AA 2024-25

Molecular Neurophysiology, 9 CFU, **code: 2fkf8x6**

Synaptic transmission in CNS, 4 CFU

Marina Sciancalepore (3CFU) and Giada Cellot (1 CFU)
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Signal transduction, 3 CFU

Paola Lorenzon

Synaptic transmission in PNS, 2 CFU

Annalisa Bernareggi

Tutorial Andrew Constanti

A preliminary course of 8h will be dedicated to reviewing notions of
Cellular Physiology of excitable cells

- Electrical membrane properties
- Voltage-gated Na^+ channels
- Transmitters and receptors

Synaptic transmission in CNS

- Electrophysiological properties of excitable cells
- Ion channels and firing properties
- Chemical & electrical synapses
- Central synapses
- Neuronal interactions
- Synaptic plasticity
- Neural networks

Suggested readings

Chapters of excellent texts:

- Principles of neuronal science, **Kandel**.
Cap. *Cell and Molecular Biology of the Neuron*

•Ion Channels of Excitable Membranes, **Hille**, Cap. 1- 5, III Ed.

•Fundamental Neuroscience. Squire et al., Cap. 6-9, 11, 37, III Ed.

- ppt files and selected papers in Moodle 2, course code: SM75972SV-2 or 972SV
- password: Calcium2024 (up to February 2025)
- recorded lectures (available offline on Teams platform)

Lectures and tutorial activities.

Examination

Written test (multiple-choice) on topics covered during the course.

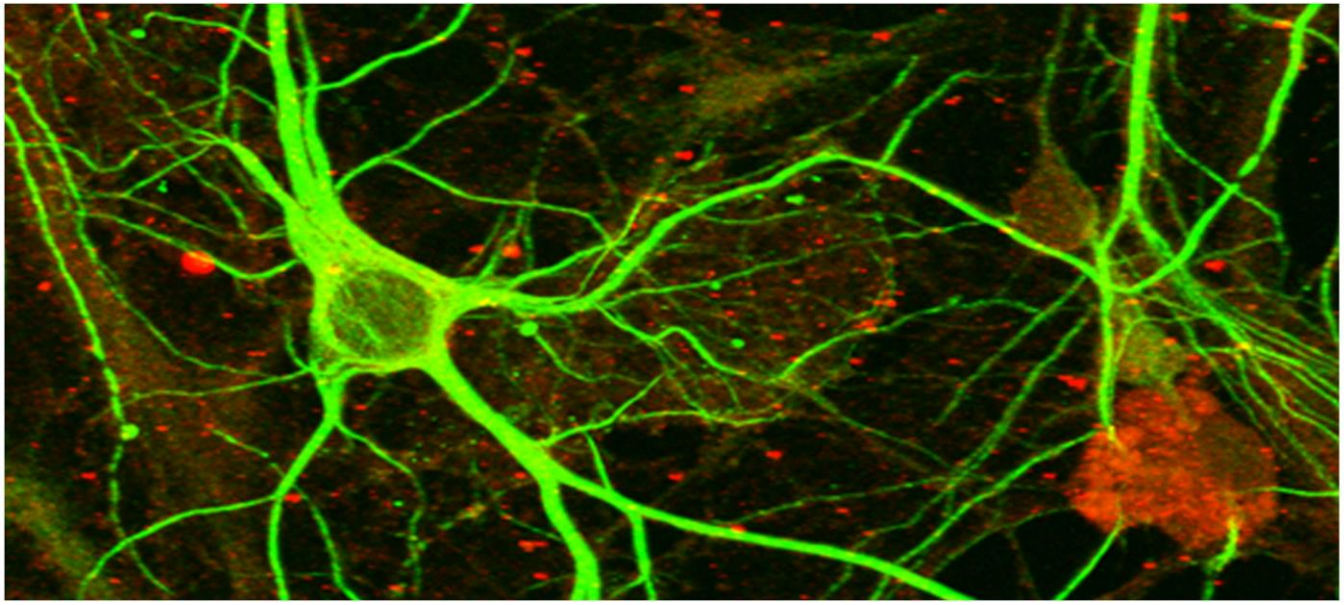
The test consists of 30 questions (10 for each part of the course).
The time limit for writing the test is 35 minutes.

The written test is passed if the total is ≥ 18/30.

