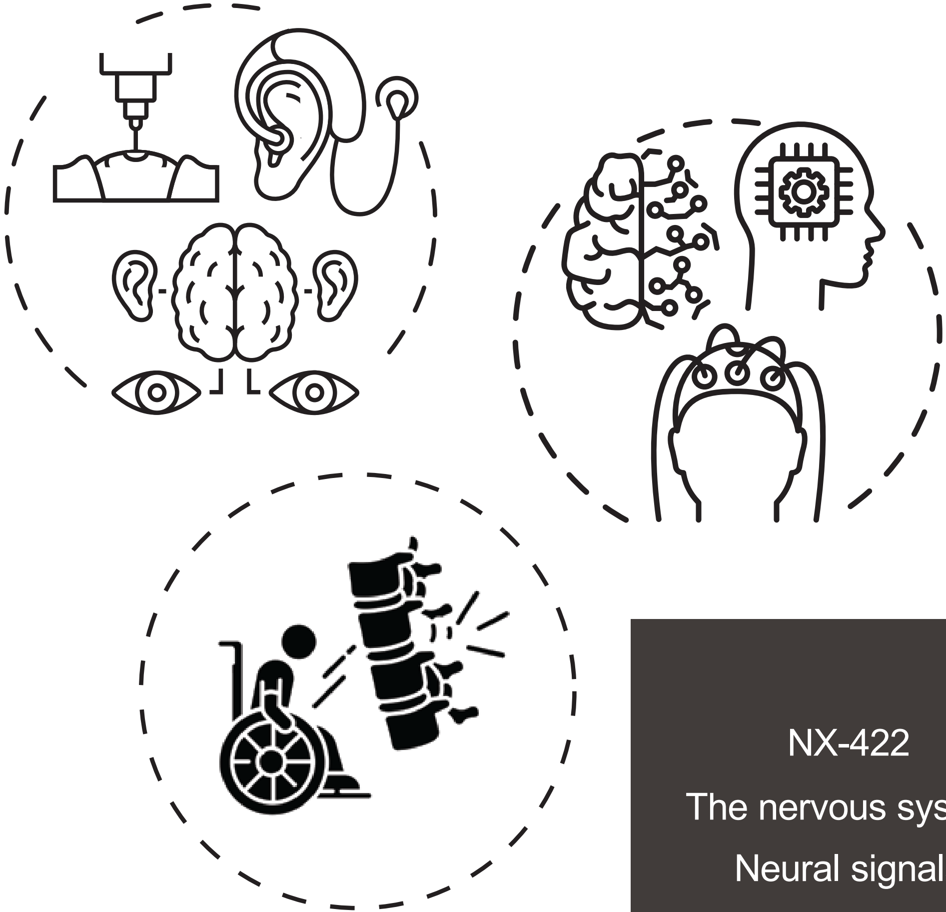
EPFL



Neural Interfaces

NX-422

The nervous system

Neural signals

Stéphanie P. Lacour

Neuro-X Institute

Neural signals

Electrocorticography **ECoG**

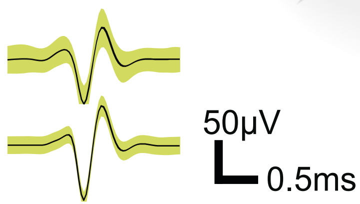
0.01 – 5 mV, < 200 Hz

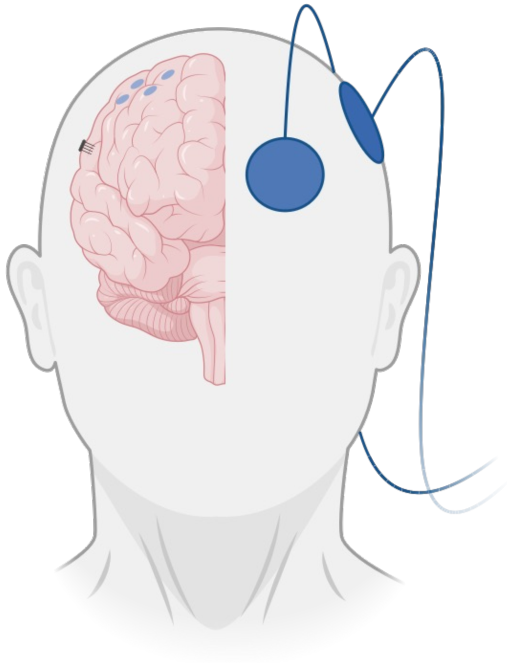
Local field potentials **LFP**

