Resting Membrane potential (V_m) or RMP

Many cells have a membrane potential (V_m) that can be measured from an electrode in the cell with a voltmeter.

neurons, muscle cells, heart cells, endocrine cells...

V_m = resting membrane potential (RMP)

= electrical potential generated by separation of charges

= voltage across the membrane

= V_{inside} - $V_{outside}$

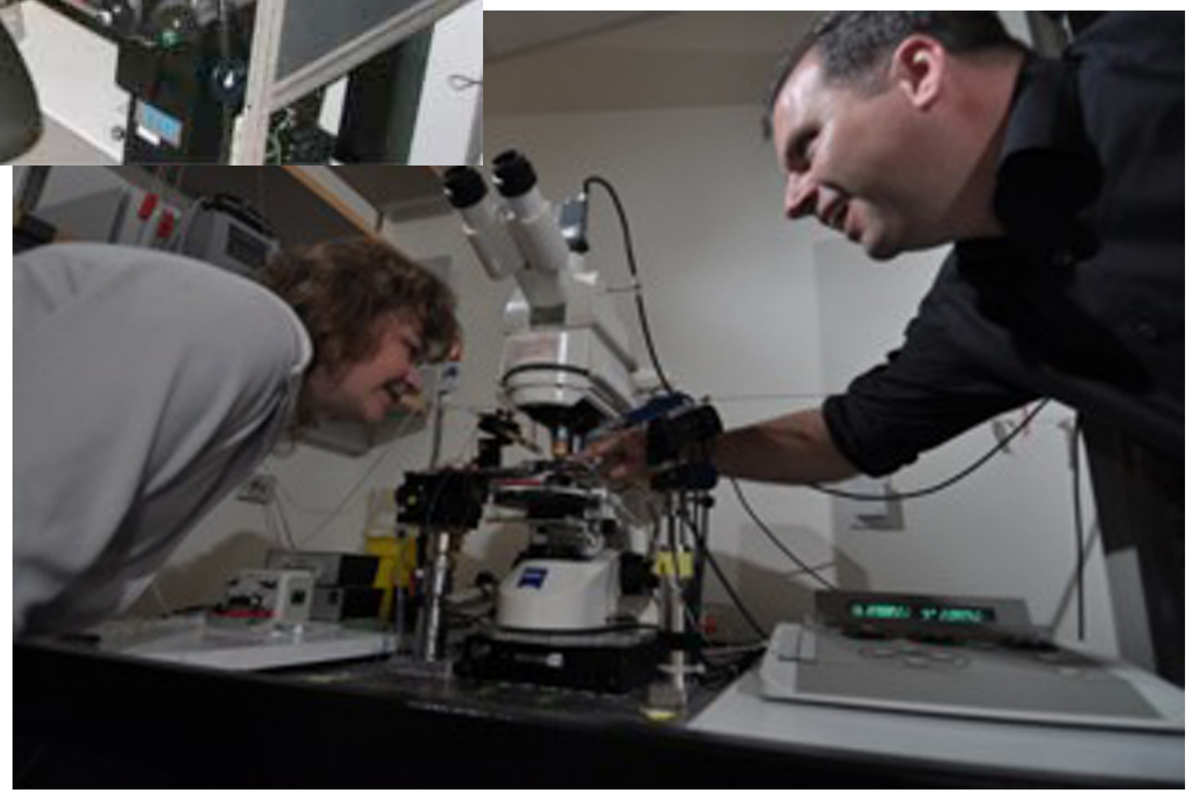
Cells have an unequal distribution of charge across their membrane:
more postiive charges on the outside; more negative charges on the inside.

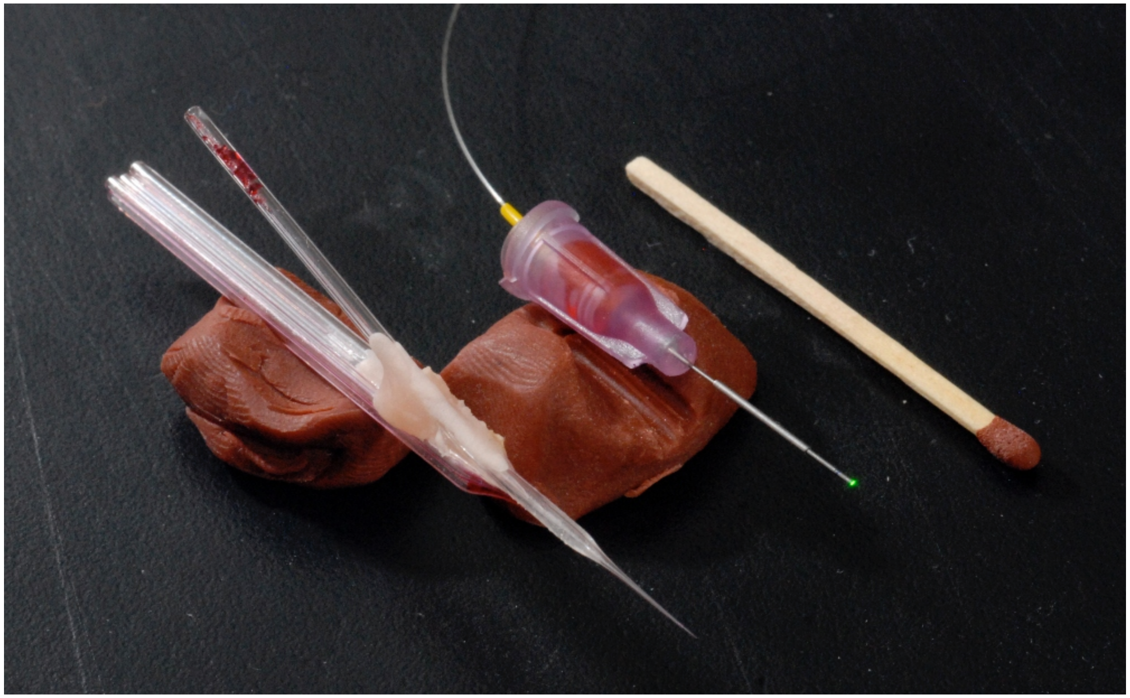
Charge separation is caused by movement of ions in and out the cell.

Ions are moved by chemical diffusion down concentration gradients and by electrical attraction, and by active transport (e.g. Na+/K+ pump.)

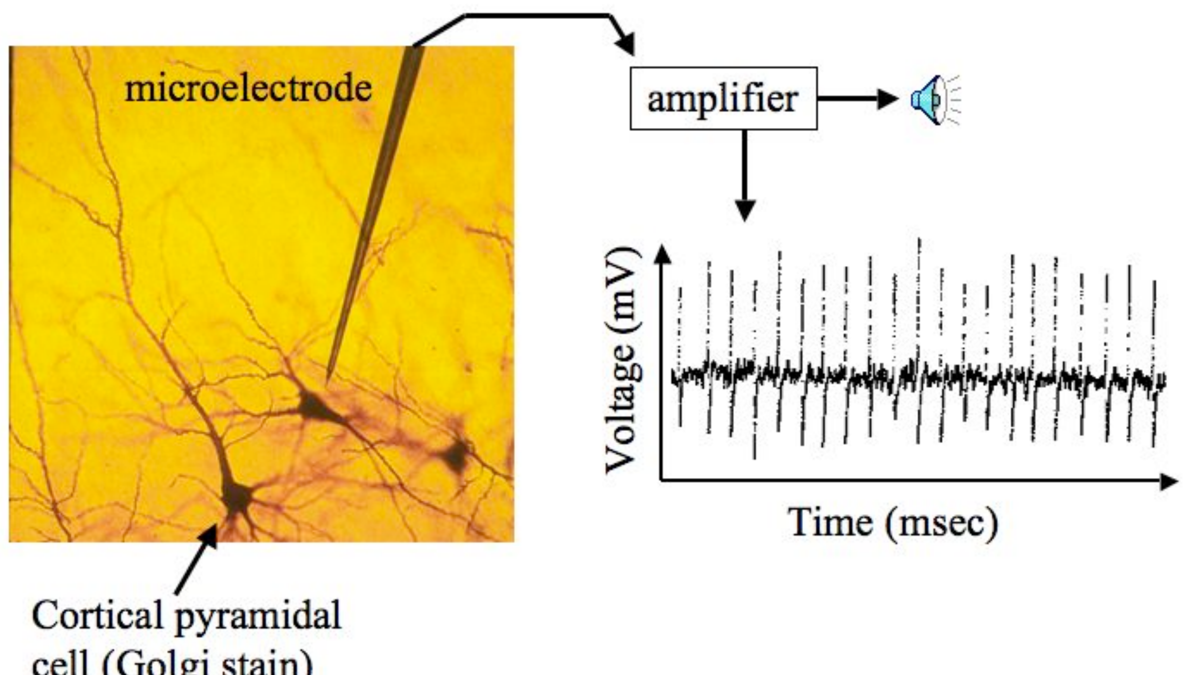
Concentration of ions inside and outside reaches equilibrium (stays constant) due to **equilibrium potential.**

http://www.youtube.com/watch?v=k48jXzFGMc8



Single-cell electrophysiology



http://www.youtube.com/watch?v=AEY-t9hyNBI

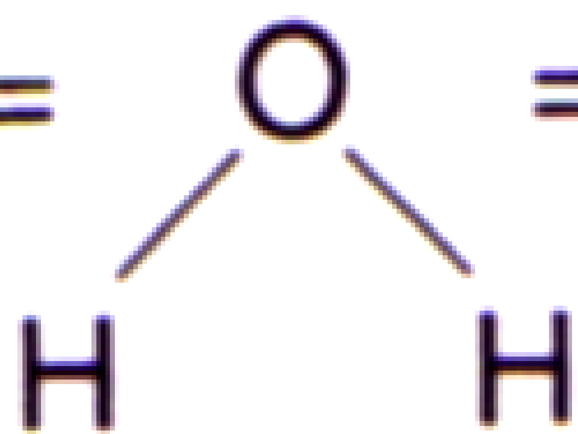
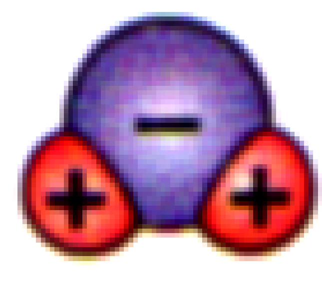
Ion Channels & Membrane Potential