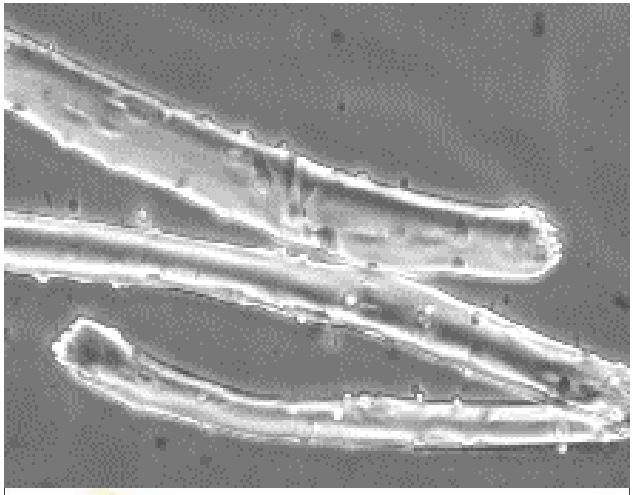
Facebook private group, students since 2004

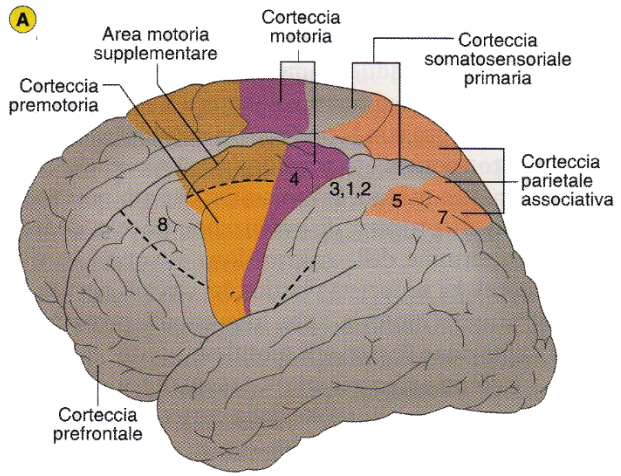
Int. Master in Neuroscience UniTS

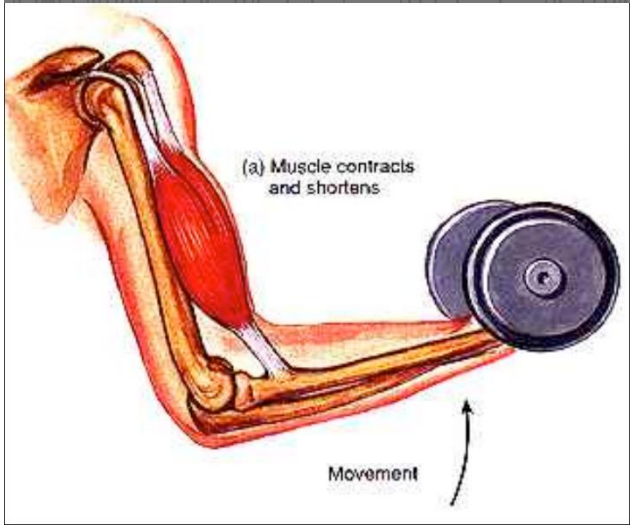
Administrator : Marina Sciancalepore



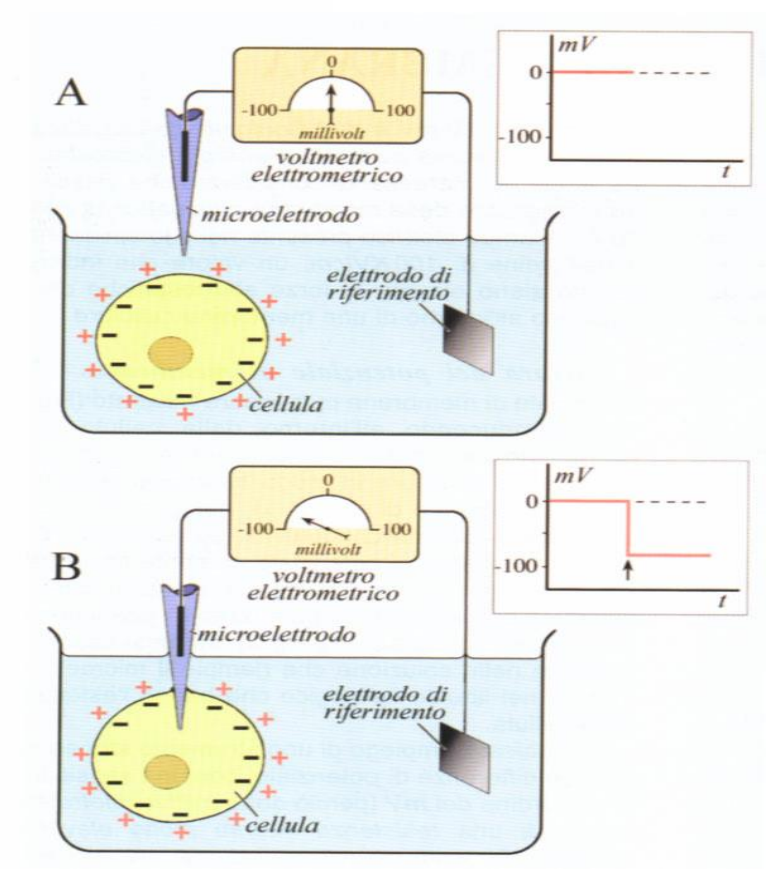
Neurons and muscle cells are electrically excitable they generate and conduct electrical signals