<1 mV, < 200 Hz

Action potentials **Spikes**

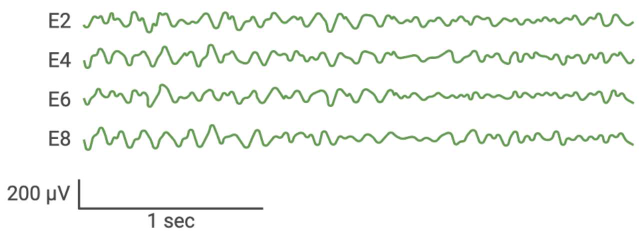
- ~ 500 µV, 0.5 – 5 kHz





Electroencephalography **EEG**

5 – 300 µV, < 100 Hz



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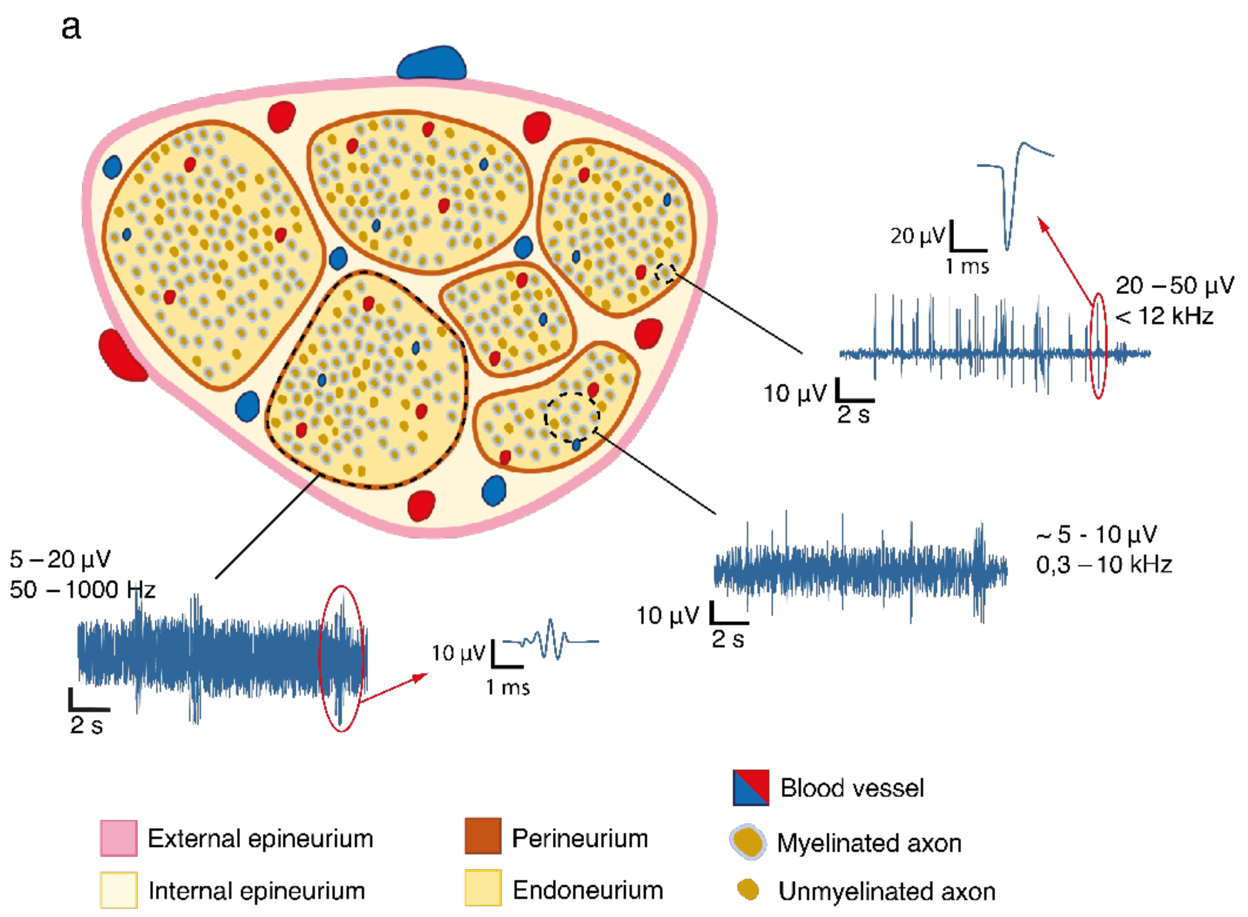
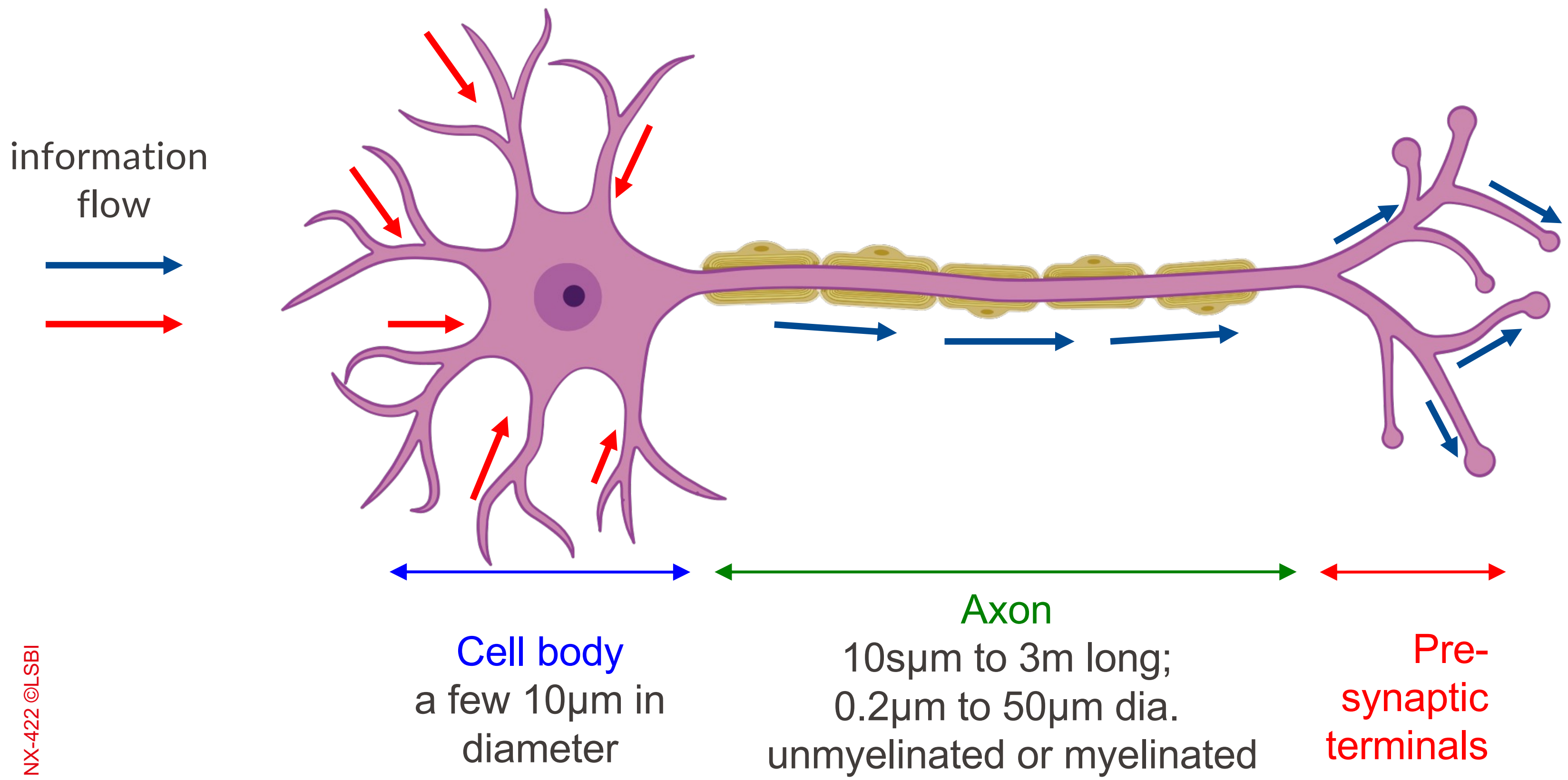
Neural signals from the peripheral nerve

