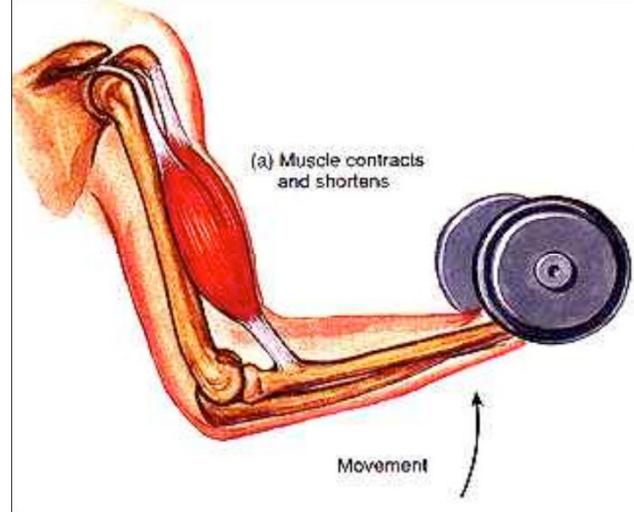# Neurons and muscle cells are electrically excitable they generate and conduct electrical signals

A

Area motoria supplementare
Corteccia motoria
Corteccia somatosensoriale primaria
Corteccia premotoria
Corteccia parietale associativa
4
3,1,2
5
7
8
Corteccia prefrontale

