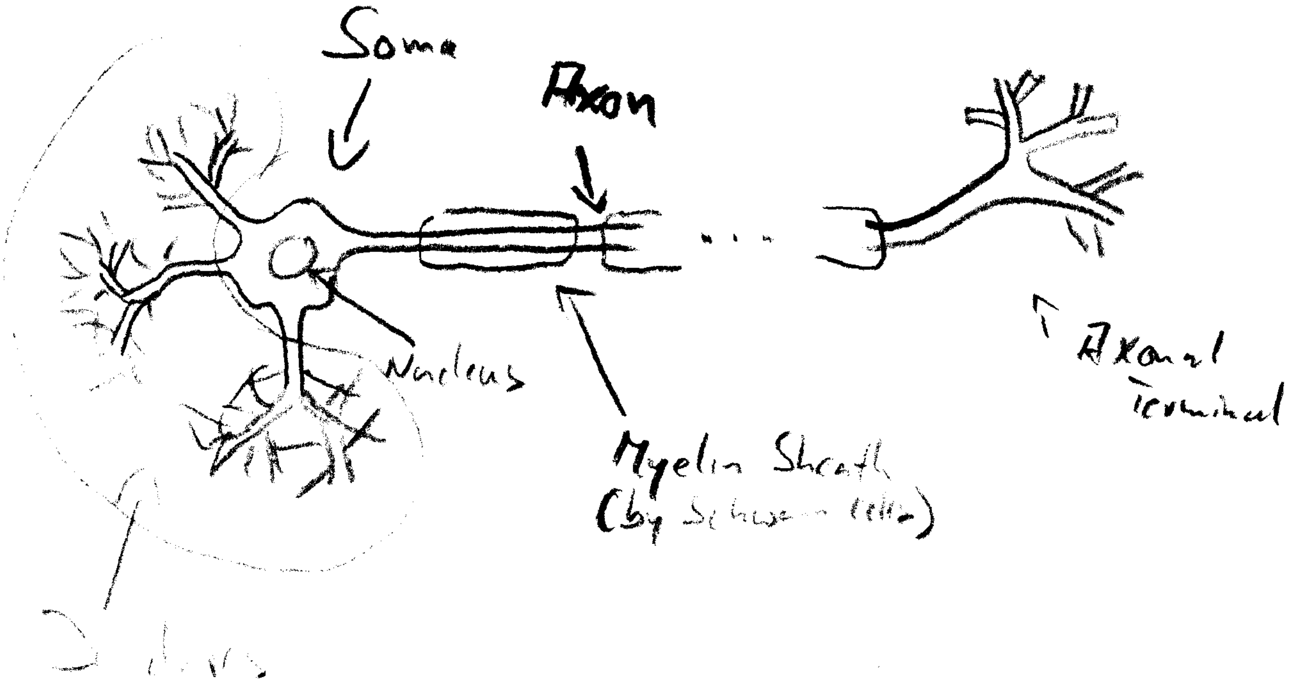
The neuron (Human Brain: 10^{11} Neurons)



Each neuron has: - cell body, hosting the nucleus, and other organelles

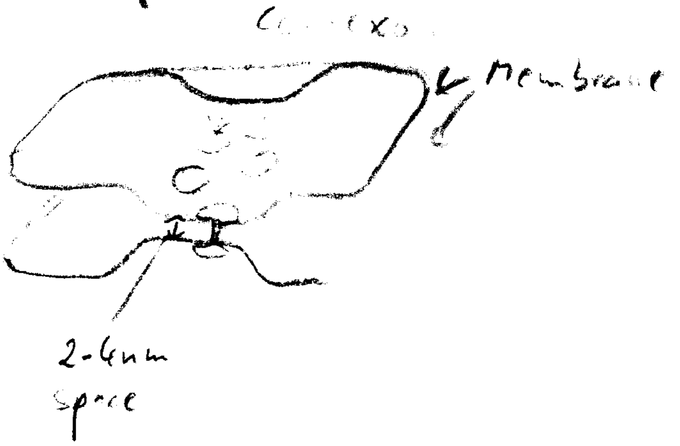
Neurites
- Axon: - can be very long (up to meters)
  - SENDS information away from the soma
  - usually myelinated, for rapid signal transport
  - Axonal terminal connects to other cells
- Dendrites: (also called dendritic branches, or dendritic processes)
  - Mostly a neuron has multiple dendrites
  - typically short (few 100 µm)
  - typically very branched
  - RECEIVE information