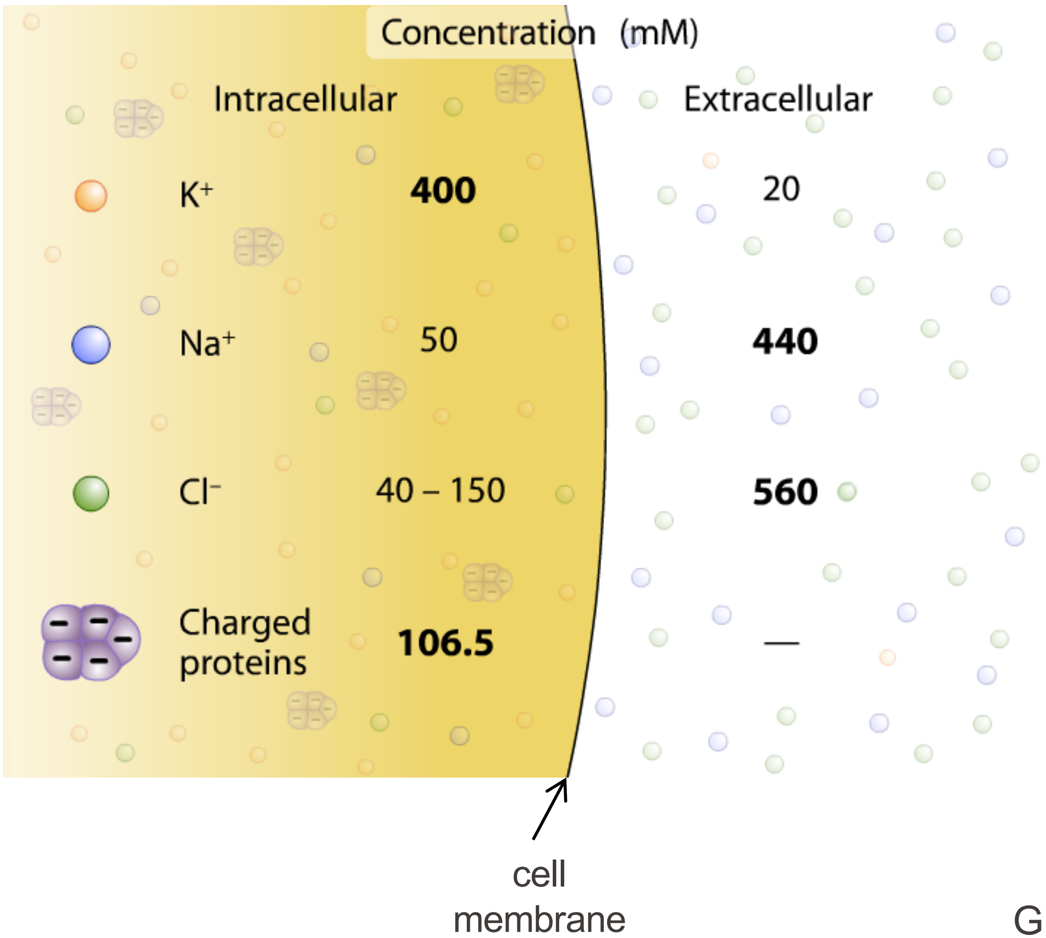


v. Paggi, O. Akouissi et al., J. Neural Eng., 2020 i

The building block: the neuron



Intra- and Extra-cellular media

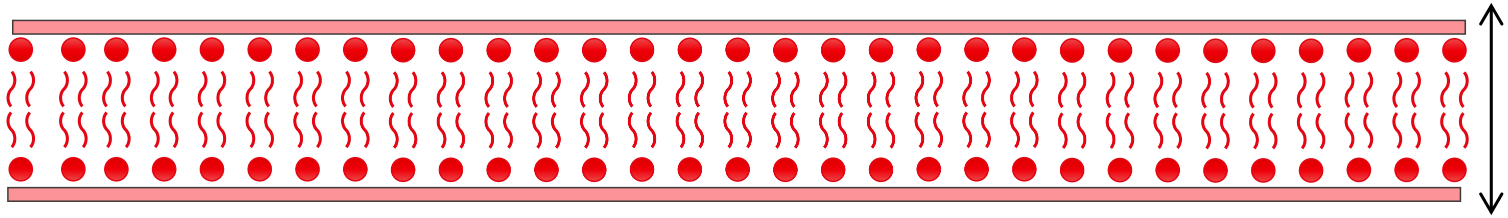


Giant axon of the squid

Neurosciences, D. Purves et al. Sylvius 4 Online

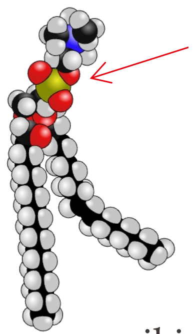
Membrane

extracellular medium



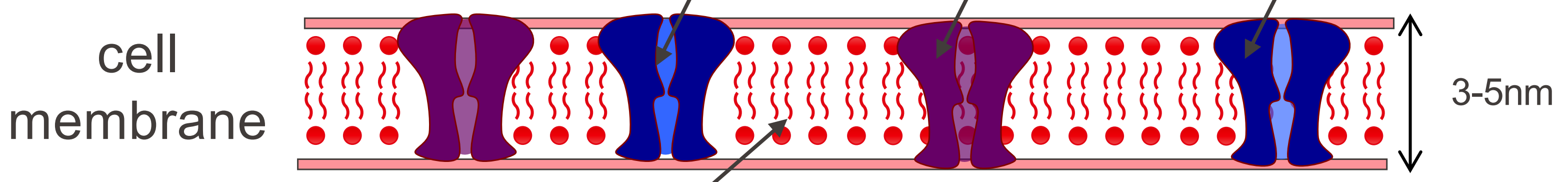
lipid bilayer

intracellular medium



wikipedia

Membrane



extracellular

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

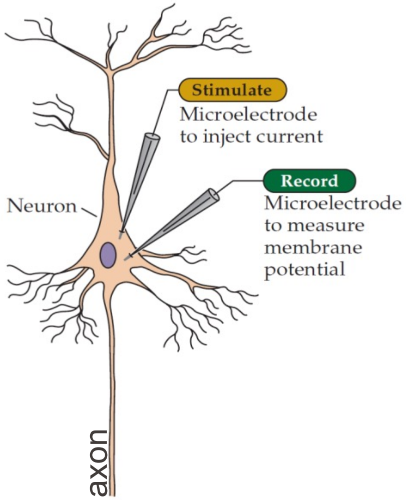
intracellular

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

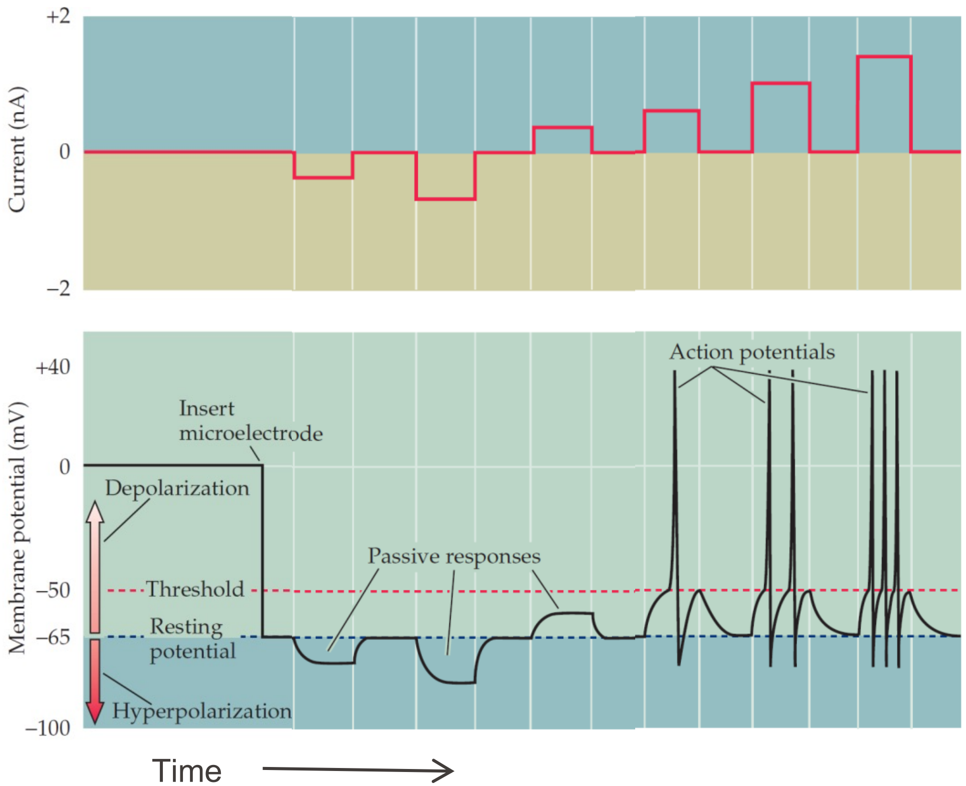
When the neuron is at rest, most ion channels are closed.

