Human Physiology PCB 4701

Membrane Potential
Fox Chapter 6 pt 2

Separation of ions across the cell membrane causes a **membrane potential**

Talk about simple spherical “cell” with membrane separating inside (intracellular) and outside (extracellular) solutions of ions

Start with simple case of just one particular ion (K+) going through its ion channel

Then look at other ions (but still one type at a time)

Then put all the ions together (K+, Na+, Cl-, Ca++, etc.…)

Next lecture, neurons — cells with multiple channels and complex morphology

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.**

Membrane potential (V_m)

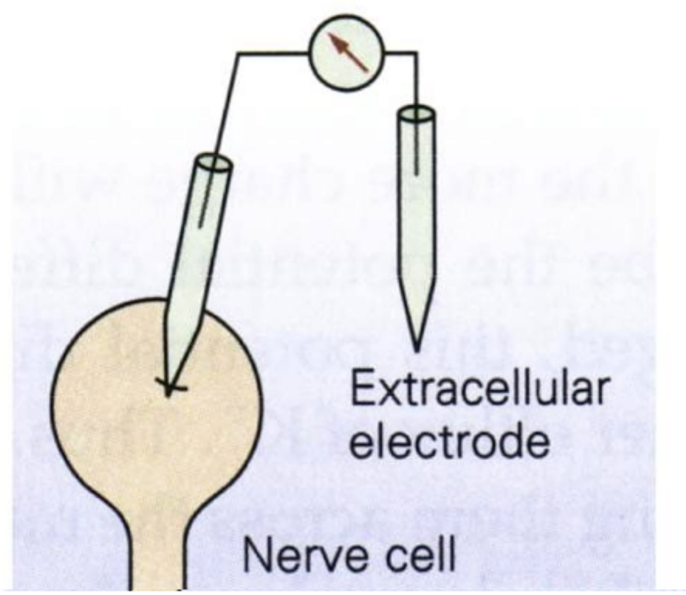
V_m = resting membrane potential

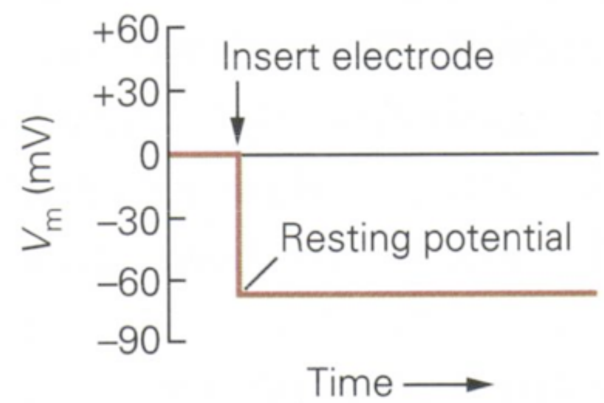
= electrical potential generated by separation of charges

