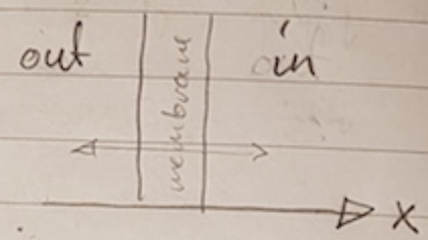
Ion pumping → sodium anomaly in <u>all animal cells</u>

<u>Summary</u>



fluxes out → in positive

forces in → out positive $\Delta\ln c_i, \Delta V, \Delta p$

linear transport $j_i = j_{p,i} - g_i \Delta\mu_i$ (passive membrane is linear!!)

flux of ion i : ⓪ $j_i = j_{pi} - g_i\, kT \ln\frac{c_{io}}{c_{ii}} - g_i v_{mi} \Delta p - g_i q_i \Delta V$

g_i – conductance through membrane

v_{mi} – molecular volume of ion i

q_i – charge of ion i

j_{pi} – ion pump flux $= \alpha_i \cdot j_p,\ j_p > 0$

Na^+ $j_{p,Na^+} = 3 j_p$, K^+ : $j_{p,K^+} = -2 j_p$

– steady state : $j_i = 0$

– assume $\Delta p = 0$

charge neutrality inside : $c_{Na,i} + c_{K,i} - c_{Cl,i} - \left|\frac{\rho_{qm}}{e}\right| = 0$

① $\Rightarrow j_{Na^+} + j_{K^+} + j_{Cl^-} = 0$

Na^+ ② $\frac{3 j_p}{g_{Na^+}} = kT \ln\frac{c_{No}}{c_{Ni}} + e\Delta V$

K^+ ③ $-\frac{2 j_p}{g_{K^+}} = kT \ln\frac{c_{Ko}}{c_{Ki}} + e\Delta V$

Cl^- ④ $0 = kT \ln\frac{c_{Clo}}{c_{Cli}} - e\Delta V$

4 equations
– c_{io} fixed
– j_p, g_i, ρ_{qm} fixed

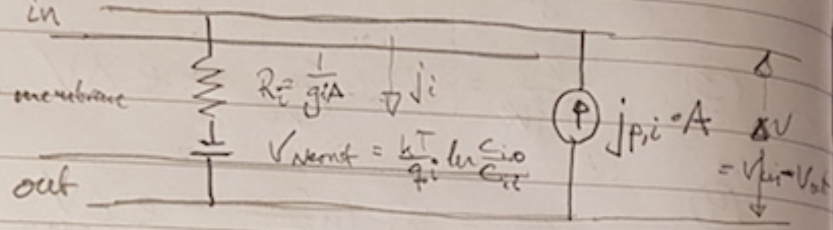
4 unknown: $c_{ii}, \Delta V$

Actual membrane potential $\Delta V = \Delta V^{Nernst} = \frac{kT}{q}\ln\frac{c_{io}}{c_{ii}}$
only for ions that permeate, but are not pumped
(here : Cl^-)

Steady state $\Delta V = V^0$ is called <u>resting potential</u>

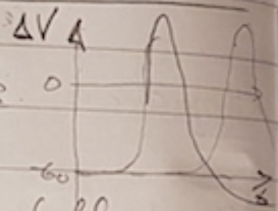
$\boxed{\text{Beware : my } g_i \cdot q_i = g_i \text{ in book}}$

Equivalent circuit



The electrophysiology of the axon:

The action potential



- When stimulated beyond a threshold the axon changes polarization for a short while and this potential pulse travels along the axon. The peak & shape is independent of the exact triggering pulse
- Travels along the axon at constant speed (0,1 - 120 m/s)
- Peak potential independent of distance
- Shape preserving pulse
- afterhyperpolarization at the end
- harder to stimulate new pulse during refractory period

