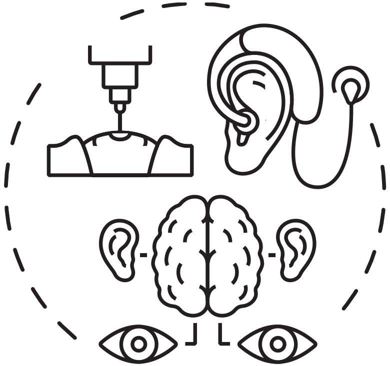
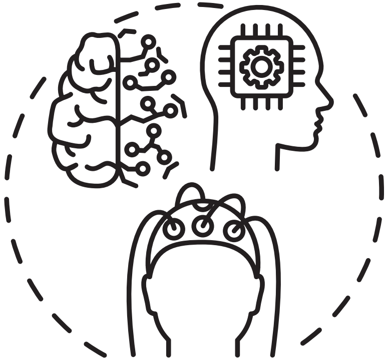




Neural Interfaces

NX-422

The nervous system

Neural signals

Stéphanie P. Lacour
Giuseppe Schiavone

Neuro-X Institute

Outline for the next 2 classes

- The nervous system
- **Neural signals**
- Neural electrodes
- Electrochemistry of bioelectrodes

Neural signals

Electrocorticography **ECoG**

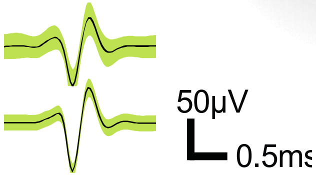
0.01 – 5 mV, < 200 Hz

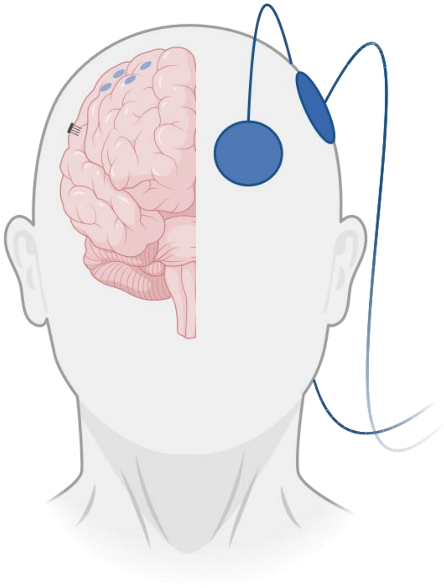
Local field potentials **LFP**

<1 mV, < 200 Hz

Action potentials **Spikes**

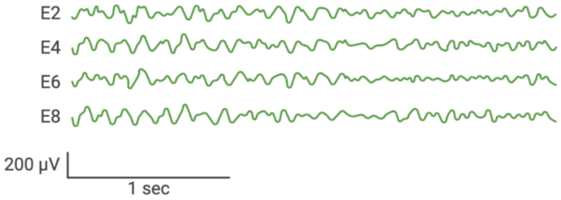
- ~ 500 µV, 0.5 – 5 kHz





Electroencephalography **EEG**

5 – 300 µV, < 100 Hz



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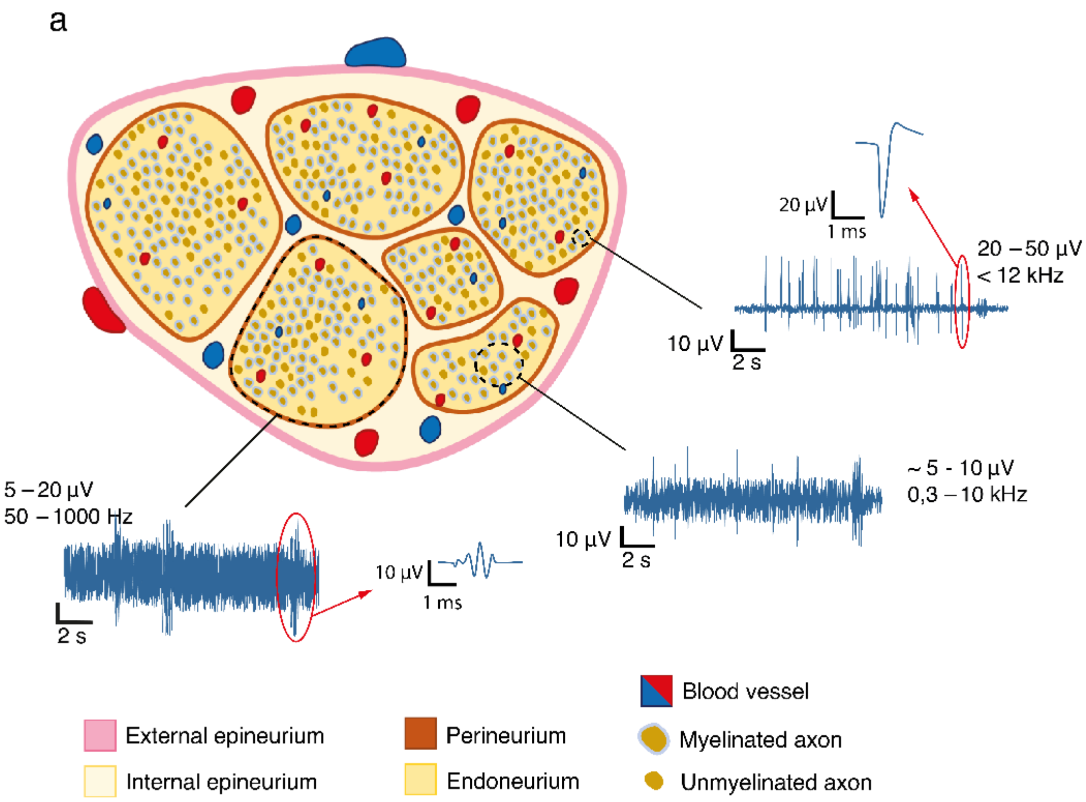
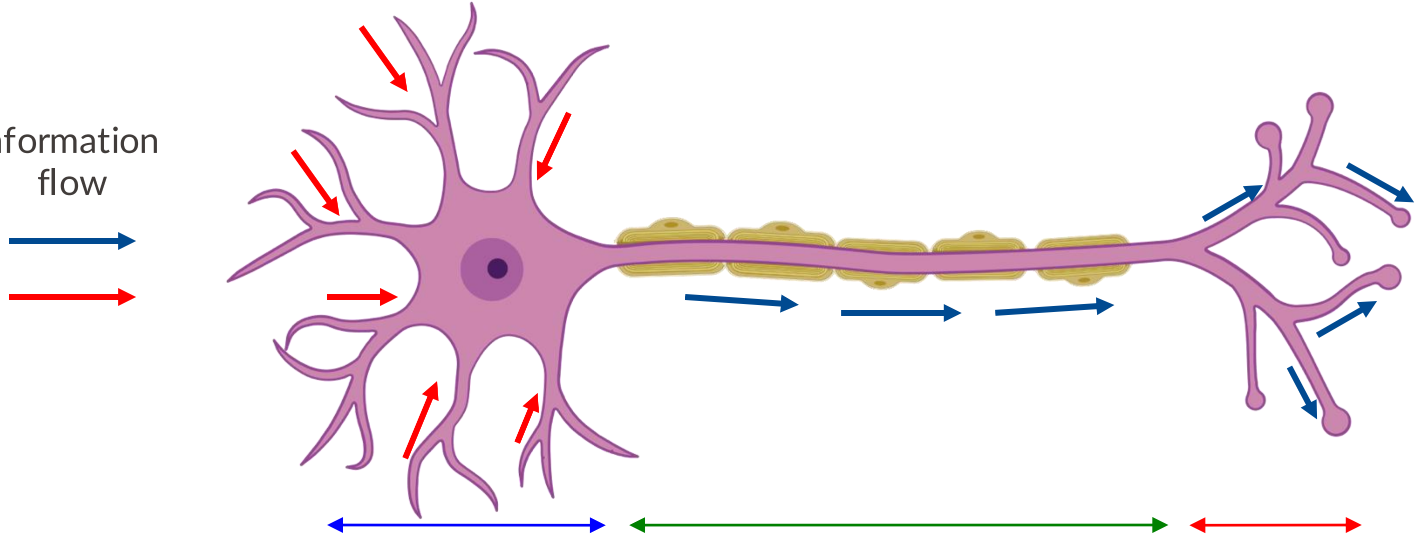
Neural signals from the peripheral nerve