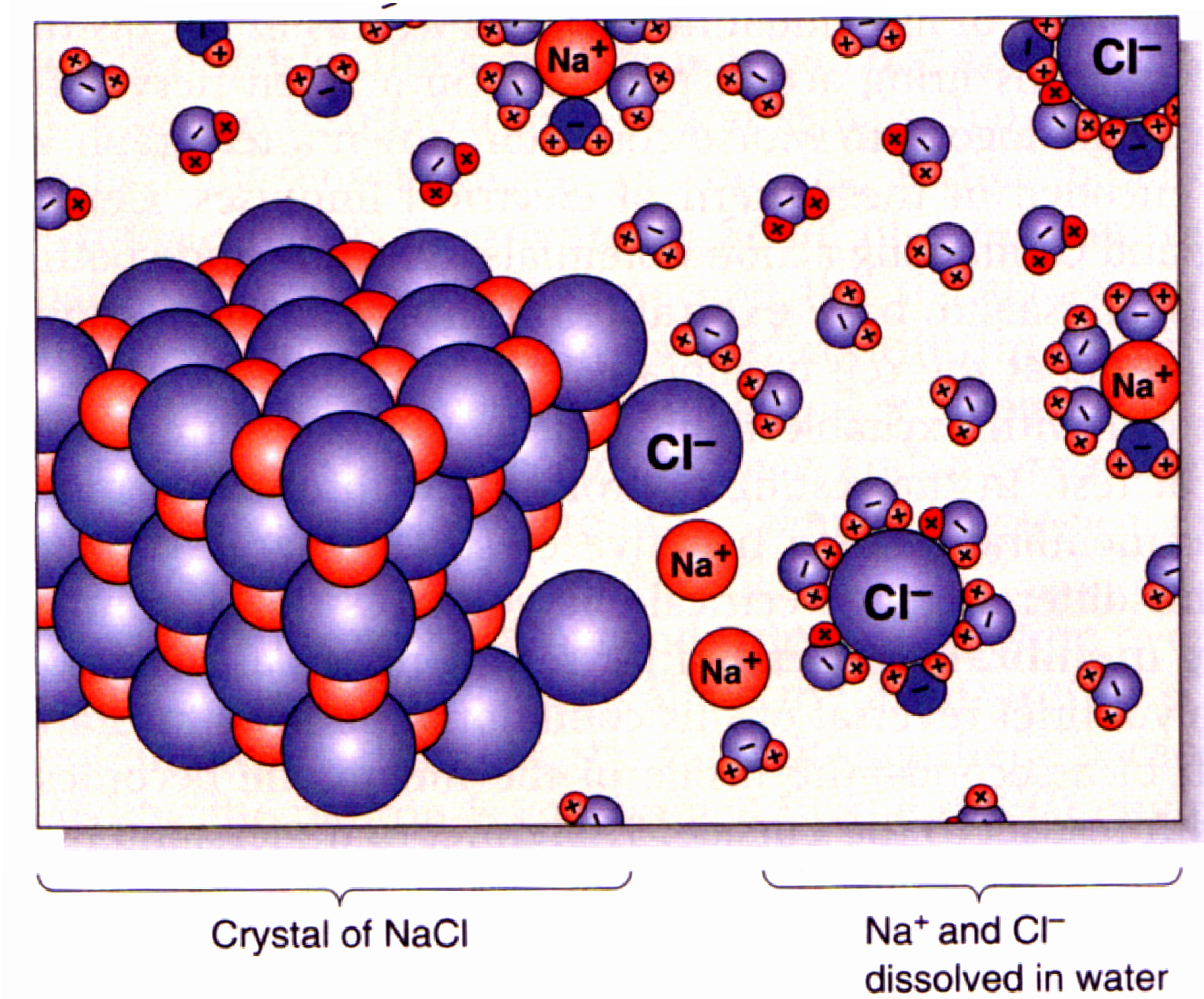
Neurons need to send signals quickly over long distances.

They utilize waves of electrical current across their membranes.

This requires that they maintain a differential distribution of charge between the inside and outside of the neuron,

and that they can switch a cross-membrane current on and off to make the signal.

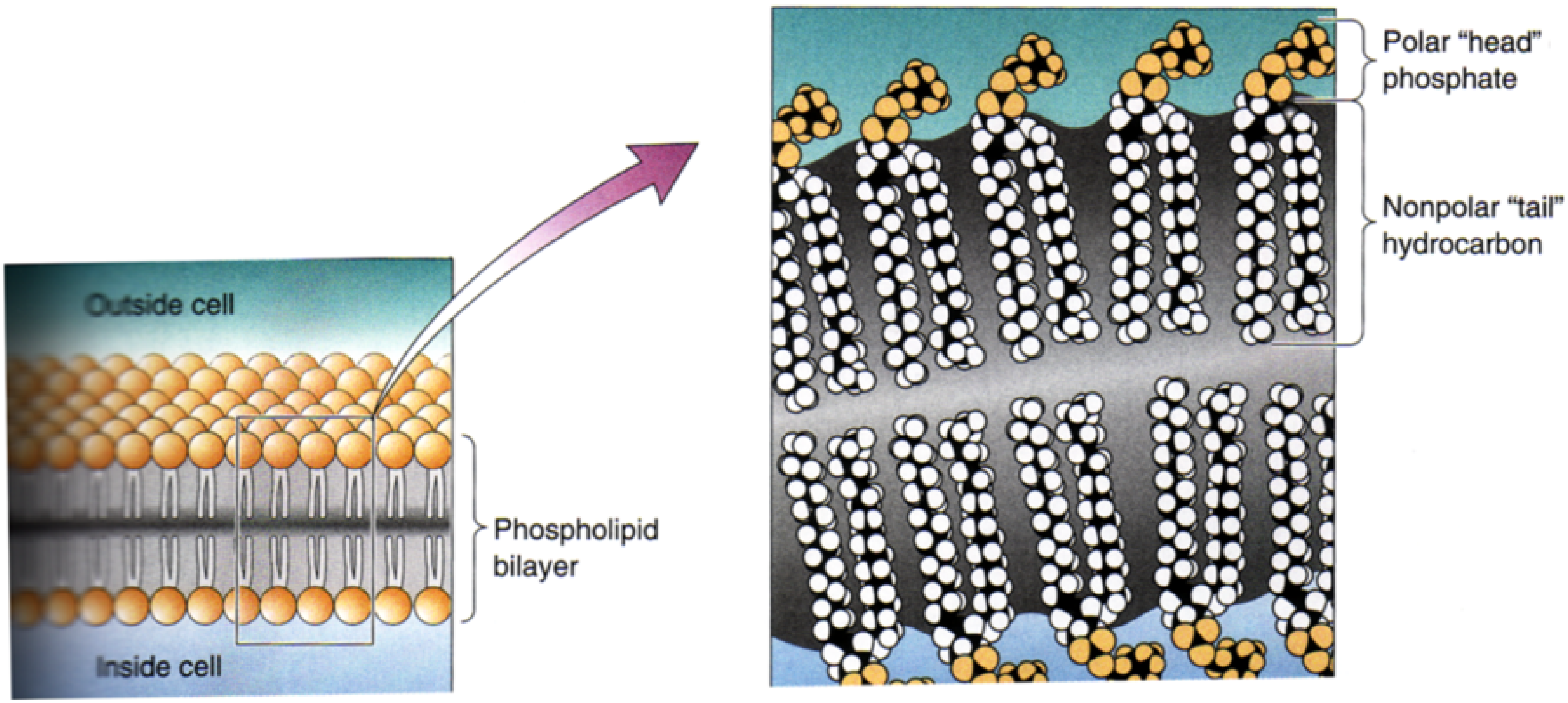
H_2O =  = 



Major ions in neuroscience:
Na+, K+, Cl-, Ca++, & protein anions (A-)

outside

[Na+] [K+]



[Na+] [K+]

inside

Na+/K+ Transporter

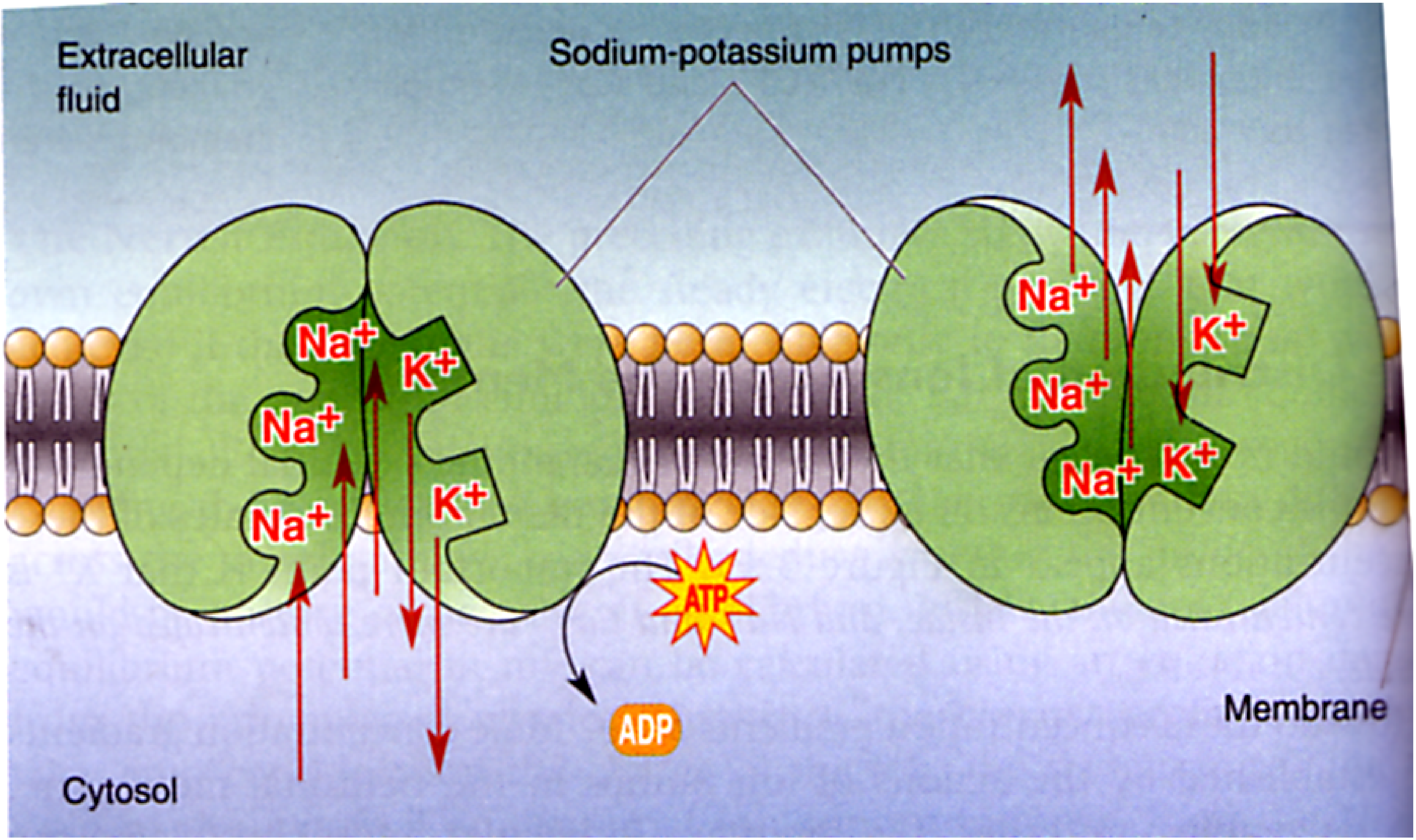
Ion	Outside (mM)	Inside (mM)
K^+	5	100
Na^+	150	15

Na ions slowly leak into cell down concentration gradient and attracted by negative charges of the cytoplasm.

