Topic B: Nerve Impulses P 347

- Last class we showed how mobile ions could set up a voltage drop ΔV across a membrane.

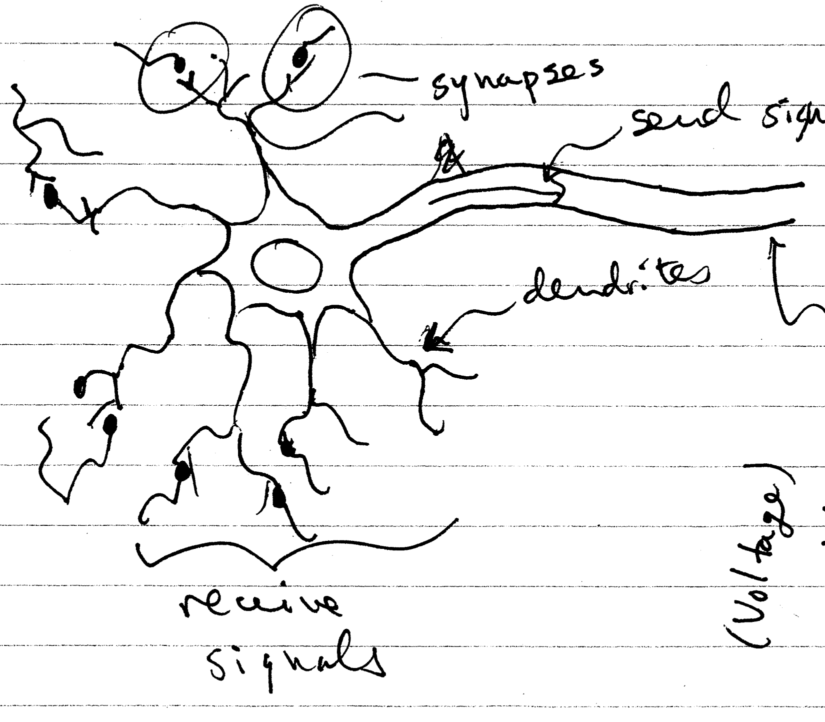
- Because of osmotic pressure that would cause the cell to lyse if equilibrium was reached, the cell actively pumps ions to be in a non-equilibrium state.

- We will see that by controlling the flow of ions through these pumps, that axons are able to change the ΔV across their membranes.

- These changes in $\Delta V \Rightarrow$ propagating electric signals

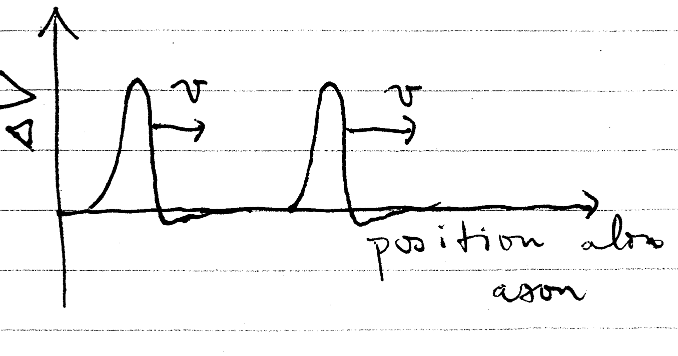
$\equiv$ nerve impulse.

Action Potentials



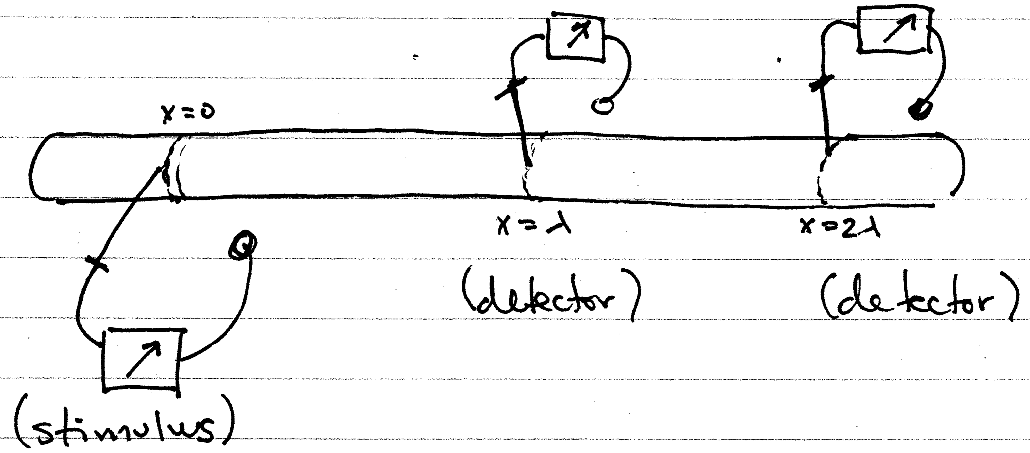
- What is the electrical signal?