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

Passive electrical properties of neurons



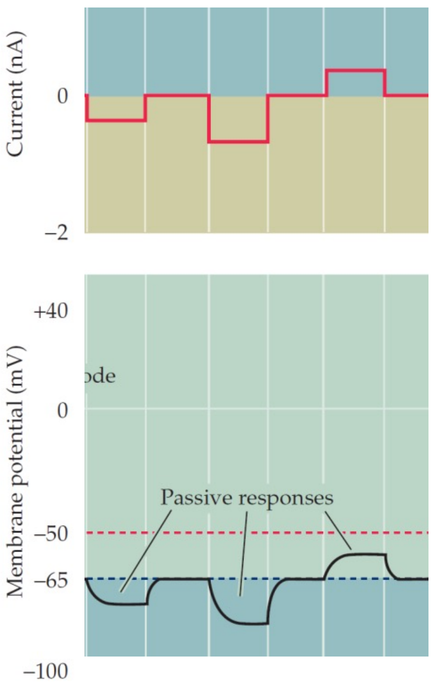
- At rest a neuron is negatively polarized with respect to the extracellular medium. **Resting potential ≈ -65mV.**



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

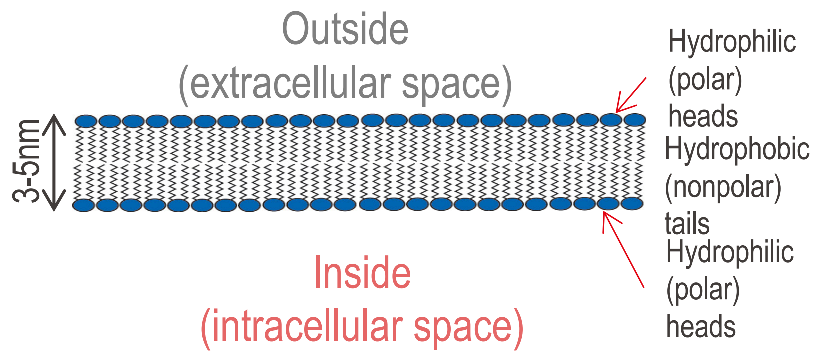
Neurosciences, D. Purves et al. Sylvius 4 (Third edition) p.33, available online

Passive electrical properties of neurons

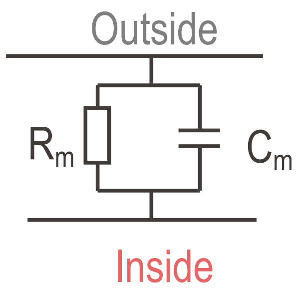


Membrane responses to hyperpolarizing and small depolarizing currents

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

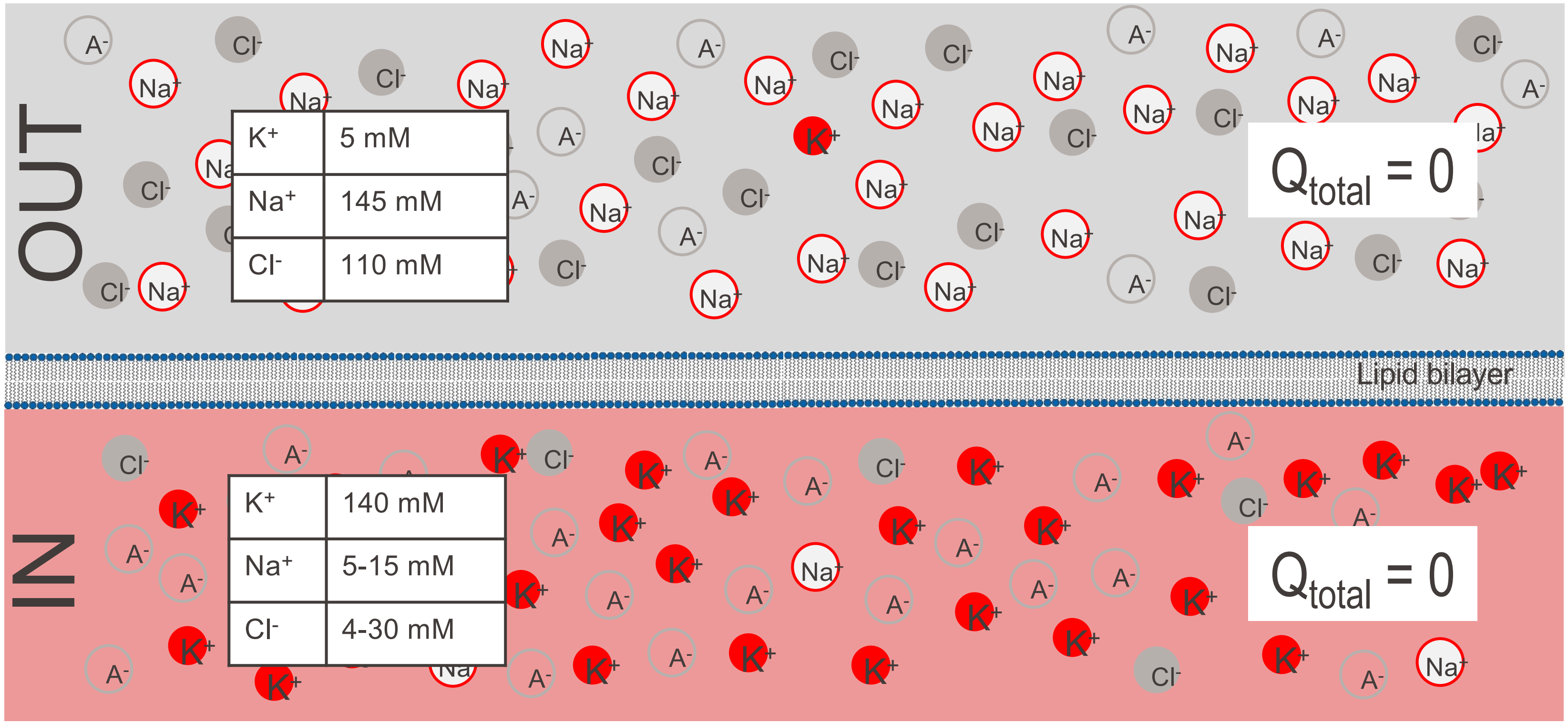


Electrical model of a cell (neuron) membrane



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

Origin of the resting potential in neurons



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

Membrane potential V_m

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

- **Nernst potential**: potential of an ion 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

K^+ potential
Na^+ potential

OUT

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

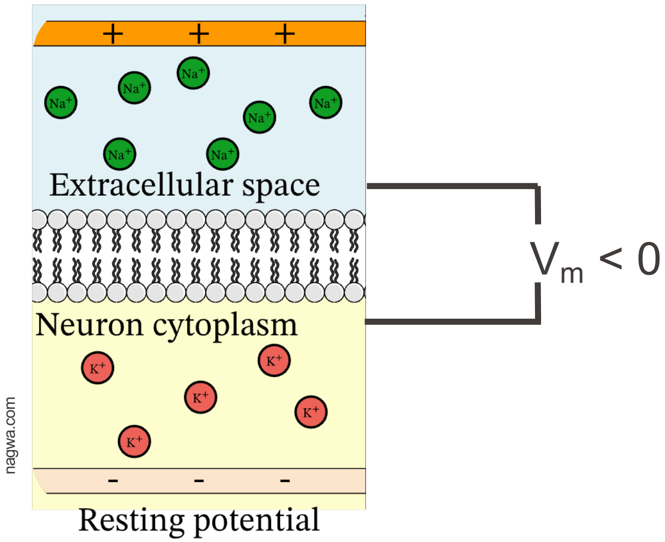
IN

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

Origin of the resting potential in neurons

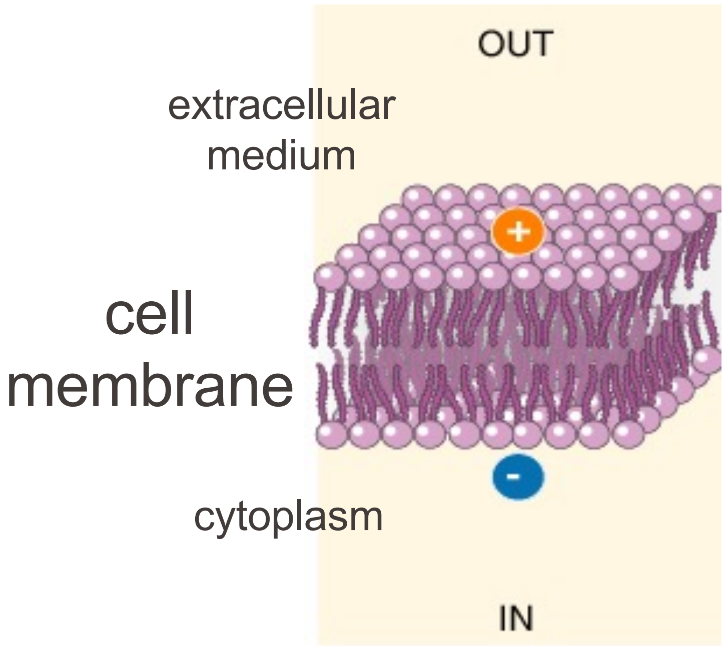
In the resting state, the membrane is permeable only (nearly) to K^+ therefore the resting membrane potential of neurons is close to the Nernst equilibrium for K^+.