Neuron actively maintains Na and K concentrations by exchanging:

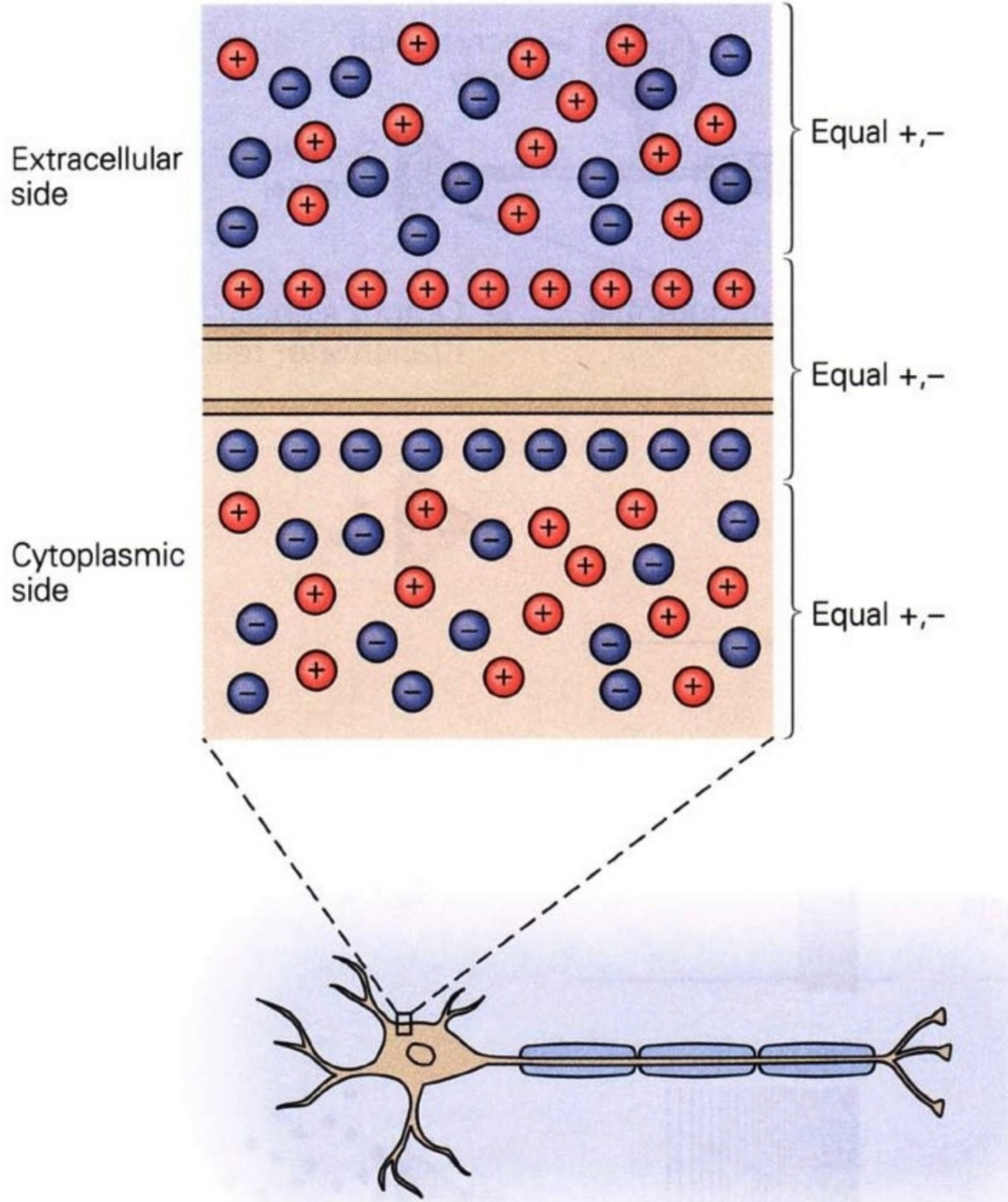
3 Na ions out for 2 K ions in for every 1 ATP molecule.

[Na+] [K+]


Extracellular fluid
Sodium-potassium pumps
Na+
Na+
Na+
K+
K+
Na+
Na+
Na+
K+
K+
ATP
ADP
Membrane
Cytosol

[Na+] [K+]

Unequal charges across the cell membrane



Membrane potential (V_m)

V_m = resting membrane potential

= electrical potential generated by separation of charges

= voltage across the membrane

= $V_{inside} - V_{outside}$

Membrane potential (V_m)

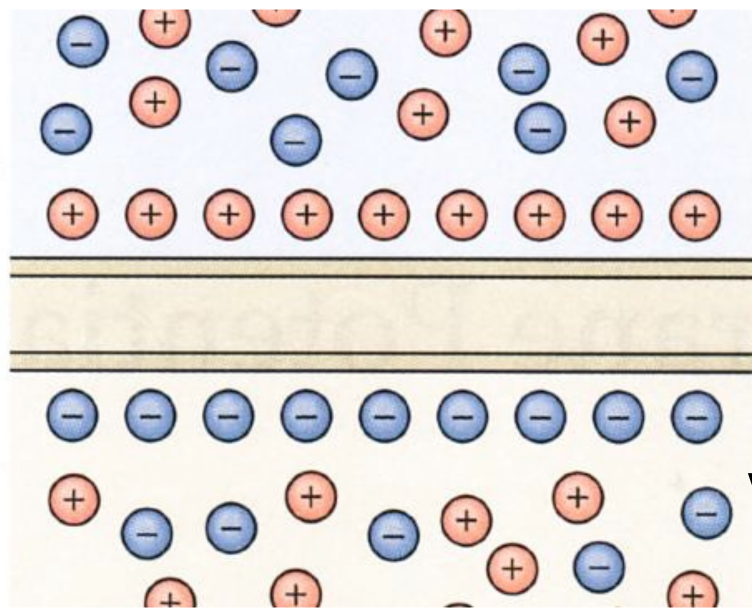
$$V_m = V_{in} - V_{out}$$

(V_{out} = 0 mV by definition)

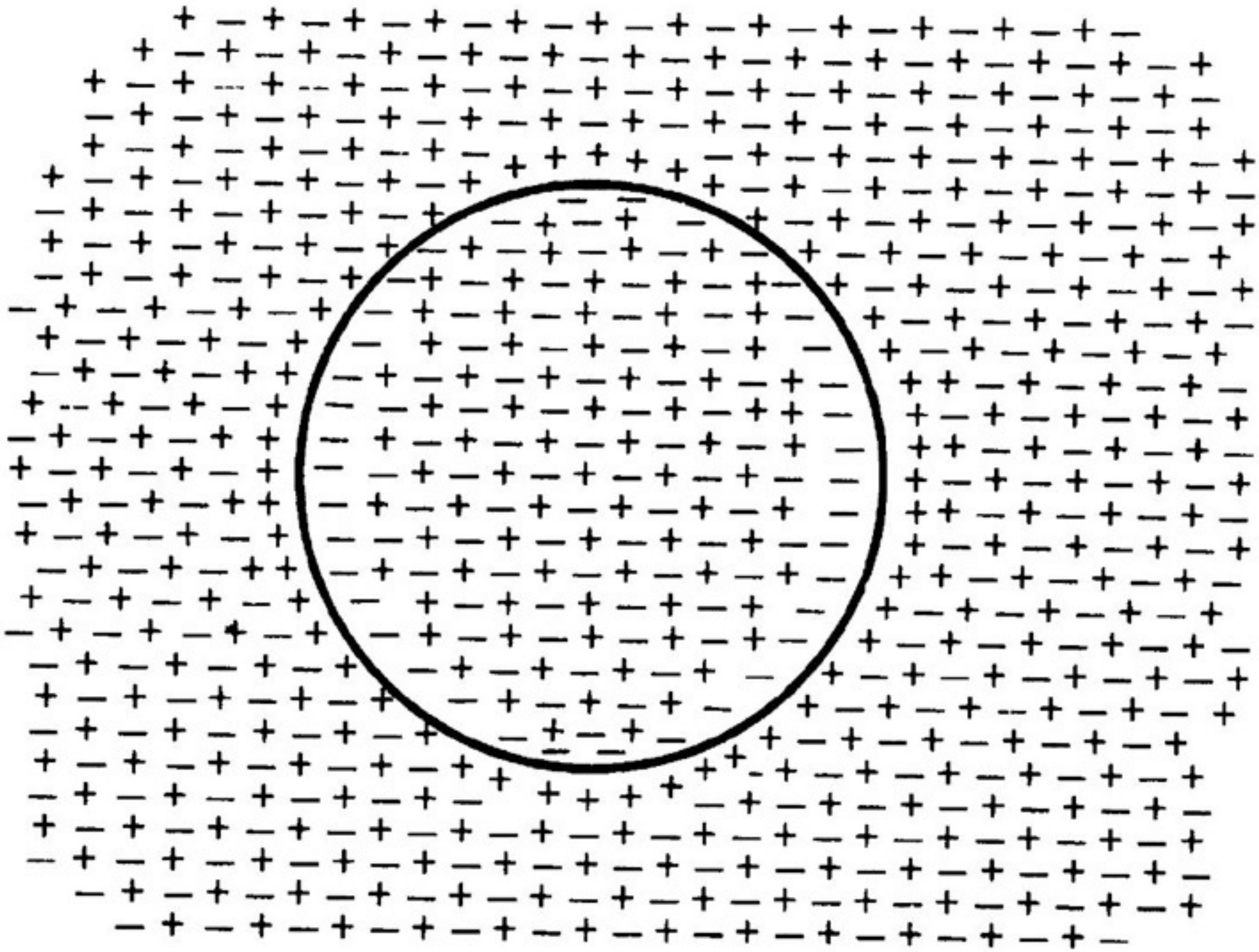
$$V_m = V_{in} - 0$$

(more negative ions inside)

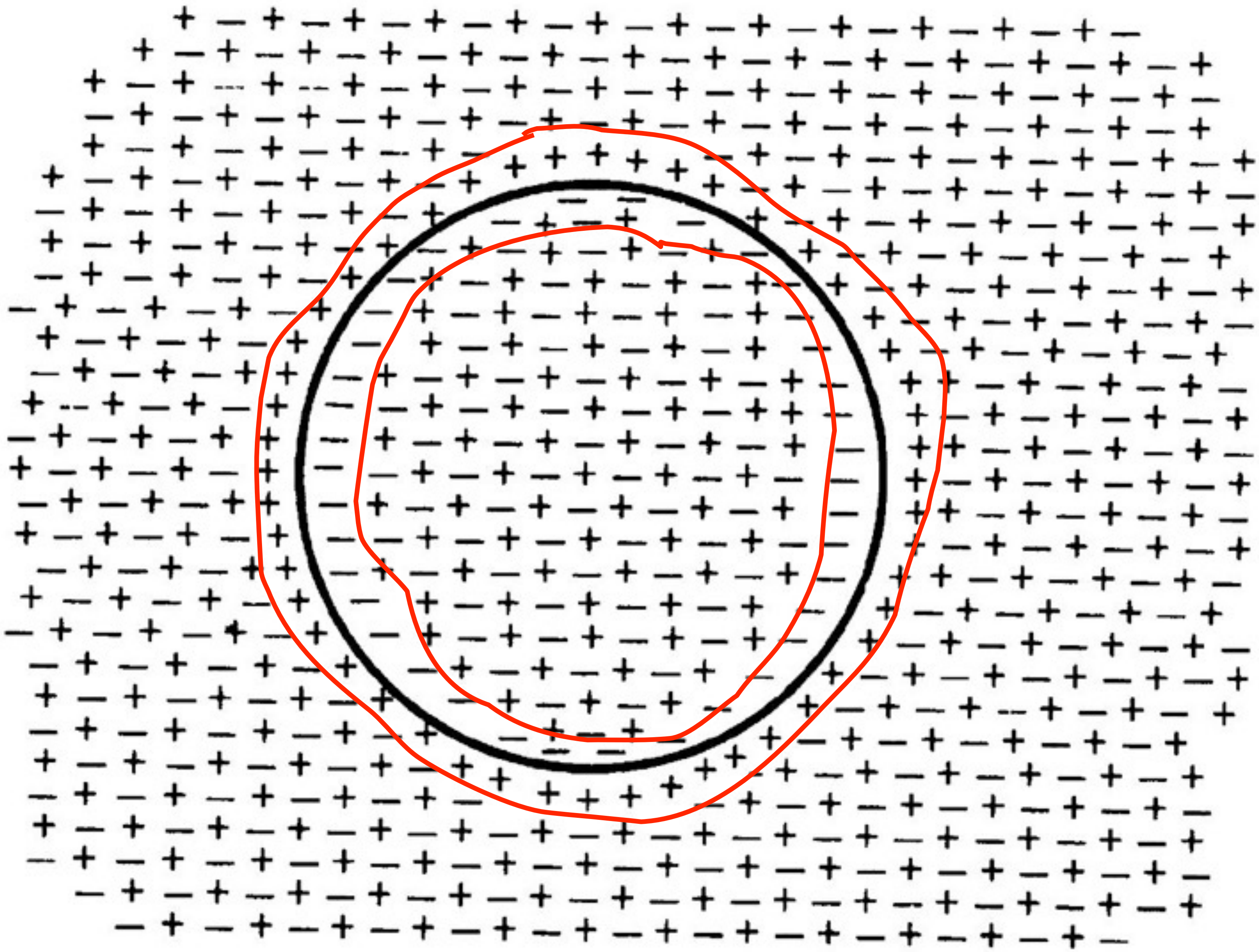
$$V_m = -60 \text{ to } -70 \text{ mV}$$



