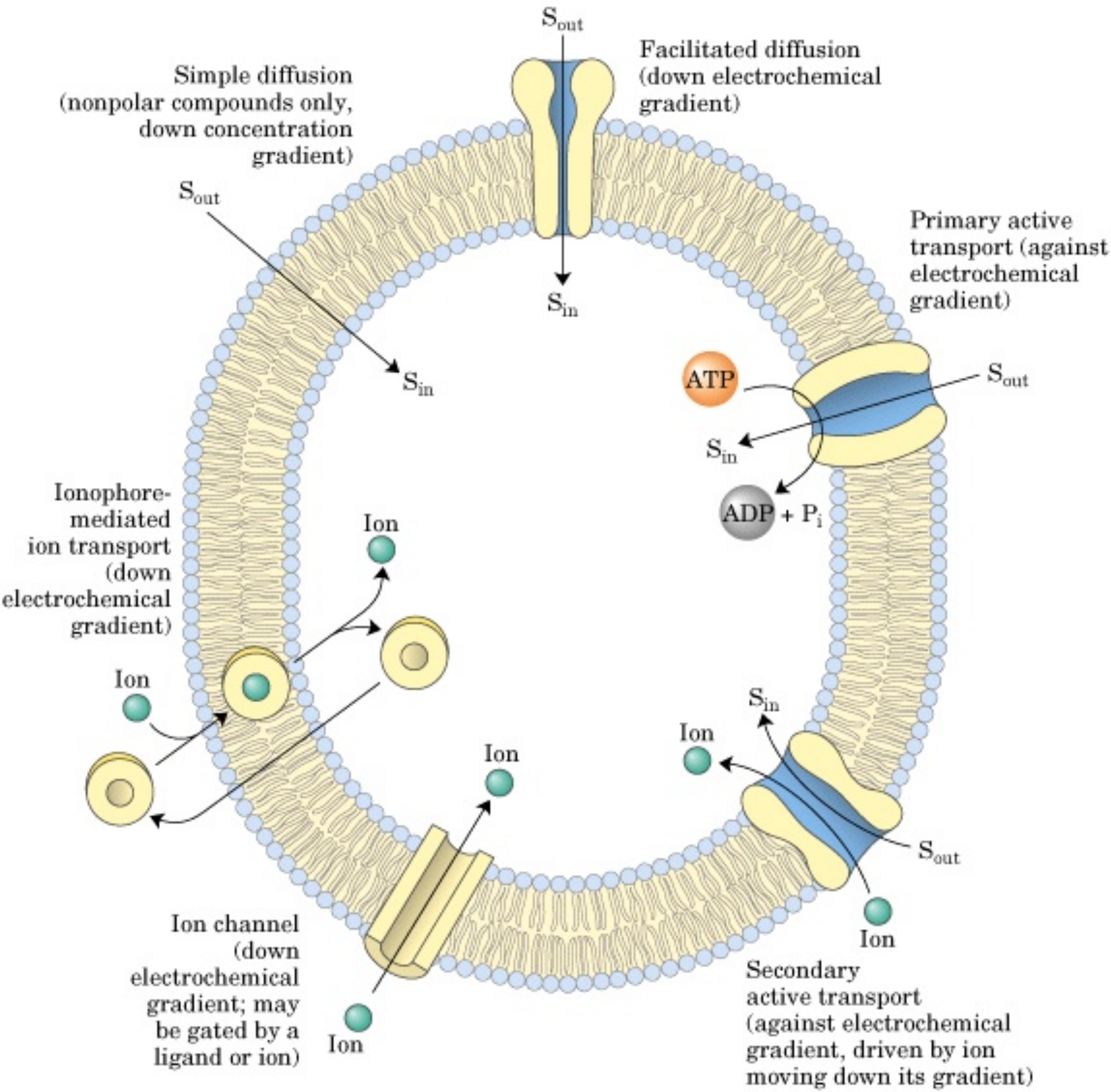
Membrane transport



Resting Potential

Requirements for cell stability

Intra- & extra-cellular solutions must each be electrically neutral.

Cell must be in osmotic balance

$[\text{particles}]_i = [\text{particles}]_e$

No net movement of ions.

The electro-diffusion model assumptions:

- *A homogeneous membrane slab*
- *A constant electric fiels*
- *Ions moving independently of ane another*
- *A constant permeability coefficient*

Iintracellular and extracellular ionic composition

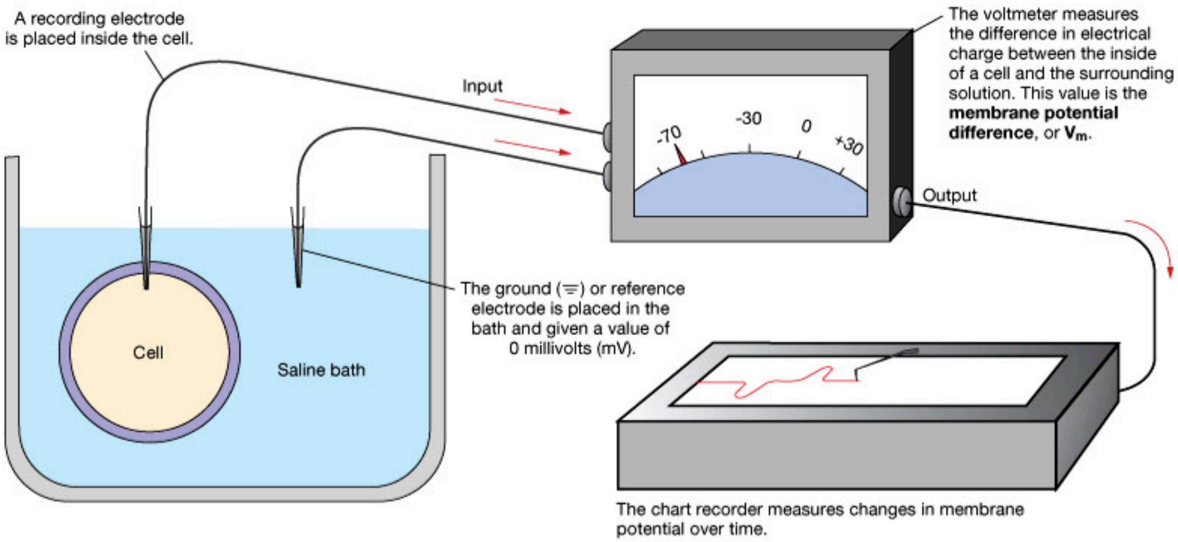
$$\Delta\mu_{in/out} = RT\ln\frac{[ion]_{in}}{[ion]_{out}} + zF\Delta\Psi_m$$

$\Delta\mu_{Na} \approx -13$ kJ/mol	**it requires a lot of energy to pump Na^+ out**
$\Delta\mu_{K} \approx +1.5$ kJ/mol	**it requires a little of energy to pump K^+ in**
$\Delta\mu_{Cl} \approx -0.5$ kJ/mol	**Cl^- is almost at equilibrium**

Extracellular				*Intracellular*		
Na^+	143	mM	>	10	mM	Na^+
K^+	4	mM	<	140	mM	K^+
Cl^-	118	mM	>	10	mM	Cl^-
A^-	10	mequiv.l^{-1}	<	132	mequiv.l^{-1}	A^-
Ca^{2+}	1.5	mM	>	0.1	μM	Ca^{2+}
Mg^{2+}	1.0	mM		1.0	mM	Mg^{2+}
HCO_3^-	24	mM	>	10	mM	HCO_3^-
pH	7.4		>	pH 7.0		