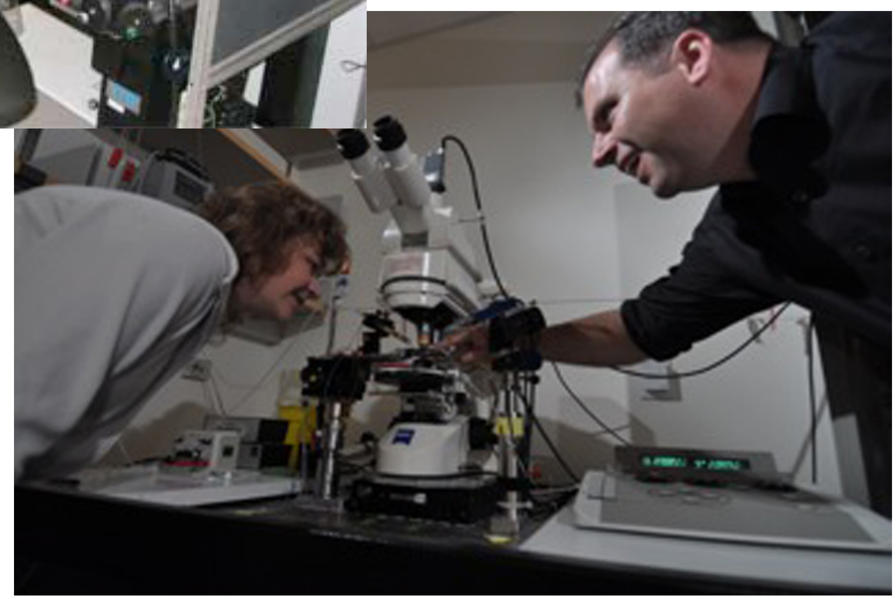
= voltage across the membrane

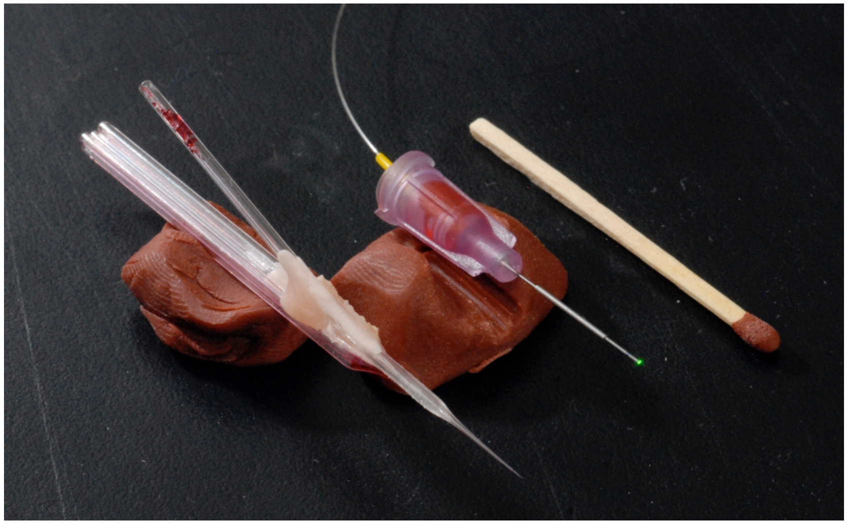
$= V_{inside} - V_{outside}$

Measuring V_m

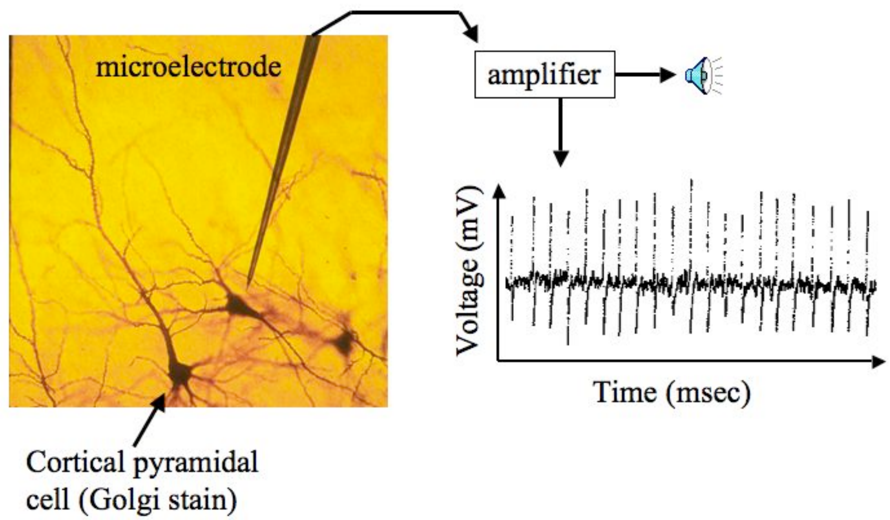








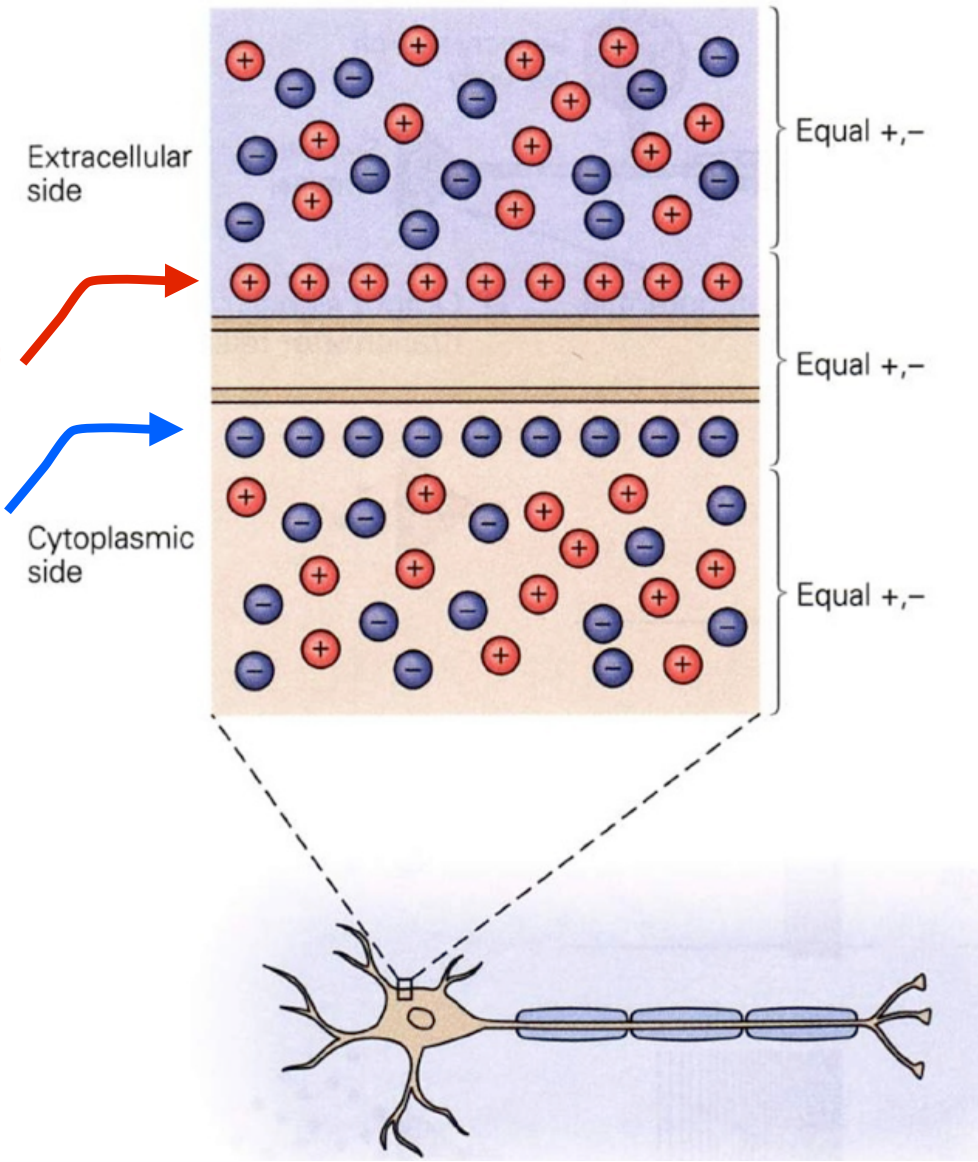
Single-cell electrophysiology



Unequal charges across the cell membrane

more + charges on **outside** of membrane

more - charges on **inside** of membrane



Membrane potential (V_m)