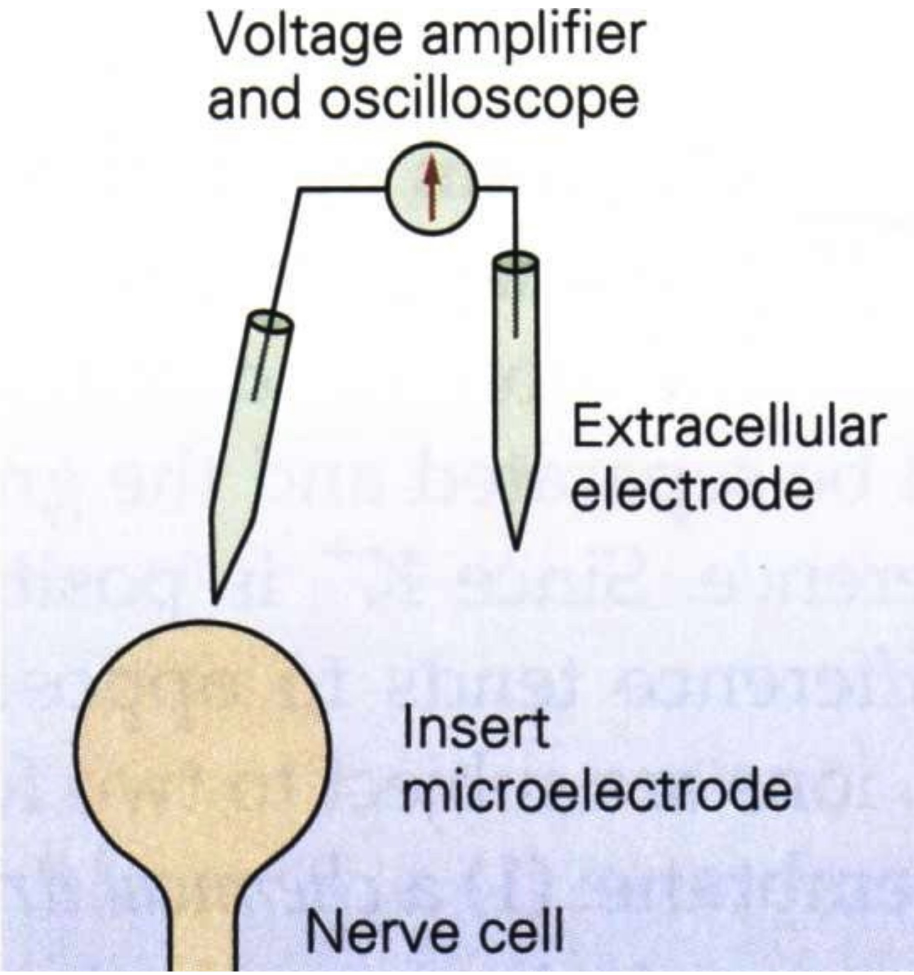
Membrane potential is caused by small number of total ions