v. Paggi, O. Akouissi et al., J. Neural Eng., 2020

The building block: the neuron

information flow

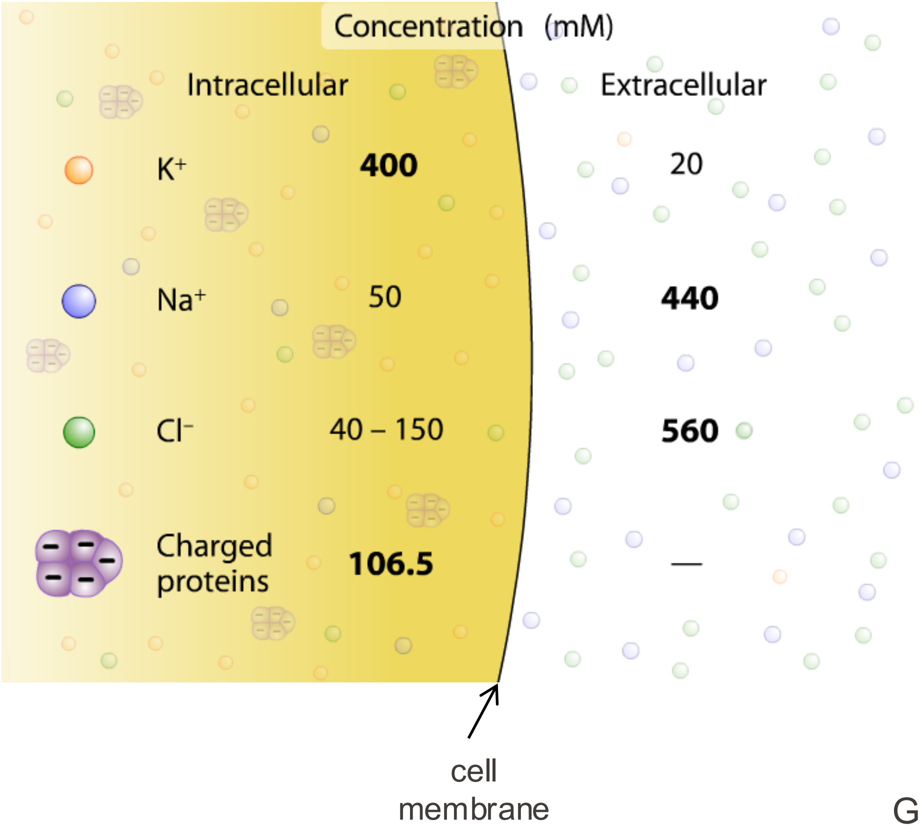


Cell body
a few 10µm in diameter

Axon
10sµm to 3m long;
0.2µm to 50µm dia.
unmyelinated or myelinated

Pre-synaptic terminals

Intra- and Extra-cellular media

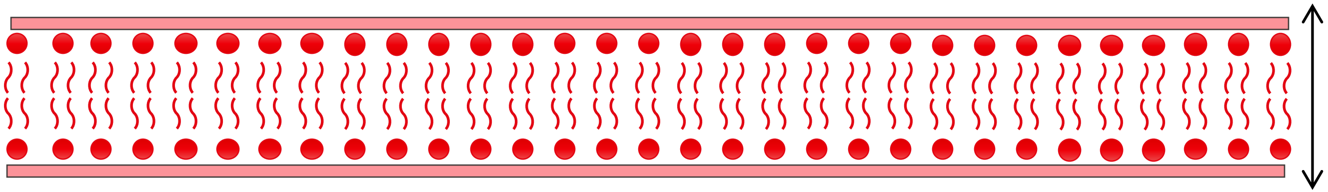


Giant axon of the squid

Neurosciences, D. Purves et al. Sylvius 4 Online

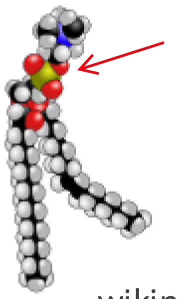
Membrane

extracellular medium



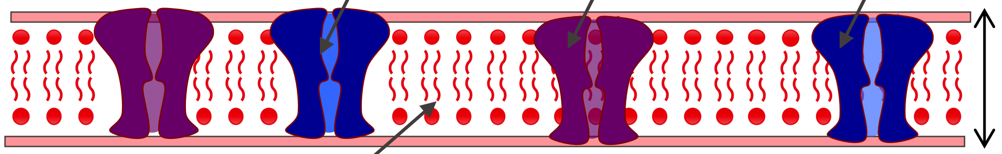
lipid bilayer

intracellular medium



wikipedia

Membrane



extracellular

K^+	5 mM
Na^+	145 mM
Cl^-	110 mM

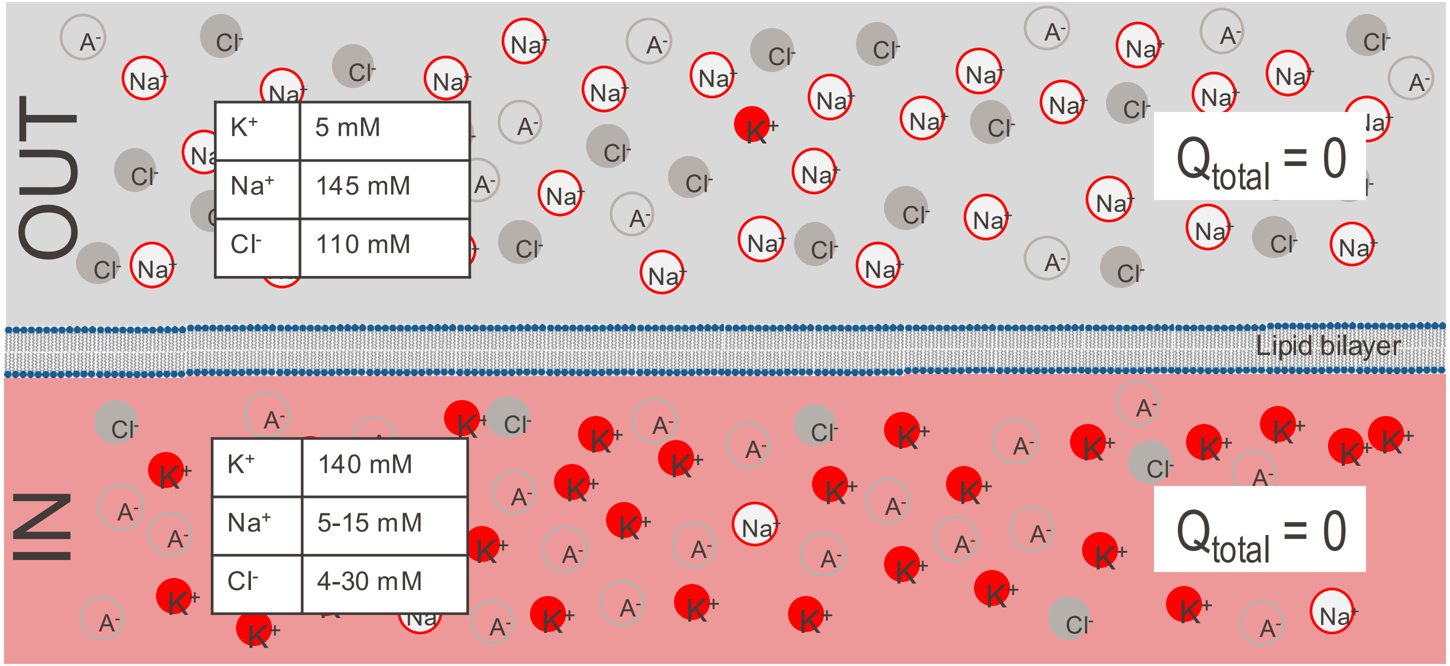
intracellular

K^+	**140** mM
Na^+	5-15 mM
Cl^-	4-30 mM

When the neuron is at rest, most ion channels are closed.

- High intracellular concentration of potassium
- Low intracellular concentration of sodium

Origin of the resting potential in neurons



K^+	5 mM
Na^+	145 mM
Cl^-	110 mM

K^+	140 mM
Na^+	5-15 mM
Cl^-	4-30 mM

- The membranes of neurons (and other cells) are polarized due to ionic concentration gradients.

Membrane potential V_m

- $V_m = V_{in} - V_{out}$

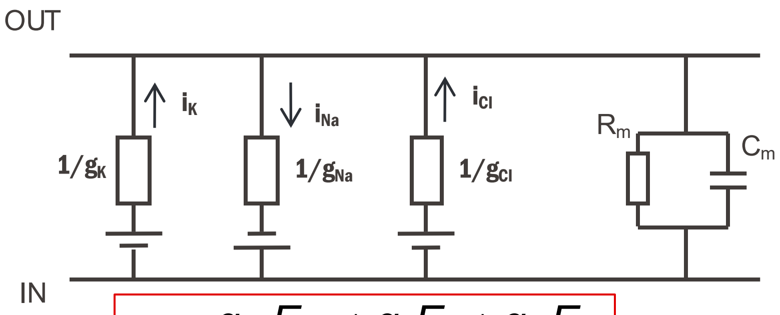
- **Nernst potential**: potential of an ion species of charge z across the membrane