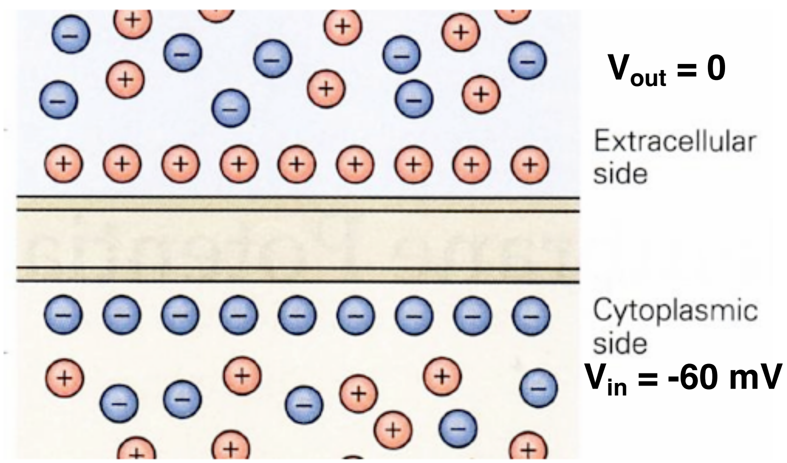
$V_m = V_{in} - V_{out}$

(V_{out} = 0 mV by definition)