The synapse (human newborn ~ 10^{15} adult: ~ 10^{14})

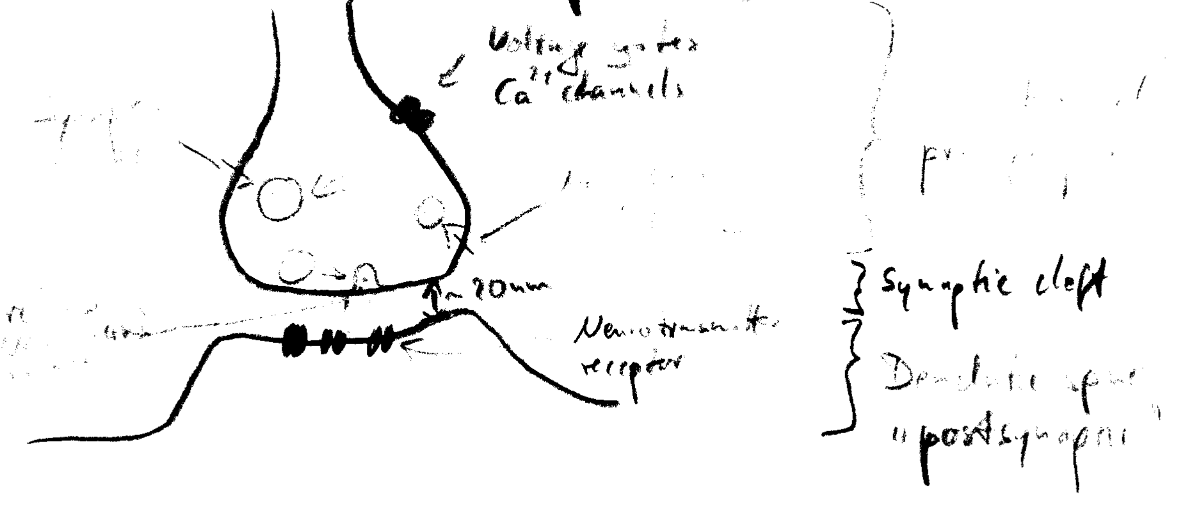
General: The synapse connects two neurons, and transmits information.

2 Types of synapses: 1) Chemical Synapses:
Information transmitted by chemical signaling (Neurotransmitters)

2) Electrical Synapses:
Membranes of two cells are closely connected so Action Potential jumps from one cell to the other



Chemical Synapses



③ Presynaptic side:

Usually the synaptic vesicles are docked to the membrane, ready to be released.
If a nerve pulse arrives ("action potential"), the voltage gated Ca^{2+} channel open → Ca^{2+} influx → this triggers exocytosis of synaptic vesicles.

Synaptic cleft: Neurotransmitter transport is diffusive:

Question: How fast?? Diffusion Equation: $\frac{\partial c(\vec{r},t)}{dt} = D \cdot \nabla^2 c(\vec{r},t)$

→ solution for a pointlike release:

$$\boxed{c(\vec{r},t) = \frac{1}{(4\pi Dt)^{3/2}} \exp\left(-\frac{\vec{r}^2}{4Dt}\right)}$$