A^- are impermeable anions

Measuring Membrane Potential Differences



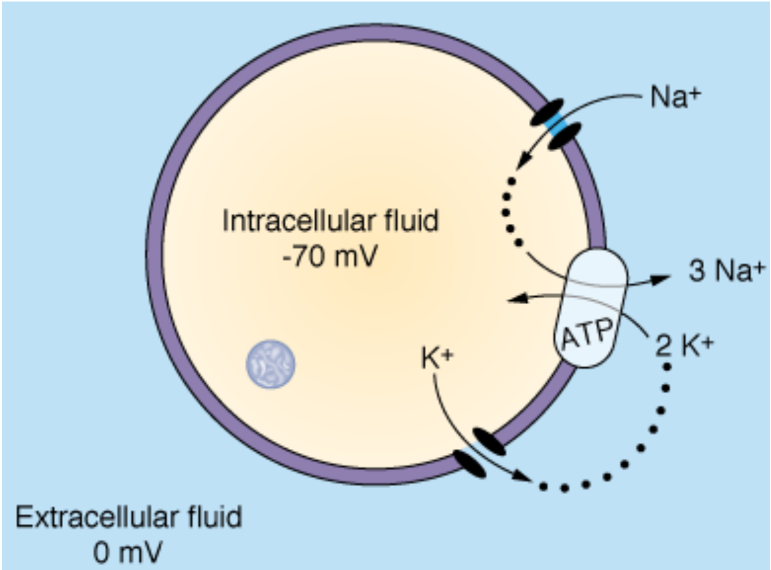
A recording electrode is placed inside the cell.

The voltmeter measures the difference in electrical charge between the inside of a cell and the surrounding solution. This value is the **membrane potential difference**, or **V_m**.

The ground (⏚) or reference electrode is placed in the bath and given a value of 0 millivolts (mV).

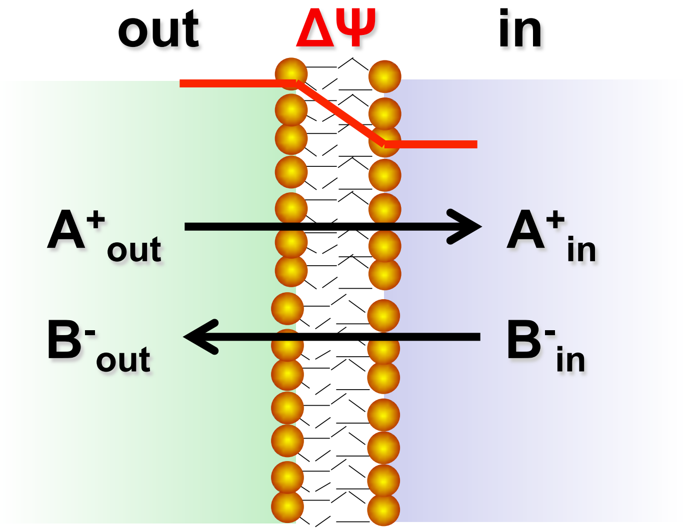
The chart recorder measures changes in membrane potential over time.

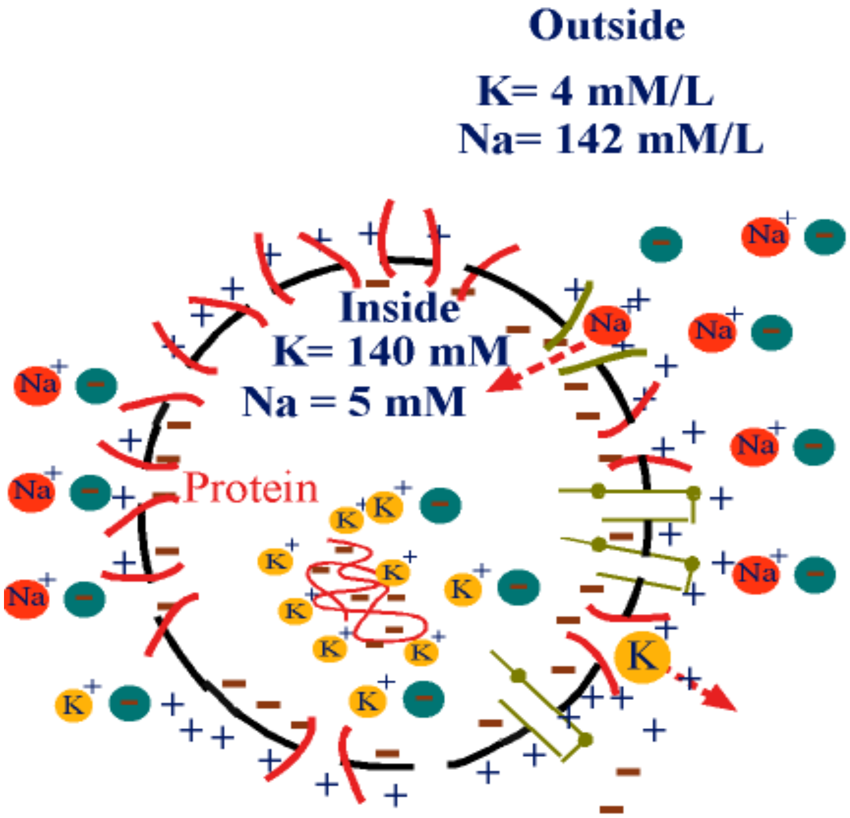
Resting Membrane Potential



of most cells is between -50 and -90 mV (average ~ -70 mV)

Donnan potentials & Donnan Equilibrium:





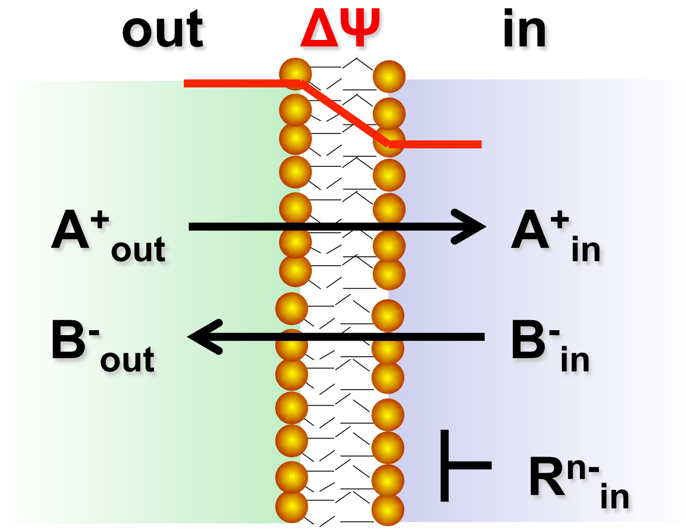
$$\Delta\Psi_{out/in} = -\frac{RT}{z_A F}\ln\frac{[A^+{}_{out}]}{[A^+{}_{in}]} = -\frac{RT}{z_B F}\ln\frac{[B^-{}_{out}]}{[B^-{}_{in}]}$$

$$z_A = -z_B = 1$$

$$\Delta\Psi = -\frac{RT}{F}\ln\frac{[A^+{}_{out}]}{[A^+{}_{in}]} = \frac{RT}{F}\ln\frac{[B^-{}_{out}]}{[B^-{}_{in}]}$$

$$\frac{[A^+{}_{out}]}{[A^+{}_{in}]} = \frac{[B^-{}_{in}]}{[B^-{}_{out}]} = \exp\left(-\frac{F\Delta\Psi}{RT}\right) \quad - \quad \textit{Donnan ratio}$$