  - $$E_{ion} = \frac{R\,T}{z\,F} \cdot \ln \frac{[ion]_{out}}{[ion]_{in}}$$

[ ] = ionic concentration (inside or outside of the cell)
R = ideal gas constant = 8.314 J/K*Mole
T = absolute temperature in K (37°C = 310K)
z = ion valence e.g. (Cl^-=-1, Ca^{2+}=+2, K^+=+1 etc…)
F = Faraday's constant 96'500 C/Mole

Electrical model for the neuronal membrane

g_x = ion conductance
E_x = Nernst potential
I_x = ion current
P_x = Permeability (Diff coeff. / thickness)



$$V_m = \frac{g_{Na}E_{Na} + g_K E_K + g_{Cl}E_{Cl}}{g_{Na} + g_K + g_{Cl}}$$

Goldman-Hodgkin–Katz voltage equation:

$$V_m = \frac{RT}{F} \ln \left(\frac{P_K[K^+]_{\text{out}} + P_{Na}[Na^+]_{\text{out}} + P_{Cl}[Cl^-]_{\text{in}}}{P_K[K^+]_{\text{in}} + P_{Na}[Na^+]_{\text{in}} + P_{Cl}[Cl^-]_{\text{out}}} \right).$$

- **Depolarization** of the membrane triggers channels opening. (Depolarization can be caused for example by a voltage/current pulse delivered via an electrode.)
- Channel opening 'creates' a **conductance** for ionic species, i.e. g_{K+} is a conductance mediated by K^+ ions, g_{Na+} is a conductance mediated by Na^+ ions.
- Conductances are **transient**.
- Transient conductances cause **transient changes in membrane potential** (these are called **Action Potentials**)