Numerical example: Squid giant axon

	$C_{i,o}$ [mM]	$C_{i,i}$ [mM]	V_i^N mV	g_i/g_{K^+}
K^+	20	400	-75	1
Na^+	440	50	+54	1/25
Cl^-	560	52	-59	1/2

g^*_{Na}/g_{K} 8

measured by diffusion of radio-active cons

equations ② & ③ $\overset{\text{eliminate } j_p}{\Longrightarrow}$

$$\Delta V = -\frac{kT}{e} \frac{\left(3 g_{K^+} \ln \frac{C_{K^+o}}{C_{K^+i}} + 2 g_{Na^+} \ln \frac{C_{Na,o}}{C_{Na,i}}\right)}{2 g_{Na^+} + 3 g_{K^+}}$$

$$= -\frac{3 g_{K^+} V^N_{K^+} + 2 g_{Na^+} V^N_{Na^+}}{2 g_{Na^+} + 3 g_{K^+}} = -72\,mV$$

according to eq ④ $V^N_{Cl^-} = \Delta V$

but $-59 \neq -72$

effect of charge balance: $\dot{j}_{Na^+} + \dot{j}_{K^+} - \dot{j}_{Cl^-} = 0$

$\Rightarrow$ correction of ④ $\Rightarrow \frac{j_p}{e g_{Cl}} = \Delta V - V^N_{Cl^-}$ $\rightarrow -\Delta V > 100\,mV$

according to Book "actual resting potential"

$$\Delta V^{actual} = -60\,mV$$

Equation ① is not really correct.

charge imbalance $\Rightarrow \Delta V$ is changed.

+ other ions are present. (and permeable?)

NB $g_i = g_i \cdot q_i$

Equation ⓪ , $\Delta p = 0$

$$j_i = j_{p,i} - g_i\,(V_i^{Nernst} - \Delta V)$$

steady state $\quad j_i = j_{p,i} - g_i\,(V_i^{N} - V^0)$

short time : ~~neglect $j_{p,i}$~~ $\quad (j_{p,i} \ll g_i(V^0 - \Delta V))$

charge balance ④ $\Rightarrow \sum j_i = 0 = \sum g_i\,(V^0 - \Delta V)$

$g_{tot} = \sum_i g_i \quad \Rightarrow$ ⑤ $\quad V^0 = \sum_i \frac{g_i}{g_{tot}} V_i^{Nernst}$ $\quad \boxed{\text{chord conductance formula}}$

$\Rightarrow V^0 = -66\,mV$

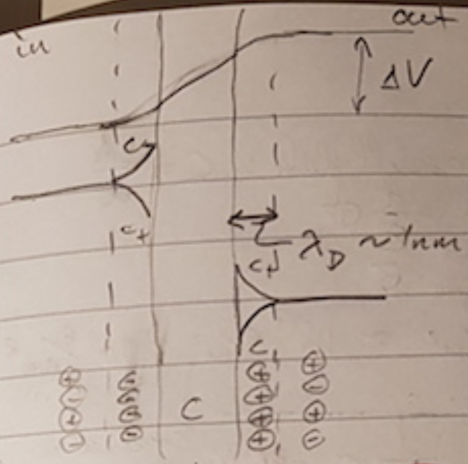
V^0 dominated by Nernst potential of ion with largest g_i

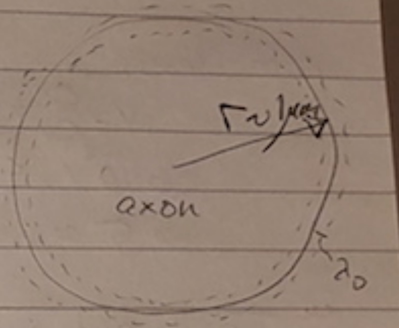
$\Rightarrow$ Different assumption adjusted steady state

result from $\Delta V = V_{cl}^{N} = -59\,mV$

and ② & ③ $\Rightarrow \Delta V = -72\,mV$

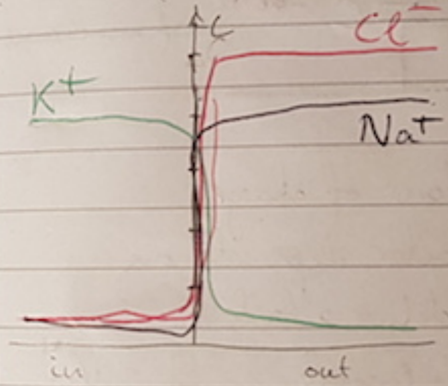
to an intermediate value





$\frac{\text{Volume ions}}{\text{Volume double layer}} \sim \frac{\lambda_D}{r} \sim 10^{-3}$