- signal $\equiv$ voltage pulse which propagates



- How does the axon set up a propagating ΔV wave?

Measuring Signals in axons

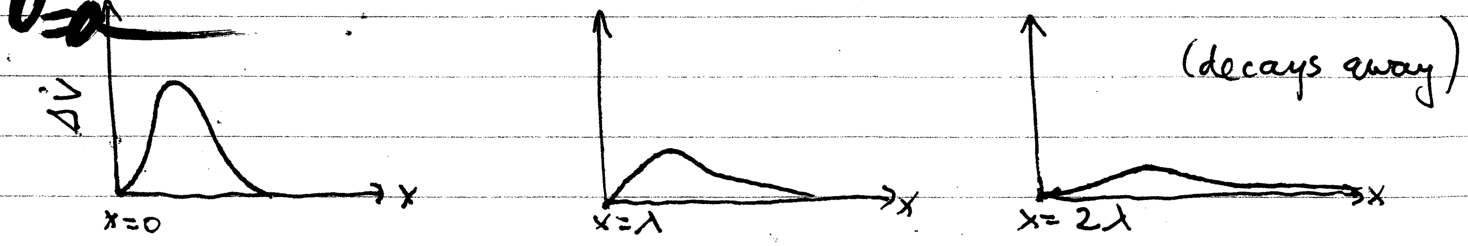


- Recall resting potential: $\Delta V_{rest} < 0$

- In expt, the stimulus "depolarizes" the membrane causing ΔV to become <u>less</u> negative.

- Detectors positioned at places down the axon measure the propagation of this stimulus down the axon.

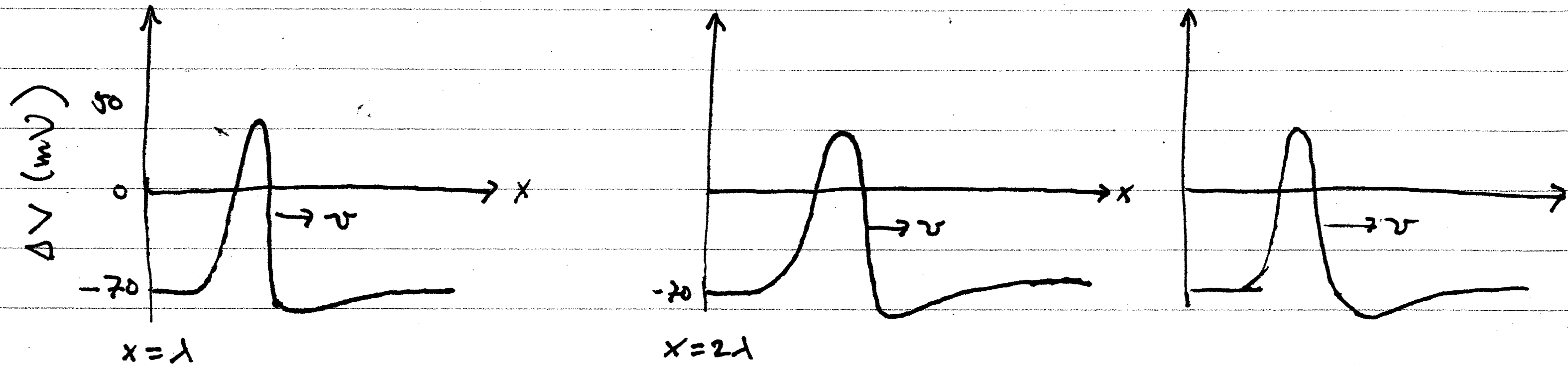
- For <u>weak</u> stimulus the response looks like a spreading & decaying wave



THIS IS NOT AN IMPULSE..

- For <u>weak</u> stimuli, the signal spreads ≡ electrotonus and is not a nerve impulse

- For <u>strong</u> stimuli (~10mV), something interesting happens ⟹ action potential ≡ propagating wave.