EPFL

K^+ potential
Na^+ potential

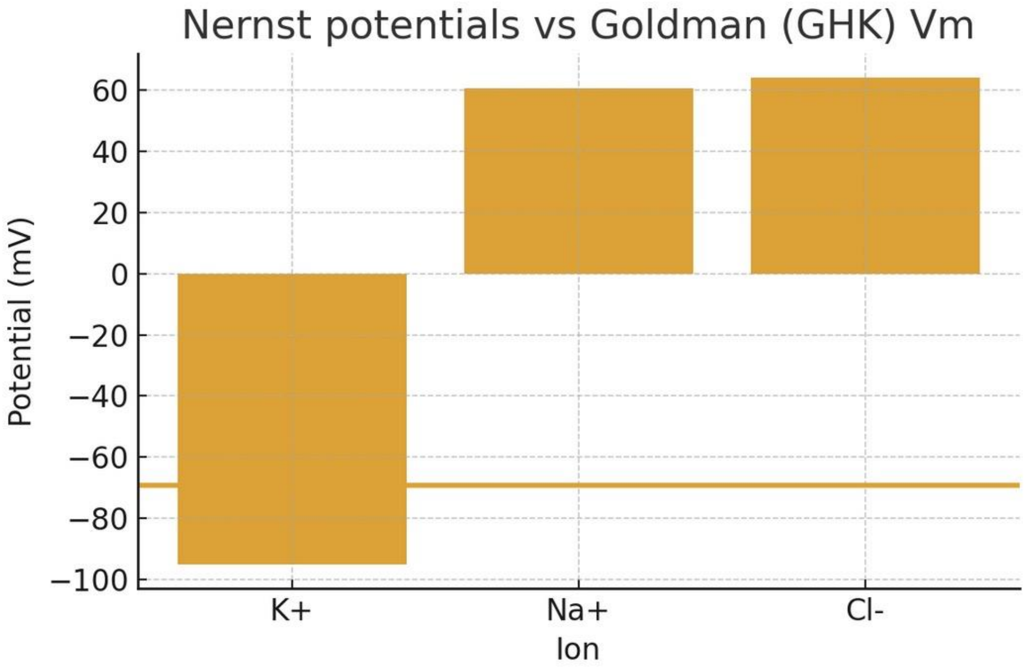
OUT

K^+	5 mM
Na^+	145 mM
Cl^-	110 mM

IN

K^+	140 mM
Na^+	5-15 mM
Cl^-	4-30 mM

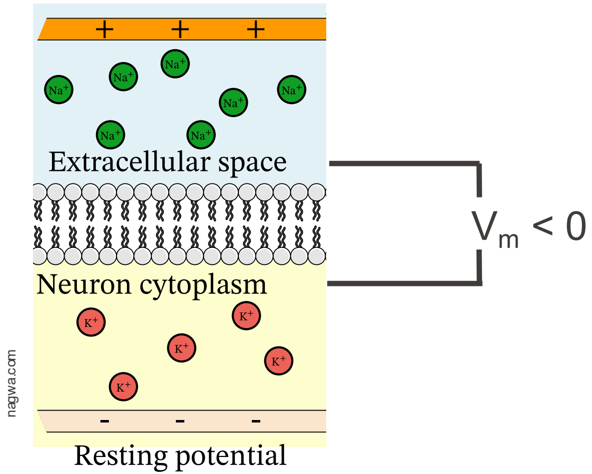
Try out the Nernst formula



Origin of the resting potential in neurons

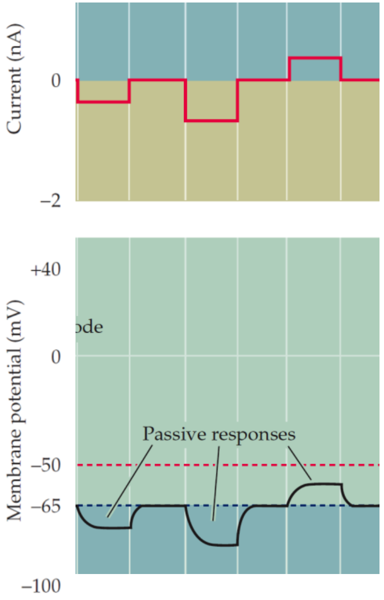
In the resting state, the membrane is permeable only (nearly) to K^+ therefore the resting membrane potential of neurons is close to the Nernst equilibrium for K^+.

The resting potential of a mammalian neuron is **-65mV.**



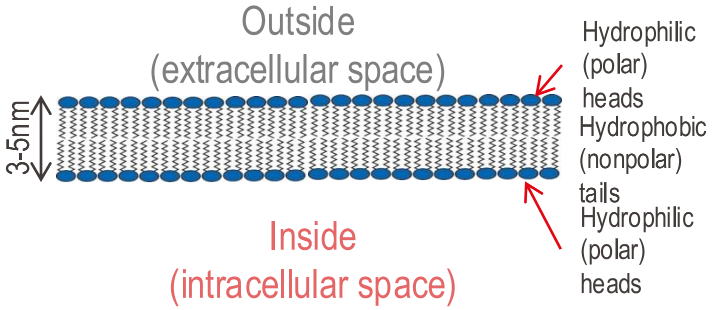
Cell types	Resting potential
Skeletal muscle cells	−95 mV
Smooth muscle cells	–60 mV
Astroglia	–80 to –90 mV
Neurons	–60 to –70 mV
Erythrocytes	–9 mV
Photoreceptor cells	–40 mV

Passive electrical properties of neurons

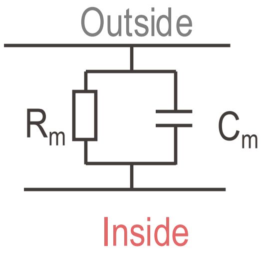


Membrane responses to hyperpolarizing and small depolarizing currents

The cell (neuron) membrane is a lipid bi-layer

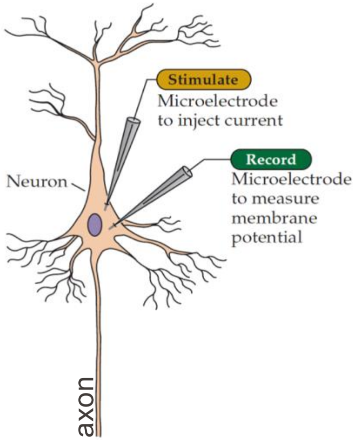


Electrical model of a cell (neuron) membrane

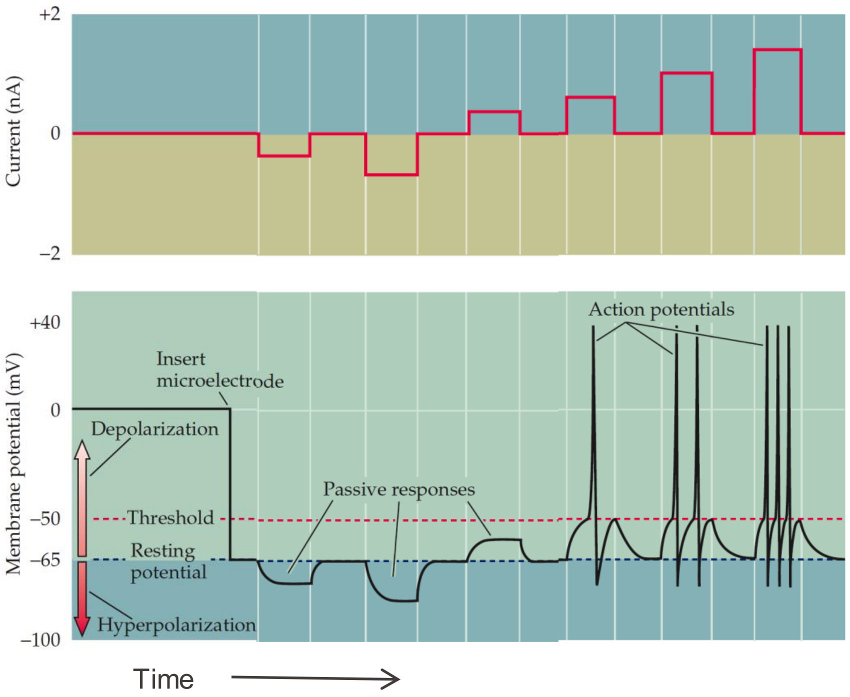


The passive electrical properties of a neuron are governed by the **membrane capacitance (C_m)** and **resistance (R_m)**

Passive electrical properties of neurons



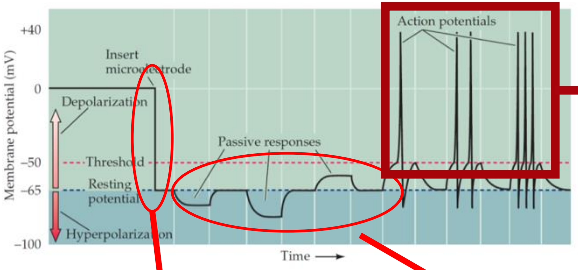
- At rest a neuron is negatively polarized with respect to the extracellular medium. **Resting potential ≈ -65mV.**



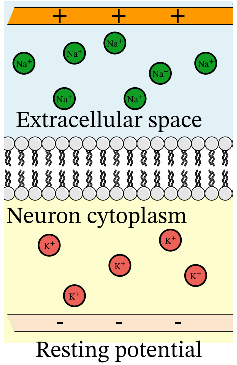
- **Hyperpolarizing current** induces only passive membrane responses.
- **Depolarizing currents** (of sufficient magnitude) trigger **action potentials** (APs).

