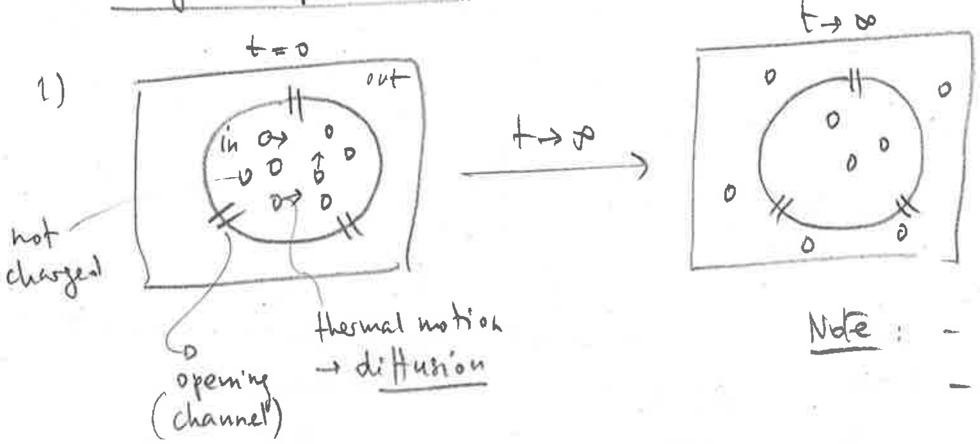
Membrane potential

Thought experiments:

1)

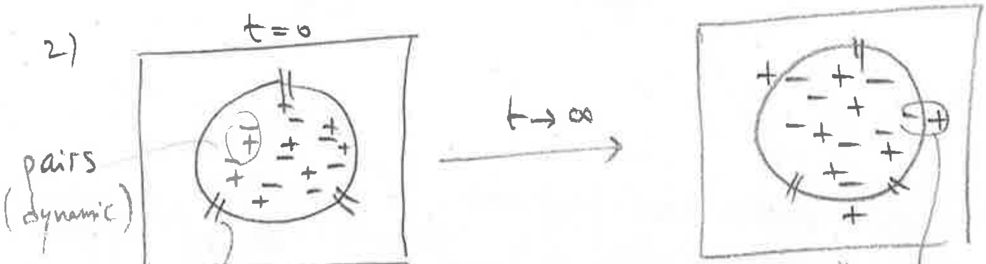


$[X]_{in} = [X]_{out}$ for $t \to \infty$

because of <u>diffusion</u>

<u>Note</u>: – macroscopic: no change
– microscopic: constant change but on average → steady state

2)



→ channel
(i) <u>selective</u> for +
(ii) no net charge $\left(\sum_{+} + \sum_{-} = 0\right)$

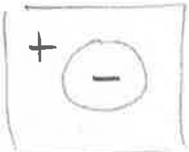
$$\boxed{[X^+]_{in} > [X^+]_{out}}$$

because inside becomes "attractive" ($V_{in} < 0$)

→ excess charge <u>on surface</u>

→ net charge

$\Rightarrow V_{in} < V_{out}$



3) Analogous for – selective channels:
$[X^-]_{in} > [X^-]_{out}$, $V_{in} > V_{out}$

This example has all the ingredients of the membrane potential in neurons

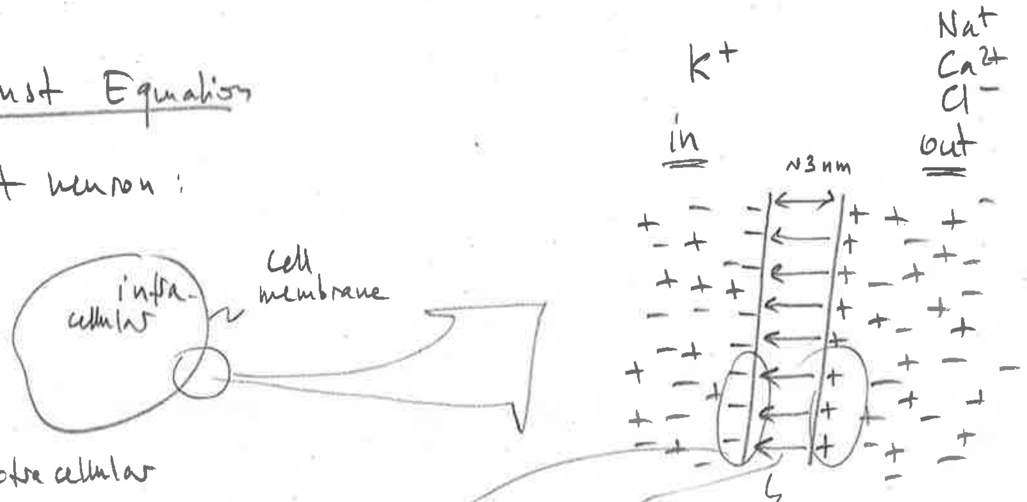
1) A physical barrier (in vs out)
2) $[X]_{in} \neq [X]_{out}$: concentration differences in vs out
3) Selective channels