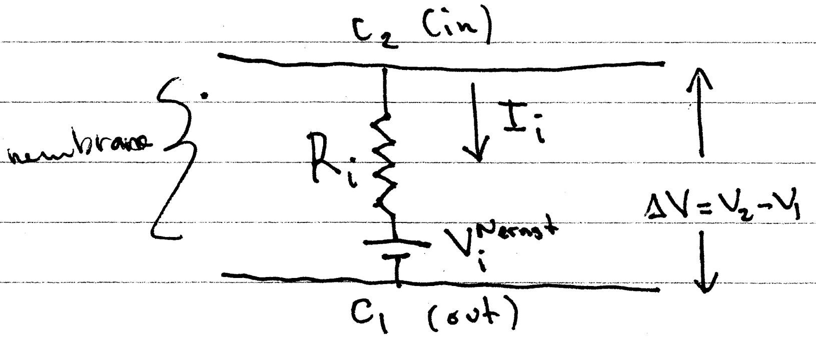


- Action potential moves at a constant speed, v. (0.1~120m/s)

- Signal does <u>not</u> decay. Shape is independent of strength of stimulus (stimulus still must be greater than a threshold)

The Circuit Diagram ~~of the Cell~~ Membrane:

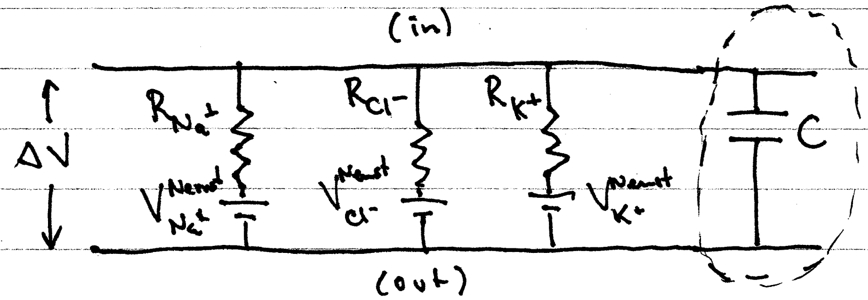
- Last class we talked about the current flow, resistance, and voltage drop for a given ionic species. We drew an electrical circuit.



$$\Delta V = I_i R_i + V_i^{Nernst}$$

(Ohmic assumption)

Multiple ions species are wired in parallel.

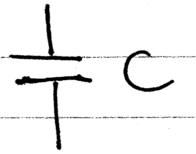


← we'll talk about this later

- As before, the resistances are different for the different ionic species.

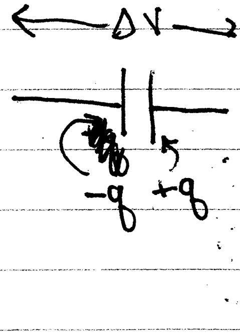
- In the analysis, that follows we will ignore the current from the pumps, as it turns out that nerve impulses function for a long time with the pumps shut off.

- What about the Capacitor:



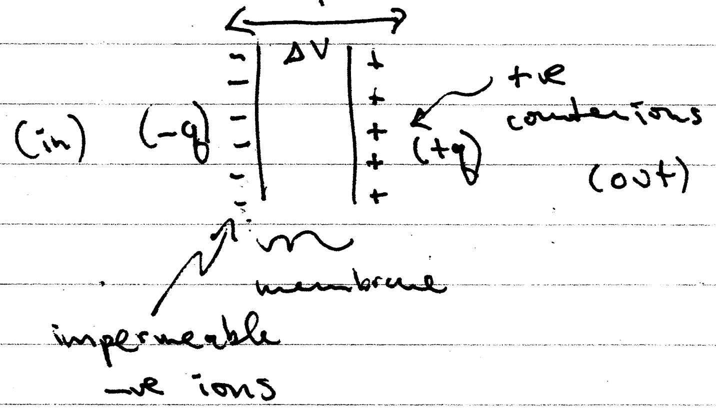
≡ a capacitor

- Capacitors store charge, no charge actually flows through them.



- The ΔV cause charge to build up on one side and the opposite charge to build up on the other.

Membrane capacitance:



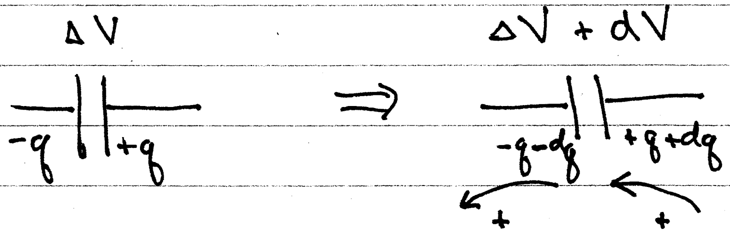
- The ΔV across the membrane sets up -q inside and a +q outside.

- How much charge is there?