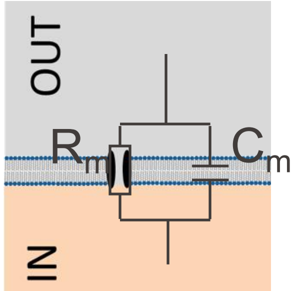
Neurosciences, D. Purves et al. Sylvius 4 (Third edition) p.33, available online

The action potential – active properties of neural cells



3. How are Action Potentials (APs) generated and what purpose do they serve?





1. **Cell membranes are polarized** (selective permeability)

2. **Passive** membrane properties determined by capacitance and leakage conductances

The action potential – active properties of neural cells

OUT

K^+	5 mM
Na^+	145 mM
Cl^-	110 mM

IN

K^+	140 mM
Na^+	5-15 mM
Cl^-	4-30 mM

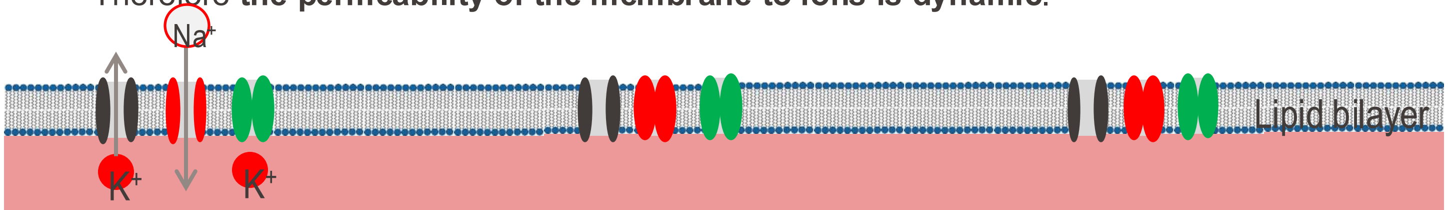
$$E_{ion} = \frac{R\,T}{z\,F} \cdot \ln \frac{[ion]_{out}}{[ion]_{in}}$$

Resting membrane potential = -65mV

What would happen if the membrane suddenly became permeable to Na^+?

Answer:
Na^+ would flow INTO the cell, the membrane will become depolarized. The cell membrane potential will 'spike' towards the Nernst equilibrium for Na^+

- The neuron membrane contains several types of ion selective channels.
- Some ion channels can act like valves (open=permeable or closed=non permeable).
- Their permeability is controlled by the membrane potential (transistor analogy).
- Therefore **the permeability of the membrane to ions is dynamic**.

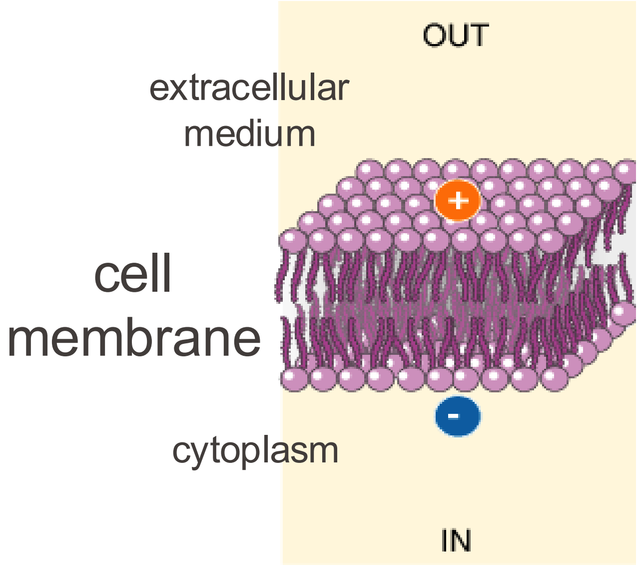


A closed K^+ voltage sensitive channel. Slow opening after local depolarization of membrane

An open voltage sensitive Na^+ channel. Fast opening is after local depolarization of membrane

A K^+ (leak) channel always open, sets up the resting potential

Membrane capacitance



Capacitance: $C = \varepsilon_0 \varepsilon_r A / d$ [μF]

(parallel plate, where A is the membrane area, d is the membrane thickness)

Capacitance per unit area: $C_m = C/A = \varepsilon_0 \varepsilon_r / d$ [$\mu F\ cm^{-2}$]

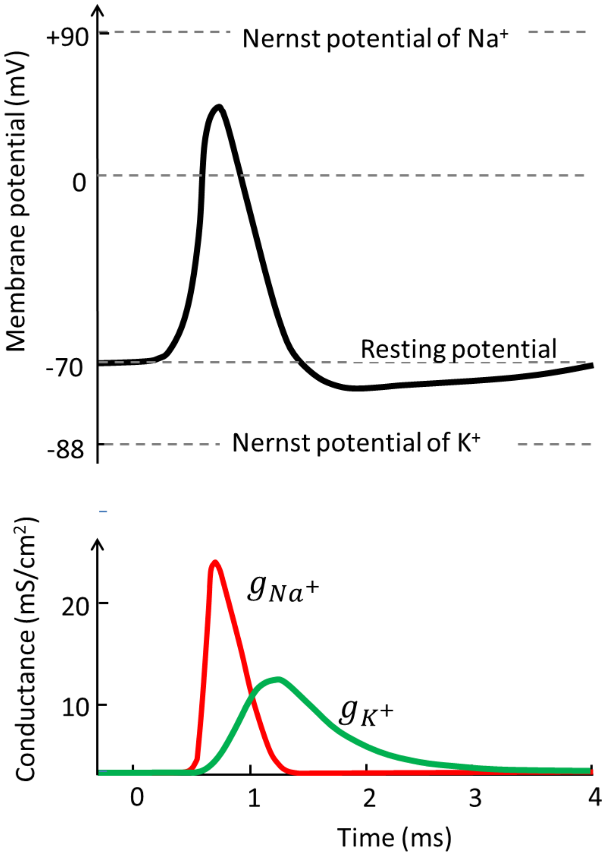
$C_m \sim 1 \mu F/cm^2$ for all nerve membranes

For an axon of diameter ***a*** and length ***L***:

$C = \varepsilon_0 \varepsilon_r 2\pi aL / d = 2\pi aL C_m$ [μF]

Capacitance per unit length: $c_m = C/L = 2\pi a C_m$ [$\mu F\ cm^{-1}$]