Donnan potentials & Donnan Equilibrium:



Electro neutrality:

$$in: \quad [A^+{}_{in}] = [B^-{}_{in}] + n[R^-{}_{in}]$$

$$out: \quad [A^+{}_{out}] = [B^-{}_{out}] = c$$

$$\frac{c}{[A^+{}_{in}]} = \exp\left(-\frac{F\Delta\Psi}{RT}\right)$$

out/in

$$\frac{c}{[B^-{}_{in}]} = \exp\left(\frac{F\Delta\Psi}{RT}\right)$$

$$c\exp\left(-\frac{F\Delta\Psi}{RT}\right) - c\exp\left(\frac{F\Delta\Psi}{RT}\right) - n[R^-] = 0$$

$$\left[\exp\left(\frac{F\Delta\Psi}{RT}\right)\right]^2 - \frac{n[R^-]}{c}\left(\frac{F\Delta\Psi}{RT}\right) - 1 = 0$$

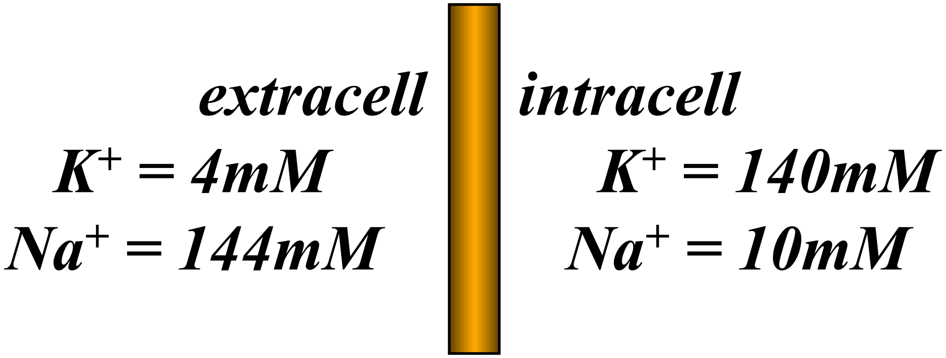
$$\exp\left(\frac{F\Delta\Psi}{RT}\right) = \frac{n[R^-]}{2c} + \sqrt{\left(\frac{n[R^-]}{2c}\right)^2 + 1} \quad \textit{and}$$

$$\boxed{\Delta\Psi = RT\ln\left(\frac{n[R^-]}{2c} + \sqrt{\left(\frac{n[R^-]}{2c}\right)^2 + 1}\right)}$$

Equilibrium potentials

If a membrane is permeable to a single ionic species the measured membrane potential can be calculated from the Nernst equation.

Cell Membrane



extracell	***intracell***
$K^+ = 4mM$	$K^+ = 140mM$
$Na^+ = 144mM$	$Na^+ = 10mM$

Membrane is permeable to K^+:

$$V_K = 61.5\log_{10}\frac{4}{140} = -95mV$$

Membrane is permeable to Na^+:

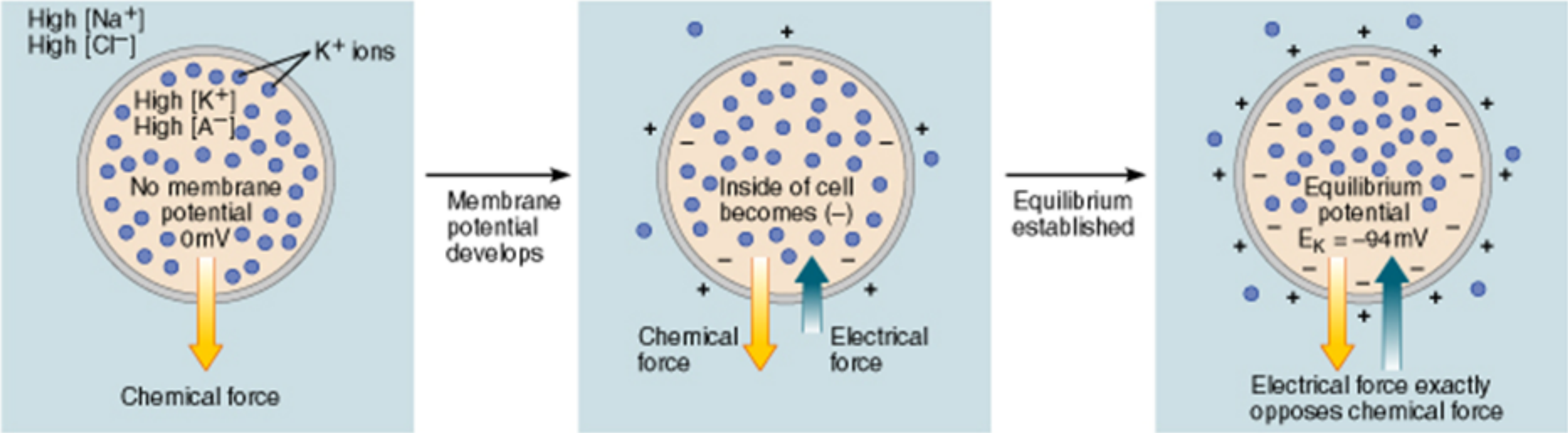
$$V_{Na} = 61.5\log_{10}\frac{144}{10} = +71mV$$