<u>Goal</u>: expression for V_{in} ($V_{out} = 0$)
- <u>dependency</u> on concentrations
- —"— temperature
- channel properties (# chan., conductance, ...)
- ion properties: X^+, X^{++}, ...

Nernst Equation

18.2

A neuron:

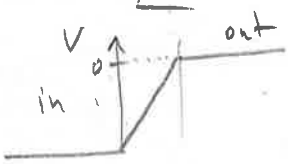


excess charge on surface

Electric field

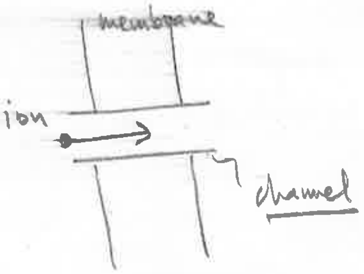
$1\,\mu m^3$ cytoplasm:
10^{10} H_2O molec.
10^8 ions
10^7 small molec. (aminoacids)
10^5 proteins

membrane: - electrical insulator
- capacitor (stores charge)
- separates in vs out



Ionic Pumps
→ cause $[X]_{in} \neq [X]_{out}$
takes a lot of Energy

Ion channels



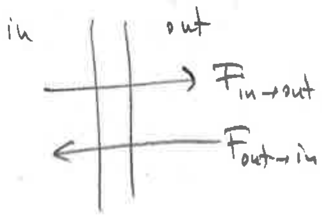
• "large" conductance compared to membrane
$g_{ch} \cong 10^4 \cdot g_{membr.}$

• selective for a ion-type ($1 : 10^4$ specificity)

Many computations in neurons:
due to - channel selectivity
- time-dependence of g_{ch}
bec. of - neurotransmitters
- Voltage
- Ca^{2+}, ... (second messengers)

Membrane potential = concentration gradients + selective channels

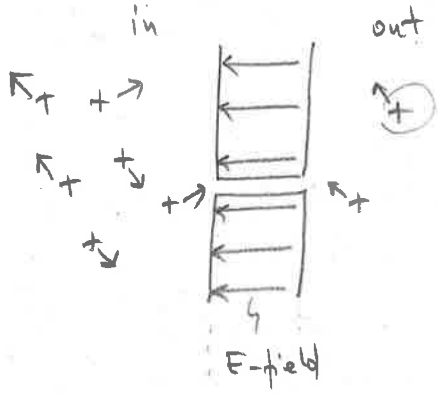
to derive: consider Flux in→out & Flux out→in
through channels



Example: – contribution of K^+

meaningful: most channels open @ rest mostly permeable to K^+

– consider steady-state = Equilibrium potential



K^+ ions

(others ions, e.g. $\ominus$, not shown)

$$\boxed{F_{out \to in} = \underbrace{\gamma}_{} \cdot [K^+]_{out}}$$

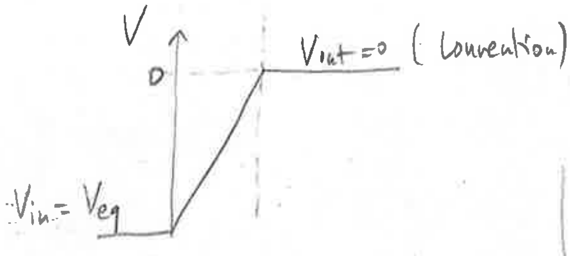
"Fraction" of ions getting to channel entrance (per unit of time)

γ: function of # channels, g_{ch}, ...