1st year physics: $\boxed{q = C(\Delta V)}$

- Capacitors store charge, and can produce currents if the voltage changes (they're like backup)

Consider



- By changing ΔV → ΔV + dV a charge +dq flowed in on one side, and flowed out on the other side!

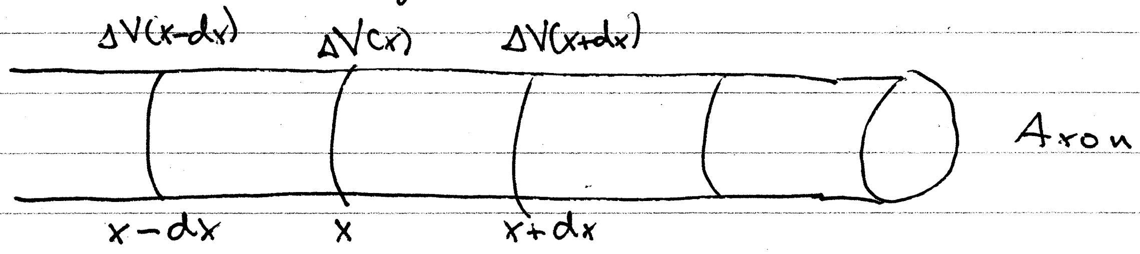
So $$\frac{dq}{dt} = \boxed{I = C\frac{d(\Delta V)}{dt}}$$

- A time varying voltage produces a current through a capacitor!

- The generation of nerve impulses lead to time varying ΔV, and thus capacitive currents become important.

Modeling of Axons:

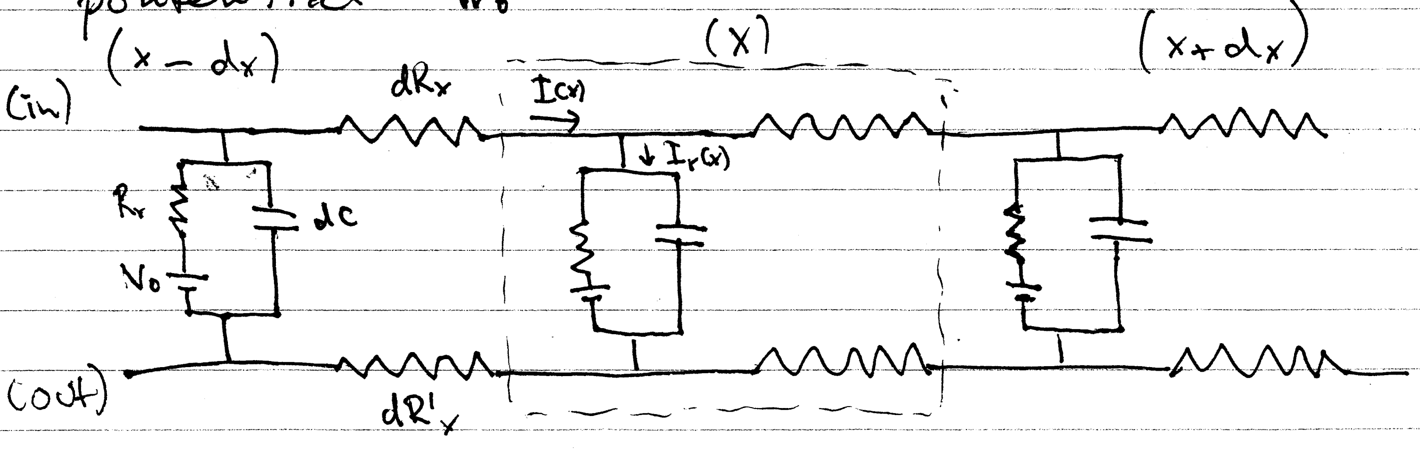
- The circuit diagram above applies to a small patch of membrane on an axon. Thus the entire axon can be viewed as a series of circuits wired together.



- Potential drop $\Delta V(x)$ changes with position x.

- Besides the radial (traverse current), there will now also be an <u>axial</u> current due to the change in ΔV along the axon.

- We will lump all the resistances into one Resistor (R_r and the Nernst potential by the steady-state pontential V_0



- The dR_x' & dR_x represent the resistance to ion transport along the axial direction outside & inside the axon respectively.

- Since no current can pile up any where, the axial current must equal the radial current.