(a) Muscle contracts and shortens

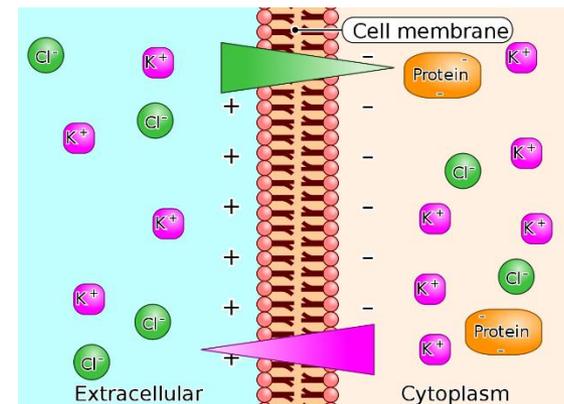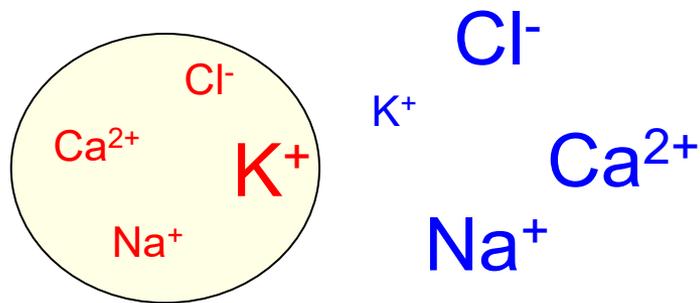Movement
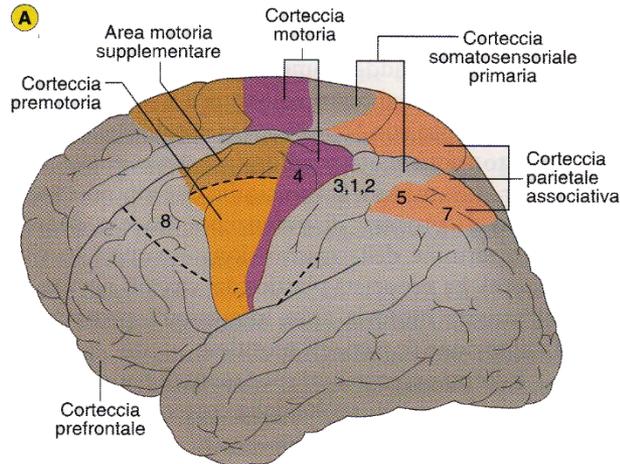
Neuronal Resting Membrane Potential ~ - 65 mV
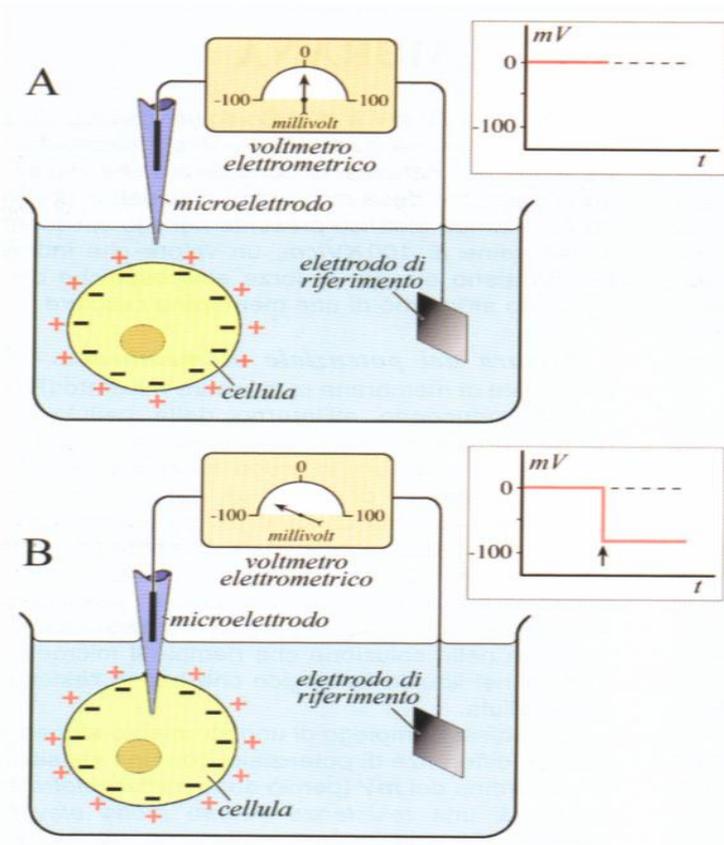
Neurons comunicate through changes in membrane potential
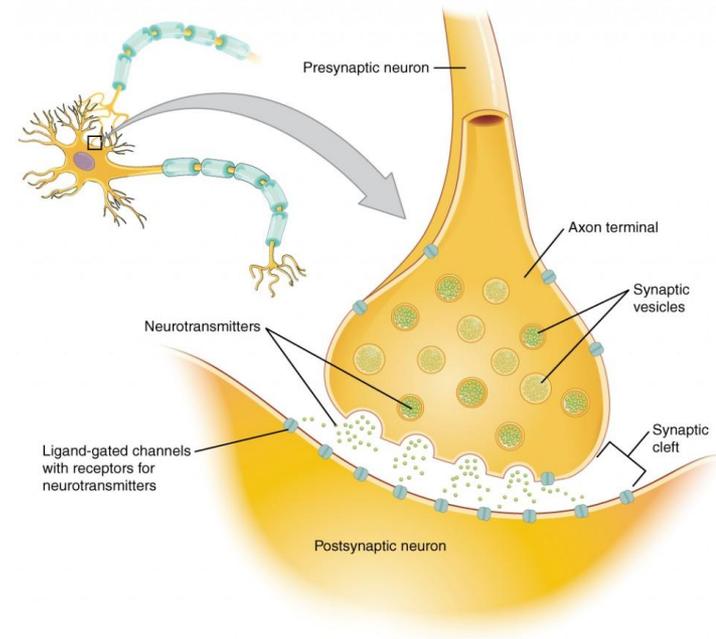
Negatively charged comparing with the outside !!