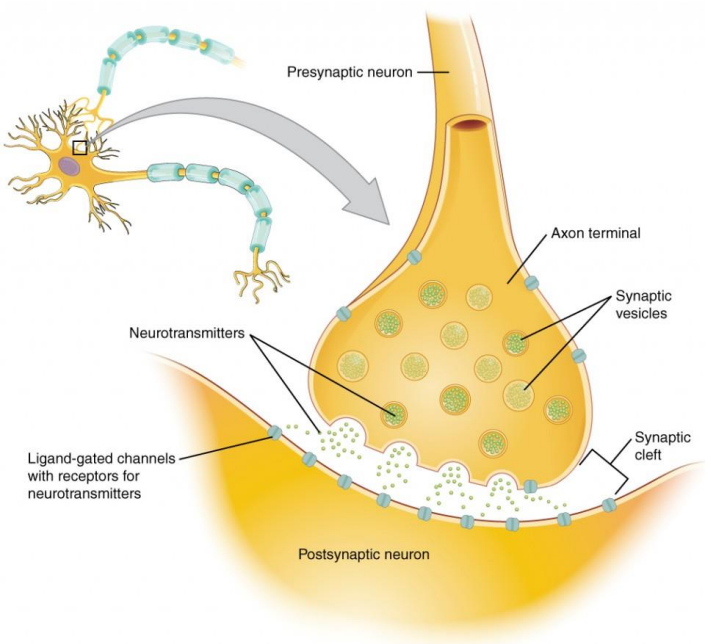




Neuronal Resting Membrane Potential ~ - 65 mV

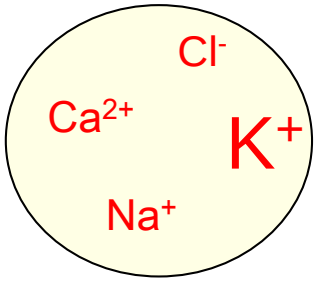


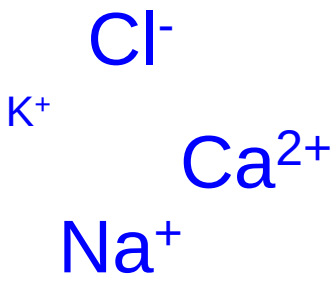
Neurons comunicate through changes in membrane potential

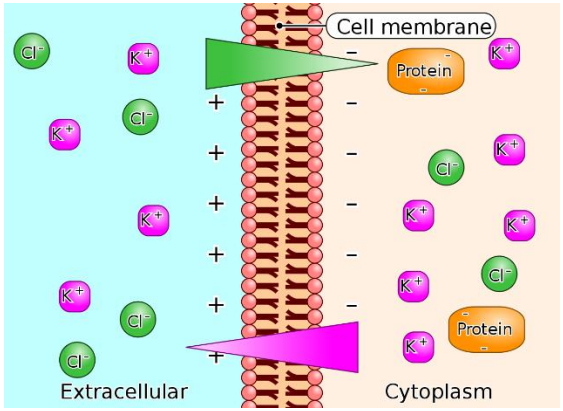


Ion distribution (in mM) at resting membrane potential

	Intracellular	*Extracellular*
Na^+	12	145
K^+	150	5.5
Cl^-	9	125
Ca^{2+}	0.0001	1.8



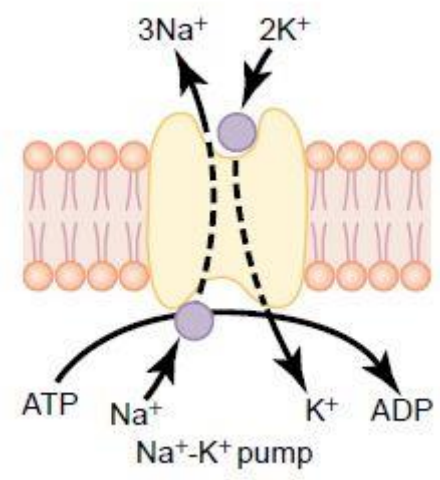




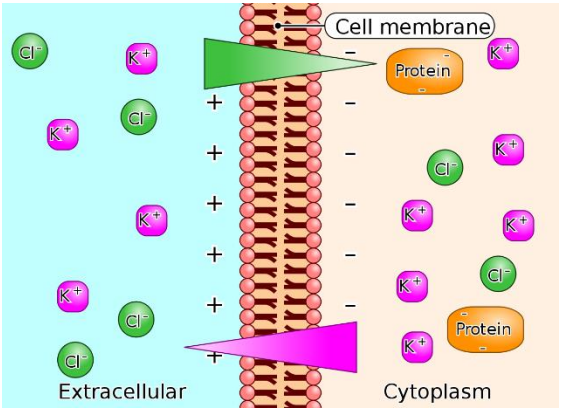
Resting membrane potential

How it is generated and maintained

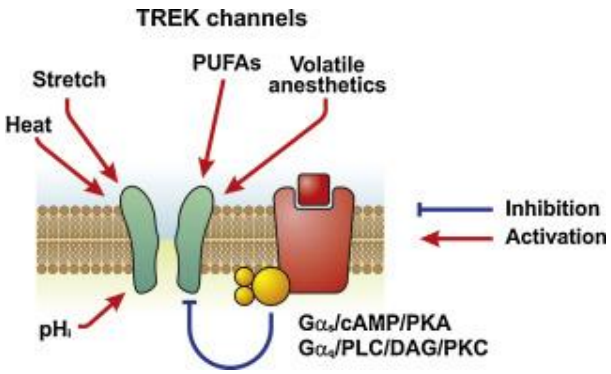
- Na^+- K^+ pumps
- Non-diffusible anions
- Membrane-selective permeability / leak channel



