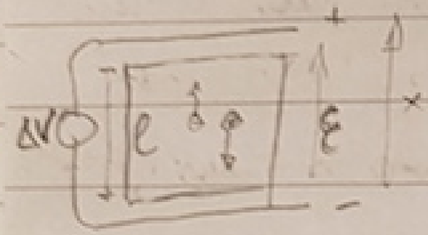
29.10.2019 Machines in membranes

Electric field $\mathcal{E} = -\frac{\Delta V}{\ell}$



Potential energy of charge:

$U(x) = -q\mathcal{E}x$, $\Delta V = \frac{\Delta U}{q}$

Force $F = -\frac{\partial U}{\partial x} = -q\mathcal{E}$ causes drift

velocity $v = \frac{F}{\xi} = -\frac{D}{kT} q\mathcal{E}$

that causes concentration gradient

Total chemical potential

$\mu = \mu_{int} + \mu_{ext} = \mu_0 + kT \ln\frac{c}{c_0} - q\mathcal{E}x$

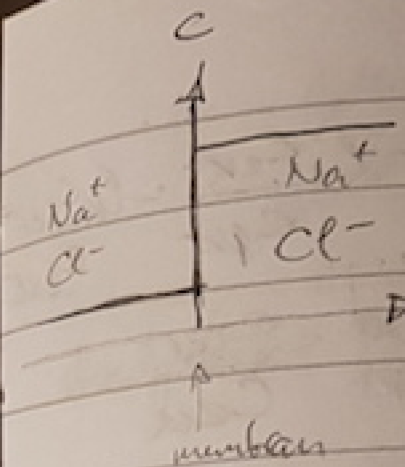
Flux $j = -D' \nabla\mu$

Equilibrium $j = 0 \Rightarrow \frac{\partial \mu}{\partial x} = 0$

$\Rightarrow kT \frac{\partial \ln c}{\partial x} = q\mathcal{E}$ $\cdot \partial x$

$kT\, \Delta \ln c = q\mathcal{E}\ell = -q\Delta V$

Nernst Potential



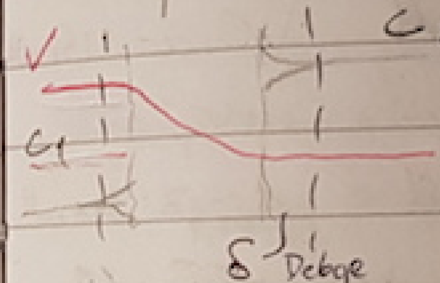
What happens when:

1 − no ions permeate

2 only one ion permeates

3 both ions permeate

2: equilibrium: $\frac{\partial \mu}{\partial x} = 0$



$\Delta V = V_{Nernst} = \frac{kT}{q} \ln\frac{c_2}{c_1}$

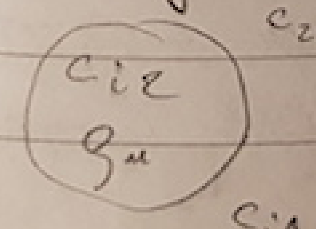
$\left(\frac{kT}{e} = \frac{1}{40}\,\text{Volt}\right)$

Multicomponent mixtures

- negatively charged macromolecules. Charge dens ρ_{m} $\rho_m/e = 125\,mM$
- K^+ c_{K^+} : $c_{1K^+} = 10\,mM$
- Na^+ c_{Na^+} $c_{1Na^+} = 140\,mM$
- Cl^- c_{Cl^-} $c_{1Cl^-} = 150\,mM$

Charge neutrality: $c_{1Na^+} + c_{1K^+} - c_{1Cl^-} = 0$ outside

$c_{2Na^+} + c_{2K^+} - c_{2Cl^-} + \rho_m/e = 0$ inside



$\rho_m = 0$

Why macromol. charges not balanced

For all permeable species

Nernst equilib: $\frac{e}{kT}\Delta V = \ln\frac{c_{2Na^+}}{c_{1Na^+}} = \ln\frac{c_{2K^+}}{c_{1K^-}} = -\ln\frac{c_{1Cl^-}}{c_{2Cl^-}}$

(Donnan potential)

$\Rightarrow$ Donnan equilibrium $\frac{c_{2Na^+}}{c_{1Na^+}} = \frac{c_{2K^+}}{c_{1K^+}} = \frac{c_{1Cl}}{c_{2Cl}}$

Solve for c_{2i}:

$c_{2Na^+} = 210\,mM$ | $c_{1Na^+} = 140\,mM$

$c_{2K^+} = 15\,mM$ | $c_{1K^+} = 10\,mM$

$c_{2Cl^-} = 100\,mM$ | $c_{1Cl^-} = 150\,mM$

few macromolecules each highly charged $c_{q,m} \approx 1\,mM$

$c_{tot,2} = 325\,mM$ | $c_{tot,1} = 300\,mM$

$\Delta\mu_{osm} = v_m kT\Delta c_{tot}$ | $\Delta c_{tot} = 25\,mM$

$\Delta V_{donnan} = -10\,mV$ | $\Delta p = kT\Delta c_{tot} = 6\cdot10^4 Pa$

$= 0{,}6\,bar$

Plants, algae, fungi, bacteria: outer rigid wall to withstand pressure

Ion pumping: $j_{i,pump}$

Nonequil. thermo: $j_i = L_i\nabla\mu_i + L_{Ti}\nabla T + \dots$

Linear if ... reversibility (very seldom not)

$\Delta\mu_i = kT\Delta\ln c_i + v_{mi}\Delta p + q(\Delta V - V_i^{Nernst})$

$j_i = L_{iu}\Delta\mu_i$ Book $L_{iu} = g_i$ conductance

steady state $j_{i,pump} = -j_i$ power series??

$\frac{j_{i,pump}}{g_i} = \underbrace{kT\Delta\ln c}_{V^{Nernst}} + c_{mi}\Delta p + q(\Delta V - \cancel{V_i^{Nernst}})$

(without pump $\Delta\mu = 0 \Rightarrow \Delta p$ ...)

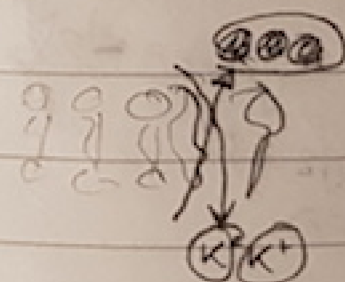
Dissipative steady state:

Entropy production rate $\sigma = \sum j_i\Delta\mu_i$

$\Rightarrow$ energy dissipation rate $\frac{\delta Q}{dt} = T\sigma$

$\Rightarrow$ Energy must be taken from somewhere

Skou: Na^+K^+ ATPase (can be put in non-living liposomes)



$3Na^+$ ↗ coupled process

$2K^+$ ↓

$[ADP] = 0{,}001$

ATP hydrolysis $ATP + H^+ \rightleftharpoons ADP$ $[ATP] = 0{,}01$

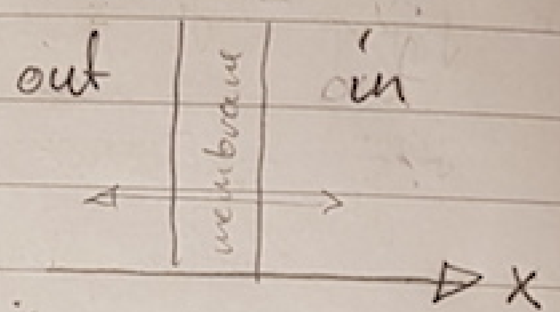
$[H^+] = 0{,}01$

? $\Delta G^0 = -12{,}4\,kT \Rightarrow K_{eq} = e^{-\frac{\Delta G_0}{kT}} \left(= \frac{[ADP]}{[ATP][H^+]}\right)_{equil.} \approx e^{23}$

$\approx -7{,}3\,kcal/mol$

Ion pumping → sodium anomaly in **all animal cells**

Summary



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 $j_i = j_{p,i} - g_i kT \ln \frac{c_{io}}{c_{ii}} - g_i v_{mi} \Delta p - g_i q_i \Delta V$

g_i − conductance through membrane

v_{mi} − molecular volume of ion i

q_i − charge of ion i

$j_{p,i}$ − 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: $c_{Na,i} + c_{K,i} - c_{Cl,i} - \left|\frac{\rho q_m}{e}\right| = 0$