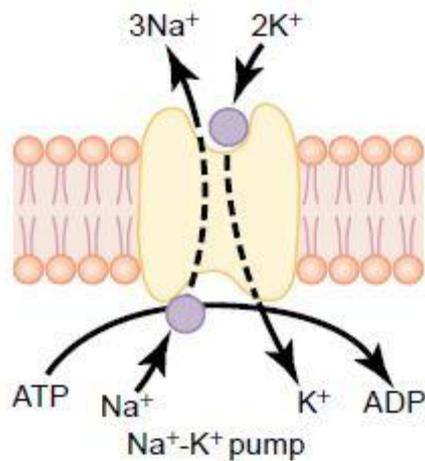# Ion distribution (in mM) at resting membrane potential

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

Cl^-

Ca^{2+} K^+ K^+

Cl^- Ca^{2+}

Na^+ Na^+
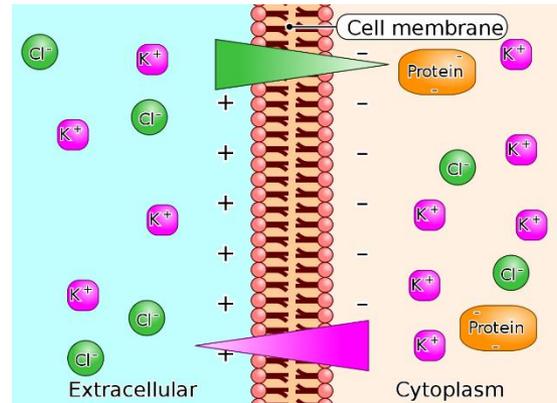
Resting membrane potential

How it is generated and maintained
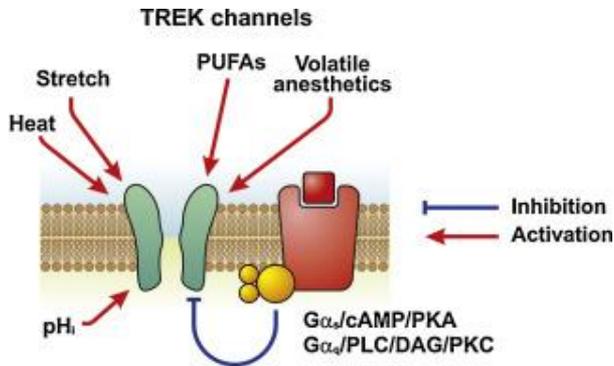
- Na$^+$- K$^+$ pumps
- Non-diffusible anions
- Membrane-selective permeability / leak channel

Primarily active transporter

Leak channels

TREK channels

Stretch

Heat

PUFAs Volatile anesthetics

Inhibition
Activation

pH_i

$G\alpha_s$/cAMP/PKA
$G\alpha_q$/PLC/DAG/PKC

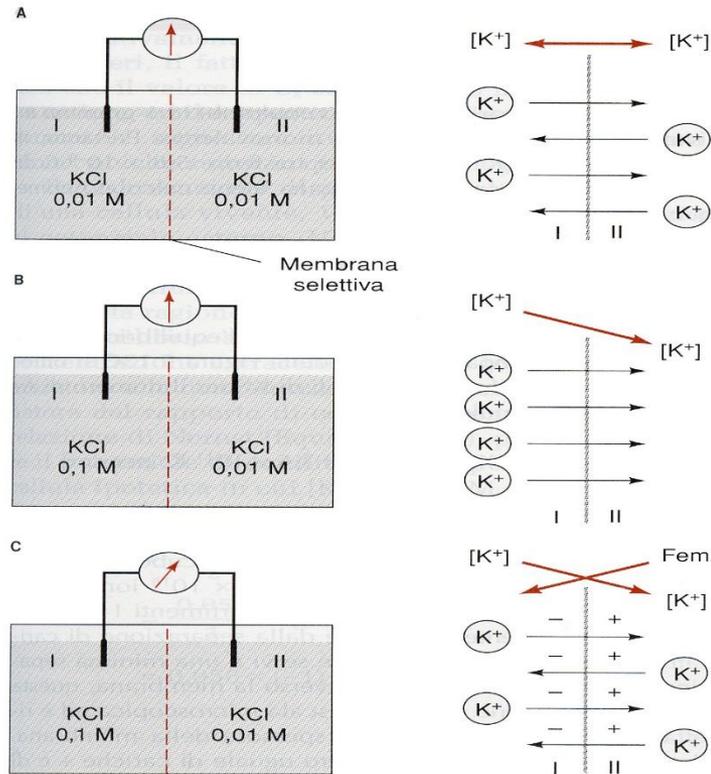**Participate in**: excitability, neuronal integration, volume regulation.