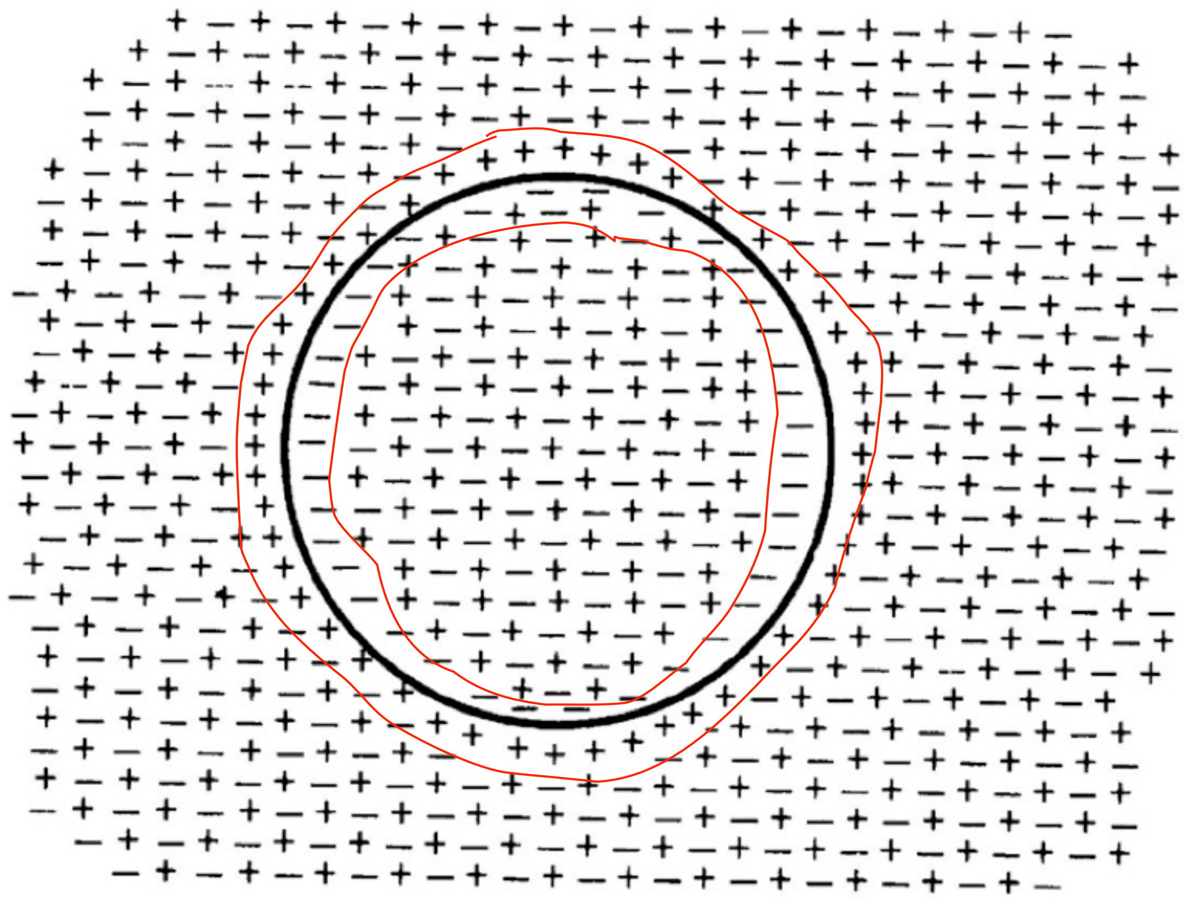
$V_m = V_{in} - 0$

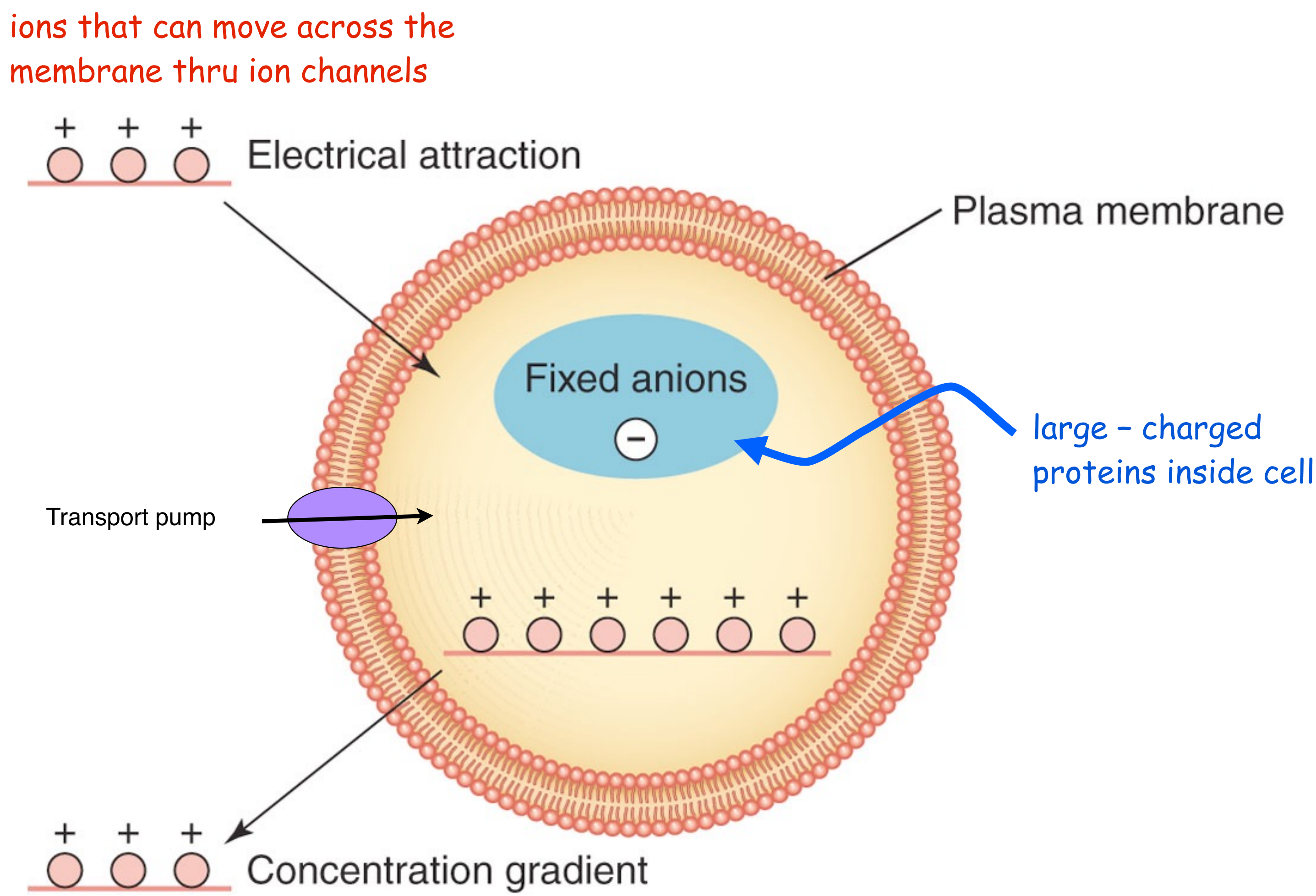
(more negative ions inside)

V_m = -60 to -70 mV



Membrane potential is caused by small number of total ions





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Equilibrium Potential for an ion (E_{ion})

Each ion species feels two forces pulling on it through open ion channels:

1. **Chemical driving force**
depends on concentration gradient across membrane

2. **Electrical driving force**
depends on electrical potential difference across membrane

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

*Example: K^+ has chemical driving force **out** of cell, but electrical driving force **into** cell.*

*Example: Na+ ions has both chemical driving force and electrical driving force **into** cell.*

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

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 an ion (E_{ion})

Each ion species feels two forces pulling on it:

1. Chemical driving force
depends on concentration gradient across membrane

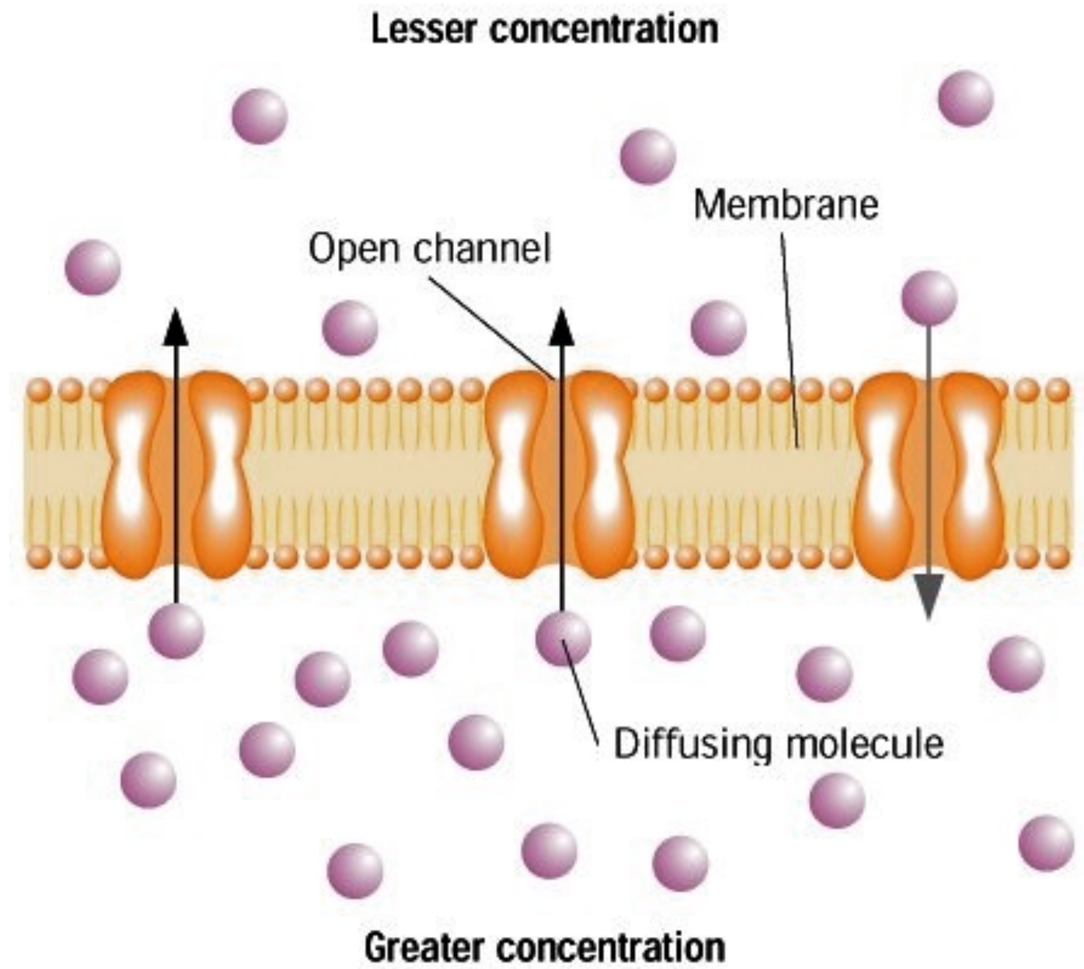
2. Electrical driving force
depends on electrical potential difference across membrane

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

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.

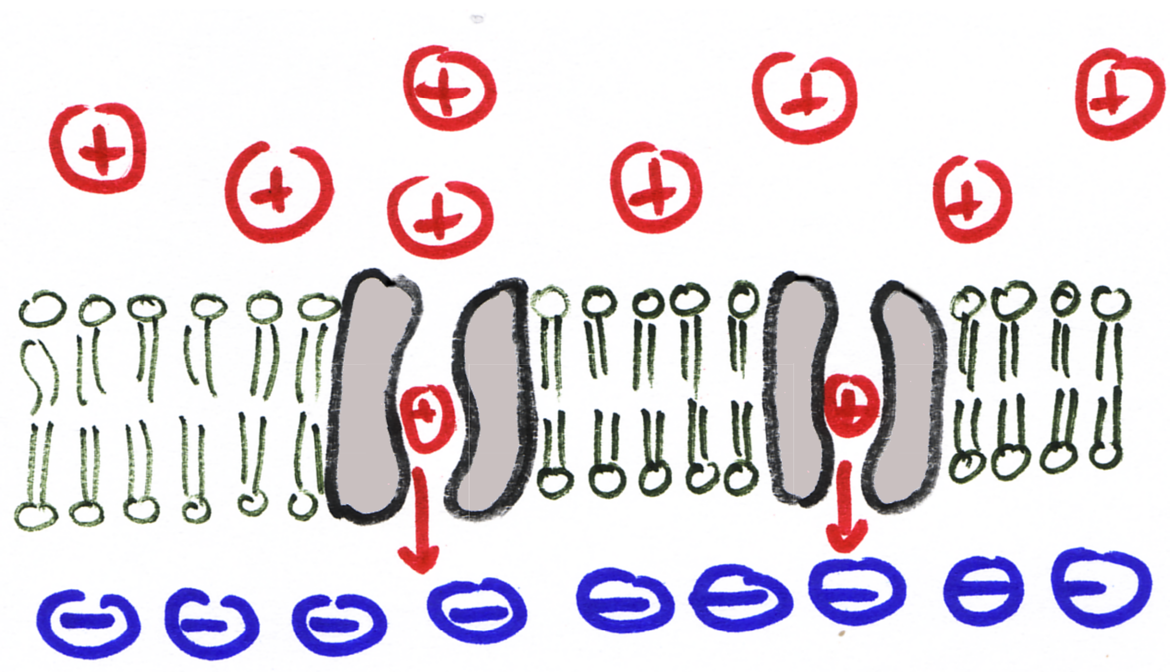
2 Forces on ions:

1. Diffusion down concentration gradient



2 Forces on ions:

2. Electrical attraction toward opposite charge

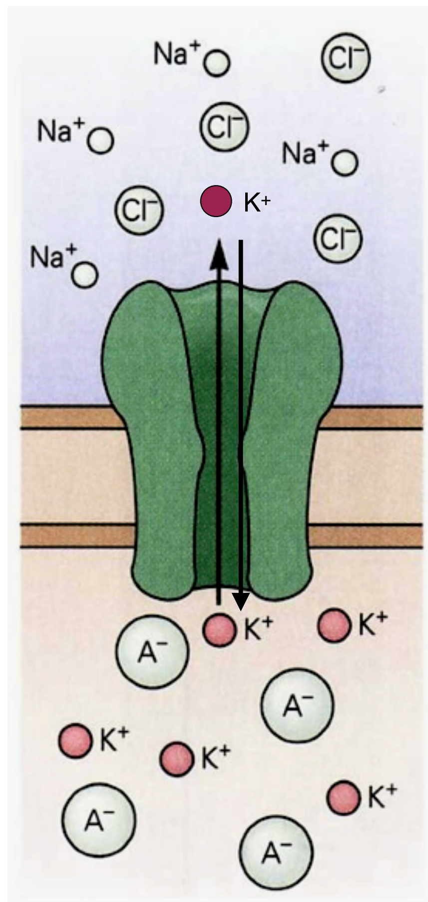


For potassium K+, chemical and electrical forces are in opposite directions

Extracellular side

Selectively permeable membrane

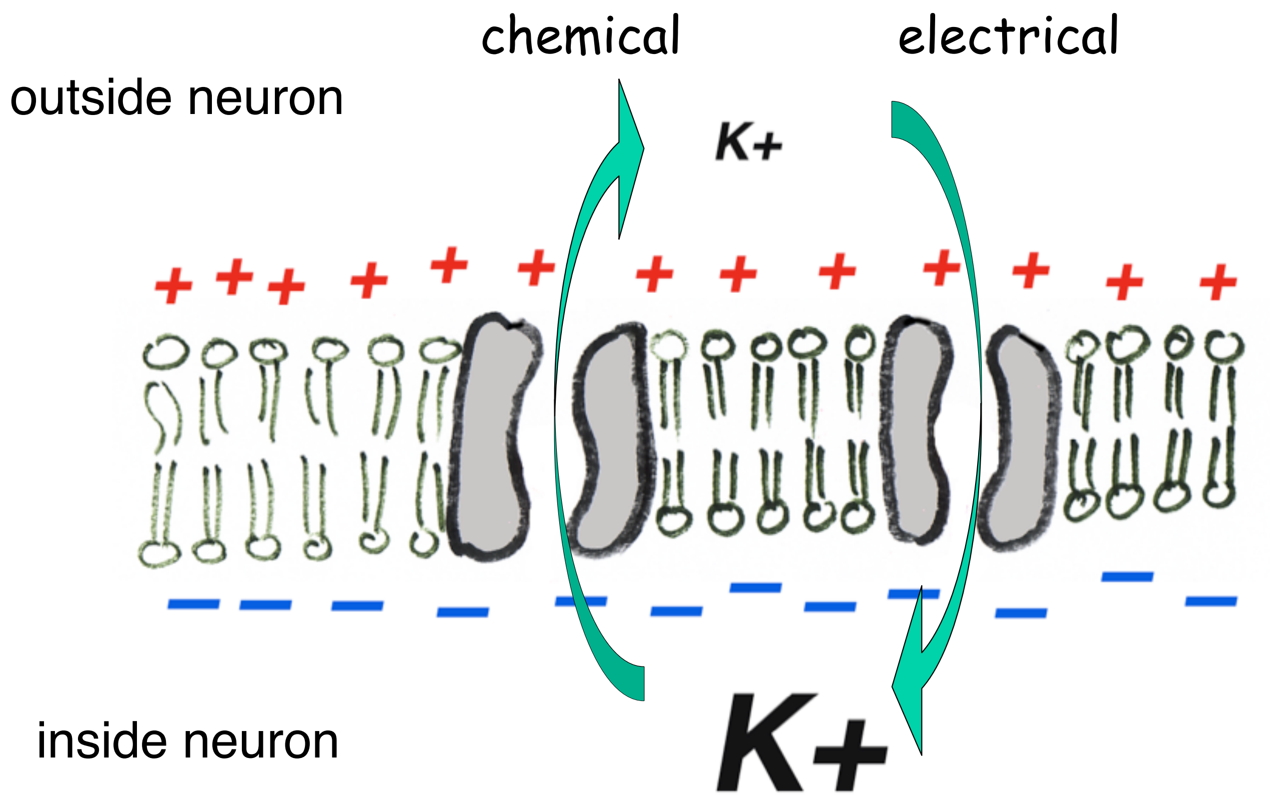
Cytoplasmic side