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

Membrane capacitance



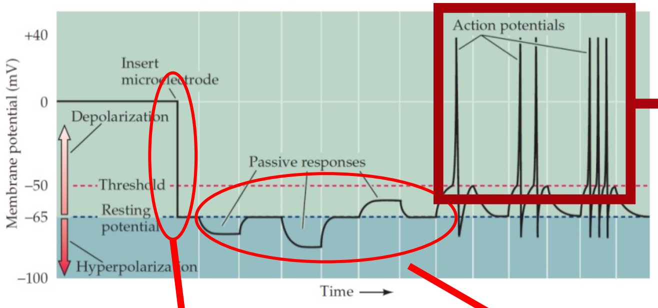
$$c_m = \frac{Q}{V_m} \ in \ \mu F / cm$$

$$C_m = 2\pi a c_m \ in \ \mu F / cm^2$$

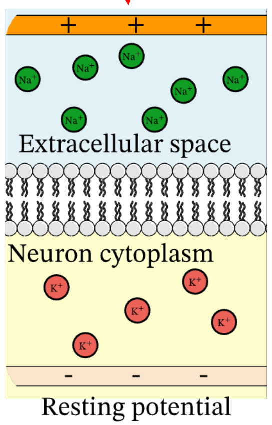
a: axon diameter
c_m: per unit length

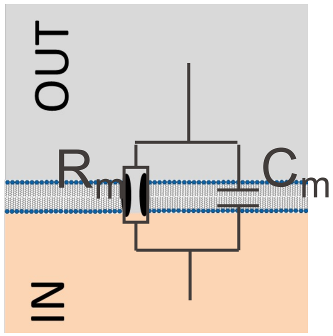
$C_m \sim 1 \mu F/cm^2$ for all nerve membranes

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

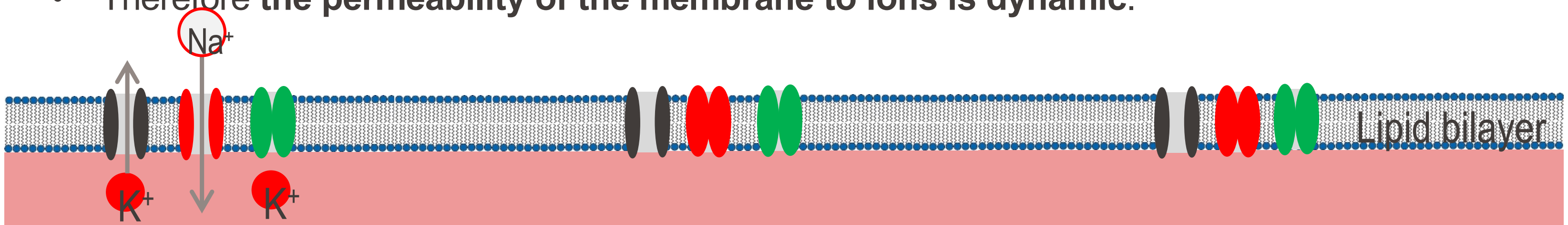
$$E_{ion} = \frac{R\,T}{z\,F} \cdot \ln \frac{[ion]_{out}}{[ion]_{in}}$$

Resting membrane potential = -65mV

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

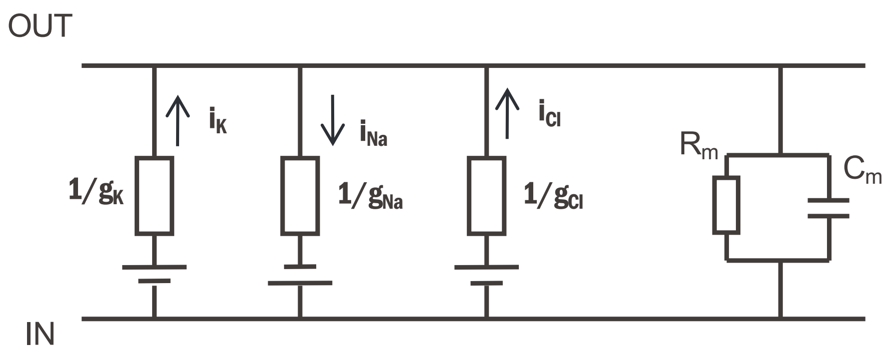
Answer:
Na^+ would flow INTO the cell, the membrane will become depolarized. The cell membrane potential will 'spike' towards the Nernst equilibrium for Na^+

- 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

Electrical model for the neuronal membrane

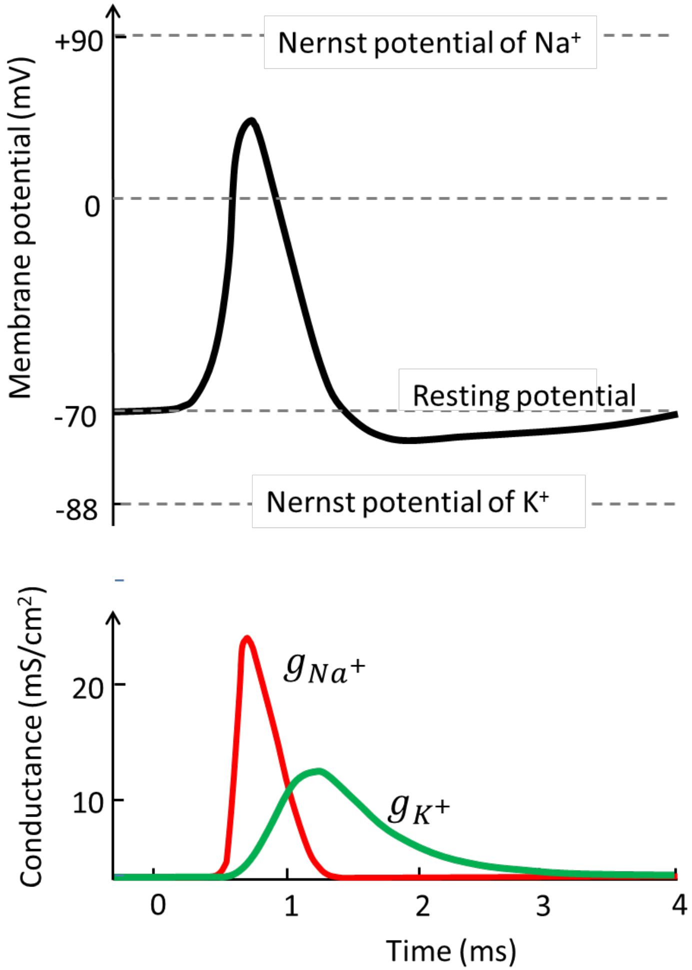


g_x = ion conductance
E_x = Nernst potential
I_x = ion current

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

- **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**)