$$V_{Cl} = \frac{RT}{F}\ln\frac{[Cl^-]_i}{[Cl^-]_o} = -45.4mV$$

$$V_{Ca} = \frac{RT}{F}\ln\frac{[Ca^{2+}]_o}{[Ca^{2+}]_i} = +40.0mV$$

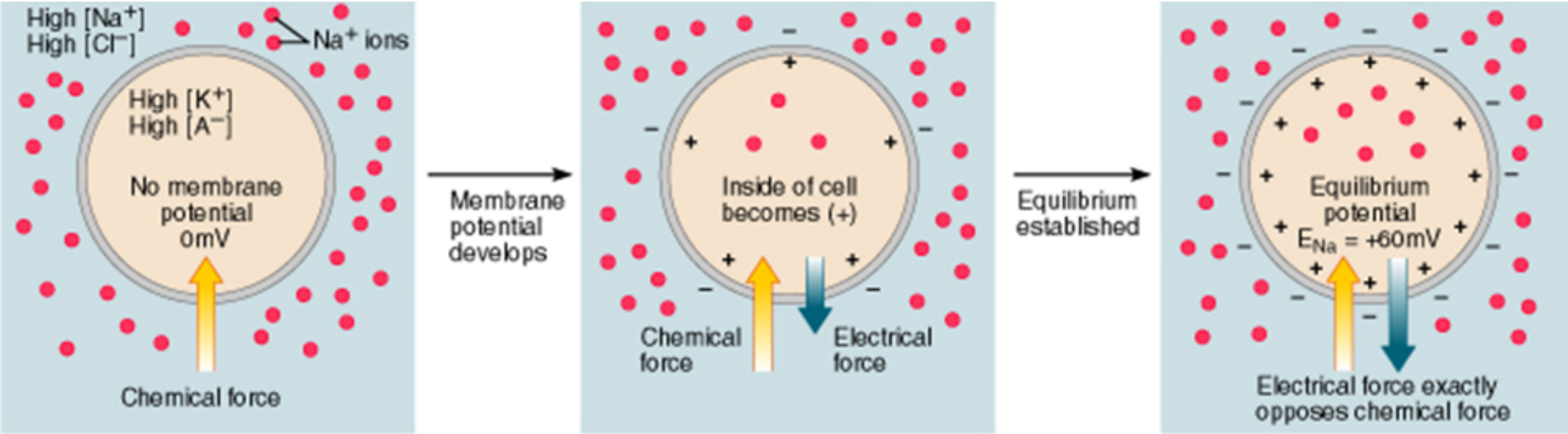
A cell permeable to K^+ only

$$E_K = \left(\frac{RT}{z}\right)\ln\frac{[K_o]}{[K_i]}$$

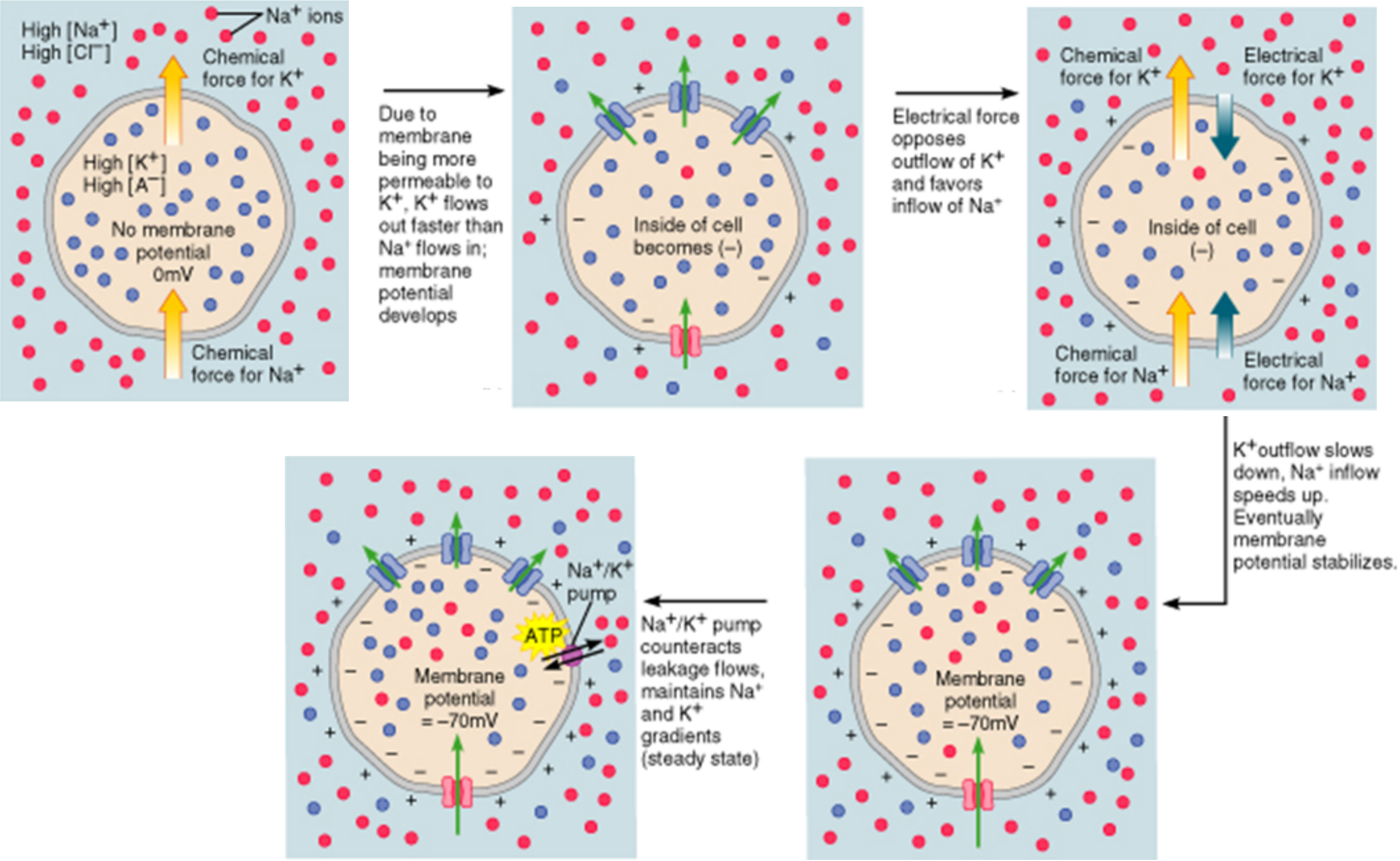


A cell permeable to Na^+ only

$$E_{Na} = \left(\frac{RT}{z}\right)\ln\frac{[Na_o]}{[Na_i]}$$



Steady state resting membrane potential



Due to membrane being more permeable to K^+, K^+ flows out faster than Na^+ flows in; membrane potential develops

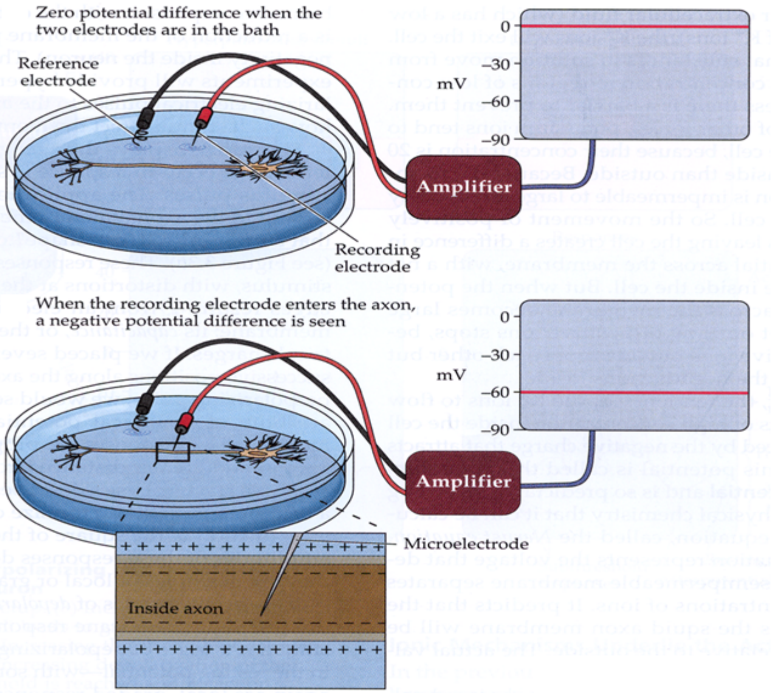
Electrical force opposes outflow of K^+ and favors inflow of Na^+

