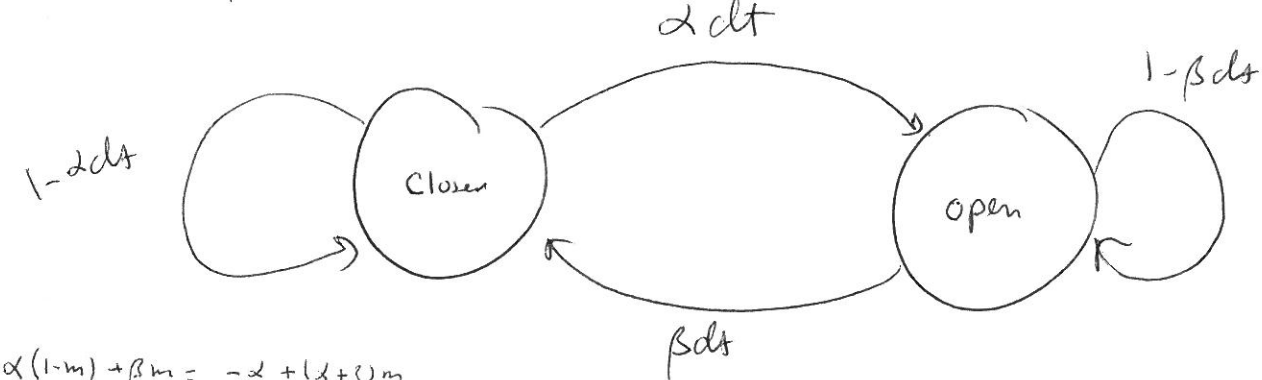
$$\frac{dm}{dt} = \alpha(v)(1-m) - \beta(v)m$$