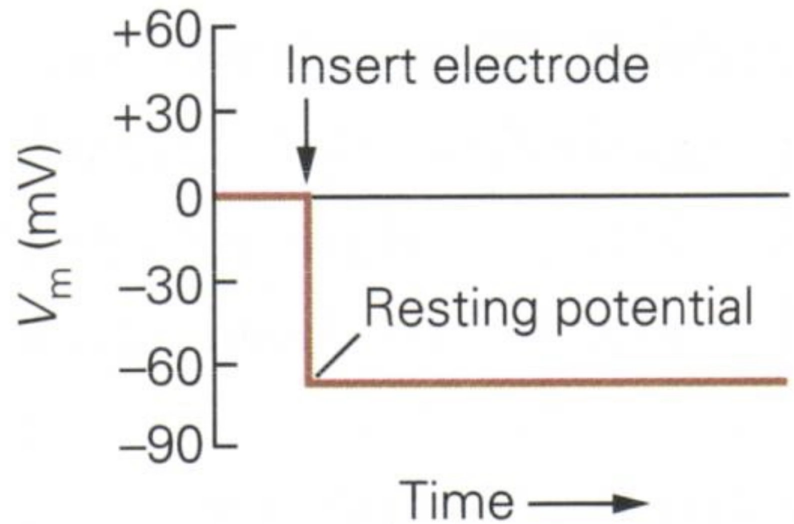


Membrane potential is caused by small number of total ions

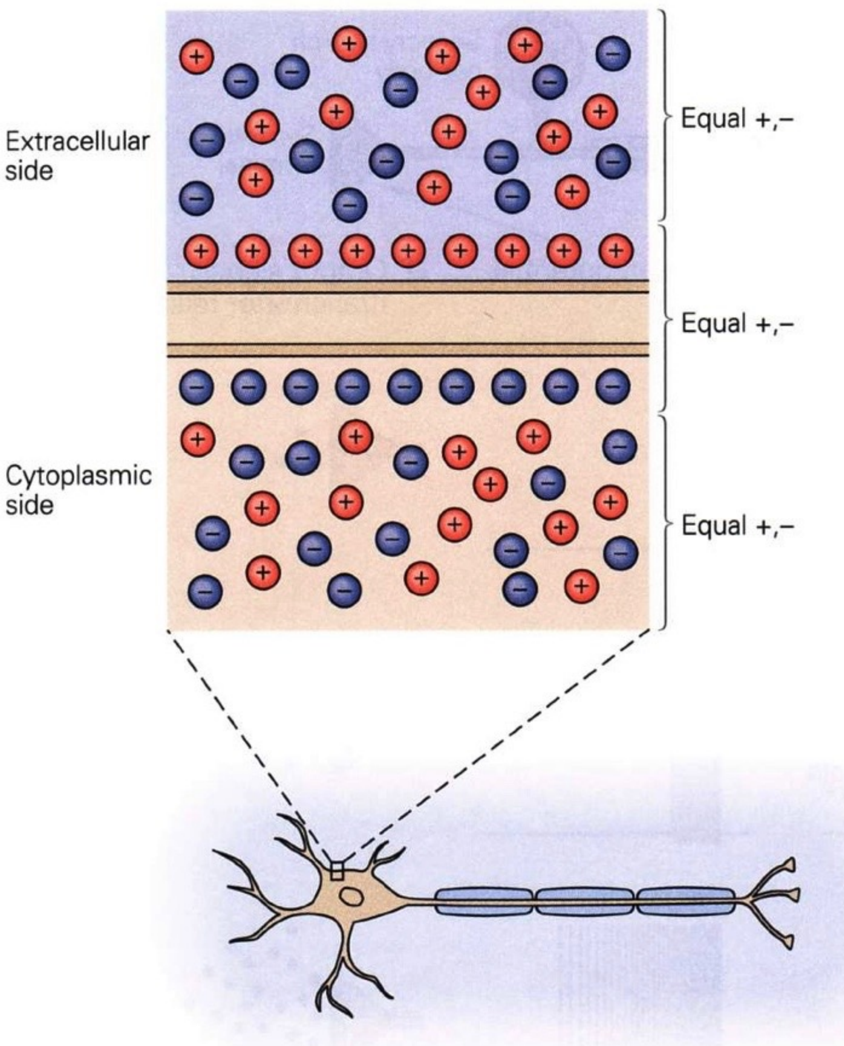


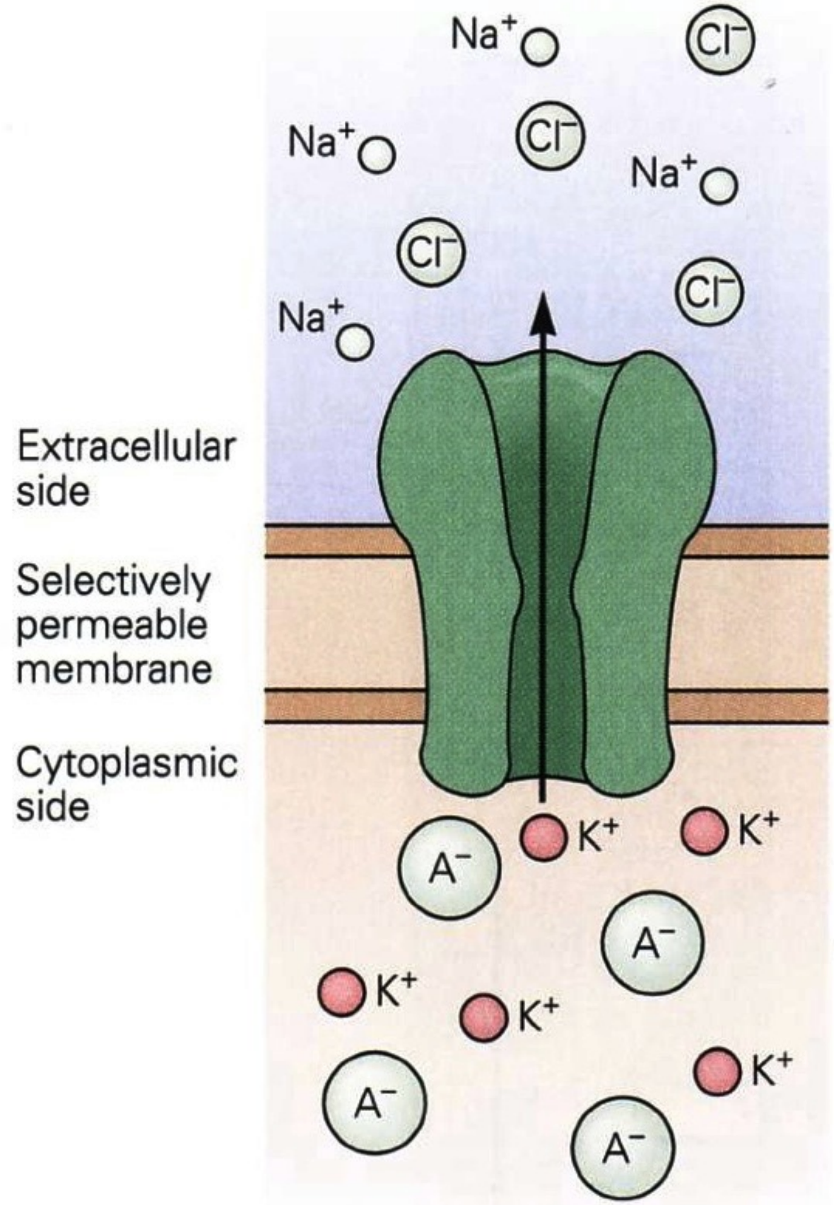
Measuring V_m



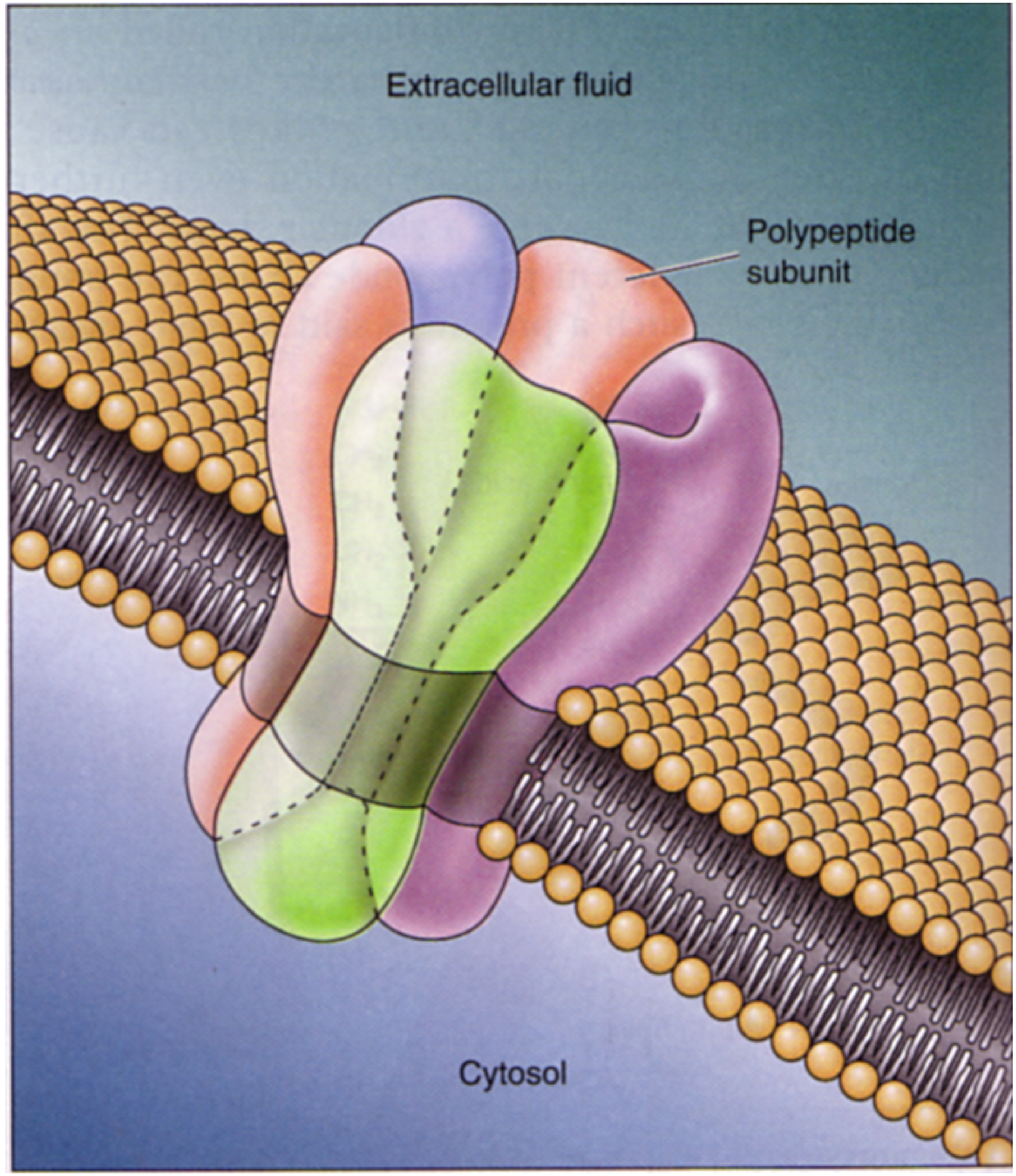


How to establish the membrane potential?





Ion Channels: proteins that span the membrane and allow ions to diffuse across the phospholipid bilayer



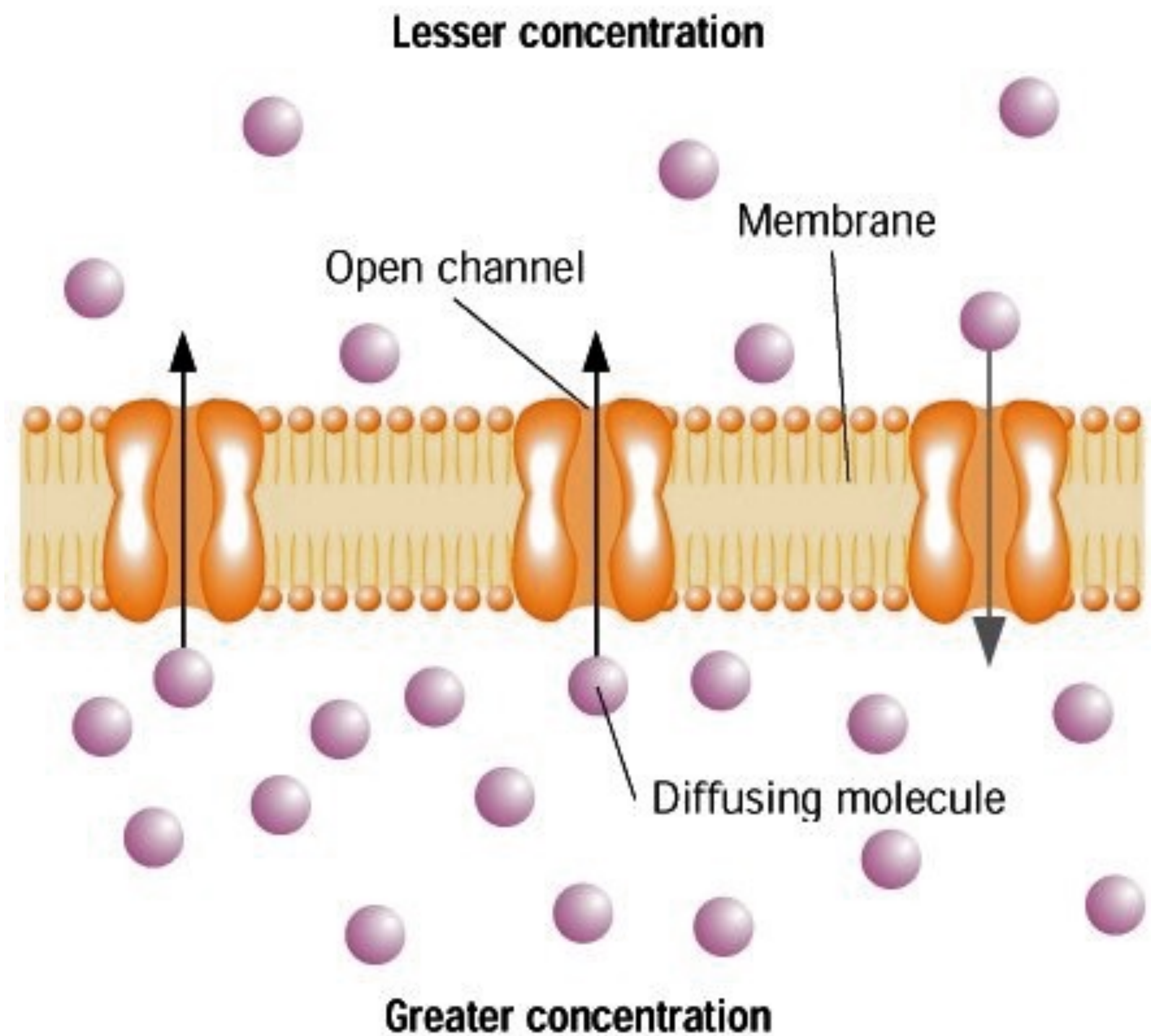
Equilibrium Potential for an ion

Each ion species feels two forces pulling on it:

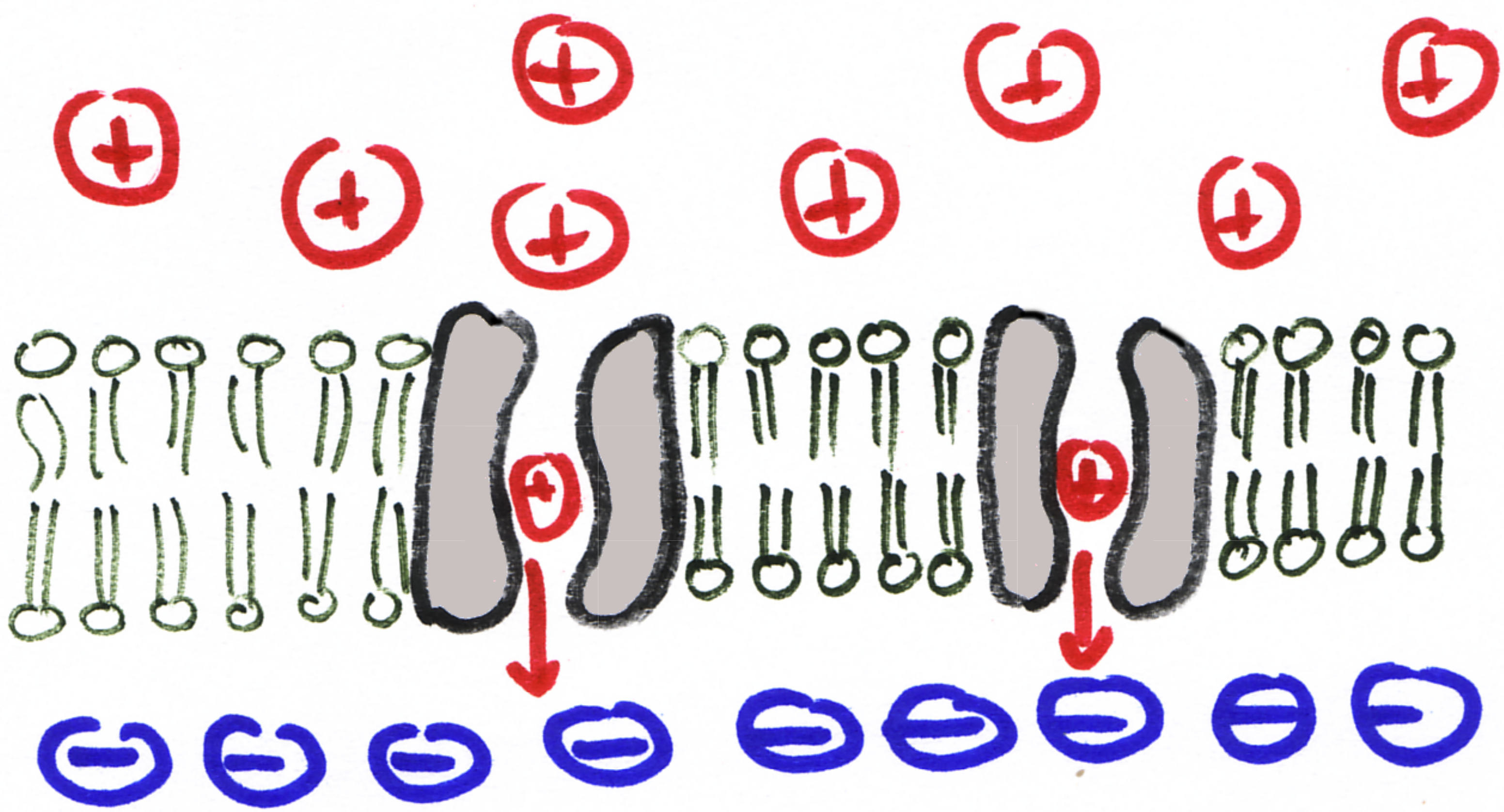
chemical driving force: depends on concentration gradient across membrane

electrical driving force: depends on electrical potential difference across membrane