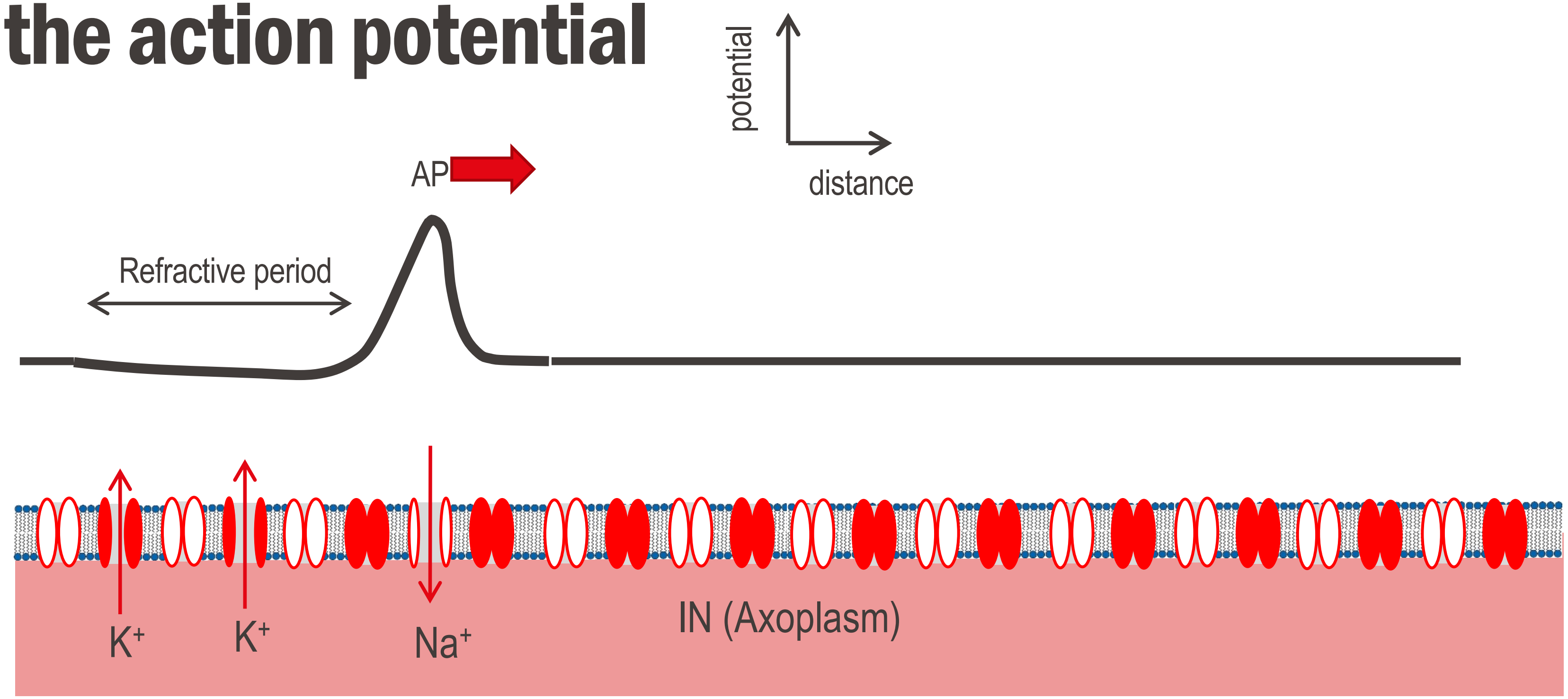
Time evolution of the Action Potential



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.

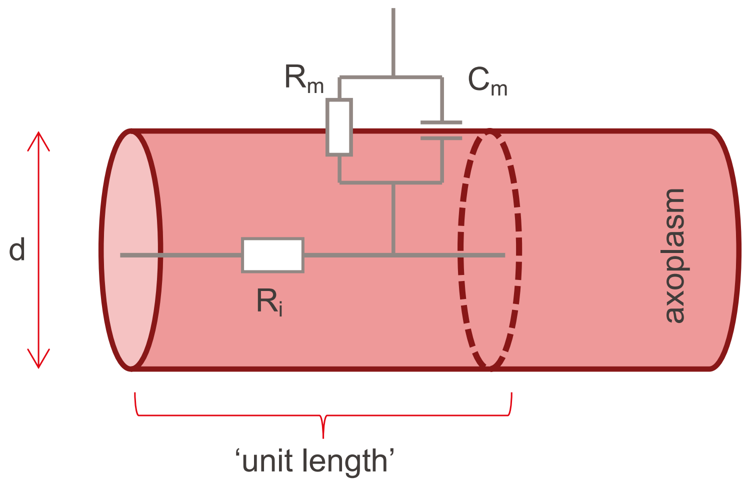
The AP lasts approximately 1ms.

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



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

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

Transmembrane resistance (i.e. Ohms):

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

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):

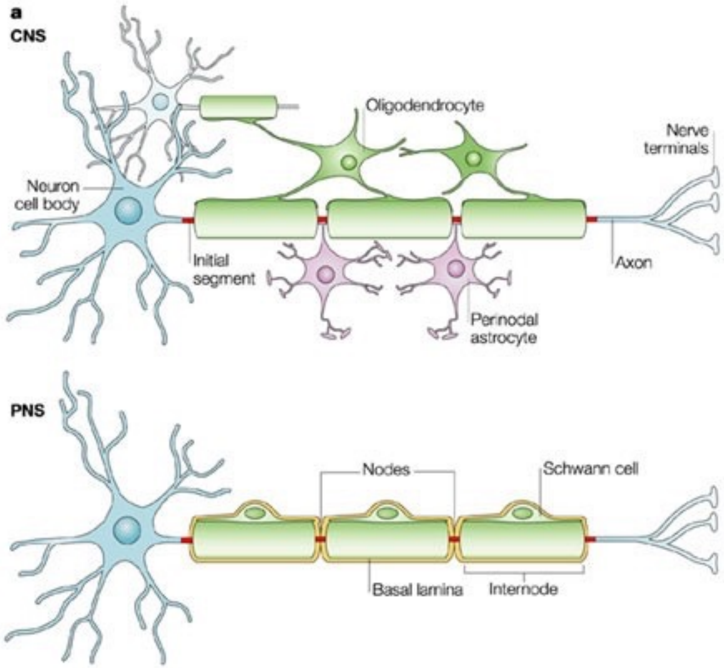
$$\lambda = \sqrt{\frac{d\, R_m}{4\, R_i}}$$