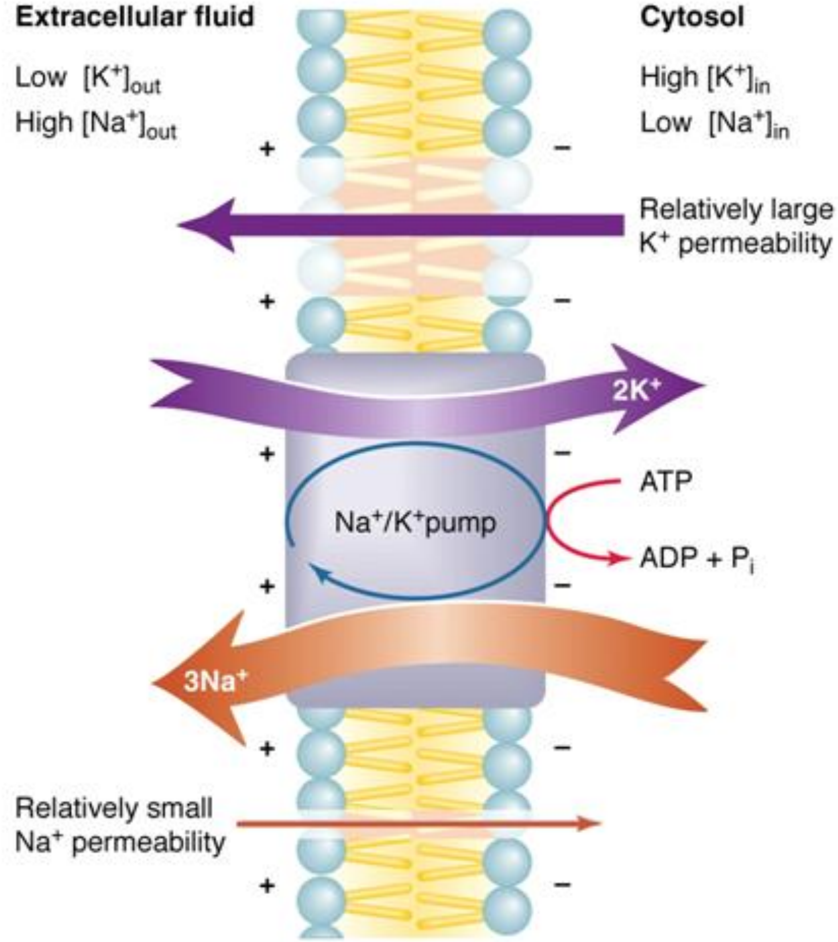
K^+ outflow slows down, Na^+ inflow speeds up. Eventually membrane potential stabilizes.

Na^+/K^+ pump counteracts leakage flows, maintains Na^+ and K^+ gradients (steady state)

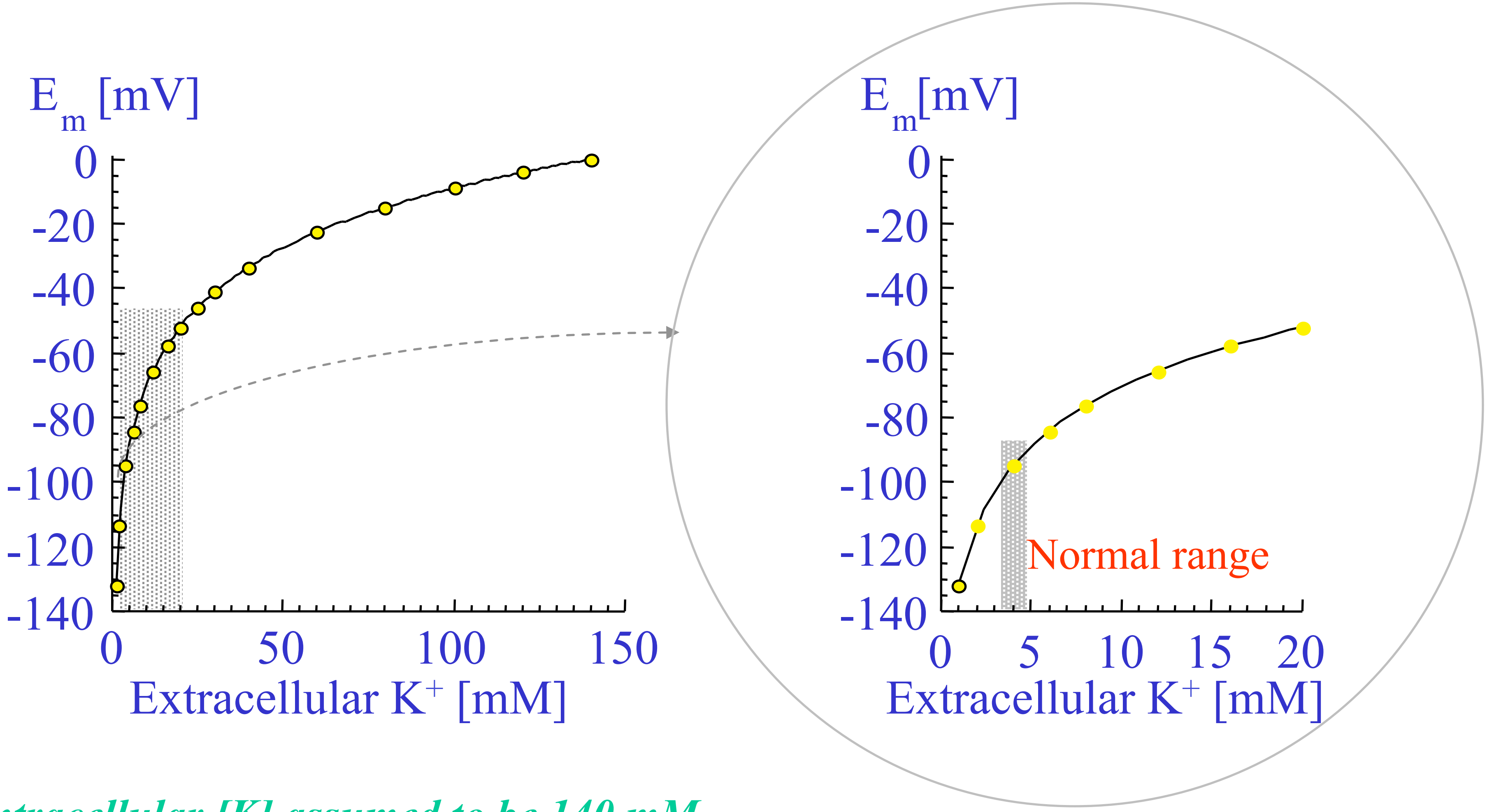
The membrane potential exists because

- **Na$^+$/K$^+$ Pump is active**
- **Na$^+$ channels is closed**
- **K$^+$ leaks**





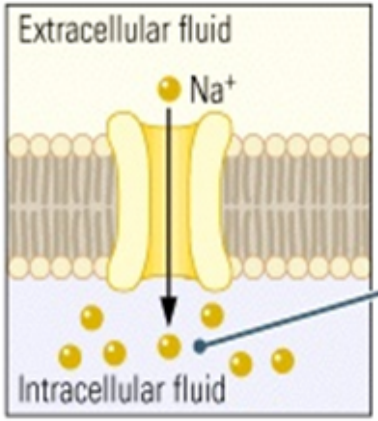
- ***The relationship between the extracellular [K] and membrane potential, E_m, is very non-linear.***
- ***Small changes of [K] around the normal level have large effects on E_m.***