Primarily active transporter



Leak channels



Participate in: excitability, neuronal integration, volume regulation.

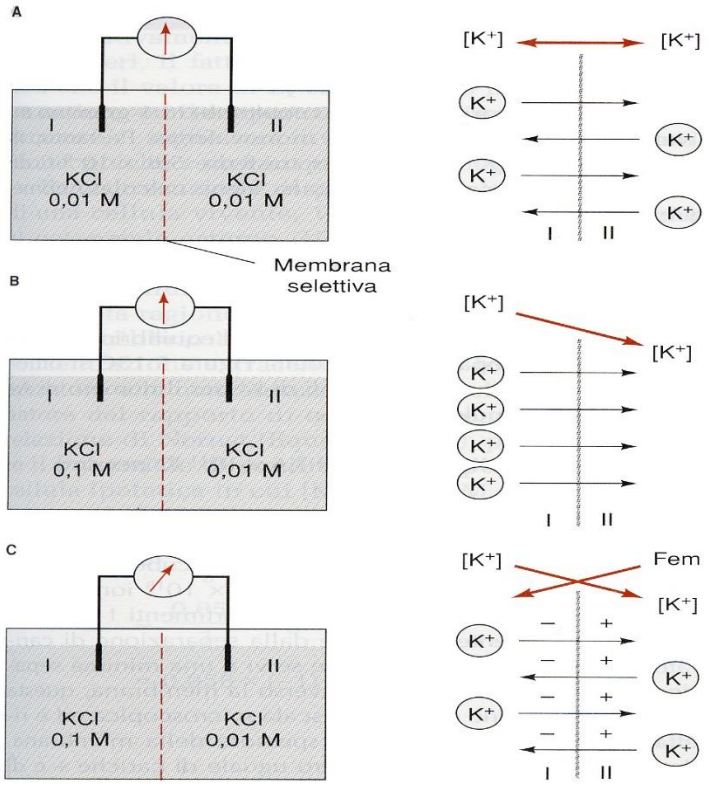
Modulated by: temperature, mechanical stretch, pH, cyclic nucleotides, kinase, phosphatases, molecular oxygen

Involved in depression, pain perception, anesthesia

High selective flux of K^+ down the electrochemical K^+ gradient

$$P_K : P_{Na} : P_{Cl^-} = 1 : 0.05 : 0.45$$

«Equilibrium potential» of diffusible ions



The Equilibrium Potential is reached when
WORK OF CHEMICAL FORCES = WORK OF ELECTRICAL FORCES