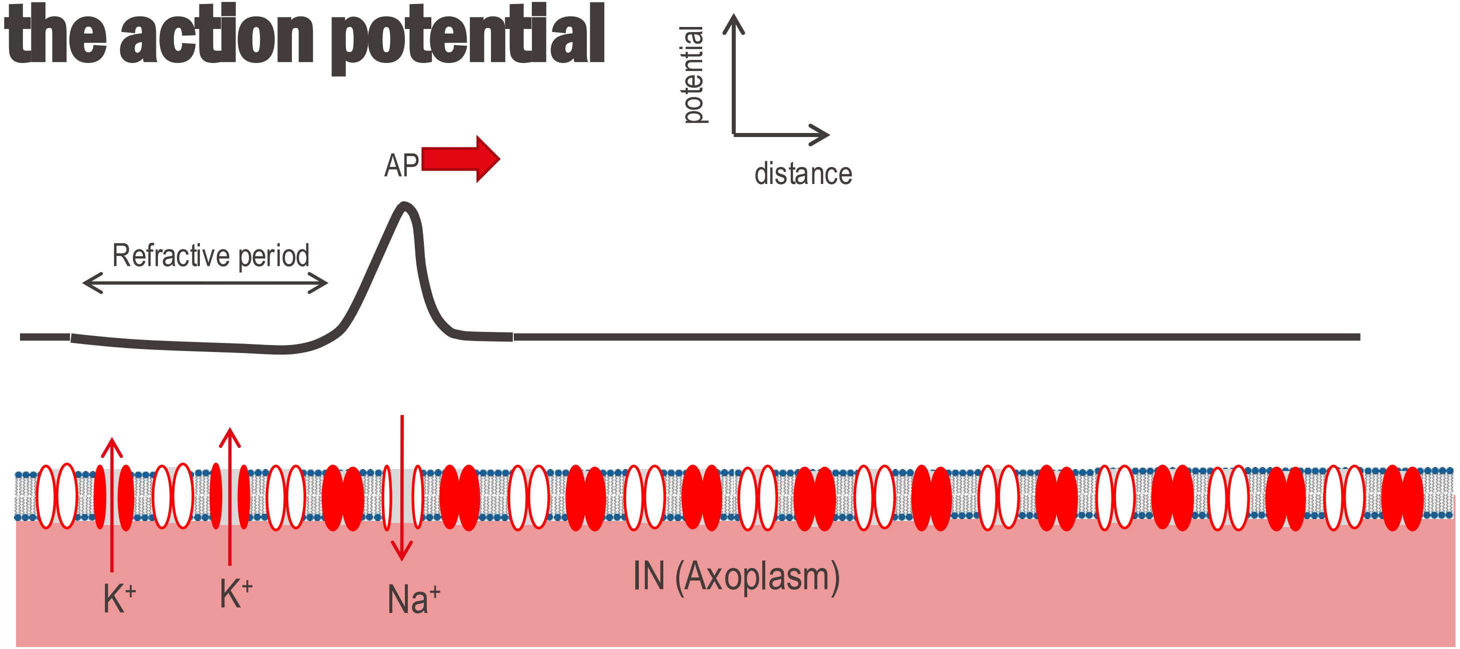
Time evolution of the Action Potential



1. Local depolarization of the neuron membrane is triggered.
2. Na^+ rushes into the cell (down concentration gradient). This is called the 'fast sodium current'.
3. Voltage sensitive K^+ channel open causing K^+ to flow out of the cell. This is called the 'delayed rectifier potassium current'.
4. The membrane potential first swings to the Na^+ Nernst potential but as the Na^+ conductance decreases and K^+ conductance increases, the cell membrane is repolarized.

The AP lasts approximately 1ms.

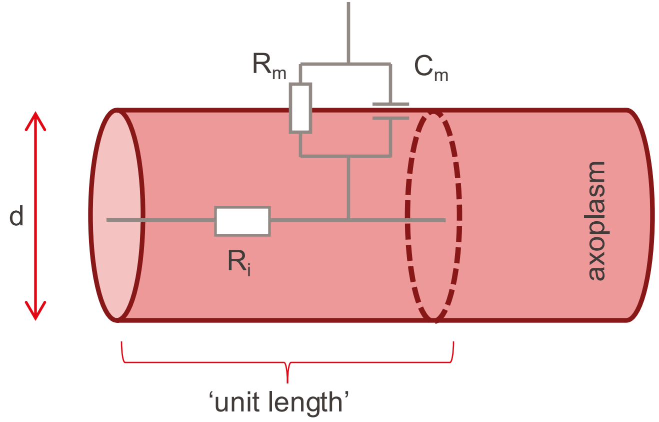
Spatial propagation of the action potential



- The AP travels along the membrane by successively depolarizing adjacent patches of membrane.
- Magnitude and duration of AP are fixed (i.e. no half amplitude or duration AP)
- The refractive period ensures the AP travels one way only
- What about the speed of propagation?

AP velocity is limited by the passive properties of axons

$$R_m = \pi\, d\, l\, r_m \qquad r_m \approx 1-20\, k\Omega / cm^2$$



Membrane capacitance (i.e. Farads per unit area):

$$C_m = \pi\, d\, l\, c_m \qquad c_m \approx 1\, \mu F / cm^2$$

Membrane conductance (i.e. Siemens per unit area):

$$G_m = \pi dl\, g_m \qquad g_m = 0.01 - 1\, mS\, cm^{-2}$$

Axoplasm resistance (i.e. Ohms):

$$R_i = \frac{4\, l\, \rho_i}{\pi\, d^2} \qquad \rho_i \approx 1\, k\Omega .cm$$

Length constant of a fiber (distance over which the potential falls by 1/e):

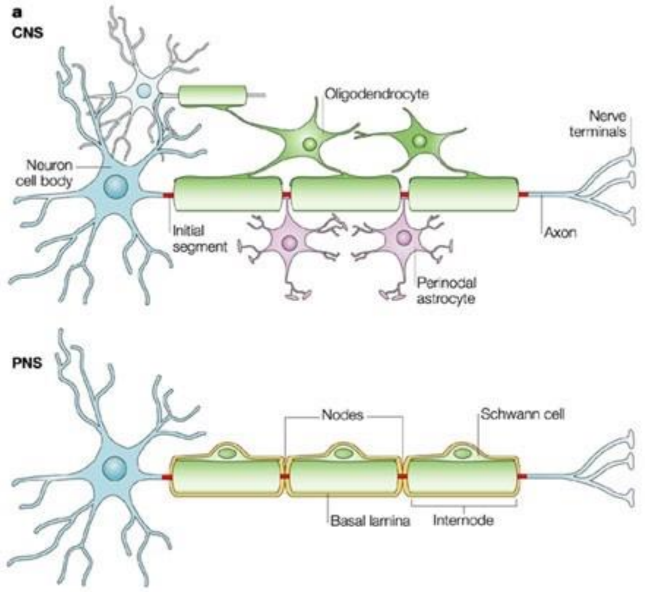
$$\lambda = \sqrt{\frac{d\, R_m}{4\, R_i}}$$

Velocity of AP propagation

$$velocity \propto \lambda / \tau_m$$

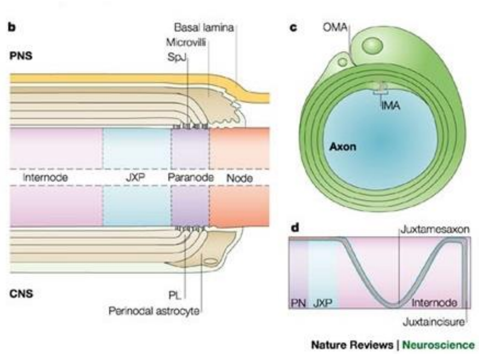
Time constant across the membrane: $\tau_m = R_m\, C_m$