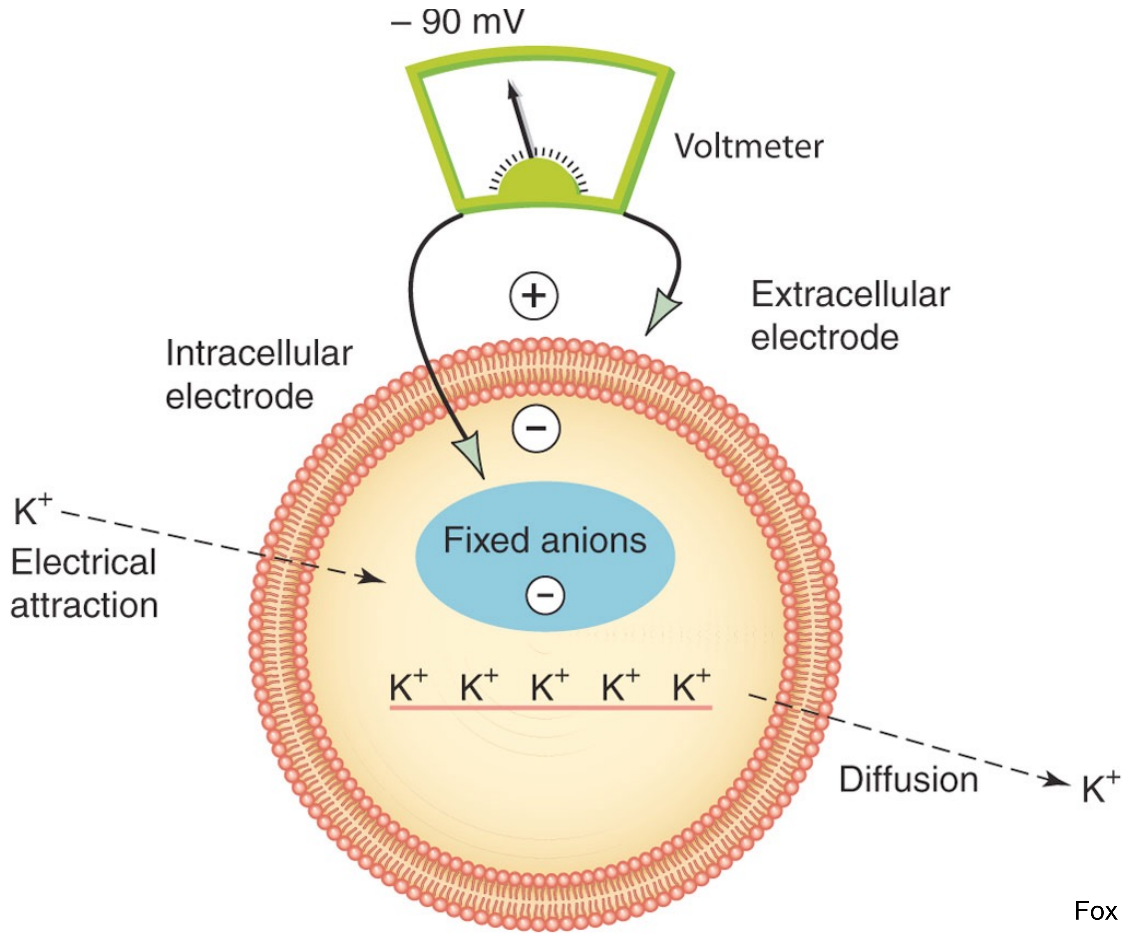
Concentration gradient for K+ moves K+ **out** of cell

Electrical gradient for K+ pulls K+ **into** the cell

Electrochemical Forces on Potassium K+ Ion



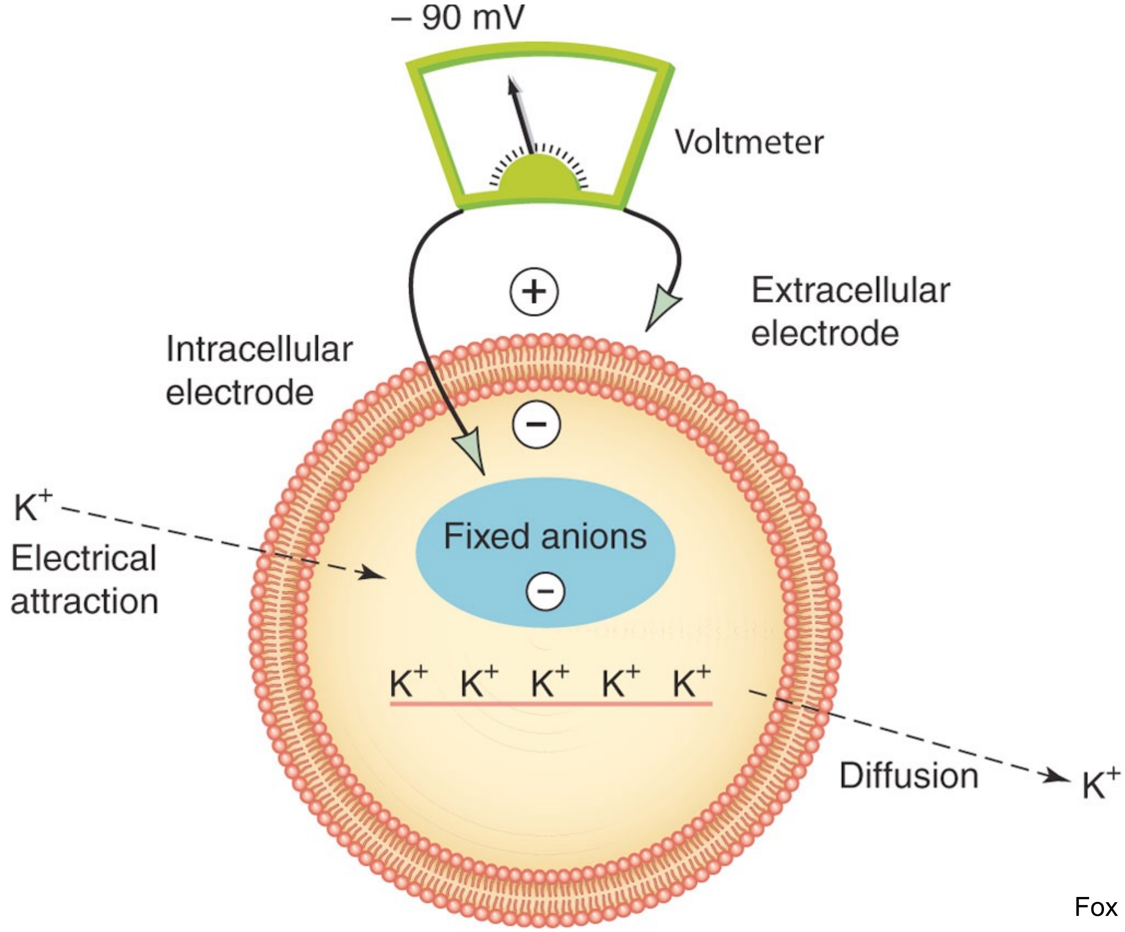
Equilibrium Potential for an ion:
Voltage at which electrical force balances chemical force