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

Velocity of AP propagation

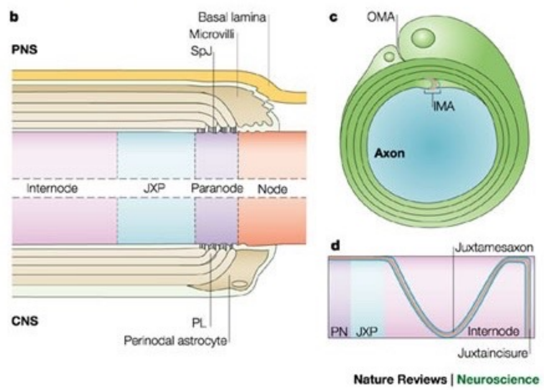
$$velocity \propto \lambda / \tau_m$$

Myelin



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

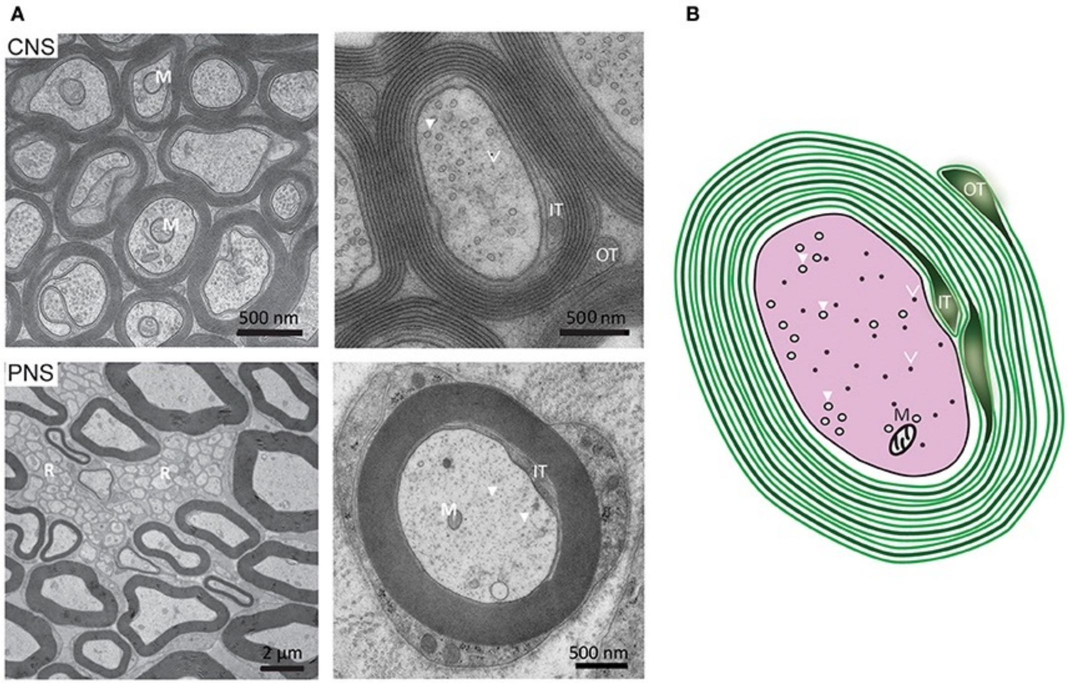
spirally wrapped myelin sheath



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

EPFL

Myelin



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

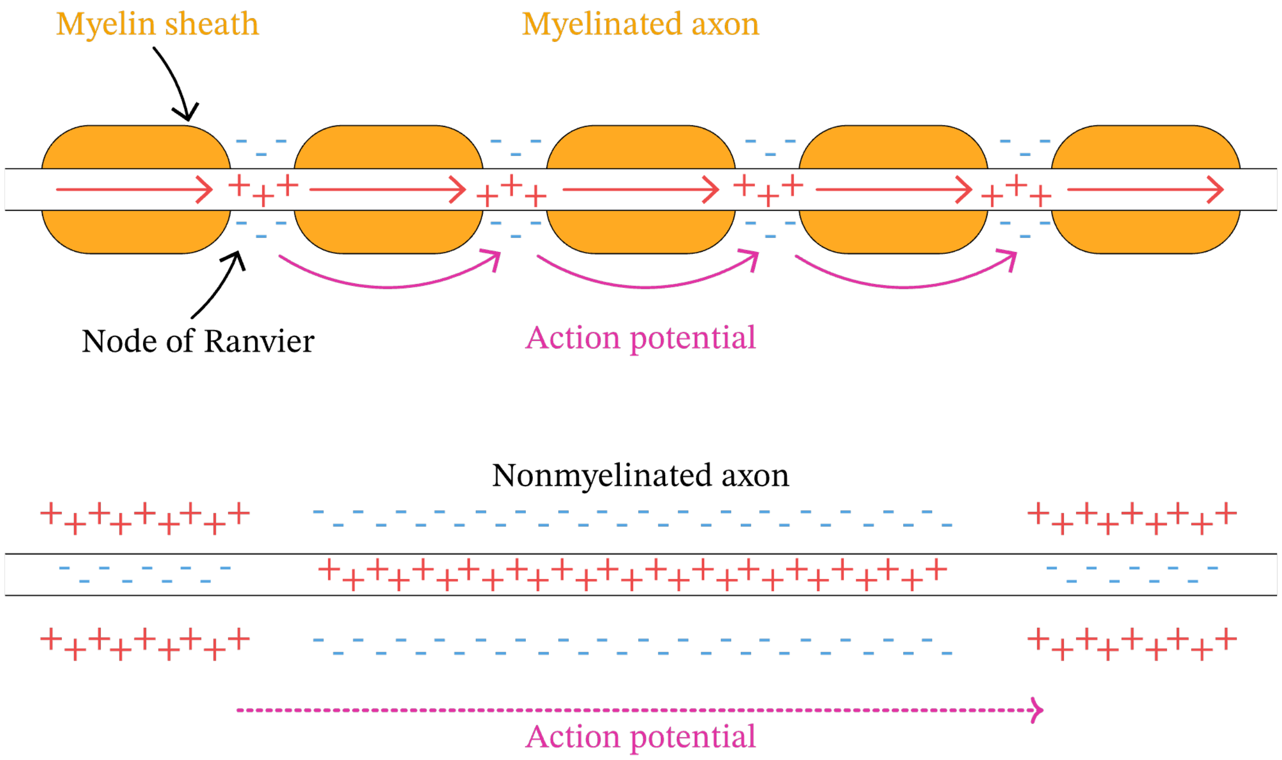
spirally wrapped myelin sheath

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

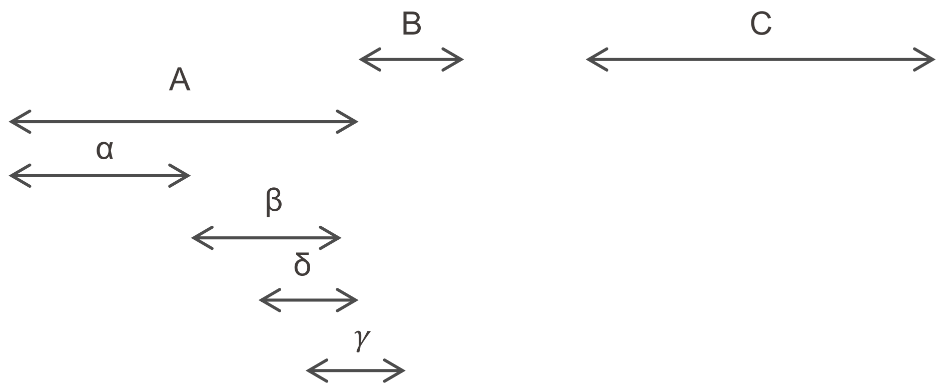
Large diameter axons are faster (squid d=1mm, needed for fast response).