$$= \alpha(v) - [\alpha(v) + \beta(v)]m$$

$$\tau(v)\frac{dm}{dt} = m_\infty(v) - m$$

$$\tau(v) = \frac{1}{\alpha(v)+\beta(v)}$$

$$m_\infty(v) = \frac{\alpha(v)}{\alpha(v)+\beta(v)}$$



$\dot{C} = -\alpha(1-m) + \beta m = -\alpha + (\alpha+\beta)m$

$\parallel$

$-\dot{m}$

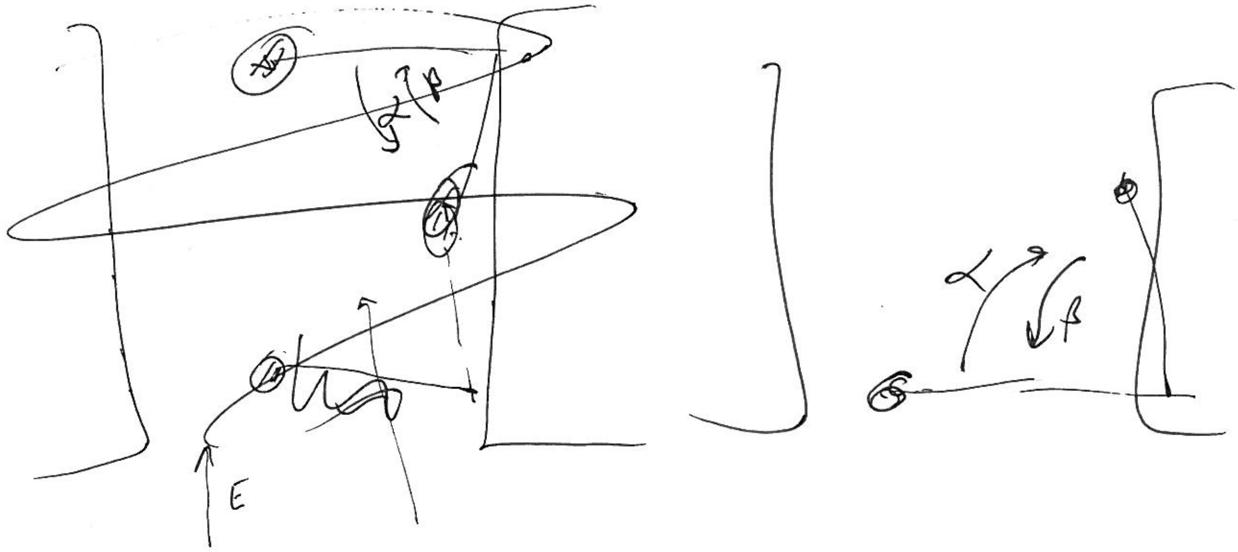
OK

$m(t+dt) = m(t)(1-\beta dt) + \overset{1-m(t)}{C(t)}(\alpha dt)$

$C(t+dt) = C(t)(1-\alpha dt) + m(t)\beta dt$

$m(t+dt) = m(t) - (\alpha+\beta)m(t) + \alpha(t)$

$\dot{m} = \alpha - (\alpha+\beta)m$



drop

voltage barm

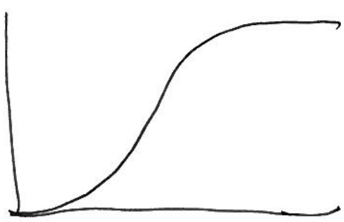
$$\alpha = A_\alpha e^{-\frac{q\delta_\alpha V}{kT}}$$

$$\beta = A_\beta e^{\frac{q\delta_\beta V}{kT}}$$

$$m_\infty = \frac{1}{1 + \frac{\beta(V)}{\alpha(V)}}$$

$V \to +\infty \qquad m_\infty \to 1$

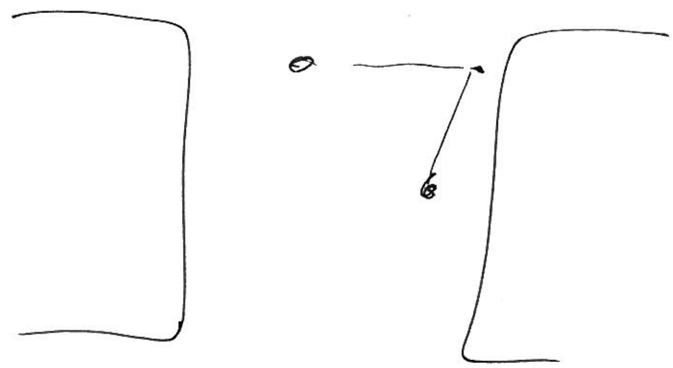
$V \to -\infty \qquad m_\infty \to 0$



14 15

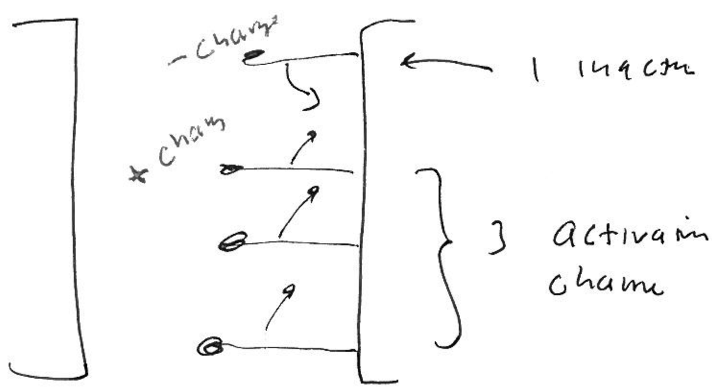
~~a tr~~

twist #1



$$\tau_h(V)\frac{dh}{dt} = h_\infty(V) - h$$

twist #2: multiple ~~ch~~ gates

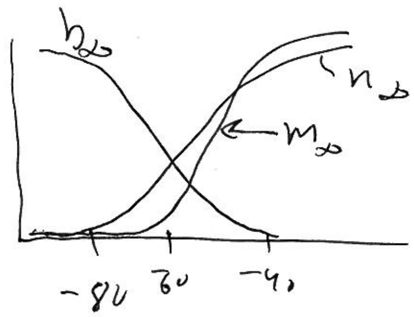


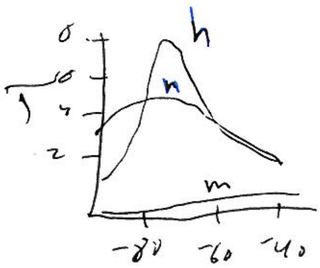
twist #3:

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

$$g_K(V) = \bar{g}_K\, n^4$$

Pg. 173, D+A





-65 mV   100 mV   -90 mV

$$C\frac{dV}{dt} = -\bar{g}_L(V - E_L) - \bar{g}_{Na} m^3 h (V - E_{Na}) - \bar{g}_K n^4 (V - E_K)$$

$$\tau\frac{dV}{dt} = -(V - E_L) - \bar{\rho}_{Na} m^3 h (V - E_{Na}) - \bar{\rho}_K n^4 (V - E_K)$$

$x = m, n, h$: $\tau_x(V)\dfrac{dx}{dt} = x_\infty(V) - x$

Hodgkin Huxley

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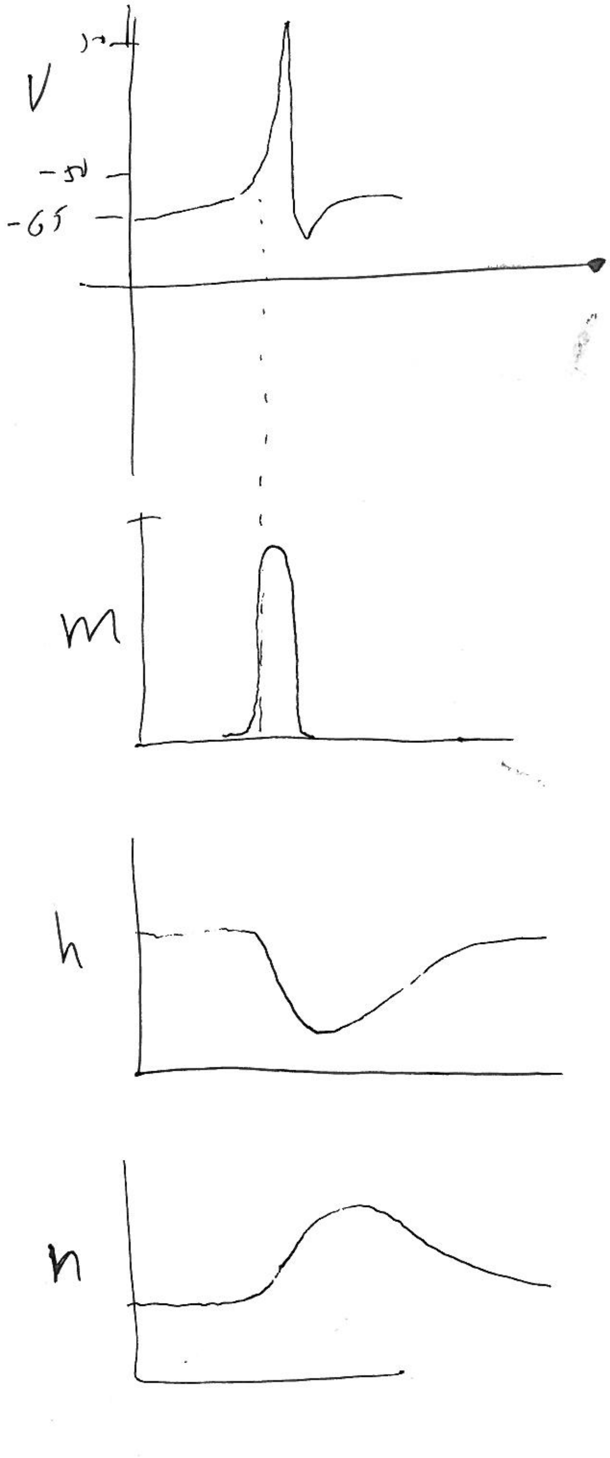


-50
-65