Force on ions:
Diffusion down concentration gradient



Force on ions:
Pulled toward opposite charge



Equilibrium Potential for an ion

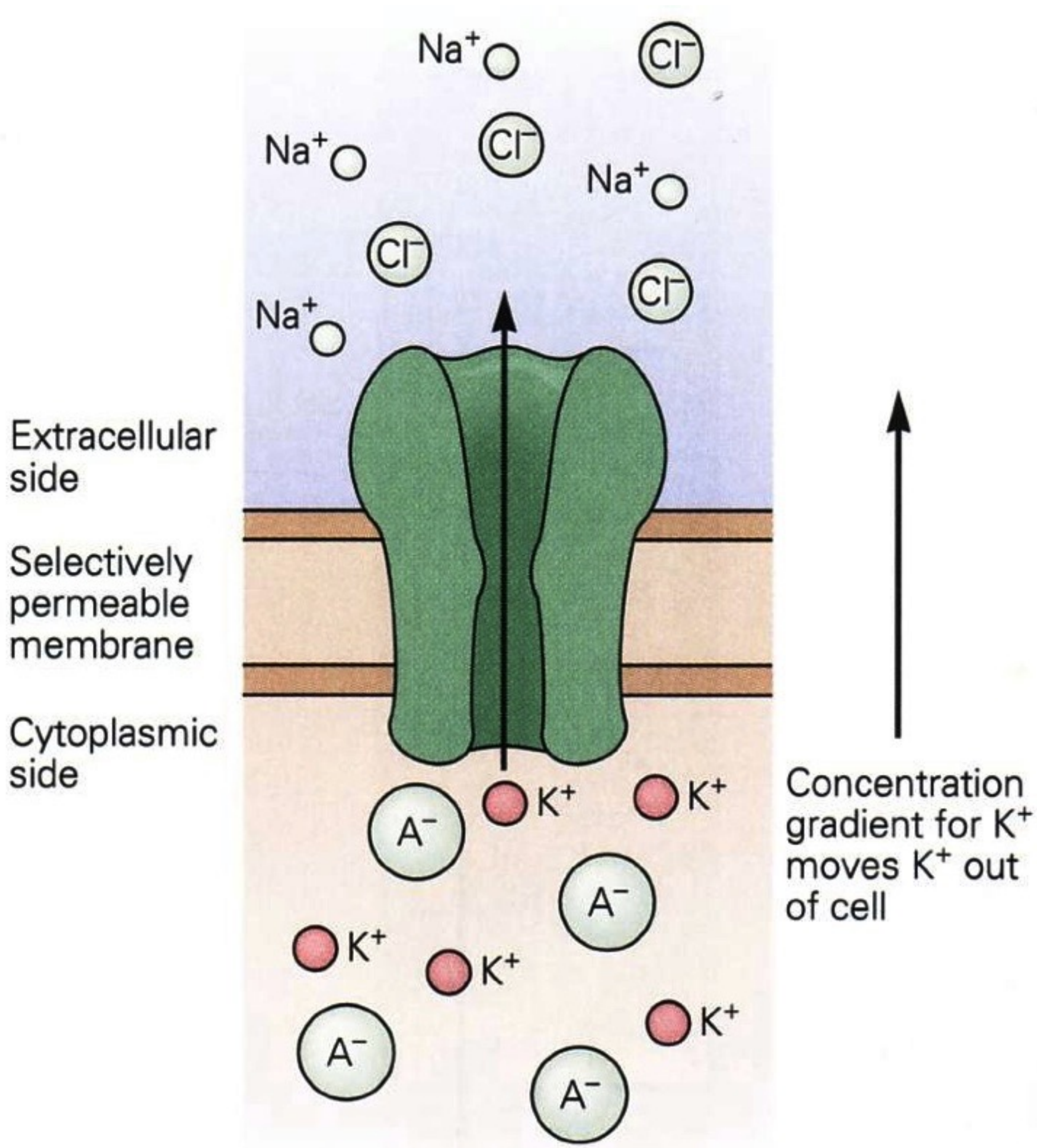
Each ion species feels two forces pulling on it:

chemical driving force: depends on
concentration gradient across membrane

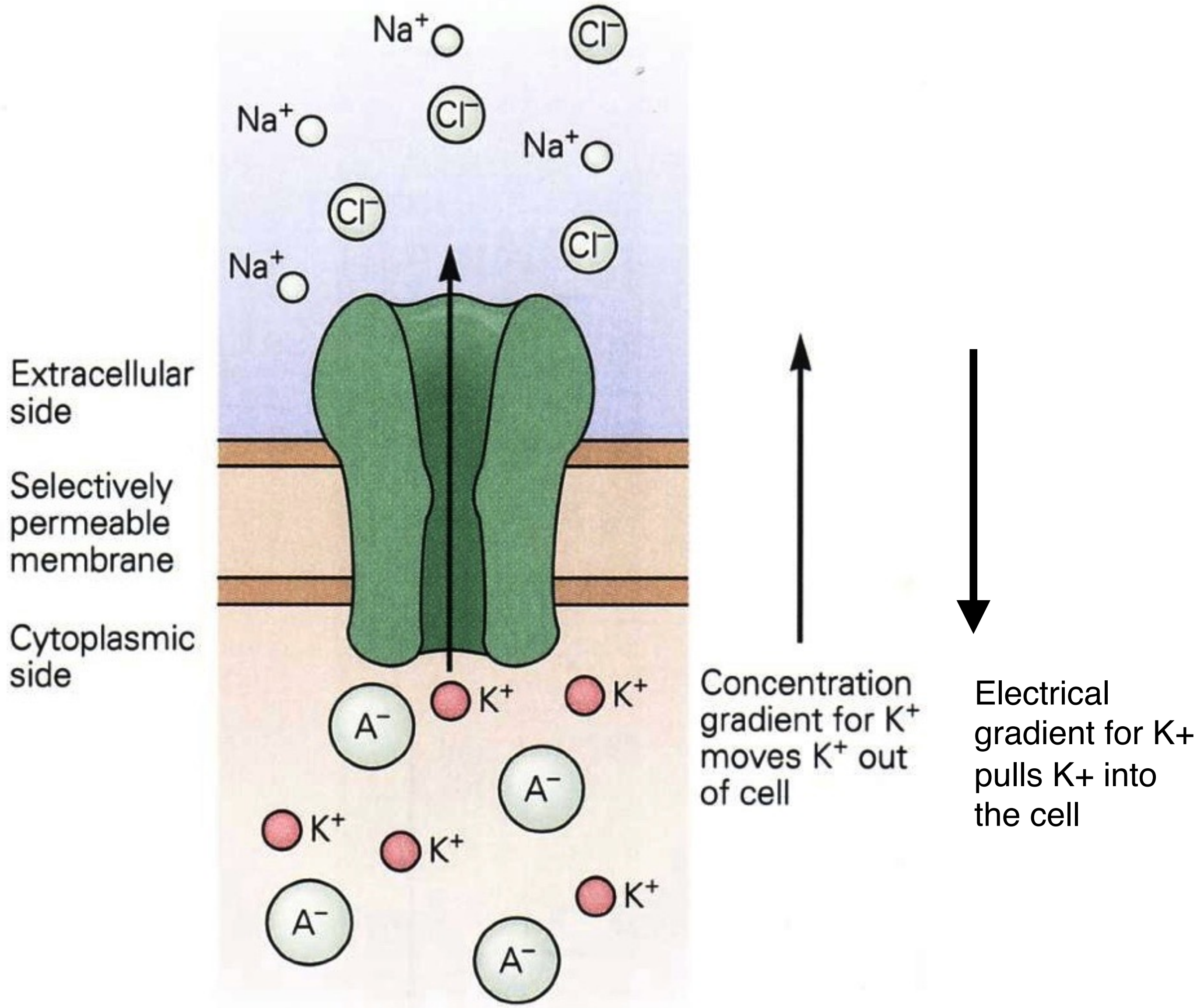
electrical driving force: depends on electrical
potential difference across membrane

these forces can act in same direction or
opposite directions across the membrane

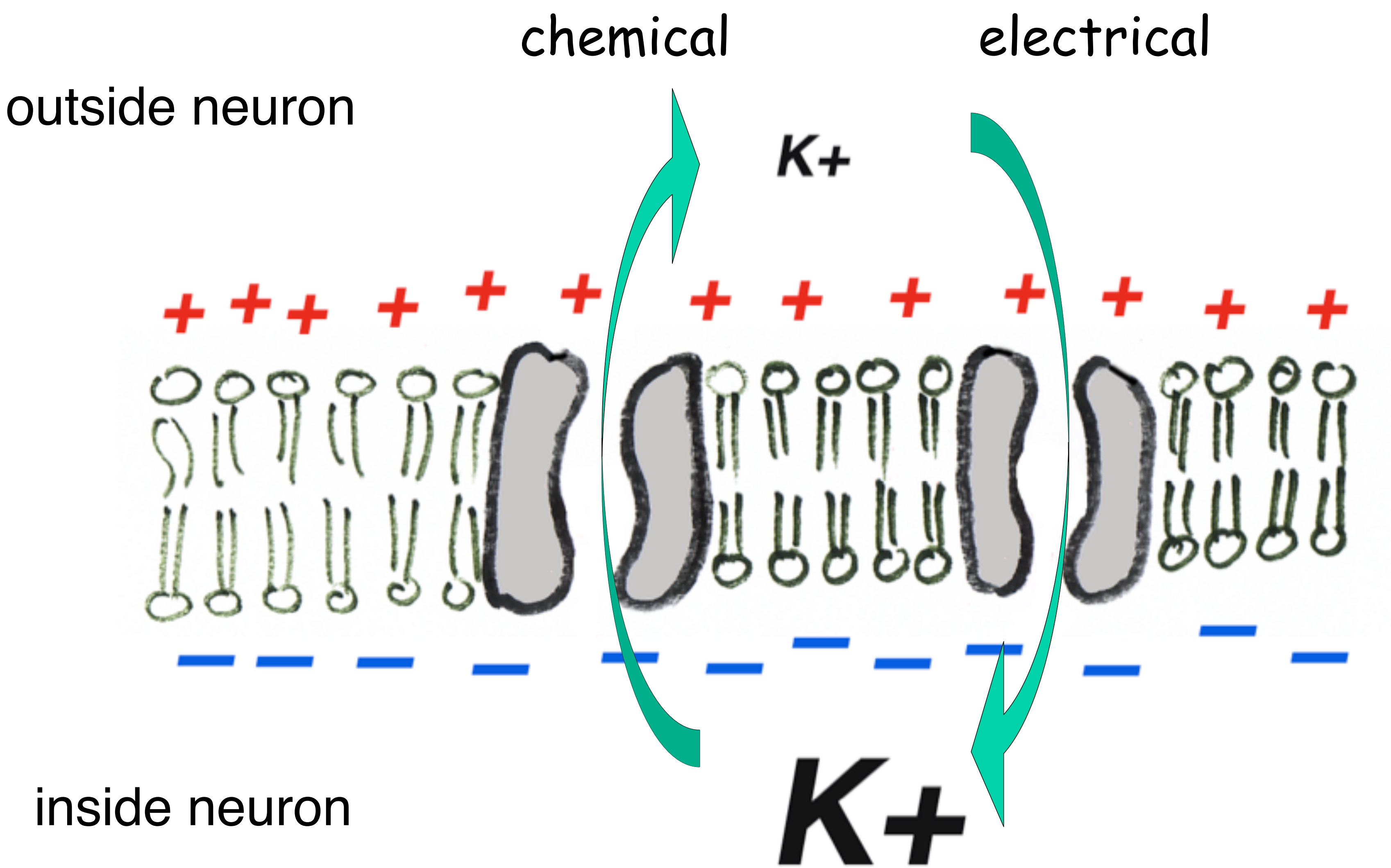
For potassium, chemical and electrical forces are in opposite directions