Myelin



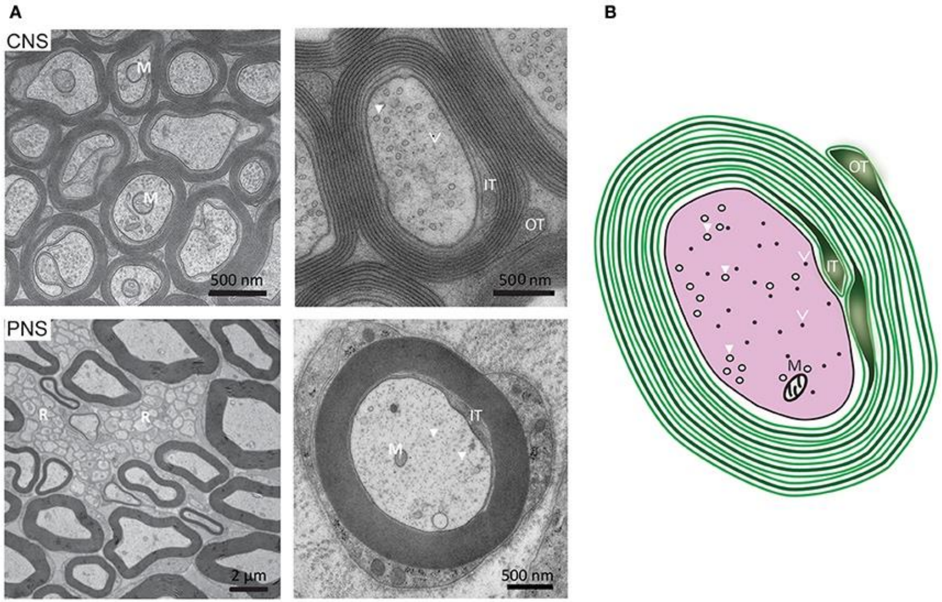
Myelin produced by **oligodendrocytes** (CNS) and **Schwann cells** (PNS)

spirally wrapped myelin sheath



Nature Reviews Neuroscience **volume 4**, pages 968–980 (2003)

Myelin



Myelin produced by oligodendrocytes (CNS) and Schwann cells (PNS)

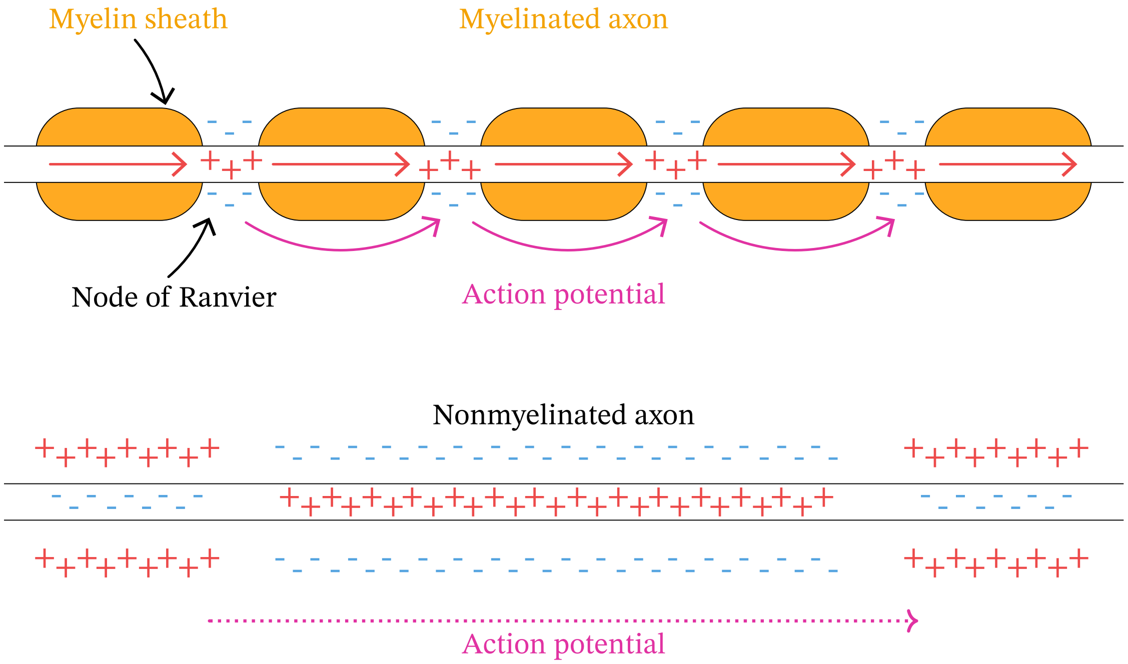
spirally wrapped myelin sheath

Electrically insulating sheath

Front. Neurosci., 11 July 2018 | https://doi.org/10.3389/fnins.2018.00467

Nodes of Ranvier

Rich in Na^{+} channels – crucial for Action potential conduction (saltatory conduction)

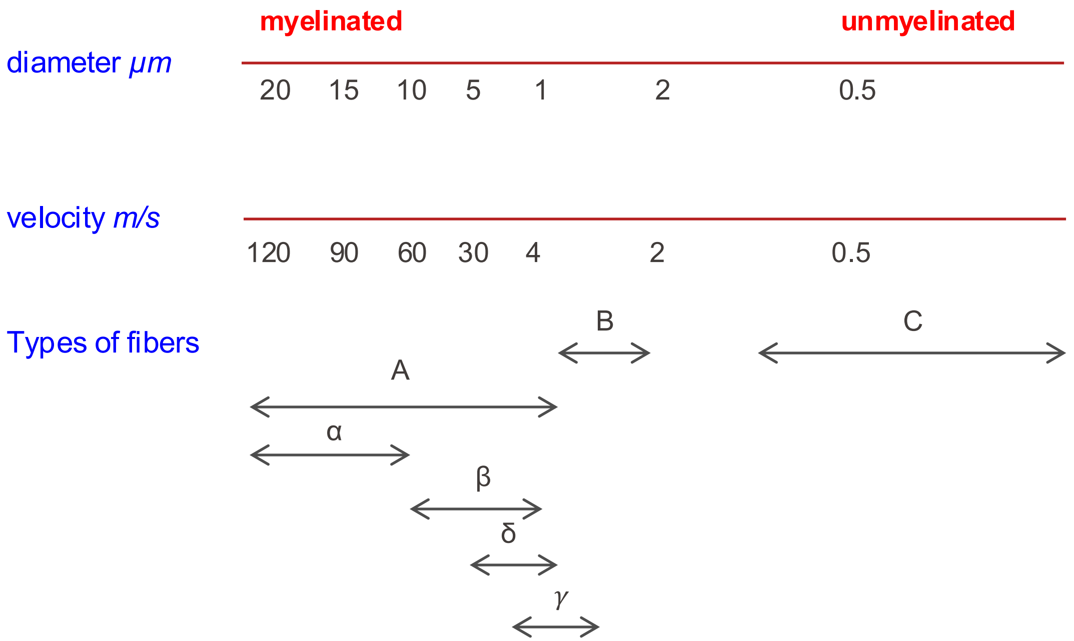


Conduction velocity of fiber types

Large diameter axons are faster (squid d=1mm, needed for fast response).

Decreasing C_m (membrane capacitance) also increases the transmission velocity.

Nature's solution is myelin (a fatty sheath wrapped around neurons).