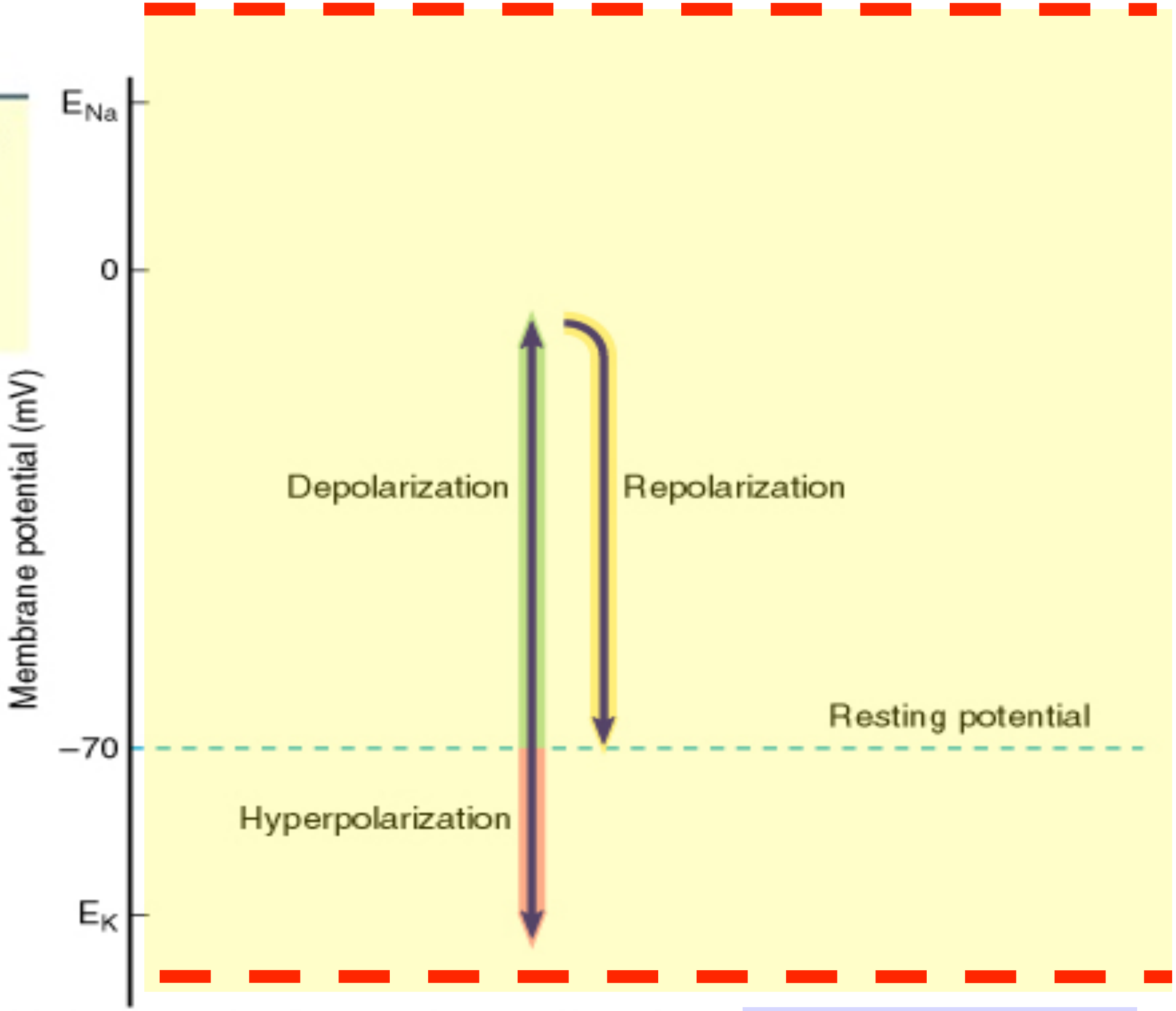
Intracellular [K] assumed to be 140 mM

The potential limits

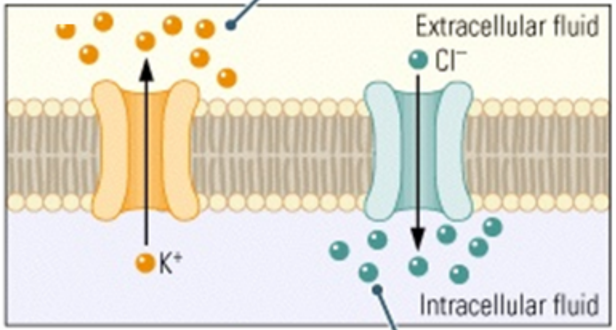
$$E_{Na} = \left(\frac{RT}{z}\right)\ln\frac{[Na_o]}{[Na_i]}$$



Depolarization is due to an influx of Na+ through normally closed Na+ channels.



Hyperpolarization is due to an efflux of K+, making the extracellular side of the membrane more positive.



An influx of Cl− also can produce hyperpolarization.

$$E_K = \left(\frac{RT}{z}\right)\ln\frac{[K_o]}{[K_i]}$$

Equilibrium potentials

Theory

- The K^+ equilibrium potential E_K, is about - 95 mV;
- The Na^+ equilibrium potential E_{Na}, is about + 71 mV.

Experiment

The measured membrane potential is between -80 and -90 mV, i.e. close to the K^+ equilibrium potential.

Deduction

- Because the resting membrane potential is close to E_K implies that the membrane is permeable to K^+

- Because the resting membrane potential is not close to E_{Na} implies that the membrane is impermeable to Na^+

A multi-ion steady-state
The Goldman-Hodgkin-Katz equation

Assumptions:

(1) The membrane is semi-permeable

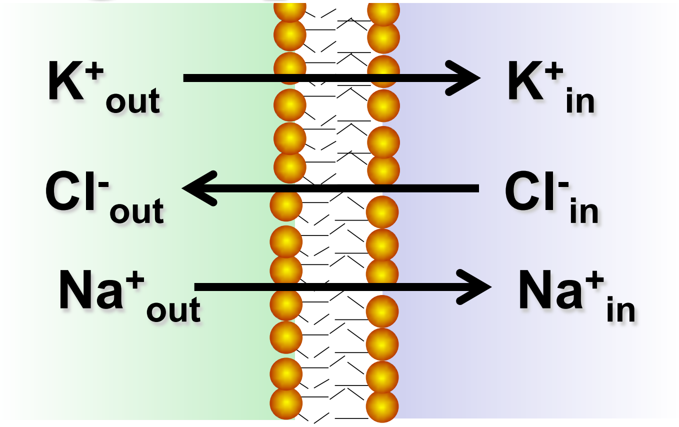
(2) A constant electrical field across the membrane.

The total current flux across the membrane ($J_m = \sum J_n$) must equal zero to keep ψ_m constant.

- If ions are in equilibrium across a membrane, then the membrane potential will be given by the Nernst equation.
- Ions are in constant flux (transport and permeation) and the capacitative charge is determined by the steady-state distribution of ions.

$$J_{total} = 0 = \sum_{cations} z_j F J_j + \sum_{anions} z_j F J_j$$

Goldman – Hodgkin – Katz voltage Equation :