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 $\quad V_m = \dfrac{RT}{z_x F} \ln \dfrac{X_e}{X_i}$

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

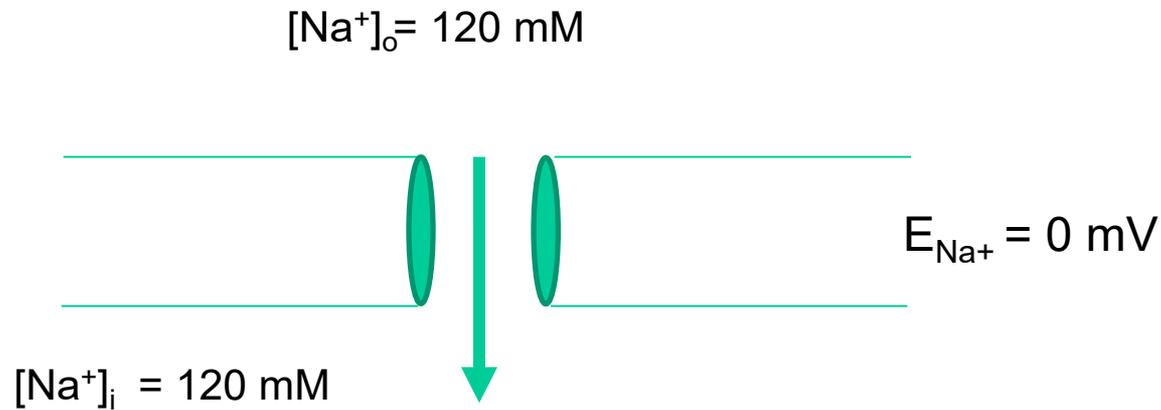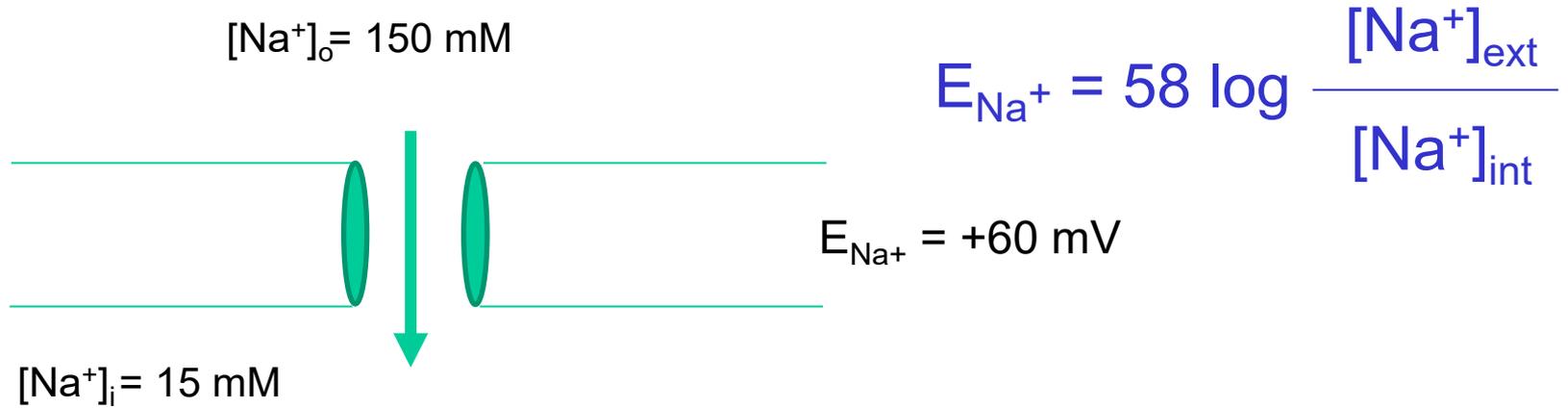# The equilibrium potential for each diffusible ion