net ion flow = 0

Fisiologia animale, Zanichelli

Equilibrium potential for each diffisible ion is calculated from…

WORK OF CHEMICAL FORCES = WORK OF ELECTRICAL FORCES

$$-RT \ln (X_i/X_e) = z_x F V_m$$

$$Vm = - RT/zF \ln (X_i/X_e)$$

Nernst equation $$V_m = \frac{RT}{z_x F} \ln \frac{X_e}{X_i}$$

At room temperature $$E_m = 58 \log \frac{X_e}{X_i}$$

The equilibrium potential for each diffusible ion

E_{Na^+} ~ +65 mV

$E_{Ca^{2+}}$ ~ +120 mV

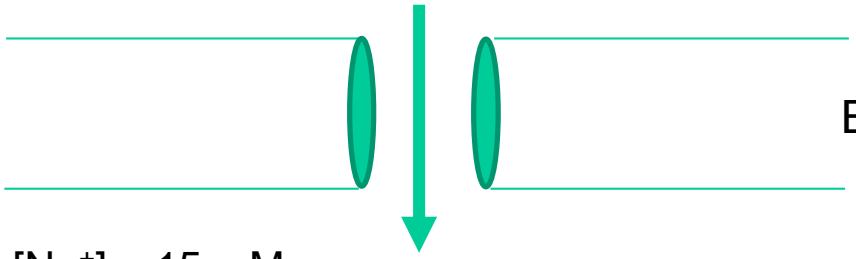
E_{K^+} ~ - 85 mV

E_{Cl^-} ~ - 66 mV

V_m = -60 mV

$[Na^+]_o$= 150 mM

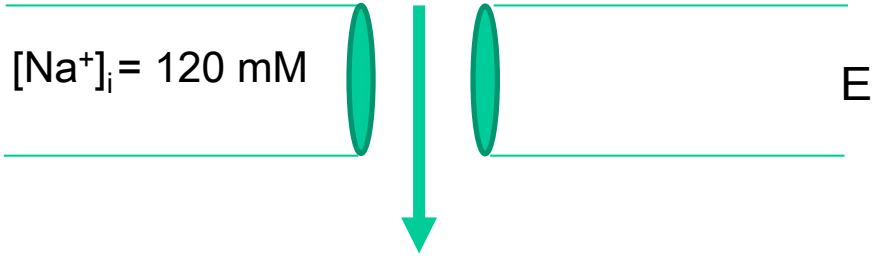
$$E_{Na^+} = 58 \log \frac{[Na^+]_{ext}}{[Na^+]_{int}}$$