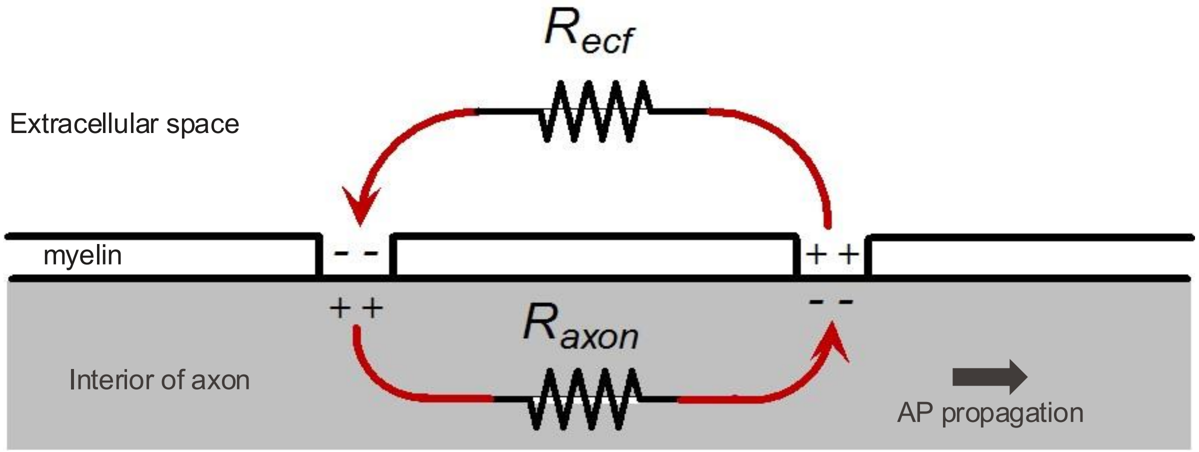
Take-home messages

- **Resting potential**:
  - concentrations of Na^+ and K^+ ions across an axon's membrane
  - maintained by the sodium–potassium pump and "leak" channels.
- **Action potential**: an all-or-nothing action
  - depolarization,
  - repolarization, hyperpolarization,
  - a refractory period
- **Speed of transmission** of an action potential
  - axon diameter
  - myelination of the neuron

In vivo

- The interface with the neurons is done **extracellularly**
  - record electrical signals using electrodes **in close proximity** to neural tissue
  - stimulate/modulate neural activity through electrical, chemical or optical neural stimulation

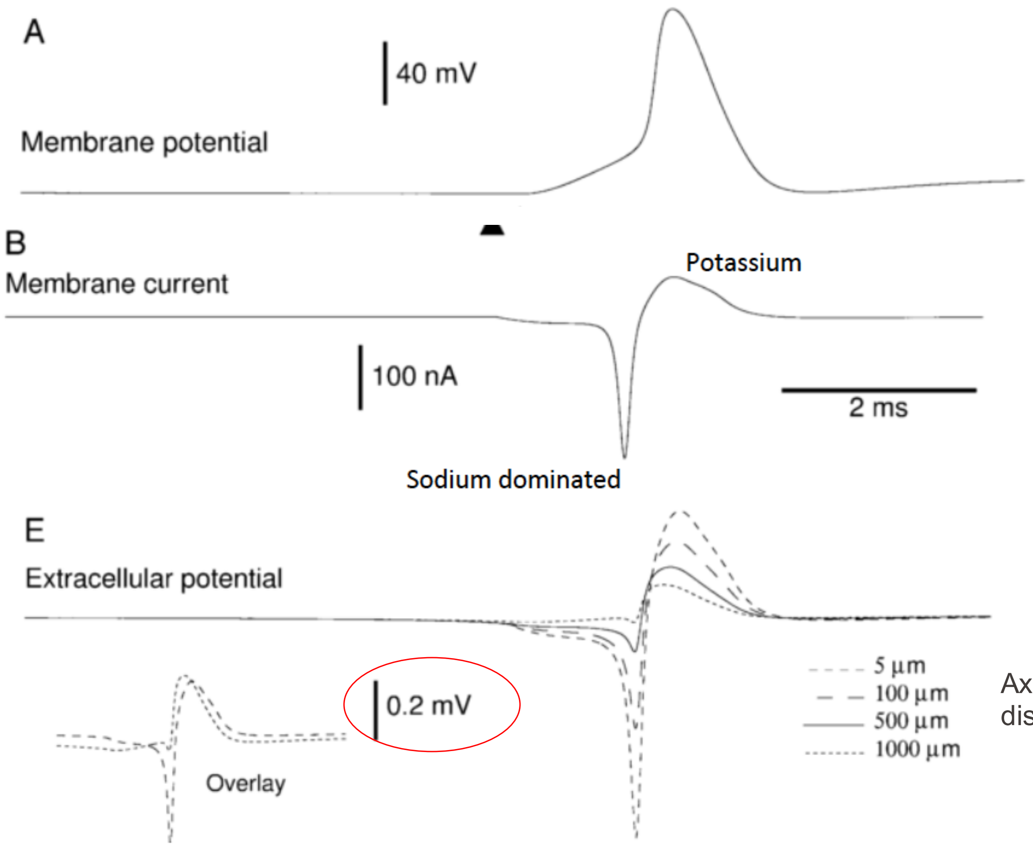
Extracellular signals are small…



$$\frac{\delta V_{out}}{\delta V_{in}} = -\frac{R_{ecf}}{R_{axon}} \quad with \; R_{axon} >> R_{ecf}$$

Recordable signals: ~5μV – 100sμV

Extracellular signals are small indeed!



Axon-electrode distance

Zooming out

Electrocorticography ECoG

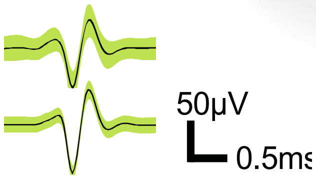
0.01 – 5 mV, < 200 Hz

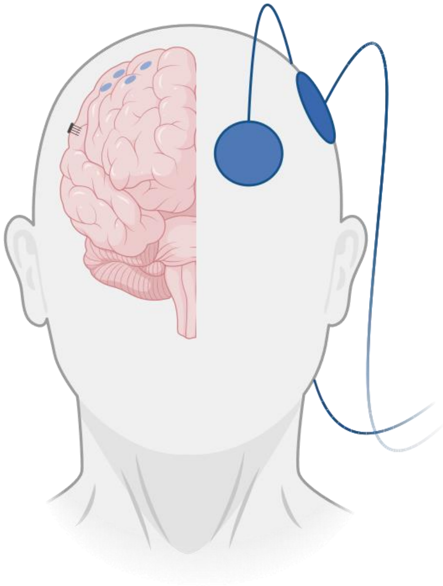
Local field potentials LFP

<1 mV, < 200 Hz

Action potentials Spikes

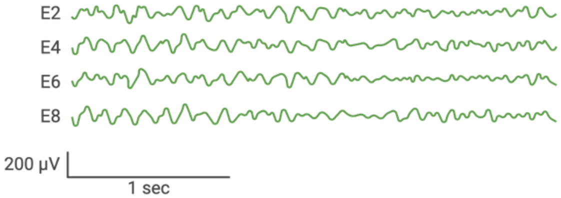
- ~ 500 µV, 0.5 – 5 kHz





Electroencephalography EEG

5 – 300 µV, < 100 Hz



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Important notions related to the design of a neural electrode

- **Position** of the electrodes
  - Far (cm-scale) or very close (µm-scale) to the electrogenic cell(s)

- **Size** of the electrodes
  - Large(cm-scale) or small (µm-scale) compared to the electrogenic cell(s)

- Select the **type** of electrophysiological signals