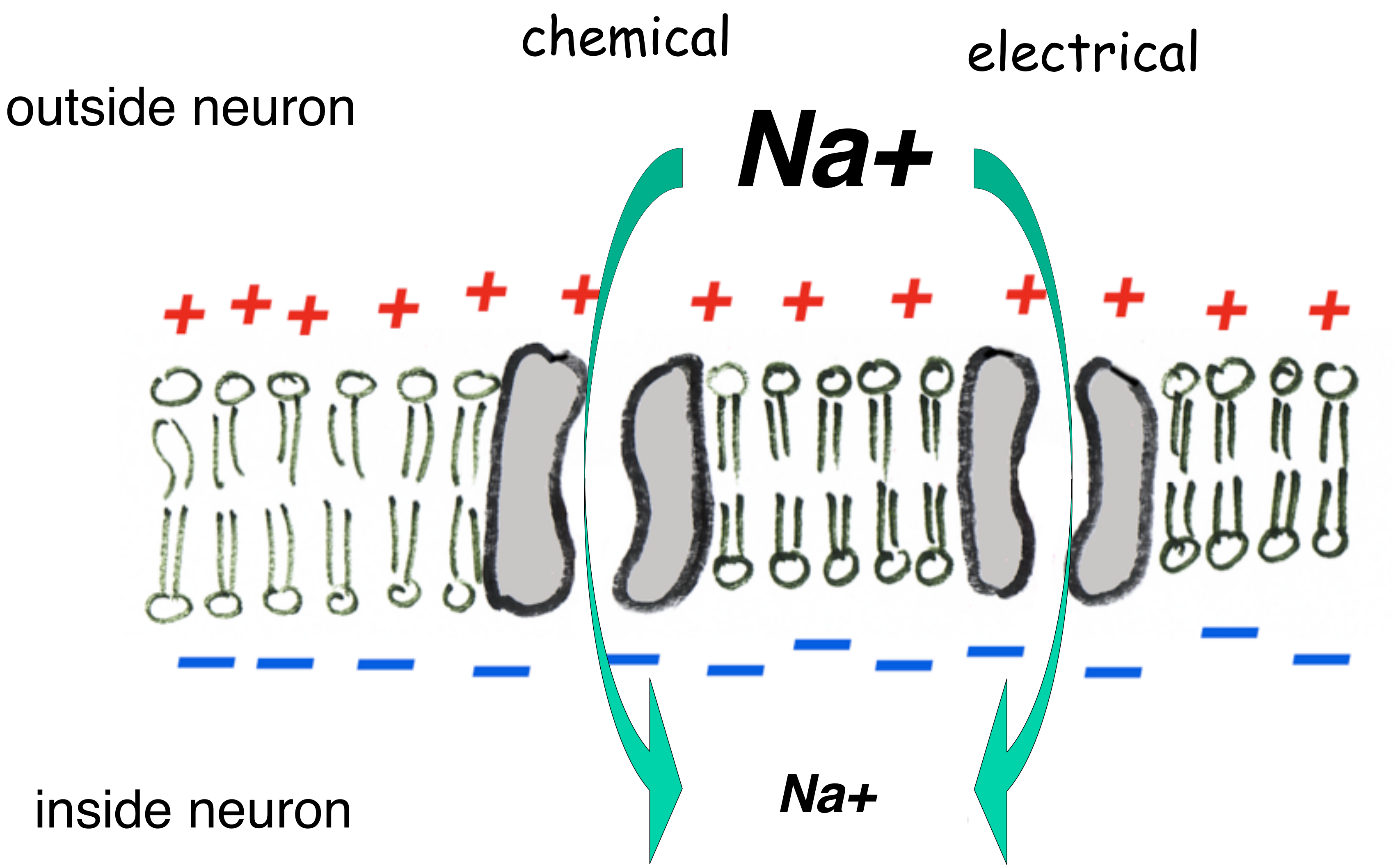
For potassium, chemical and electrical forces are in opposite directions



Electrochemical Forces on Potassium K^+ Ion



Electrochemical Forces on Sodium Na+ Ion



Equilibrium Potential for an ion

Each ion species feels two forces pulling on it:

chemical driving force: depends on concentration gradient across membrane

electrical driving force: depends on electrical potential difference across membrane

these forces can act in same direction or opposite directions across the membrane

the electrical potential that balances the concentration gradient is called the equilibrium potential.

Equilibrium Potential for an ion

If there are open channels for an ion, the electrical and chemical driving forces will try to force the ions to move across the membrane.

the ion will move across the membrane until the change in electrical charge causes the cell's V_m to reach the ion's equilibrium potential.

Equilibrium Potential for one ion across the membrane

https://www.youtube.com/watch?v=4kx9_0YwShE

Distribution of Ions in Mammalian Neurons

Ion	Outside (mM)	Inside (mM)	Ratio Out : In	E_{ion}
K^+	5	100	1:20	?
Na^+	150	15	10:1	?
Ca^{++}	2	0.0002	10,000:1	?
Cl^-	150	15	10:1	?

Calculating the Equilibrium Potential

Given the concentrations of ions inside and outside of a neuron, we can calculate its Equilibrium Potential using the **Nernst Equation**

Nernst Equation

E_{ion} is the "equilibrium potential" for a single permeant ion

E_{ion} (mV) = RT / zF • log ($[ion]_{out}$ / $[ion]_{in}$)

R = gas constant
T = temperature (kelvin)
z = valence
F = Faraday constant

E_{ion} (mV) = 62 / charge • log ($[ion]_{out}$ / $[ion]_{in}$)

at 37 C

Distribution of Ions in Mammalian Neurons

Ion	Outside (mM)	Inside (mM)	Ratio Out : In	E_{ion}
K^+	5	100	1:20	?
Na^+	150	15	10:1	?
Ca^{++}	2	0.0002	10,000:1	?
Cl^-	150	15	10:1	?

Nernst Equation for K^+

$$E_{ion}\ (\mathrm{mV}) = 62 \,/\, \mathrm{charge} \cdot \log\left([\mathrm{ion}]_{out} \,/\, [\mathrm{ion}]_{in}\right)$$

$$E_{K^+}\ (\mathrm{mV}) = 62 \,/\, +1 \cdot \log\left(5\ \mathrm{mM} \,/\, 100\ \mathrm{mM}\right)$$

$$= 62 \,/\, +1 \cdot \log\left(.05\right)$$

$$= 62 \,/\, +1 \cdot -1.3$$

$$= -80\ \mathrm{mV}$$

Nernst Equation for Na^+

$$E_{ion} = 62 / \text{charge} \cdot \log ([\text{ion}]_{out} / [\text{ion}]_{in})$$

$$E_{Na^+} = 62 / +1 \cdot \log (150 \text{ mM} / 15 \text{ mM})$$

$$= 62 / +1 \cdot \log (10)$$

$$= 62 / +1 \cdot \log (1)$$

$$= +62 \text{ mV}$$

Nernst Equation for Cl^-

$$E_{ion} = 62 / \text{charge} \cdot \log([ion]_{out} / [ion]_{in})$$

$$E_{Cl^-} = 62 / -1 \cdot \log(100\ \text{mM} / 10\ \text{mM})$$

$$= 62 / -1 \cdot \log(10)$$

$$= 62 / -1 \cdot 1$$

$$= -62\ \text{mV}$$

Nernst Equation for Ca++

$$E_{ion} = 62 / \text{charge} \cdot \log ([ion]_{out} / [ion]_{in})$$

$$E_{Ca++} = 62 / +2 \cdot \log (2\text{ mM} / .0002\text{ mM})$$

$$= 62 / +2 \cdot \log (10{,}000)$$

$$= 62 / +2 \cdot 4$$

$$= 123\text{ mV}$$

Nernst Equation

$$E_{K^+} = 62 / +1 \cdot \log (5\text{ mM} / 125\text{ mM})$$
$$= -80\text{ mV}$$

$$E_{Na^+} = 62 / +1 \cdot \log (150\text{ mM} / 15\text{ mM})$$
$$= +62\text{ mV}$$

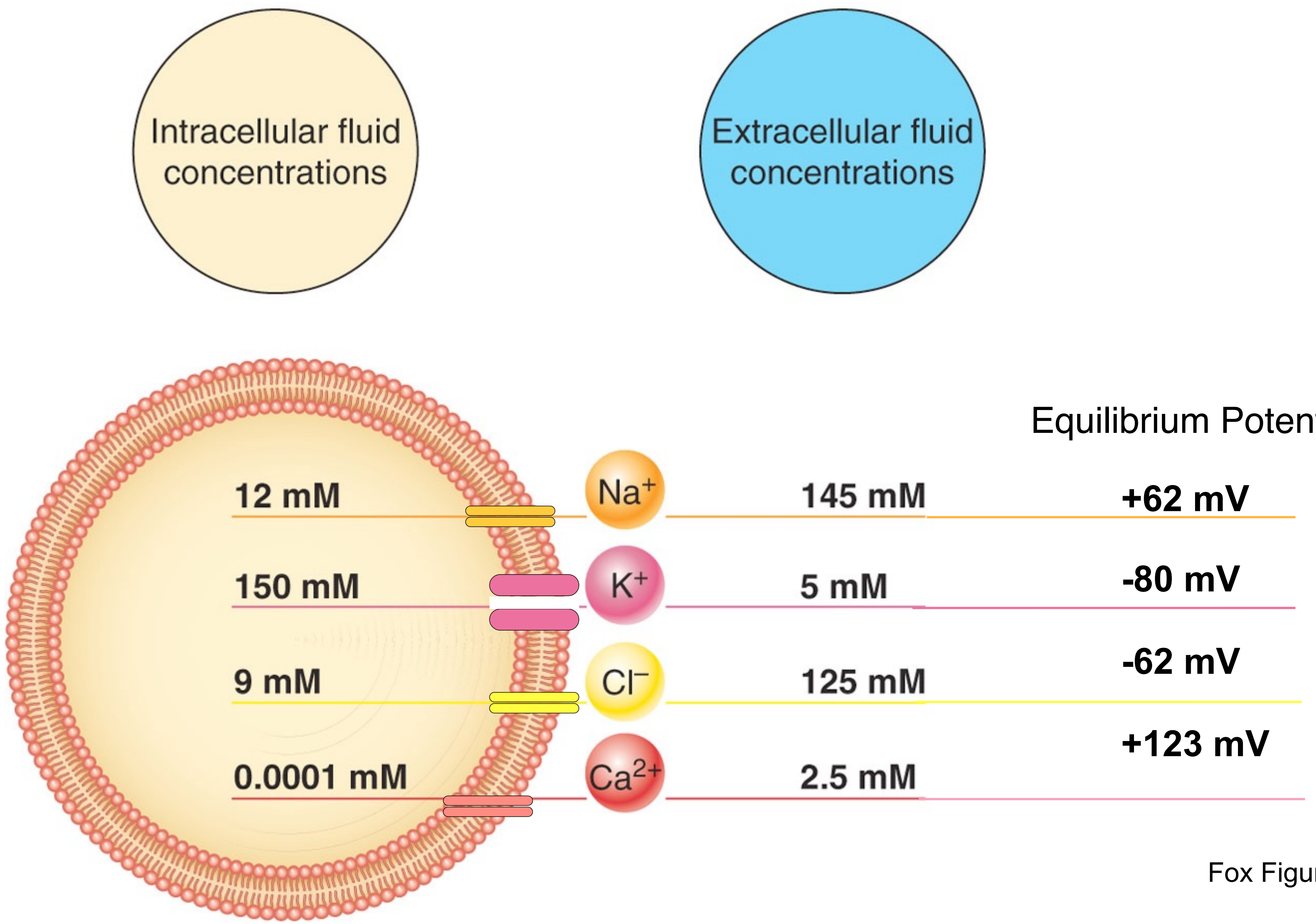
$$E_{Cl^-} = 62 / -1 \cdot \log (100\text{ mM} / 10\text{ mM})$$
$$= -62\text{ mV}$$

$$E_{Ca++} = 62 / 2 \cdot \log (2\text{ mM} / .0002\text{ mM})$$
$$= 123\text{ mV}$$

But how to calculate overall membrane potential?