$$\boxed{F_{in \to out} = \gamma \cdot [K^+]_{in} \cdot \underbrace{e^{\frac{qV_{eq}}{k_B T}}}_{}}$$

Fraction of ions with thermal energy > qV

$\left(V_{eq} < 0 \Rightarrow e^{\frac{qV}{k_B T}} < 0 \right)$



@ Equilibrium $F_{out \to in} = F_{in \to out}$

$$\frac{[K^+]_{out}}{[K^+]_{in}} = e^{\frac{qV}{k_B T}}$$

$$\Rightarrow \boxed{V_{eq} = \frac{k_B T}{q} \cdot \ln \frac{[K^+]_{out}}{[K^+]_{in}}}$$ Solutions for K^+

in general: $$\boxed{V_{eq} = \frac{k_B T}{qz} \cdot \ln \frac{[X]_{out}}{[X]_{in}}}$$ Nernst Equation

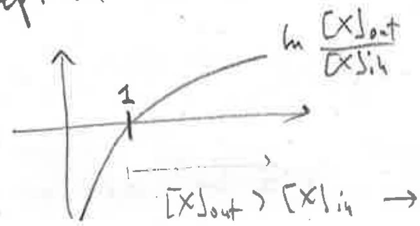
charge of ion

Holds for channels selective to 1 ion type

otherwise: use GHK-Equation (below)

From Nernst Eq.:

- $T\uparrow \Rightarrow |V|\uparrow$: more thermal energy $\Rightarrow$ more ions can cross the potential barrier in vs. out
- $|z|\uparrow \Rightarrow |V|\downarrow$: bec. larger Energy barrier ($\Delta E = zqV$)
- change in charge sign (z) $\Rightarrow$ change in sign (V)
- dep. on concentration:



$[X]_{out} > [X]_{in} \rightarrow V > 0$ (for $z > 0$)

$[X]_{in} > [X]_{out} \rightarrow V < 0$ (for $z > 0$)

Approximate concentrations in neurons:

	[in] mM	[out] mM	Veq mV
K^+	400	20	−75
Na^+	50	440	+55
Cl^-	52	560	−60
Ca^{2+}	10^{-4}	10	+140

For example: K^+ $\ln \frac{20}{400} = \ln \frac{1}{20} = -1 \cdot \ln 20 \cong -3 \longrightarrow -3 \cdot 25 = -75\,mV$

$k_B = 1.38 \cdot 10^{-23}\ J/K$ Boltzmann constant

$q = 1.60 \cdot 10^{-19}\ C$

$T \cong 300\ K$

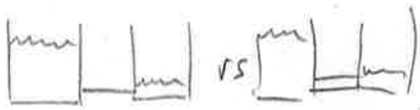
$\frac{k_B T}{q} \cong 24 - 27\ mV$

cold & warm blooded animals

Note: V_{eq} does not depend on g

e.g. # of channels, g_{ch}, ...

But: - time-to-equilibrium does depend on it



- V_∞ for external current does depend on g_L!

(see next lecture)

Note: we assumed $\left([X]_{in/out} @ t=0\right) = \left([X]_{in/out} @ t=\infty\right)$

Is this assumption ok?

Consider capacitance of the membrane

$C_m = c_m \cdot A$ — c_m: specific capacitance; A: Area

$c_m \cong 10\, nF/mm^2$

$A \cong 0.01 - 0.1\, mm^2$

$\Rightarrow C_m \cong 0.1 - 1\, nF$

- How many ions needed to get $V_m = -70\, mV$?

$C_m = \frac{Q_m}{V_m}$ $\quad Q_m = C_m \cdot V_m = 10^{-9} \cdot 70 \cdot 10^{-3}\, C = 7 \cdot 10^{-11}\, C$

($C_m = 1\, nF$)

$\# \text{ions} = \frac{Q_m}{q} = \frac{7 \cdot 10^{-11}}{1.6 \cdot 10^{-19}} \cong 10^{9}$ ions

- How many ions in a neuron?