E_{Na+} = +60 mV

$[Na^+]_i$= 15 mM

$[Na^+]_o$= 120 mM

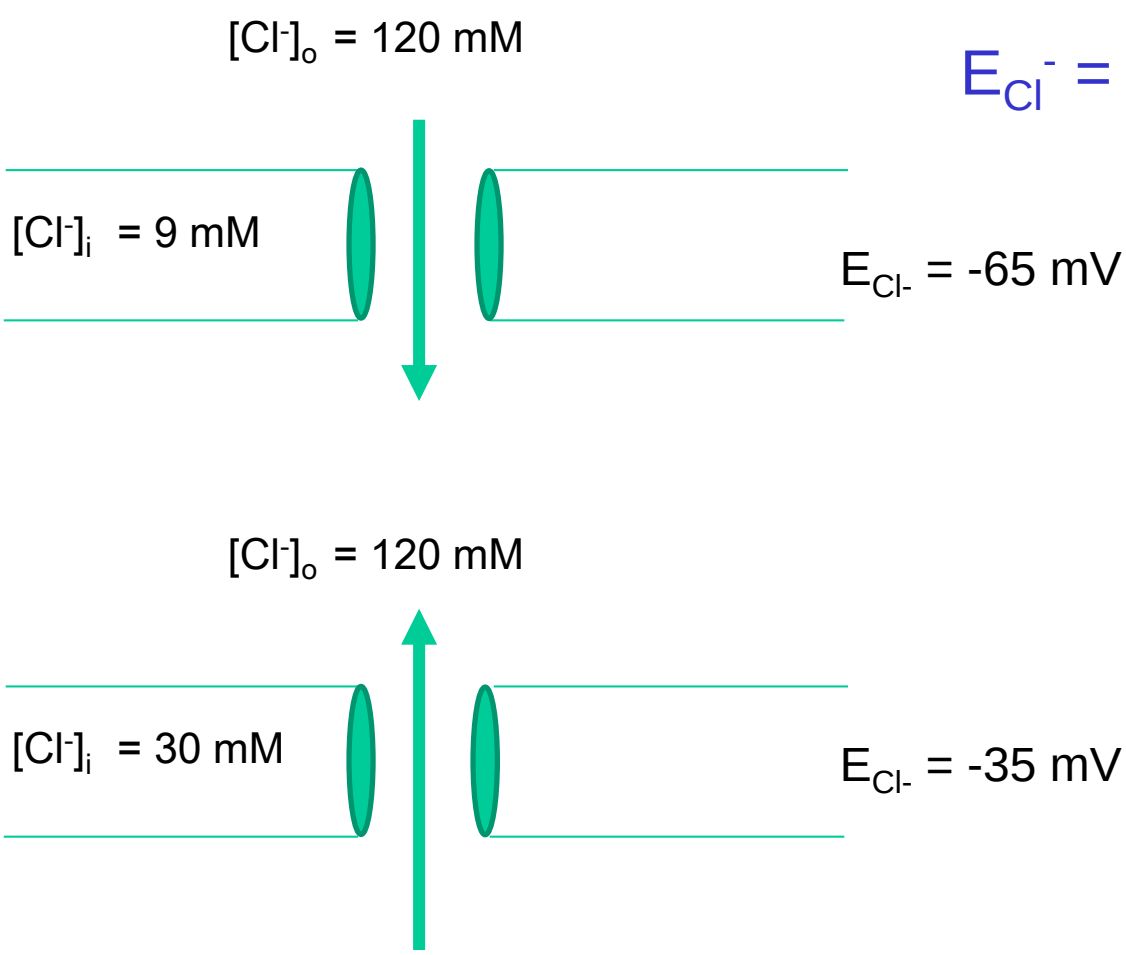


$[Na^+]_i$= 120 mM

E_{Na+} = 0 mV

V_m = -60 mV

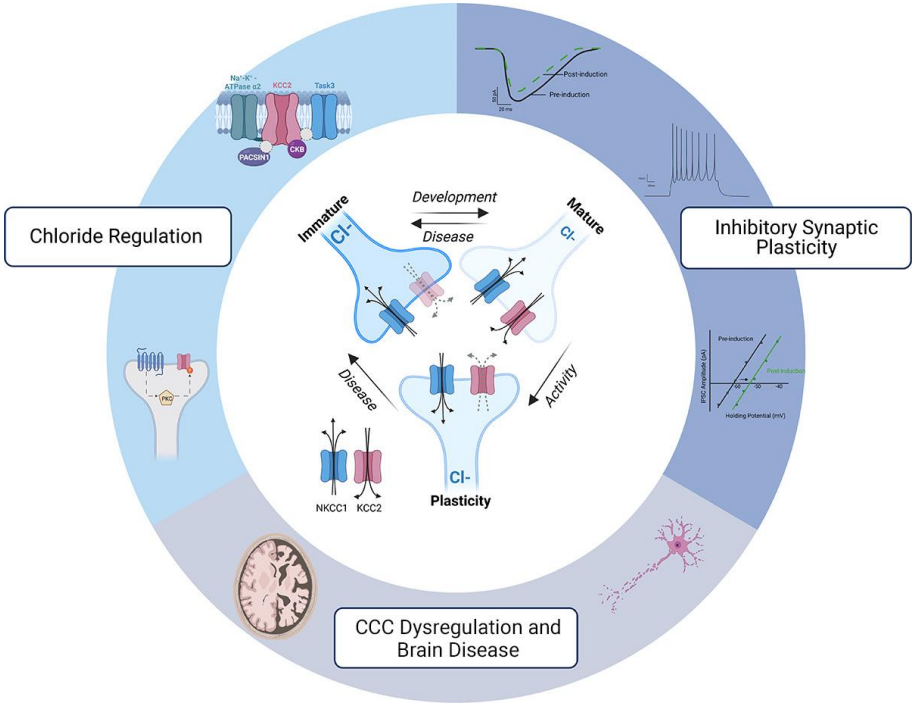
$$E_{Cl^-} = -58 \log \frac{[Cl^-]_{ext}}{[Cl^-]_{int}}$$

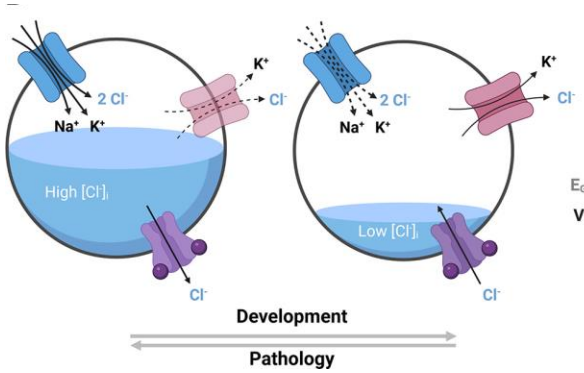


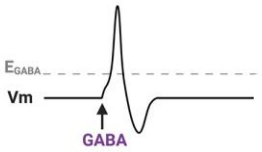
In neurons the chloride gradient is primarily mediated by two secondarily active cation-chloride cotransporters which are developmentally regulated

Na^+, K^+- 2 Cl^- (NKCC1)

K^+-Cl^- (KCC2)







Impaired Cl^- homeostasis:

Brain injury:

- Hypoxy
- Encephalopathy
- Brain edema

Neurodevelopmental, neuropsychiatric and neurological disorders

Because a given set of ions is present, membrane potential is given by

Goldman-Hodgkin-Katz Equation

$$\mathbf{Vm} = \frac{RT}{F} \ln \frac{[K^+]_e P_K + [Na^+]_e P_{Na} + [Cl^-]_i P_{Cl}}{[K^+]_i P_K + [Na^+]_i P_{Na} + [Cl^-]_e P_{Cl}}$$