Axial current: $I_{axial} = I_x(x) - I_x(x+dx) = -\frac{dI}{dx}. dx$

Radial current: $I_r(x) = I_{OHm}(x) + I_{cap}(x)$ ⇑ capacitance

$$= \frac{(V - V_0)}{R_R} + C\frac{dV}{dt}$$

Now, $I_x(x) = -\frac{(V(x+dx) - V(x))}{dR_x} = -\frac{V(x+dx) - V(x)}{dx}\frac{1}{\xi}$ ← resistan /lengt

$$= -\frac{1}{\xi}\frac{dV}{dx}$$

So $I_{axial} = I_r$

$$\Rightarrow \frac{1}{\xi}\frac{d^2V}{dx^2} = \frac{(V - V_0)}{R_R} + C\frac{dV}{dt}$$

let $\tau = R_e C$ & $\sqrt{R_R/\xi} = \lambda$ & $v = V - V_0$

$$\Rightarrow \boxed{\lambda^2\frac{d^2v}{dx^2} - \tau\frac{dv}{dt} = v} \equiv \text{cable eqn}$$

- The cable equation gives the spatial and temporal dynamics of the pontential across the membrane ASSUMING that the circuit captures all the physics

- We will see that this equation DOES NOT give a propagating wave — it's incomplete.

Solution to cable equation:

let $w(x,t) = e^{t/\tau} v(x,t)$ & sub into cable eqn

$$\Rightarrow \quad \frac{\lambda^2}{\tau} \frac{d^2 w}{dx^2} = \frac{dw}{dt} \equiv \text{Diffusion eqn for } w$$

- Diffusion equation DOES NOT have any propagating wave solutions.

- However, $v(x,t) = e^{-t/\tau} w(x,t)$ which has decaying dynamics which DOES describe the behaviour of axons when their stimulus is weak.

- Q: What then causes a propagating impulse?

Voltage Gated Ion Pumps:

- What did we need to get a genetic switch?

Ⓐ positive feedback Ⓑ cooperativity.

- A nerve impulse is a switch between a state of low (resting) voltage and high (impulse) voltage.

- How do we get feedback & cooperativity in generating the membrane ~~pote~~ potential?

- We already saw the answer last week:

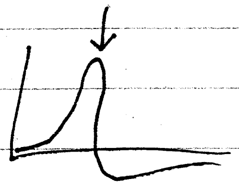
  If $g_{K+} >> g_{Na} \Longrightarrow \Delta V \approx V_{K+}^{Nernst} \approx -60\,mV$

  BUT

  If $g_{Na^+} >> g_{K+} \Longrightarrow \Delta V \approx V_{Na+}^{Nernst} \approx +40\,mV$

- Thus need the membrane to "switch" its conductance properties.

- Expt find that @ peak of action potential



$$g_{K^+} \approx \underline{\underline{0.05\, g_{Na^+}}} \approx 2 g_{Cl^-}$$

so $$g_{Na^+} \approx 20\, g_{K+} \quad @ \text{ peak}$$

- The key: the conductance of an ionic species *depends* on the membrane voltage, $g_i(V)$ — it's *not* a constant.

Thus: $$I_i = g_i(\Delta V)\,(\Delta V - V_i^{Nernst})$$

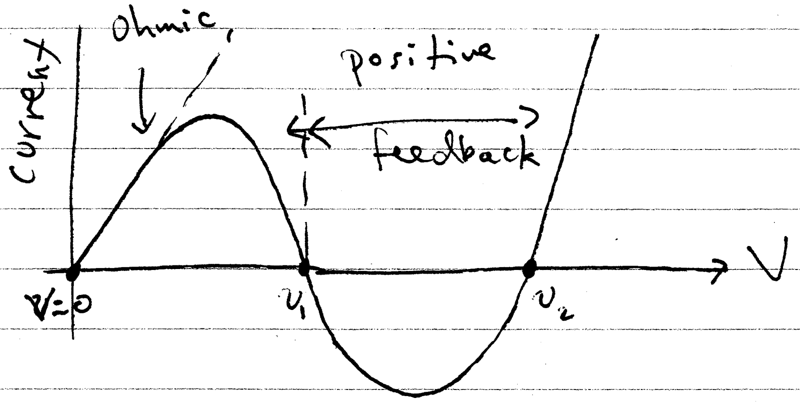
- because g_i is not constant with ΔV, the system is *no* longer ohmic.

Nonlinearity:

simple model: $g_{Na^+}(V) = g^0_{Na^+} + BV^2$

$\rightarrow$ conductance increases with voltage

Result:



- Thus if the voltage passe v_1, then positive feed back kicks in and we move towards the stable voltage v_2 — this is the threshold behavior we wanted.

- Thus nerve impulses rely on a cooperative positive feed back in order to function.