Volume of neuron $\cong 10^{6}\, \mu m^3$ ($\Leftrightarrow$ "radius" $= 10 - 100\, \mu m$)

$\Rightarrow$ contains 10^{14} ions

$\Rightarrow$ only $1 : 10^{5}$ ions contribute to membrane potential @ rest
(if only 1 type was involved ... see below)

$\Rightarrow$ assumption seems ok

But: $\left.\begin{array}{l} C_m \,\&\, Q_m \propto r^2 \\ \text{Volume} \propto r^3 \end{array}\right\}$ things get worse for smaller radius

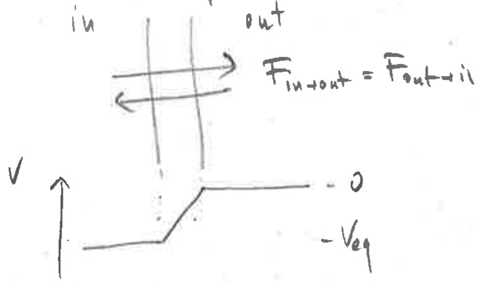
$\Downarrow$

ratio $\propto \frac{1}{r}$

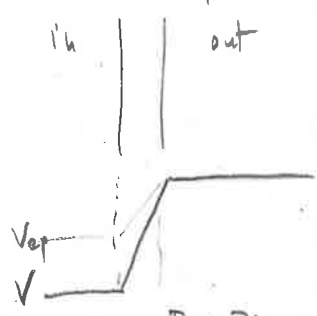
- What if potential $V \neq V_{eq}$?

Consider K^+

@ V_{eq}



$V < V_{eq}$

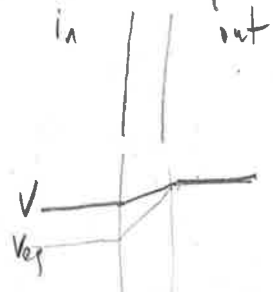


$\leftarrow F_{out \to in}$ unchanged

$\rightarrow F_{in \to out}$ smaller

Bec. ΔE larger

$V > V_{eq}$

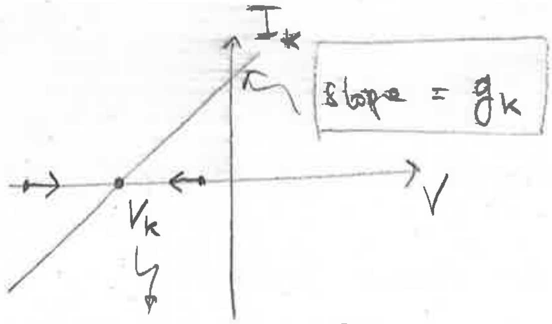


$\leftarrow F_{out \to in}$ unchanged

$\rightarrow F_{in \to out}$ larger

Bec. ΔE smaller

Net current I_K: $\xleftarrow{K^+ \text{ in}}$ $\Rightarrow V \uparrow$; $\xrightarrow{K^+ \text{ out}}$ $\Rightarrow V \downarrow$



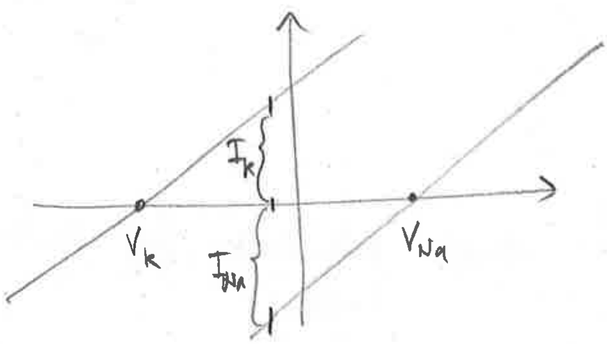
Bottom Line: (i) I_K tries to pull V towards V_K

(ii) Pull is stronger if g_K is larger

- Consider 2 channel types

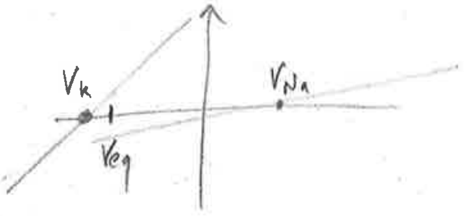
e.g. K^+ : $V_K = -70\,mV$

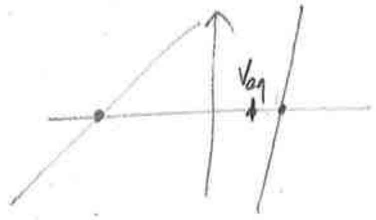
Na^+ : $V_{Na} = +50\,mV$



New V_{eq} given by $I_K = -I_{Na}$

V_{eq} depends on conductances of g_{Na} & g_K :