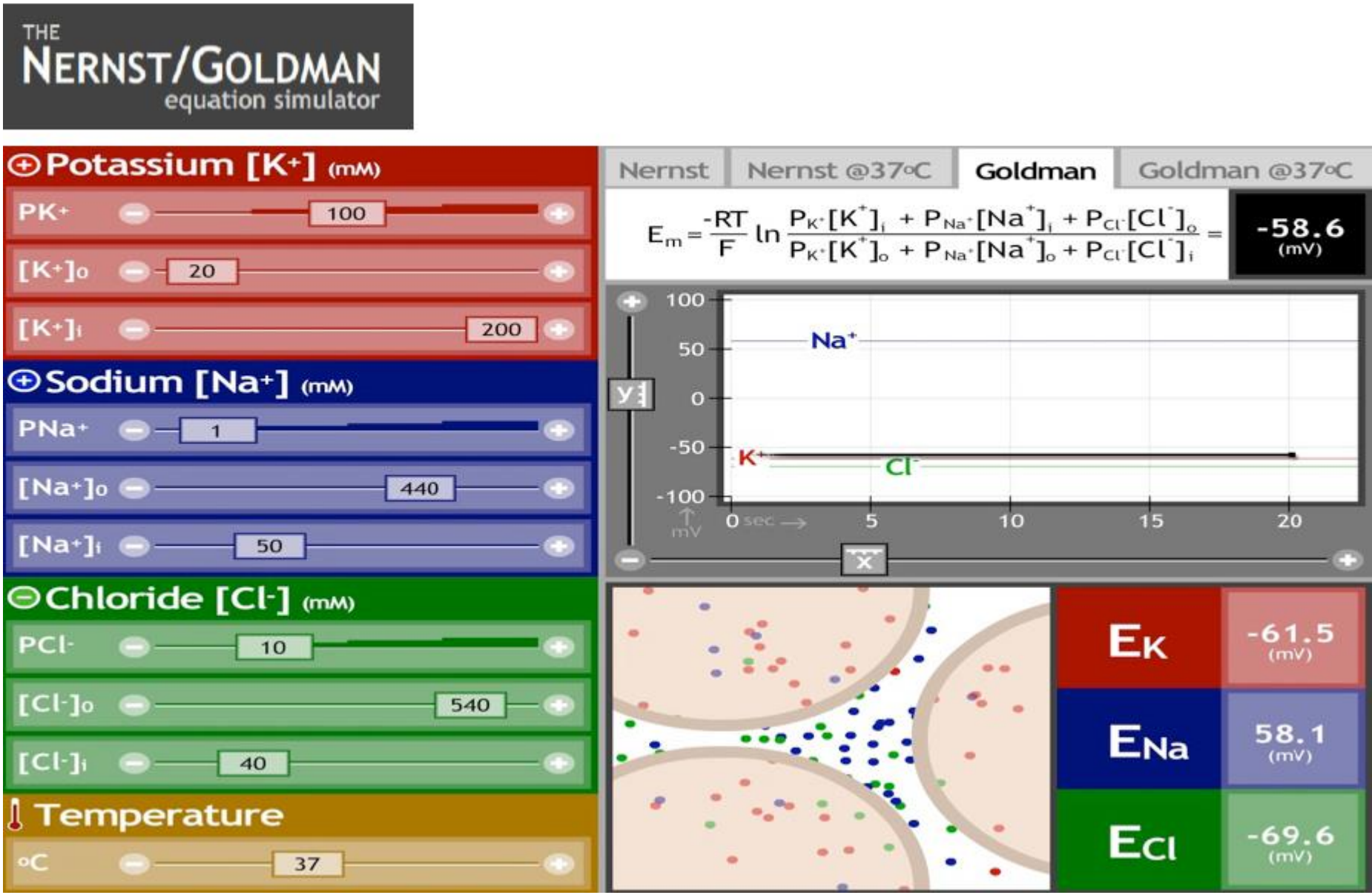
Each ion will move down its electrochemical gradient

The contribution of each ion is determined by:

- its *concentration difference across the membrane*
- its *relative permeability*.

https://www.physiologyweb.com/calculators/ghk_equation_calculator.html

Equilibri di membrana



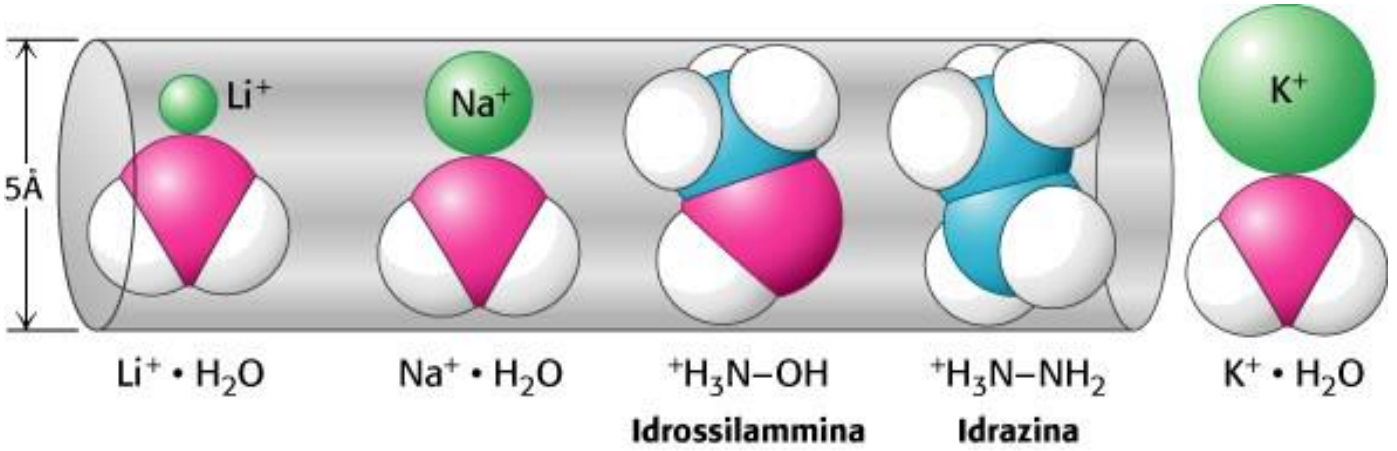
Ions cross membranes
due to the presence of channel proteins
forming hydrophilic pores across membranes