$$J_{Na} + J_K - J_{Cl} = 0$$

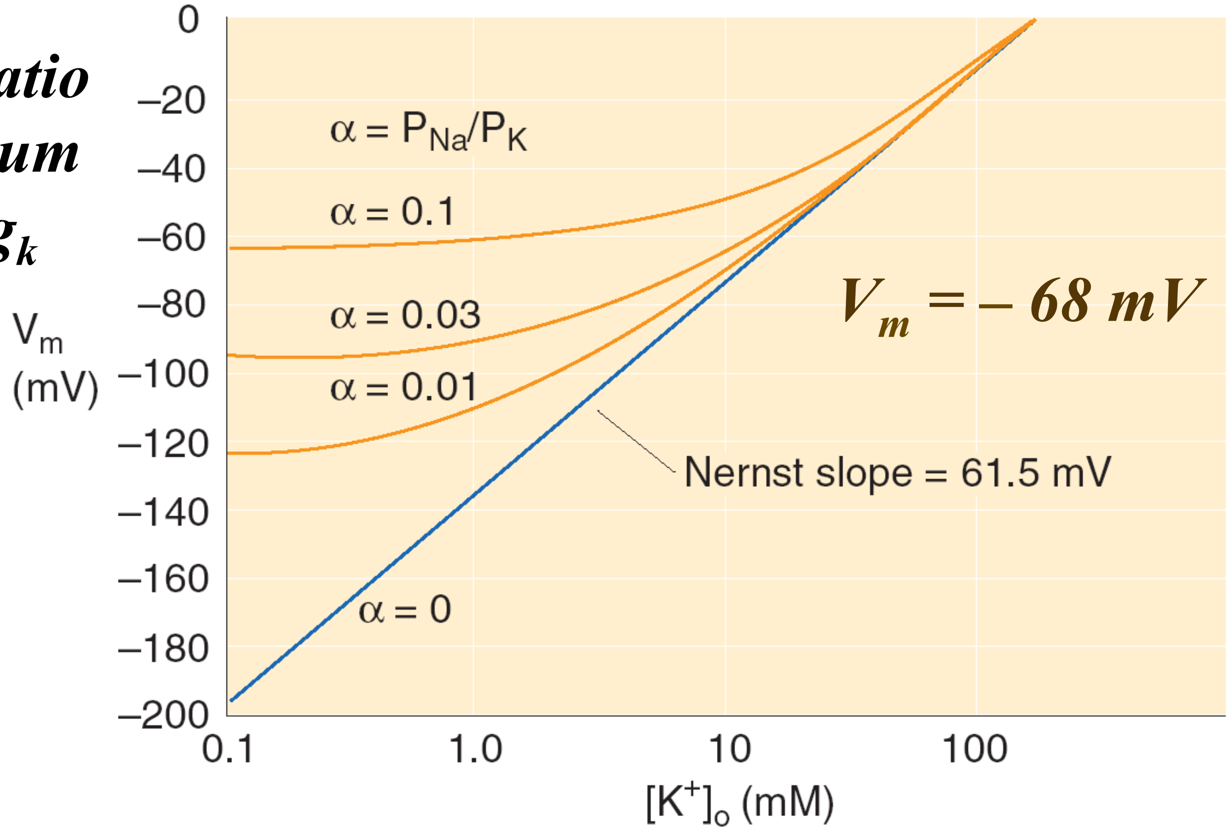
$$\frac{P_K[K^+_{in}]\exp\left(\frac{F\Delta\Psi}{RT}\right) - P_K[K^+_{out}]}{1-\exp\left(\frac{F\Delta\Psi}{RT}\right)} + \frac{P_{Na}[Na^+_{in}]\exp\left(\frac{F\Delta\Psi}{RT}\right) - P_{Na}[Na^+_{out}]}{1-\exp\left(\frac{F\Delta\Psi}{RT}\right)}$$

$$+\frac{P_{Cl}[Cl^-_{in}]\exp\left(-\frac{F\Delta\Psi}{RT}\right) - P_{Cl}[Cl^-_{out}]}{1-\exp\left(-\frac{F\Delta\Psi}{RT}\right)} = 0$$

$$\mathbf{P_K : P_{Na} : P_{Cl} = 1 : 0.04 : 0.45}$$

$$\Delta\Psi = \frac{RT}{F}\ln\frac{P_K[K^+_{out}] + P_{Na}[Na^+_{out}] + P_{Cl}[Cl^-_{in}]}{P_K[K^+_{in}] + P_{Na}[Na^+_{in}] + P_{Cl}[Cl^-_{out}]}$$

V_m depends on the ratio of sodium to potassium conductance, g_{Na}/g_k

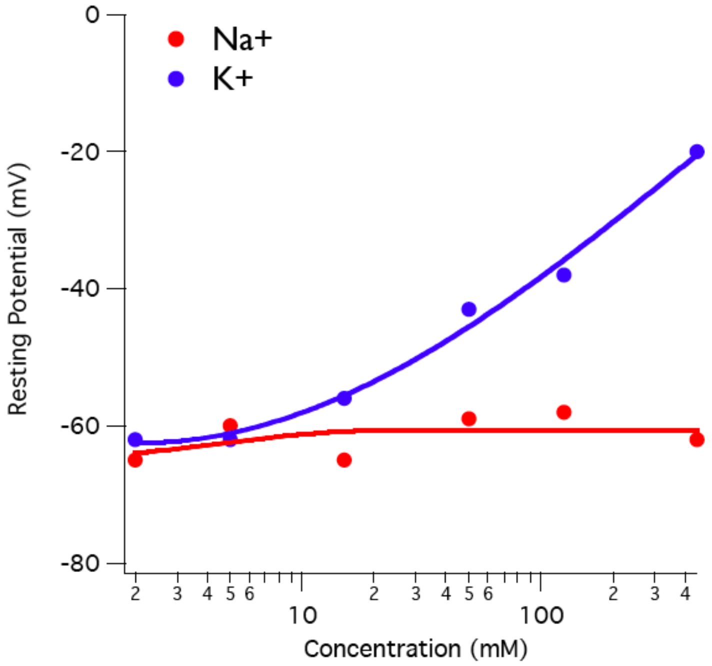


$V_m = – 68\ mV$

- *At rest $g_{Na} << g_k$ – the membrane potential is close to the potassium equilibrium potential*

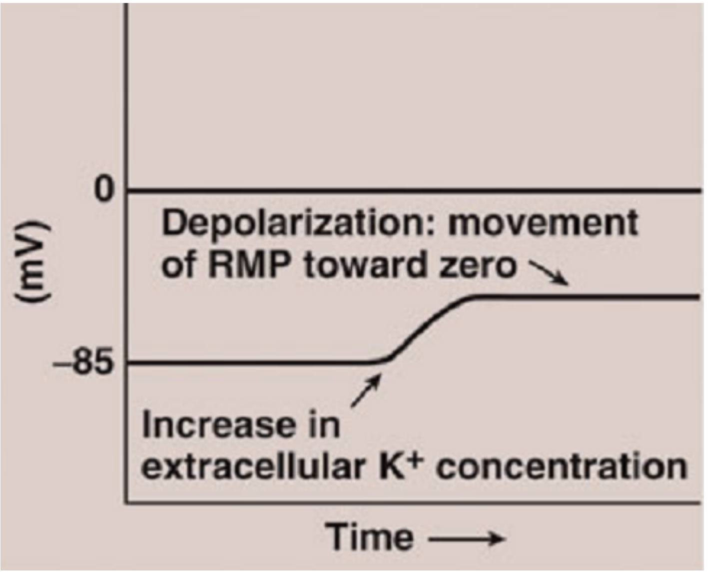
- *At rest $g_{Na} > 0$ – the membrane potential is "pulled" slightly away from V_K.*