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

Na^+ ② $\frac{3 j_p}{g_{Na^+}} = kT \ln \frac{c_{Na,o}}{c_{Na,i}} + e\Delta V$

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

Cl^- ④ $0 = kT \ln \frac{c_{Cl,o}}{c_{Cl,i}} - e\Delta V$

4 equations − c_{io} fixed

− $j_p, g_i, \rho q_m$ fixed

4 unknown: c_{ii}, ΔV

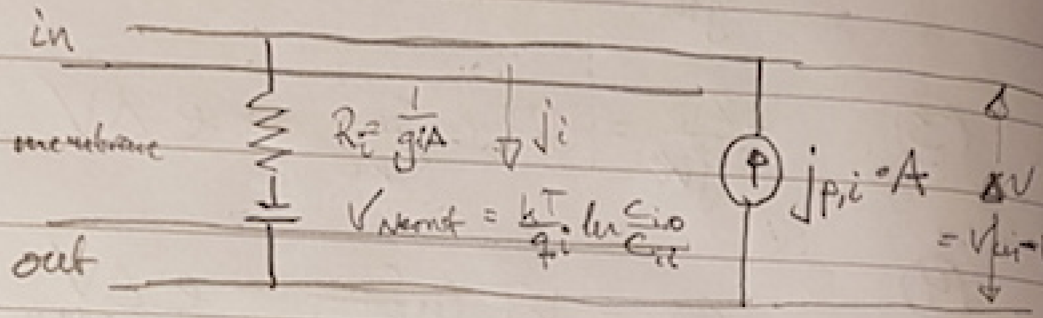
Actual membrane potential $\Delta V = \Delta V^{Nernst} = \frac{kT}{q} \ln \frac{c_{io}}{c_{ii}}$

only for ions that permeate, but are not pumped (here: Cl^-)

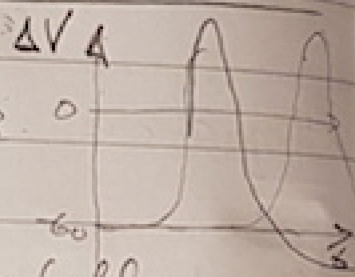
Steady state $\Delta V = V^0$ is called <u>resting potential</u>

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

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_{K^+}/g_{Na^+} 8

measured by diffusion of radioactive comp.

equations ② & ③ $\xRightarrow{\text{eliminate } j_p}$

$$\Delta V = -\frac{kT}{e} \frac{\left(3 g_{K^+} \ln \frac{c_{Ko}}{c_{Ki}} + 2 g_{Na^+} \ln \frac{c_{Nao}}{c_{Nai}}\right)}{2 g_{Na^+} + 3 g_{K^+}}$$

$$= -\frac{3 g_{K^+} V_{K^+}^N + 2 g_{Na^+} V_{Na^+}^N}{2 g_{Na^+} + 3 g_{K^+}} = -72 \text{ mV}$$

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

but $-59 \neq -72$

effect of charge balance: $j_{Na^+} + j_{K^+} - j_{Cl^-} = 0$

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

according to book "actual resting potential"

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

Equation ① is not really correct.

charge imbalance $\Rightarrow$ ΔV 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 $j_i = j_{p,i} - g_i (V_i^N - V^0)$

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

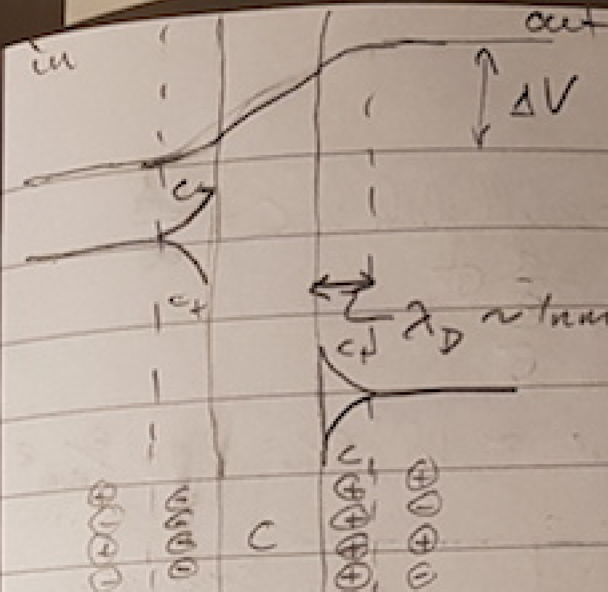
charge balance (4) $\Rightarrow \sum j_i = 0 = \sum g_i (V^0 - \Delta V)$