$$E_{Na^+} \sim +65 \text{ mV}$$

$$E_{Ca^{2+}} \sim +120 \text{ mV}$$

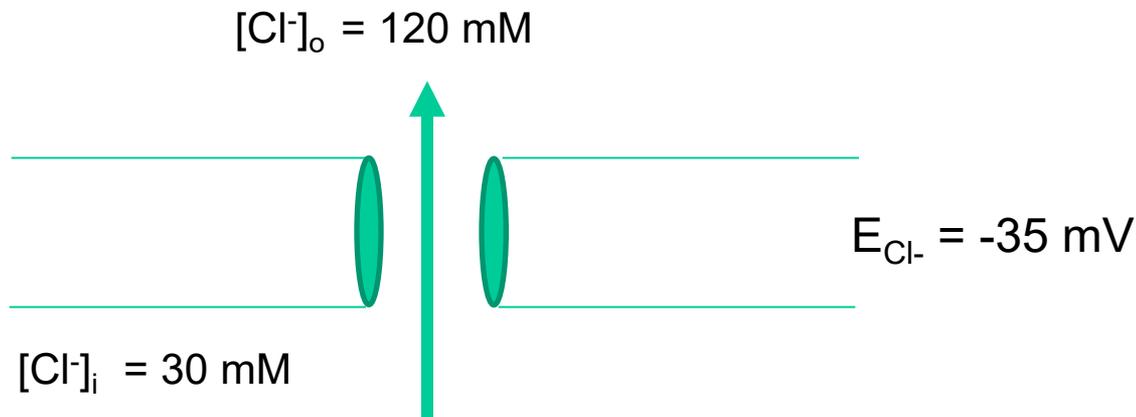$$E_{K^+} \sim -85 \text{ mV}$$

$$E_{Cl^-} \sim -66 \text{ mV}$$

$V_m = -60$ 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

$E_{Na+} = 0$ mV

$[Na^+]_i = 120$ mM

$V_m = -60$ mV

$[Cl^-]_o = 120$ mM

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

$E_{Cl-} = -65$ mV

$[Cl^-]_i = 9$ mM

$[Cl^-]_o = 120$ mM

$E_{Cl-} = -35$ mV

$[Cl^-]_i = 30$ mM
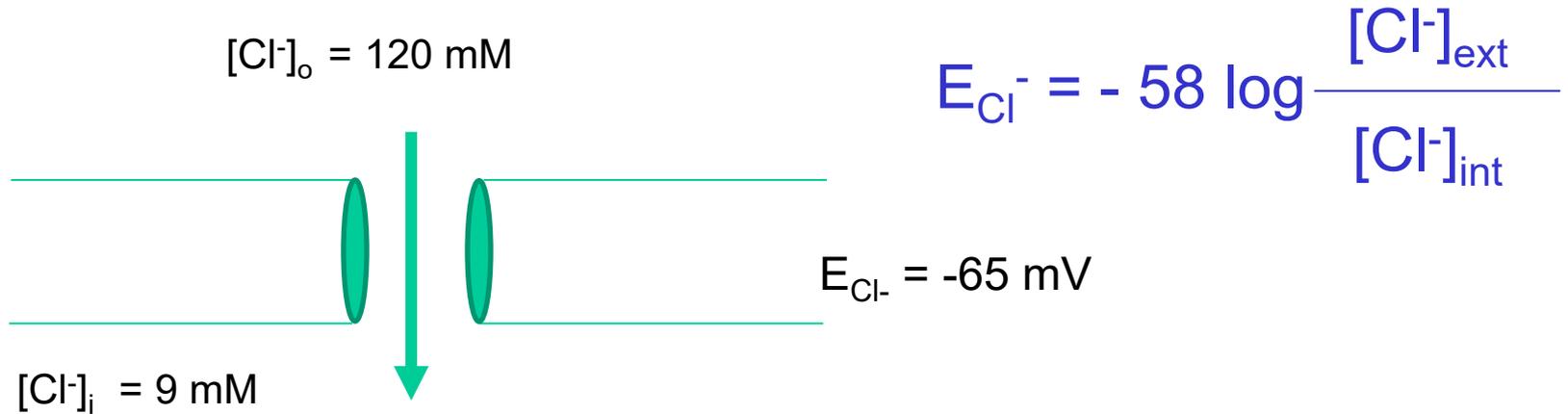
The electrochemical driving force = $(V_m - V_{eq})$