(squid giant axon $r \sim 1\,mm$)

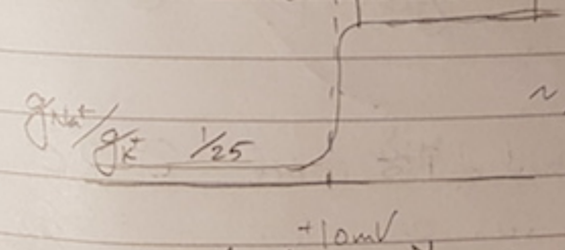


(Volume ions) $\cdot\, \Delta C_i$ = energy store

n_{ions} needed to move to change $\Delta V \propto$ volume of double layer!

Main mechanism of action potential :

(see fig 12.15)



$$\Rightarrow V^0 = \frac{1}{g_{tot}}\left(g_{Na^+} V_{Na^+}^{N} + g_{K^+} V_{K^+}^{N} + g_{Cl^-} V_{Cl^-}^{N}\right)$$

$$= \frac{1}{1+8+\frac{1}{2}}\left(8 \cdot 54 - 75 - \tfrac{59}{2}\right) = \underline{34\,mV}$$

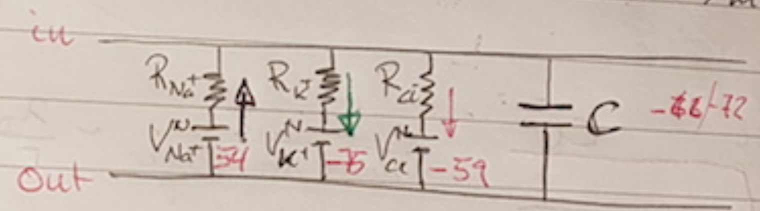
capacitance

parallel plate: $C = \frac{\varepsilon A}{d}$

$$V = \frac{Q}{C} = \frac{qd}{\varepsilon A} = \frac{d}{\varepsilon}\sigma$$

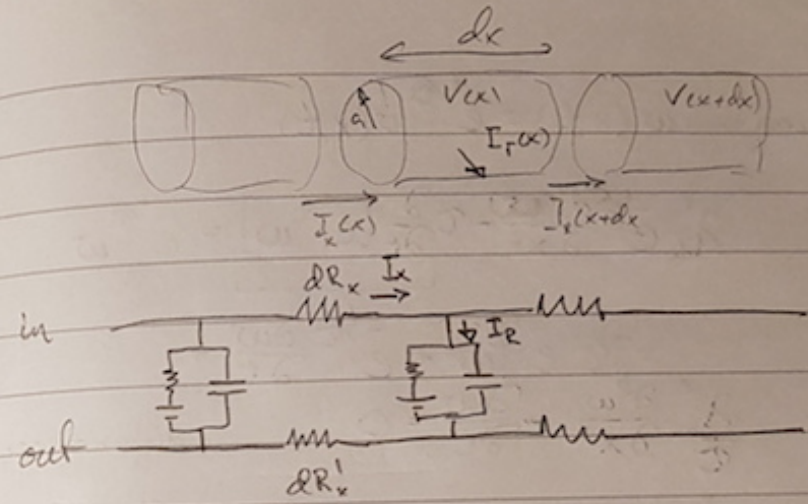
$$6 \cdot 10^{-2} V = \frac{10^{-9}}{10^{-11}} \cdot \sigma$$

$$\Rightarrow \sigma \simeq 6\ C/m^2 \approx 10^{-19}\ e/m^2 \simeq 10\ e/nm^2$$



small area of membrane

- constant (small) flow of charge
- charging of capacitor depends on which channel delivers fastest
- rest state: g_{K^+} largest $\Rightarrow \frac{Q}{C} \sim V^N_{K^+}$
- activated state g_{Na^+} largest $\Rightarrow \frac{Q}{C} \sim V^N_{Na^+}$
- Time constant of RC circuit $\tau = R \cdot C$ $= C/g_{tot}$



charge balance

change in axial current = radial current + charge buildup

$$-\frac{dI_x}{dx} \cdot dx = 2\pi a \left(j_{q,r}(x) + C\frac{dV}{dt} \right) dx$$

$$\pi a^2 H \frac{d^2V}{dx^2} = 2\pi a \left(j_{q,r}(x) + C\frac{dV}{dt} \right)$$

$$j_{q,r} = (V - V^0) g_{tot} = v\, g_{tot} \quad \left(= v\, g_{tot}(v) \right)$$