↑ Gauss function, that spreads in time

But: How can we estimate the time to pass the gap?
Look at standard deviation σ of Gaussian.
Normal distribution in 1D

$$g(\vec{x}) = \frac{1}{\sigma\sqrt{2\pi}} \cdot \exp\left(-\frac{(\vec{x}-x_0)^2}{2\sigma^2}\right)$$

← n is Dimension

=> 3D · (if same σ)

$$\Rightarrow 2\sigma^2 3 = 4Dt$$

=> to pass 20nm gap:

$$t = \frac{3}{2}(20 \cdot 10^{-9}\,m)^2 \cdot \frac{1}{D}$$

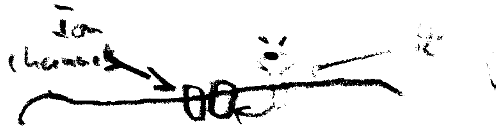
$$\approx 600 \cdot 10^{-8} \approx 6 \cdot 10^{-6}\,s$$

$$\approx \underline{\underline{6\,\mu s}}$$

Diffusion constant:
Stokes - Einstein relation $D = \frac{k_B T}{6\pi\eta \cdot r}$

$$\approx 10^{-10}\,\frac{m^2}{s}$$

④ Postsynaptic Side



Neurotransmitter binds to receptor
→ Receptor opens nearby ion channels
→ change in membrane potential, called „postsynaptic potential".

The activation can lead to:

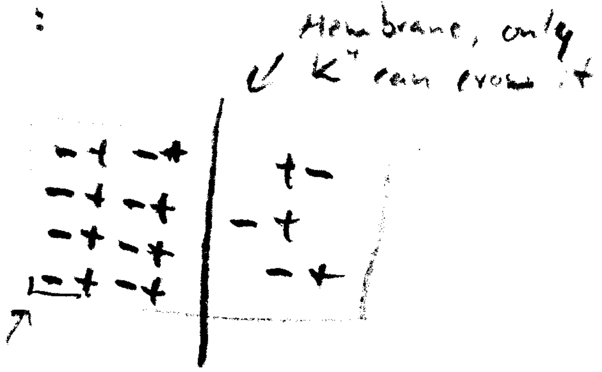
- depolarizing of the membrane potential
  ↳ action potential is initiated
  ⇒ **Exitatory Synapse**
- hyperpolarizing of membrane potential
  ↳ action potential is supressed
  ⇒ **Inhibitory Synapse**
  (Influx of Cl^-, efflux of K^+

[illegible]

⑤ Membrane Potential I

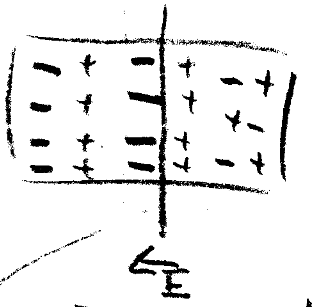
Origins from ion concentration gradients across the membrane.

Simple example :



$$c^l_{KCl} > c^r_{KCl}$$

Since the KCl concentration on the left is higher than on the right, osmotic pressure will ~~th~~ drive K^+ ions to the right



This results in a charge difference across the membrane => A membrane potential, with an electrical field that forces + to the left an - to the right

At equilibrium, the net flux due to the concentration difference is the same as the potential driven flux.

The equilibrium can be calculated by the „Nernst Equation"

Nernst Equation

$$\Delta V = \frac{R\cdot T}{z\cdot F}\cdot \ln\frac{C_o}{C_i}$$

membrane potential

R: gas constant = $k_B \cdot N_A$

Boltzmann constant

Avogadro constant

T: Temperature

z: valence of the ion (1 for K^+, -1 for Cl^-)

F: Faradays constant = $e \cdot N_A$

Elementary Charge

C_o and C_i = outside and inside concentration of the ion

Derivation: Consider the Energy to move ion against potential difference:

$$\Delta E^V_x = z\cdot e\cdot \Delta V$$, in Mole: $\underline{\Delta E^V_M = z\cdot F\cdot \Delta V}$