$g_K \gg g_{Na}$

$\underline{V_{eq} \approx V_K}$

$g_K \ll g_{Na}$

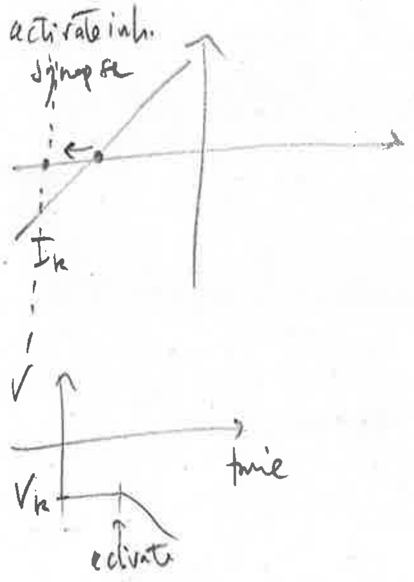
$\underline{V_{eq} \approx V_{Na}}$

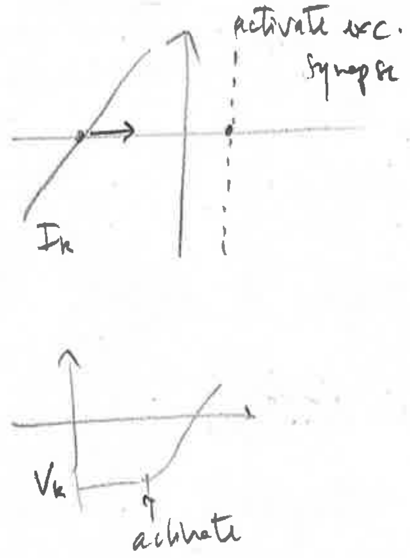
A lot of computations in neurons based on this process !

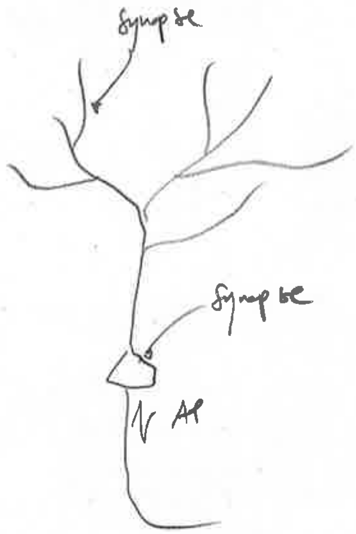
1) open a channel type with $V_{reversal}$

2) V is pulled towards $V_{reversal}$

<u>Example</u> : Inhibitory & Excitatory synapses :







• What if channels are permeable to more ion types ?

<u>GHK - Equation</u> :
$$\boxed{V = \frac{k_B T}{q} \cdot \ln \frac{P_K \cdot [K]_{out} + P_{Na} \cdot [Na]_{out} + P_{Cl} \cdot [Cl]_{in}}{P_K \cdot [K]_{in} + P_{Na} [Na]_{in} + P_{Cl} \cdot [Cl]_{out}}}$$

$\underline{P = \text{permeability}}$

18.8

Questions / Corrections

- V_{inh} vs V_{rest}

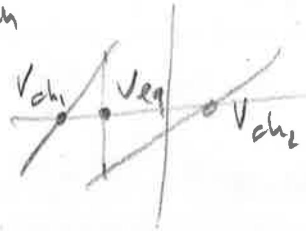
  V_{rest} vs V_{K^+}

  V_{inh} vs. V_{Cl^-}

- The role of pumps

- When 2 channel types are open

  $V_{eq} \neq V_{ch_1}$ & $V_{eq} \neq V_{ch_2}$



@ Equilibrium $\left.\begin{array}{l} I_{ch_1} \neq 0 \\ I_{ch_2} \neq 0 \end{array}\right\} \Rightarrow$ the concentrations do change

→ need pumps to revert concentration gradient

Literature: Dayan & Abbott, Theoretical neuroscience (online)

chapters 5 & 6