$\Rightarrow$ non-linear

$$\tau = RC = C/g_{tot}$$

$$\lambda_{ax} = \sqrt{aH/2g_{tot}}$$

H - conductivity

$$\Rightarrow \boxed{\lambda_{ax}^2 \frac{d^2v}{dx^2} - \tau\frac{dv}{dt} = v}$$

linear cable equation

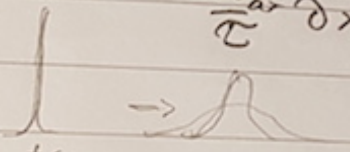
Solution $\quad w(x,t) = e^{t/\tau} v(x,t)$

$$\lambda_{ax}^2 e^{-t/\tau} \frac{\partial^2 w}{\partial x^2} - \tau \boxed{\frac{\partial}{\partial t}\left[e^{-t/\tau} w\right]} = e^{-t/\tau} w$$

$$= -\frac{1}{\tau} e^{-t/\tau} w + e^{-t/\tau} \frac{\partial w}{\partial t}$$

$$\Rightarrow \quad \frac{\lambda_{ax}^2}{\tau} \frac{\partial^2 w}{\partial x^2} - \frac{\partial w}{\partial t} = 0$$

diffusion eq.

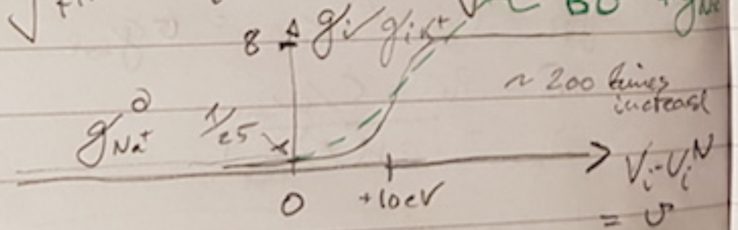


$$v(x,t) = \frac{c \cdot e^{-t/\tau}}{\sqrt{t}} e^{-\frac{x^2 \tau}{4t\lambda_{ax}^2}}$$

$e^{-t/\tau} \Rightarrow$ not area preserving

Voltage gating

$$\dot{j}_{q,r} = \sum_i (V - V_i^N) g_i(V) \sim B v^2 + g^0_{Na^+}$$

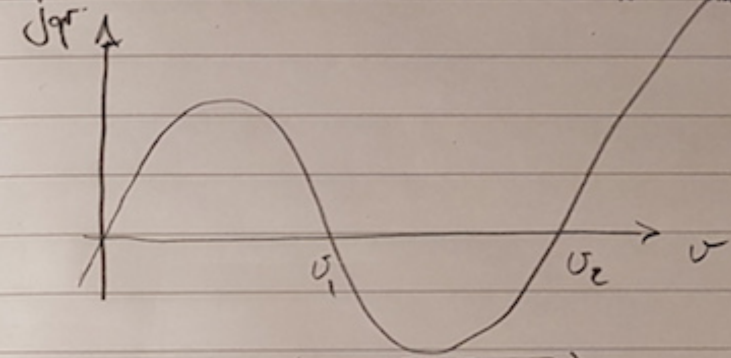


$$g_{Na^+}(v) = g^0_{Na^+} + B v^2$$

$$\Rightarrow \quad \dot{j}_{q,r} = \sum_0 (V - V_i^N) g_i^0 + (V - V^N_{Na^+}) B v^2$$

$$\Rightarrow \quad j_{qr} = v\, g^0_{tot} + (v - H) B v^2$$

$$H = V^N_{Na^+} - V^0$$



$$v_{1,2} = \frac{1}{2}\left(H \mp \sqrt{H^2 - 4 g^0_{tot}/B}\right)$$

$$v_1 v_2 = \frac{g^0_{tot}}{B}$$

nonlinear cable equation $\Rightarrow$

$$\boxed{\lambda_{ax}^2 \frac{\partial^2 v}{\partial x^2} - \tau \frac{\partial v}{\partial t} = \frac{v(v - v_1)(v - v_2)}{(v_1 v_2)}}$$