For transport efficiency, channels have an advantage over carriers in that **up to 100 million ions can pass through one open channel each second—**a rate 10^5 times greater than the fastest rate of transport mediated by any known carrier protein

Ion channel selectivity

1) Steric factors (**pore size**)

1) Rings of acidic residues (Glu, Asp) at the edges of the pore (**selectivity filter**)



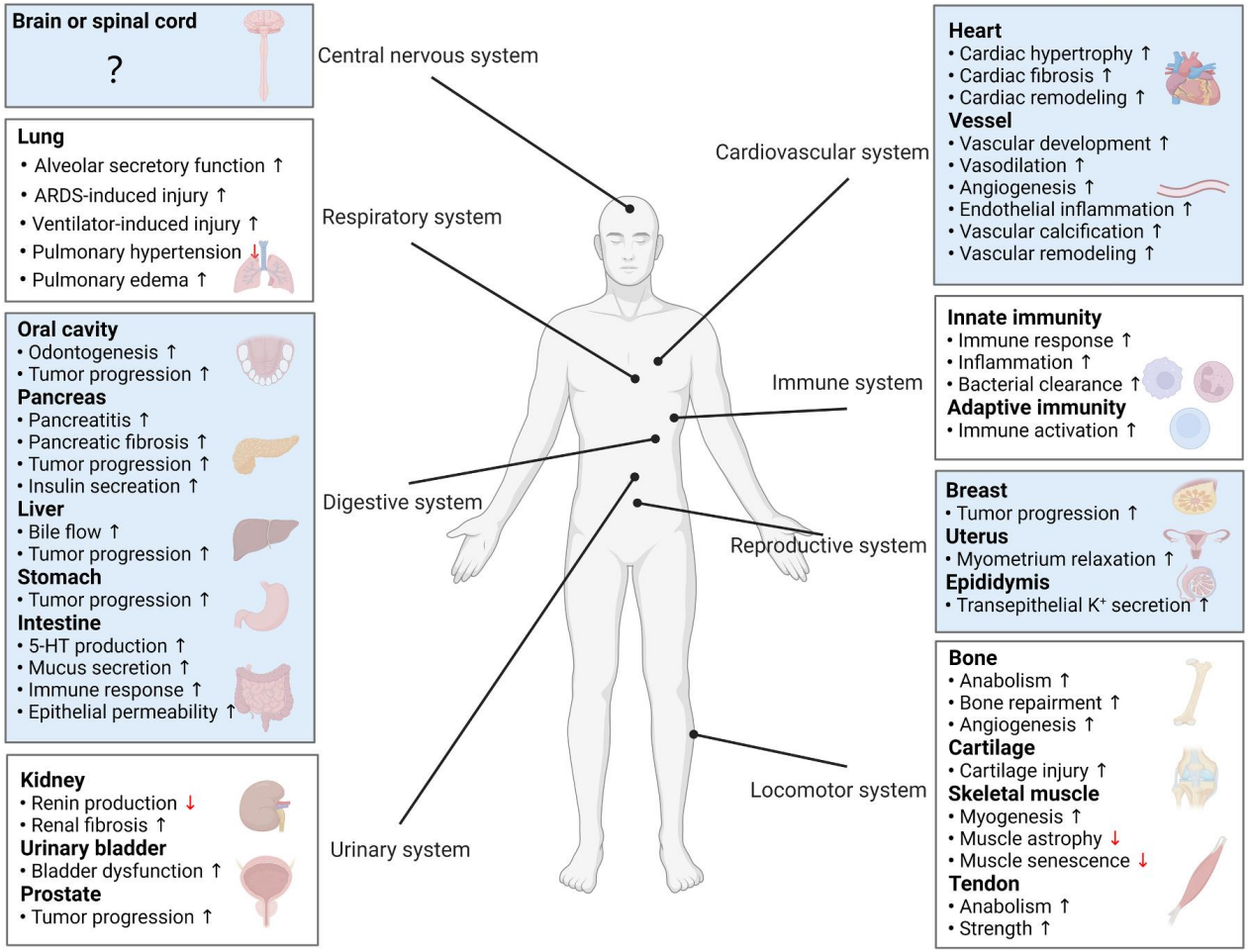
The main stimuli that are known to cause ion channels to open are:

- a change in the voltage across the membrane *(voltage-gated channels)*
- the binding of a ligand *(ligand-gated channels).*
- a mechanical stress *(mechanically gated channels)*

The activity of many ion channels is regulated, in addition, by protein phosphorylation and dephosphorylation.

The functions of Piezo1 channel activation in different organ systems.

Probably involved in neuronal development, including neurogenesis (Esfandiari et al., 2012), neuronal migration (Minegishi et al., 2018), polarization, and axonal and dendrite morphogenesis.



Zong et al., Ageing Research Reviews, 2023