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

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

	myelinated						unmyelinated
diameter *μm*	20	15	10	5	1	2	0.5
velocity *m/s*	120	90	60	30	4	2	0.5

Types of fibers



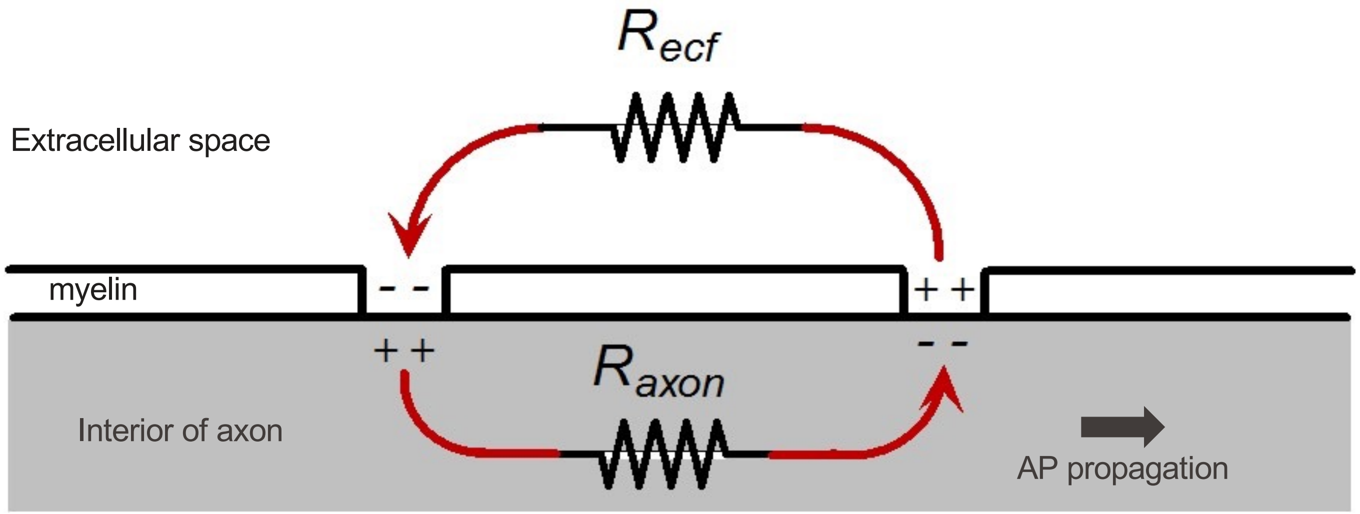
Take-home messages

- **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

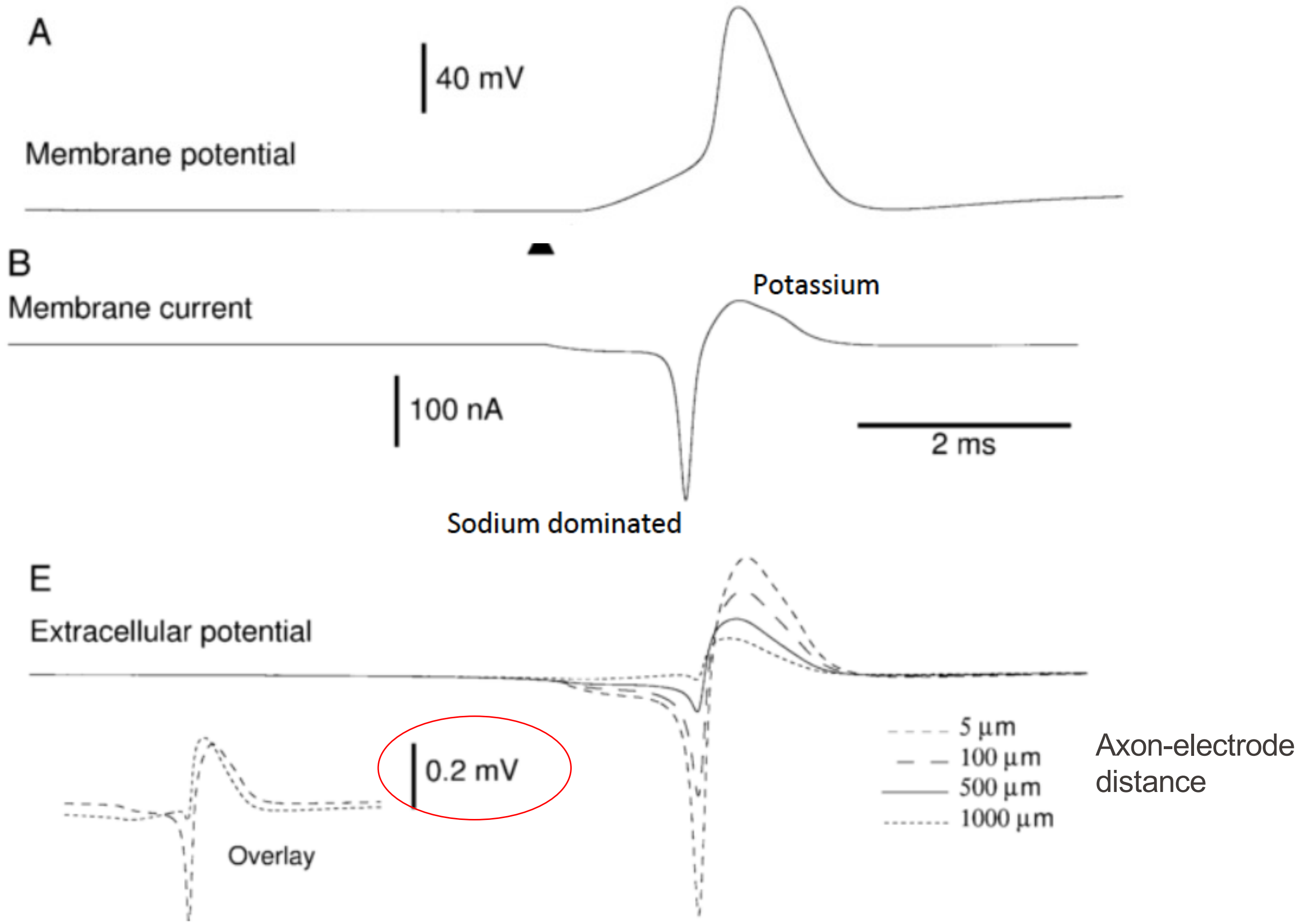
Extracellular signals are small…



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

Recordable signals: ~5μV – 100sμV

Extracellular signals are small indeed!



Zooming out

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<1 mV, < 200 Hz

Action potentials **Spikes**

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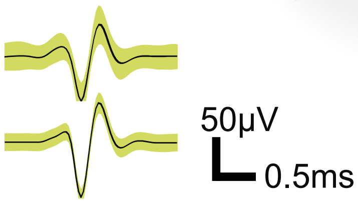

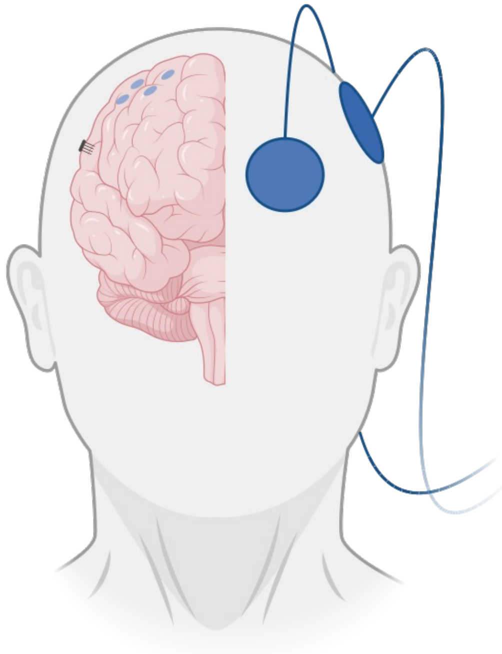

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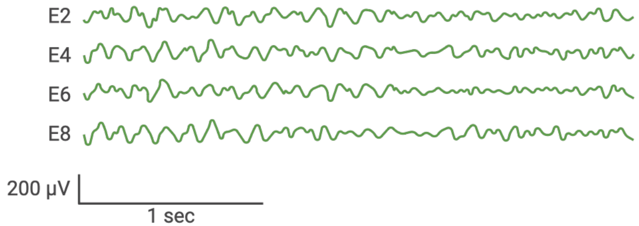

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Important notions related to the design of a neural electrode

- **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