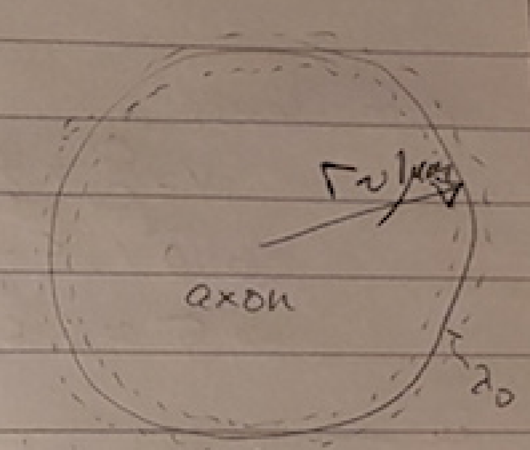
$g_{tot} = \sum_i g_i \Rightarrow$ (5) $V^0 = \sum_i \frac{g_i}{g_{tot}} V_i^{Nernst}$ chord conductance formula

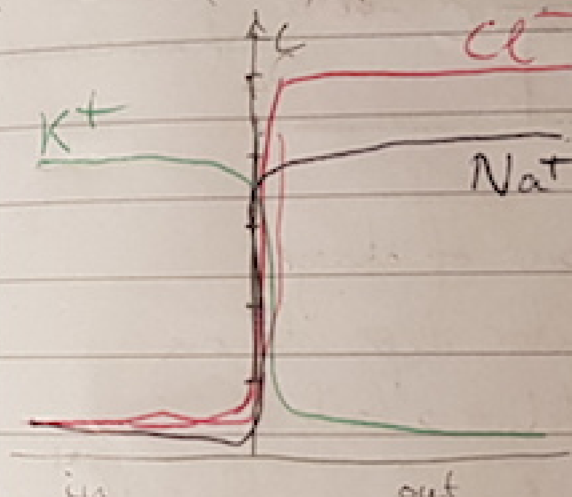
$\Rightarrow V^0 = -66 mV$

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







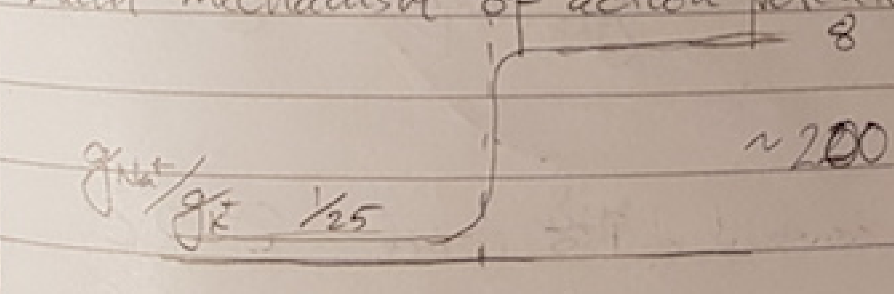
$\frac{\text{Volume ions}}{\text{Volume double layer}} \sim \frac{\lambda_D}{r} \sim 10^{-3}$

(squid giant axon $r \approx 1mm$)

(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 (2.15))

~ 200 times higher

+10mV

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

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

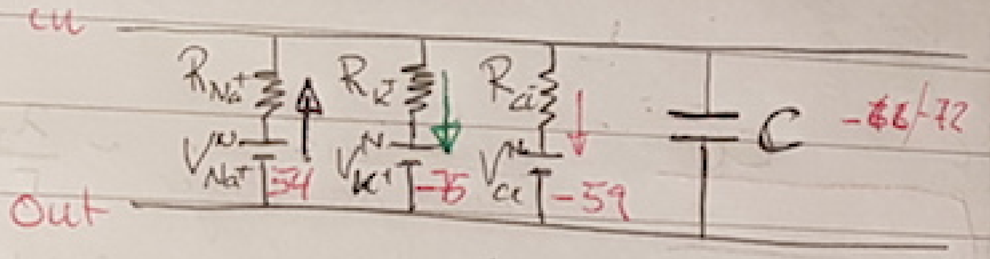
capacitance

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

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

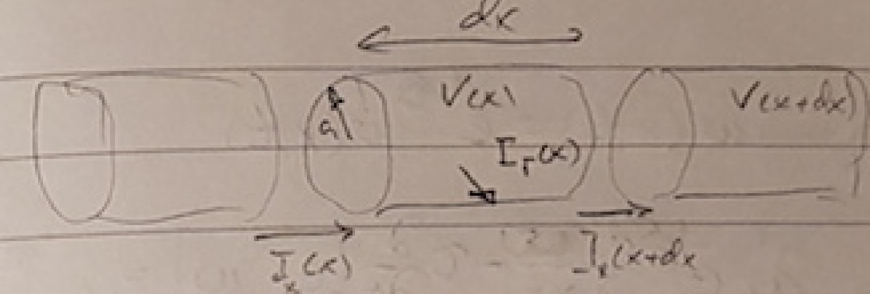
$$6 \cdot 10^{-2} V = \frac{10^{-9}}{10^{-11}} \cdot \sigma$$