Consider Energy to move along concentration gradient:

Boltzmann:

$$\frac{C_o}{C_i} = \exp\left(\frac{\Delta E^c}{k_B T}\right) \Rightarrow \Delta E^c = k_B T\cdot \ln\frac{C_o}{C_i}$$

in Mole: $\Delta E^c_M = RT\cdot \ln\frac{C_o}{C_i}$

=> if the Energy balances in Equilibrium

$$\Rightarrow z\cdot F\cdot \Delta V = RT\ln\frac{C_o}{C_i}$$

$$\Rightarrow \boxed{\Delta V = \frac{RT}{z\cdot F}\cdot \ln\frac{C_o}{C_i}}$$

$$= \frac{k_B T}{z\cdot e}\cdot \ln\frac{C_o}{C_i}$$

Membrane Potential II

Ion concentrations in Neurons [mM]

		Intracell	Extracell
Potassium	K^+	140	5
Sodium	Na^+	[redacted] 12	105
[redacted]			
Calcium	Ca^{2+}	10^{-4}	1-2

} results in ~ -55mV

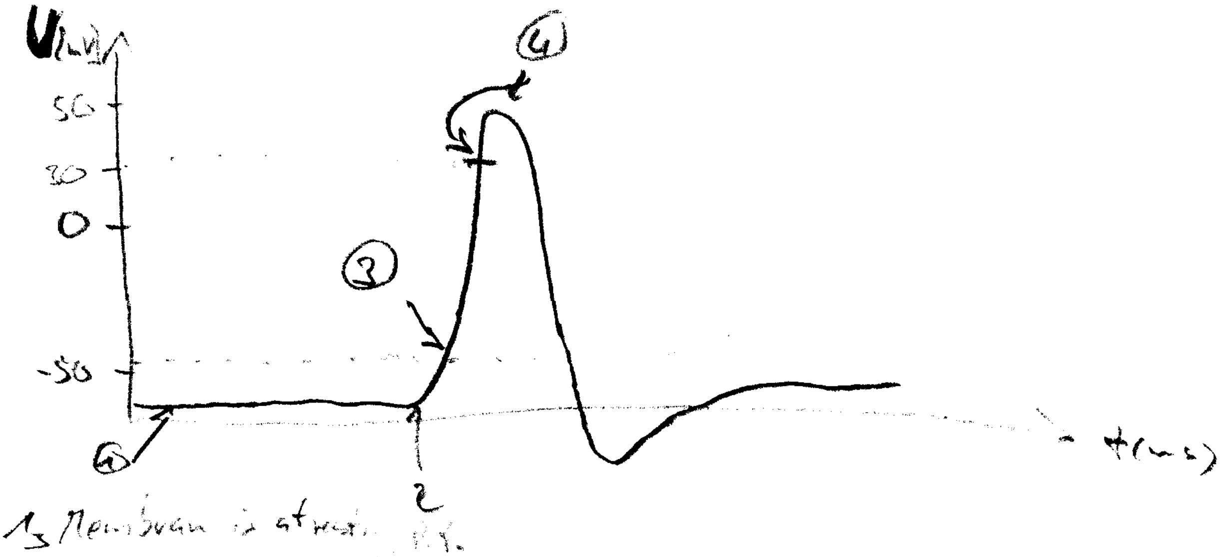
What is the potential for several ions?