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*.

Equilibri di membrana
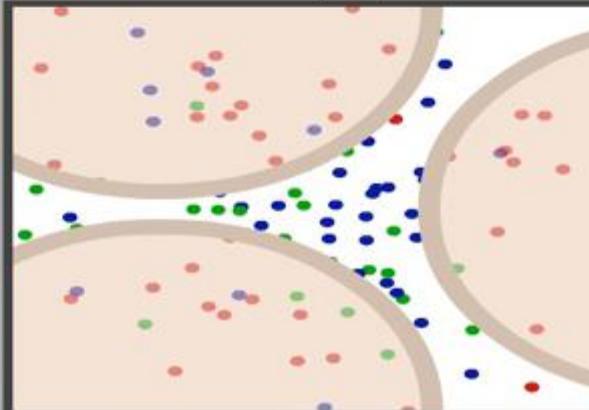
**Ions cross membranes
due to the presence of channel proteins**
forming hydrophilic pores across membranes

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**)

$Li^+ \cdot H_2O$ $Na^+ \cdot H_2O$ $^+H_3N-OH$ $^+H_3N-NH_2$ $K^+ \cdot H_2O$

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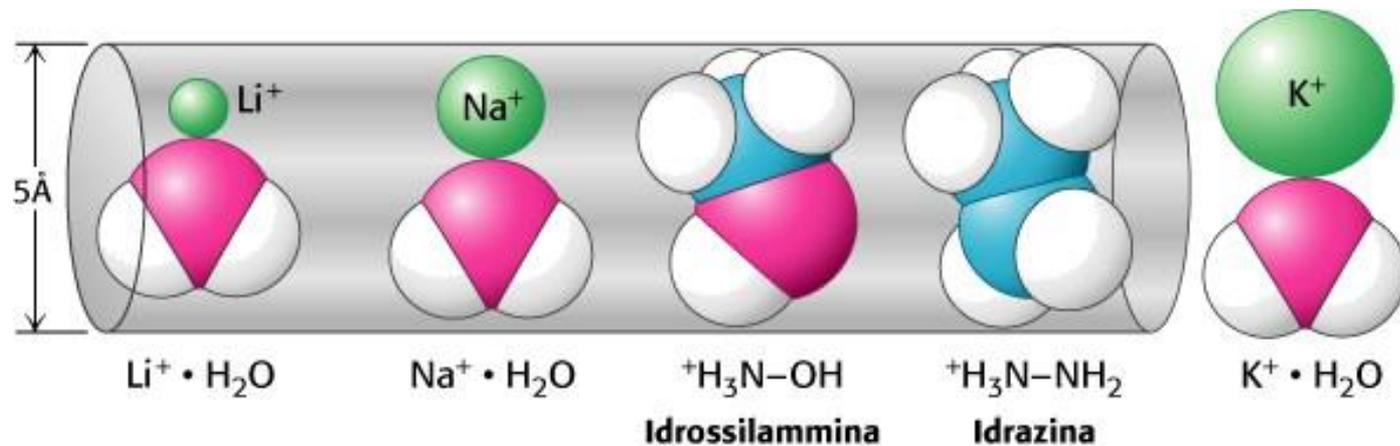
The main stimuli that are known to cause ion channels to open are:

- 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.