Membrane Potential (V_m) for a cell:

Each ion contributes to overall membrane potential



Fox Figure 6.26

Distribution of Ions in Mammalian Neurons

Ion	Outside (mM)	Inside (mM)	Ratio Out : In	E_{ion} (mV)
K^+	5	100	1:20	-80
Na^+	150	15	10:1	+62
Ca^{++}	2	0.0002	10,000:1	123
Cl^-	150	15	10:1	-62

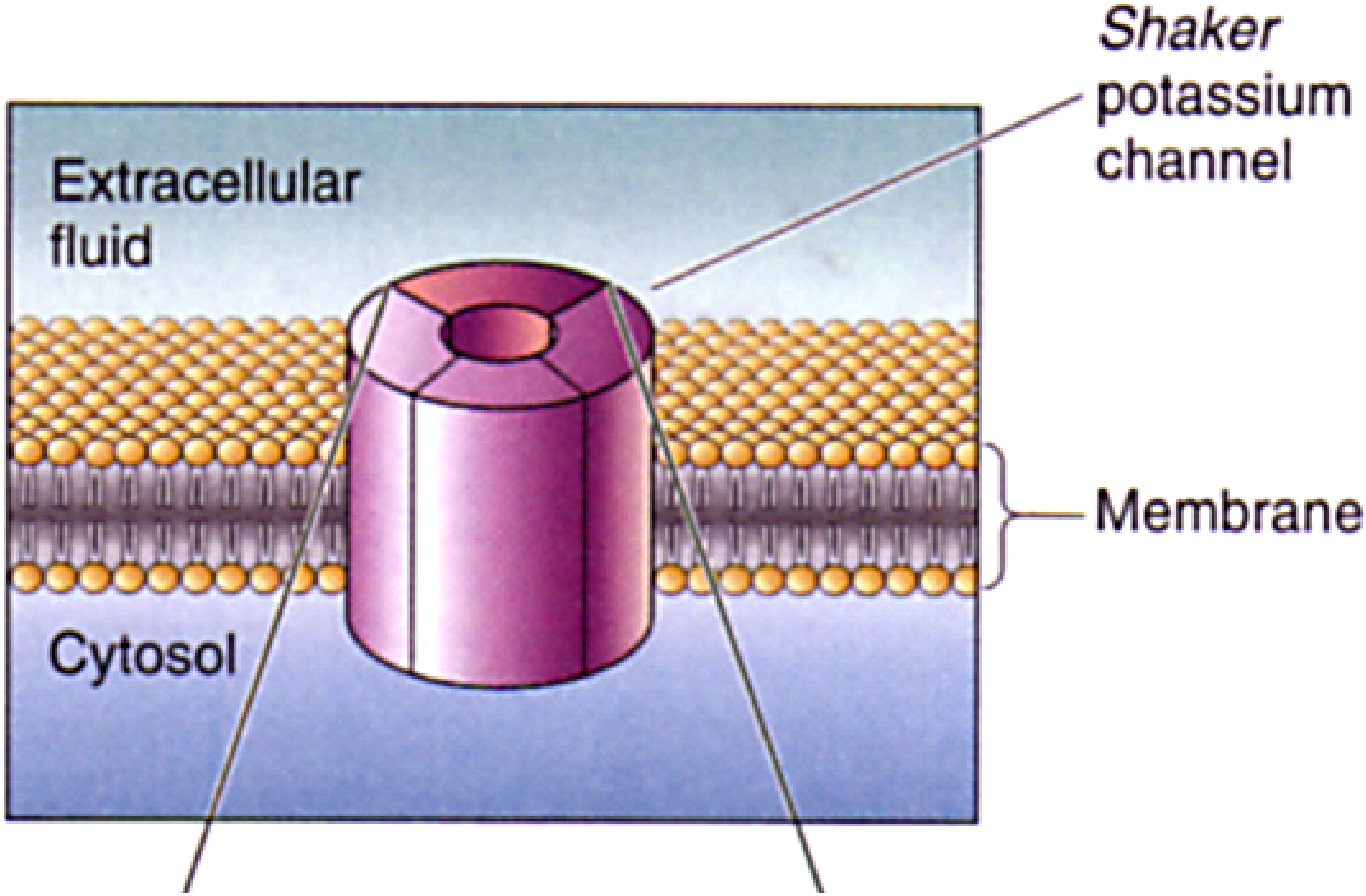
But how to calculate overall membrane potential?

Equilibrium Potential for an ion

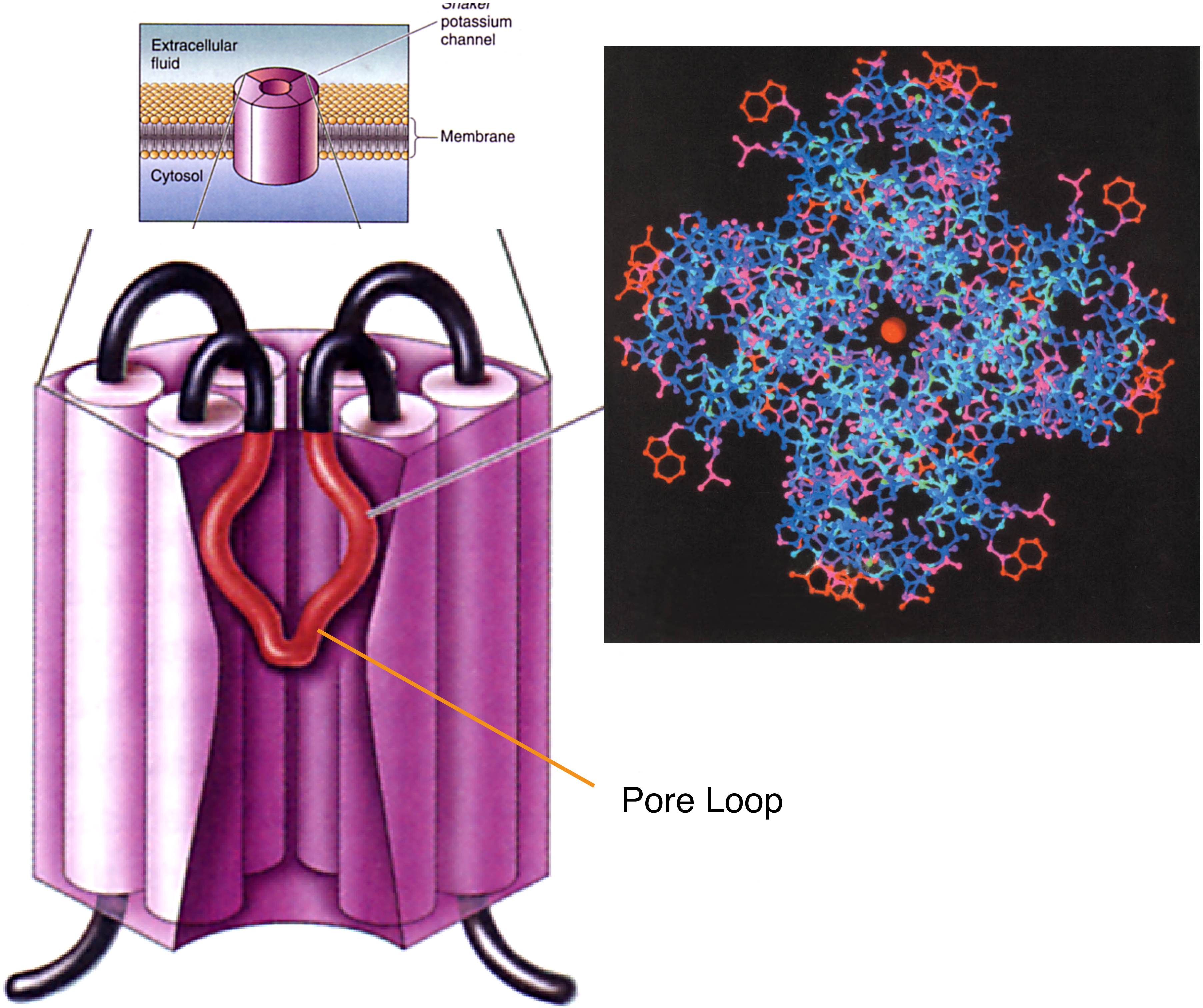
If there are open channels for an ion, the electrical and chemical driving forces will try to force the ions to move across the membrane.

the ion will move across the membrane until the change in electrical charge causes the cell's V_m to reach the ion's equilibrium potential.

Because the cell is selectively permeable to ions, some ions can move across the membrane , while ions with closed ion channels cannot move across the membrane.



Protein structure of K+ channel makes it selective for K+
(i.e. Na+, Cl-, Ca++ can't get through)


potassium
channel
Extracellular
fluid
Membrane
Cytosol
Pore Loop

Ion flux

number of ions that are crossing the membrane

ion flux = (electrical force + chemical force)

x membrane permeability for that ion

In the resting neuron,

Lots of open K^+ channels, so K^+ flux can be large.

Very few open Na^+ channels, so Na^+ flux is low.

Neuron actively controls concentrations of Na^+ & K^+

So, V_m lies in between Equilibrium Potentials of K^+ and Na^+

Permeability of Ions in Mammalian Neurons

	Outside	Inside (mM)	E_{ion}	Permeab.
K^+	5	125	-81	1.0
Na^+	150	15	+62	0.04
Cl^-	100	10	-62	0.045

Because K+ has the highest permeability, it has the highest flux and so contributes the most to the overall membrane potential.

Goldman Equation

Goldman Equation is the compromise potential reached accounting for each permeant ion.

$$V_{membrane} = 62 \log \frac{P_K[K^+]_o + P_{Na}[Na^+]_o + P_{Cl}[Cl^-]_i}{P_K[K^+]_i + P_{Na}[Na^+]_i + P_{Cl}[Cl^-]_o}$$

P_X = relative permeability of ion X

$[X]_i$ = concentration of X inside cell

$[X]_o$ = concentration of X outside cell

Goldman Equation

$$V_m = 62 \log \frac{1[5]_o \quad + .04[150]_o \quad + .05[10]_i}{1[125]_I \quad + .04[15]_i \quad + .05[100]_o}$$

$$V_m = -65 \text{ mV}$$

V_m approaches the Equilibrium Potential of

the most permeable ion.

Distribution of Ions in Mammalian Neurons

	Outside	Inside (mM)	E_{ion}	Permab.
K^+	5	125	-80	1.0
Na^+	150	15	-62	0.04
Cl^-	100	10	-62	0.045

V_m= -65 mV

Change of Concentration leads to change of V_m

	Outside	Inside (mM)	E_{ion}	Permab.
K^+	150	150	0	1.0
Na^+	150	15	+62	0.04
Cl^-	100	10	-62	0.045

V_m = +0 mV

Change of Permeability leads to change of V_m

	Outside	Inside (mM)	E_{ion}	Permab.
K^+	5	125	-80	1.0
Na^+	150	15	-62	20
Cl^-	100	10	-62	0.045

V_m = +49 mV

Changing the Membrane Potential

https://www.youtube.com/watch?v=qNvtIW8LPRw