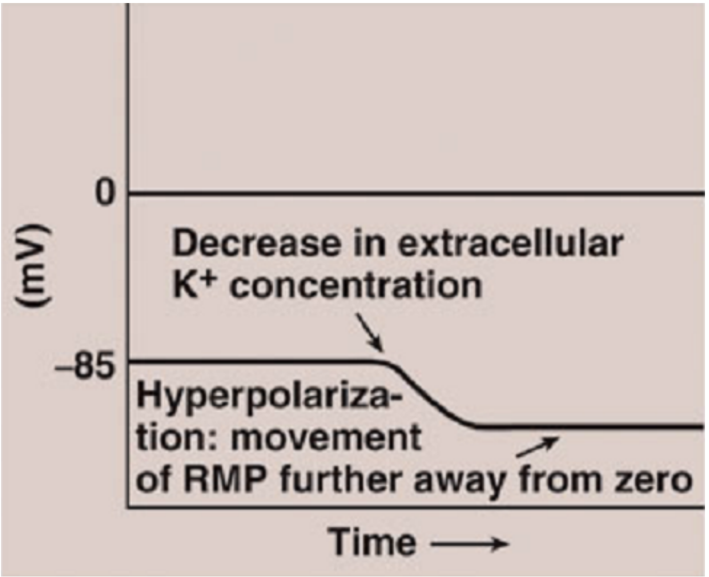
Changes in Resting Membrane Potential

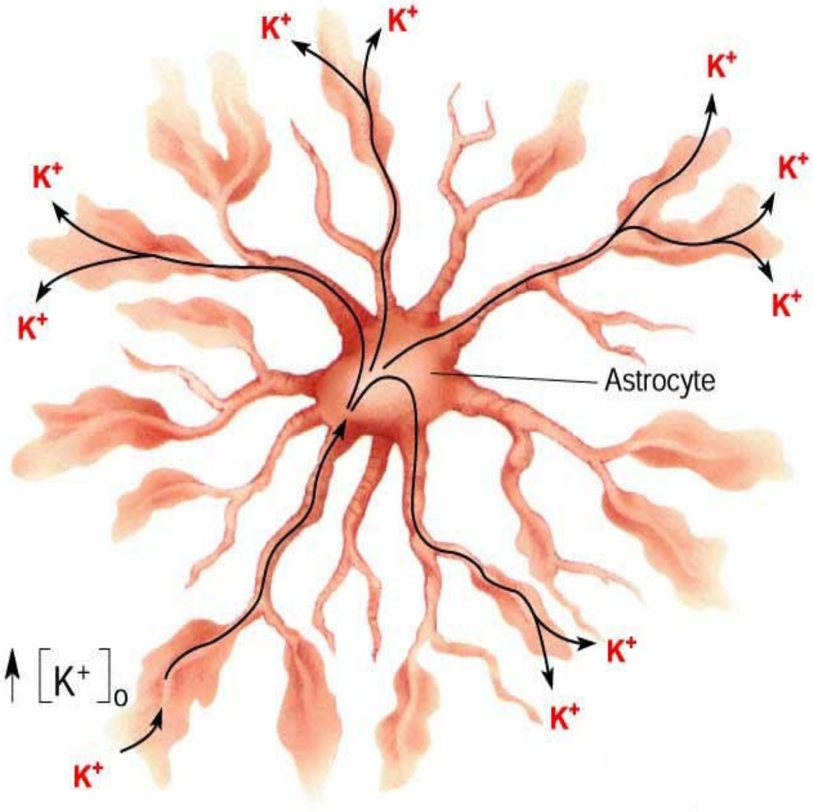


Resting potential strongly depends upon the external K^+ concentration

Resting potential is independent of external Na^+ concentration







Neurones become depolarised and die if they are exposed for too long to high concentrations of extracellular K^+.

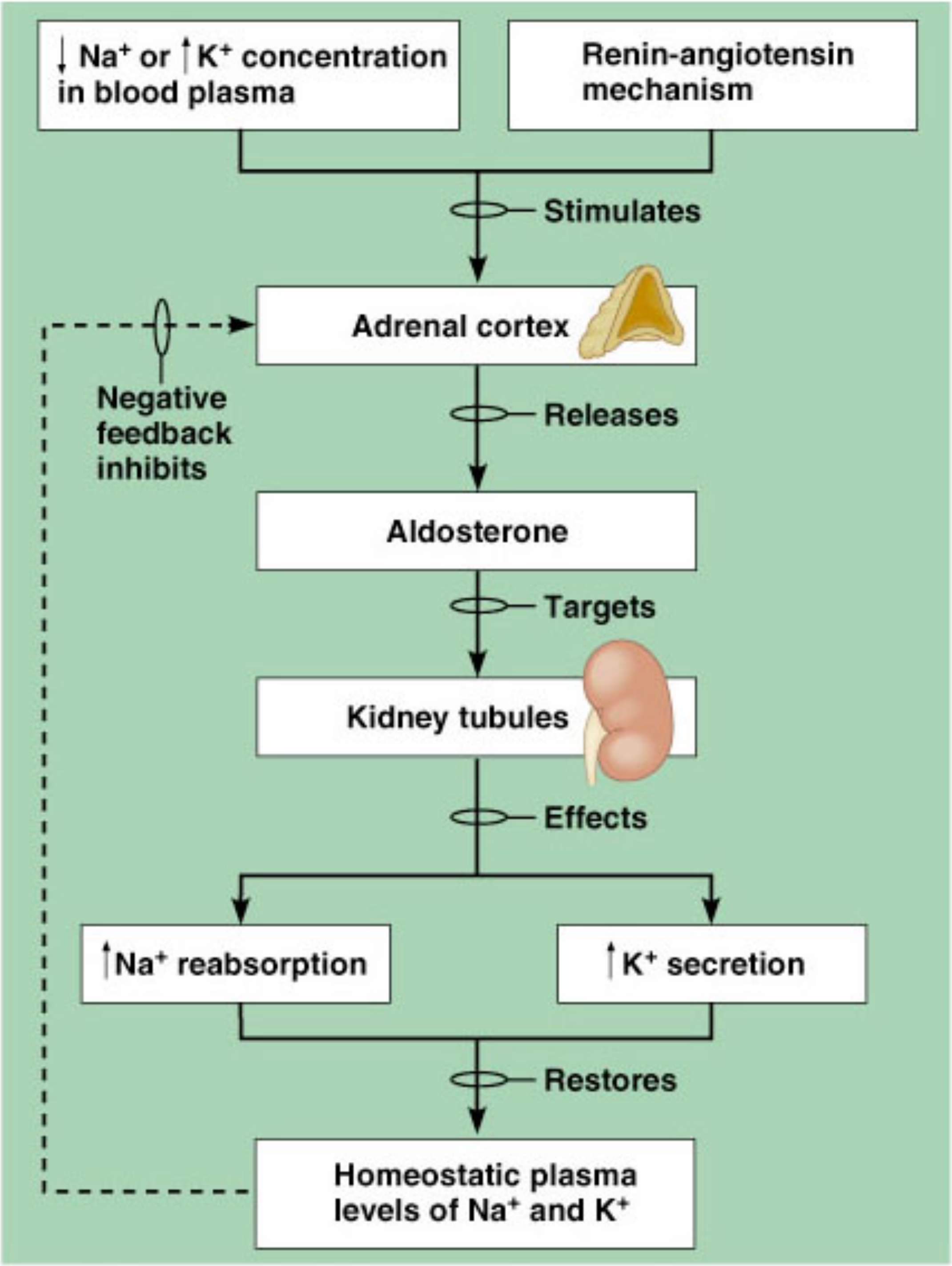
Astrocytes and other neuroglia have very high resting K^+ permeabilities – in fact their resting potentials are very close to the Nernst potential for K^+.

They are effective K^+ buffers.

Increases in extracellular K^+, caused by leakage from nearby neurones, are ‘mopped up’ by astrocytes.

One strategy for the treatment of stroke and epilepsy is to increase the efficiency of these glial cells as K^+ buffers, limiting neuronal damage.

Regulation of Ions Balance: Aldosterone



↓ Na^+ or ↑ K^+ concentration in blood plasma

Renin-angiotensin mechanism

Stimulates

Adrenal cortex

Negative feedback inhibits

Releases

Aldosterone

Targets

Kidney tubules

Effects

↑ Na^+ reabsorption

↑ K^+ secretion

Restores

Homeostatic plasma levels of Na^+ and K^+