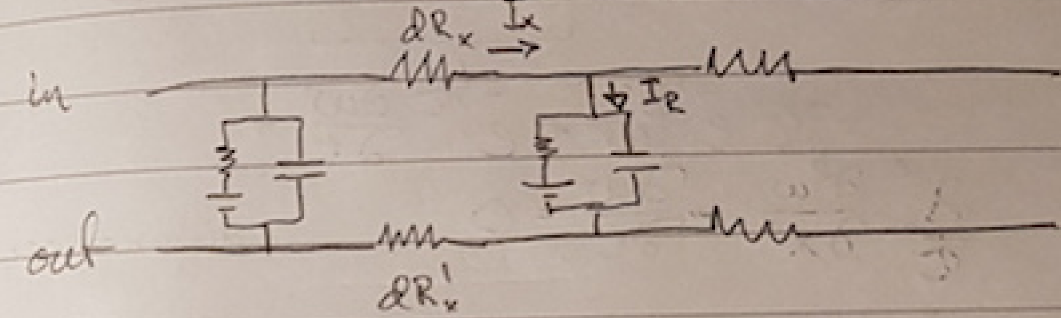
$$\Rightarrow \sigma \simeq 6\ C/m^2 \approx 10^{-19}\ e/m^2 \simeq 10\ e/nm^2$$



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

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

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

$$j_{qr} = (V - V^0) g_{tot} = v\, g_{tot} \quad (= v\, g_{tot}(v))$$

$\Rightarrow$ non-linear

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

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

κ - conductivity

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

linear cable equation

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

$$\lambda_{ax}^2 e^{-t/\tau}\frac{\partial^2 w}{\partial x^2} - \tau \underbrace{\frac{\partial}{\partial t}\left[e^{-t/\tau} w\right]}_{= -\frac{1}{\tau} e^{-t/\tau} w + e^{-t/\tau}\frac{\partial w}{\partial t}} = e^{-t/\tau} w$$

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

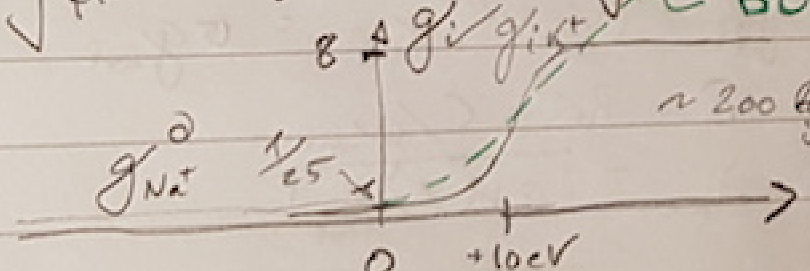
diffusion eq.

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

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

Voltage gating

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

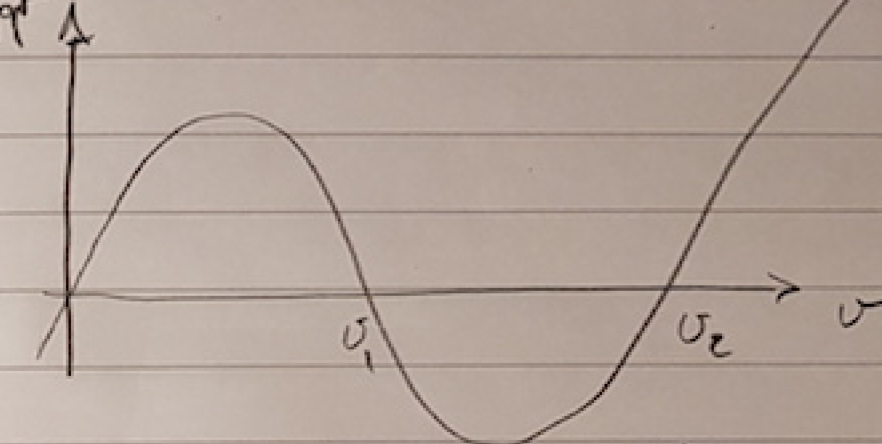


$$g_{Na^+}(v) = g^0_{Na^+} + Bv^2$$

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

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

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



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

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

nonlinear cable equation =>

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