~~Imgine Imagine~~

Goldman Equation:

$$\cancel{F}\ \Delta V = \frac{RT}{F} \cdot \ln\left(\frac{P_{Na}[Na^+]_o + P_K[K^+]_o + P_{Cl}[Cl^-]_i}{P_{Na}[Na^+]_i + P_K[K^+]_i + P_{Cl}[Cl^-]_o}\right]$$

The action potential



1. Membran is at resting [illegible]
2. A synapse on an adjacent neuron raise the potential
3. If the potential ~~increases~~ -50mV, voltage gated Na^+ open for a short time => Na^+ rushes into the cell => Potential increases further, the cell depolarizes and reaches maximum being at a ca. 50mV (the Na^+ channel only open briefly, then activated Na^+-K^+-Pumps restore the concentrations

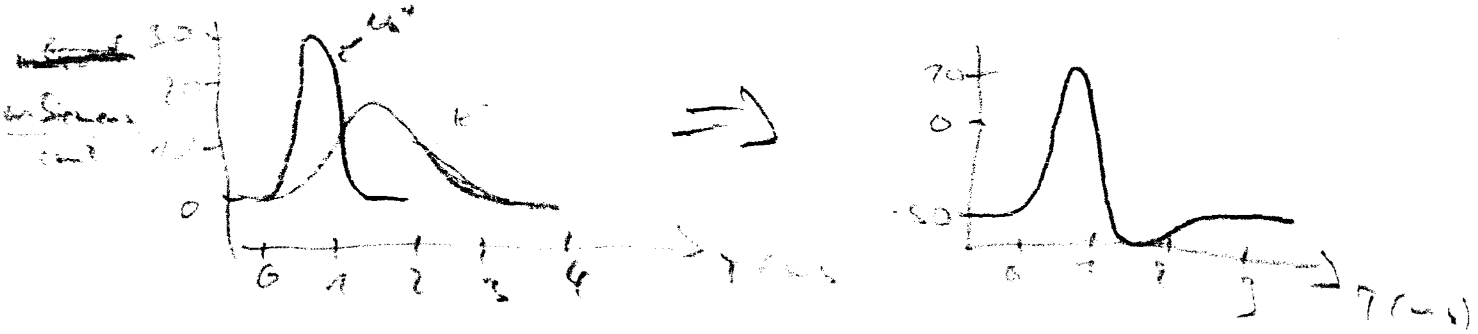
④ at about +30 mV voltage gated potassium channels open => K^+ rushes out, and reduces the potential

=> Potential returns to resting potential

However: for the next action potential, the ~~old~~ voltage gated channel need to be reactivated. In the mean time, called "refractory ~~#~~ period" no action potential can be sent.

Mathematical Model by Hodgkin & Huxley

=> Conductance for Na^+, and K^+ follows:



Model:

$$C_m \frac{dV_m}{dt} = G_{Na}(E_{Na} - V_m) + G_K \cdot (E_K - V_m) + G_L(E_L - V_m)$$

$$G_{Na} = \bar{g}_{Na} \cdot m^3 \cdot h$$

m: activation state variable

h: inactivation variable

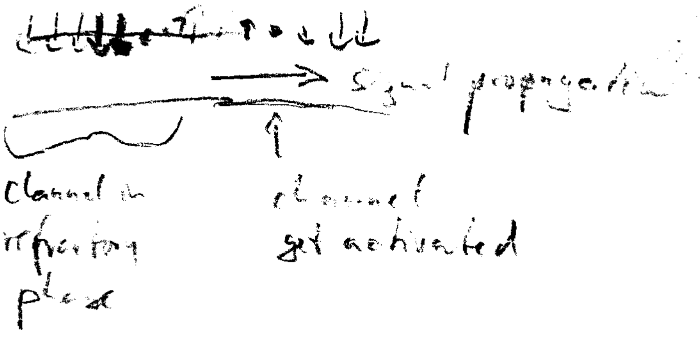
$$G_K = \bar{g}_K \cdot n^4$$

$$n(t) = n_\infty(V) - (n_\infty(V) - n(0)) \cdot e^{-t/\tau}$$

n: activation state variable

E

E-field changing direction



Speed of propagation: How far does the depolarized ~~mem~~ membrane influence other channel?

This depends on the conductivity of the membrane. By Myelation, the conductivity is increased

=> faster signal propagation, from ~ 0.5-10 $\frac{m}{s}$ to ~ 150 $\frac{m}{s}$