Fox Figure 6.25

Equilibrium Potential for an ion:

Voltage at which electrical force balances chemical force



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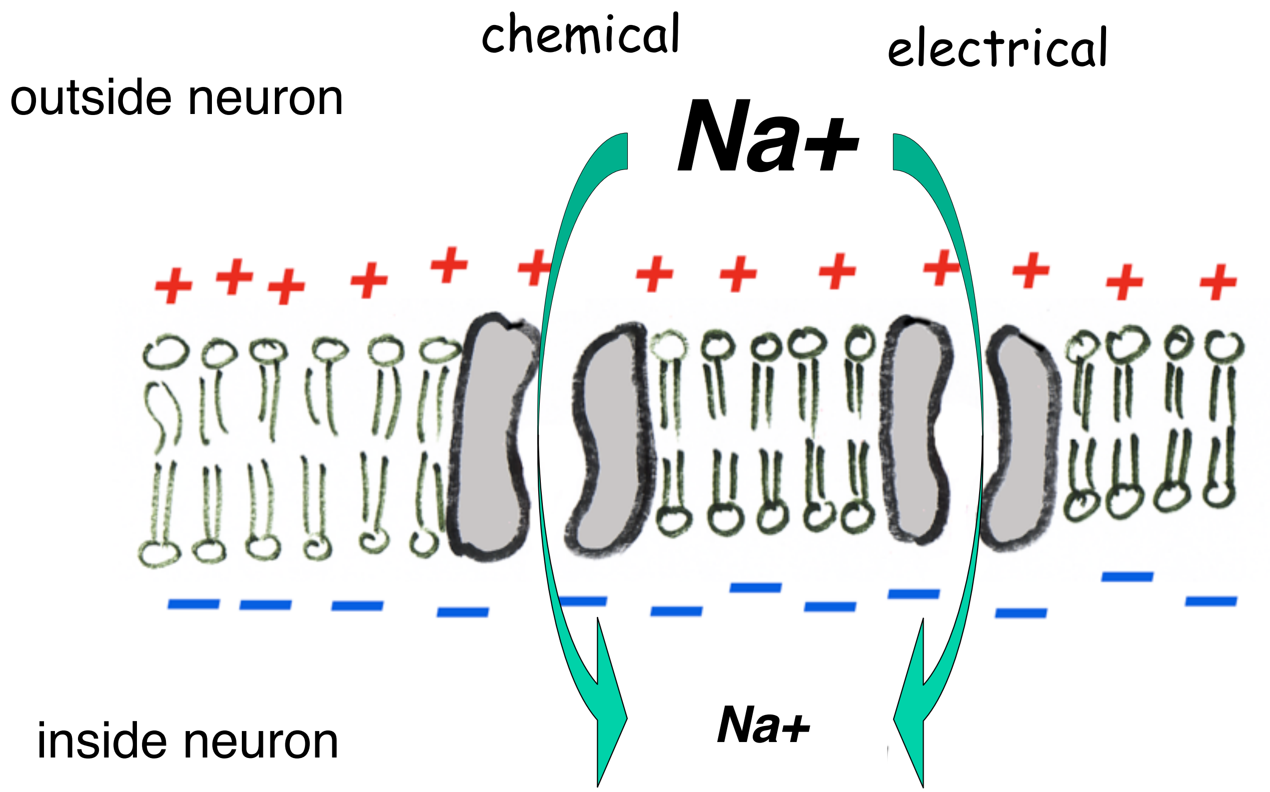
Electrochemical Forces on Sodium Na+ Ion



Calculating the Equilibrium Potential

Given the concentrations of ions inside and outside of a neuron, we can calculate its Equilibrium Potential (E_{ion}) in mV using the Nernst Equation.

$$E_{ion} = 61 / \text{charge} \cdot \log([\text{ion}]_{out} / [\text{ion}]_{in})$$

Multiple ions can move across the cell membrane, and each ion will have its own Equilibrium Potential, depending on the intracellular/extracellular concentations and the ion's charge.

e.g. Na^{+}, K^{+}, Cl^{-}, Mg^{2+}

Ion Flux

Because the cell is **selectively permeable** to ions, some ions can move easily across the membrane thru open ion channels **(high flux)**, while ions with few channels or closed ion channels cannot move across the membrane **(low flux)**.

Membrane potential (V_m) or RMP

The cell's overall membrane potential (V_m) is a combination of the E_{ion} of all the ions that can permeate the membrane, with a greater contribution for the ions with the greatest permeability (i.e. with the most open ion channels).

Need to know & apply Nernst Equation to find E_{ion} for a simple case!

Nernst Equation

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

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

R = gas constant

T = temperature (kelvin) *(assume 37 C)*

z = valence

F = Faraday constant

$E_{ion} = 61 / charge \cdot \log([ion]_{out} / [ion]_{in})$

Need to know & apply Nernst Equation to find E_{ion} for a simple case!

Nernst Equation for K^+

$$E_{ion}\ (mV) = 61 / charge \cdot \log([ion]_{out} / [ion]_{in})$$

$$E_{K^+}\ (mV) = 61 / +1 \cdot \log(5\ mM / 150\ mM)$$

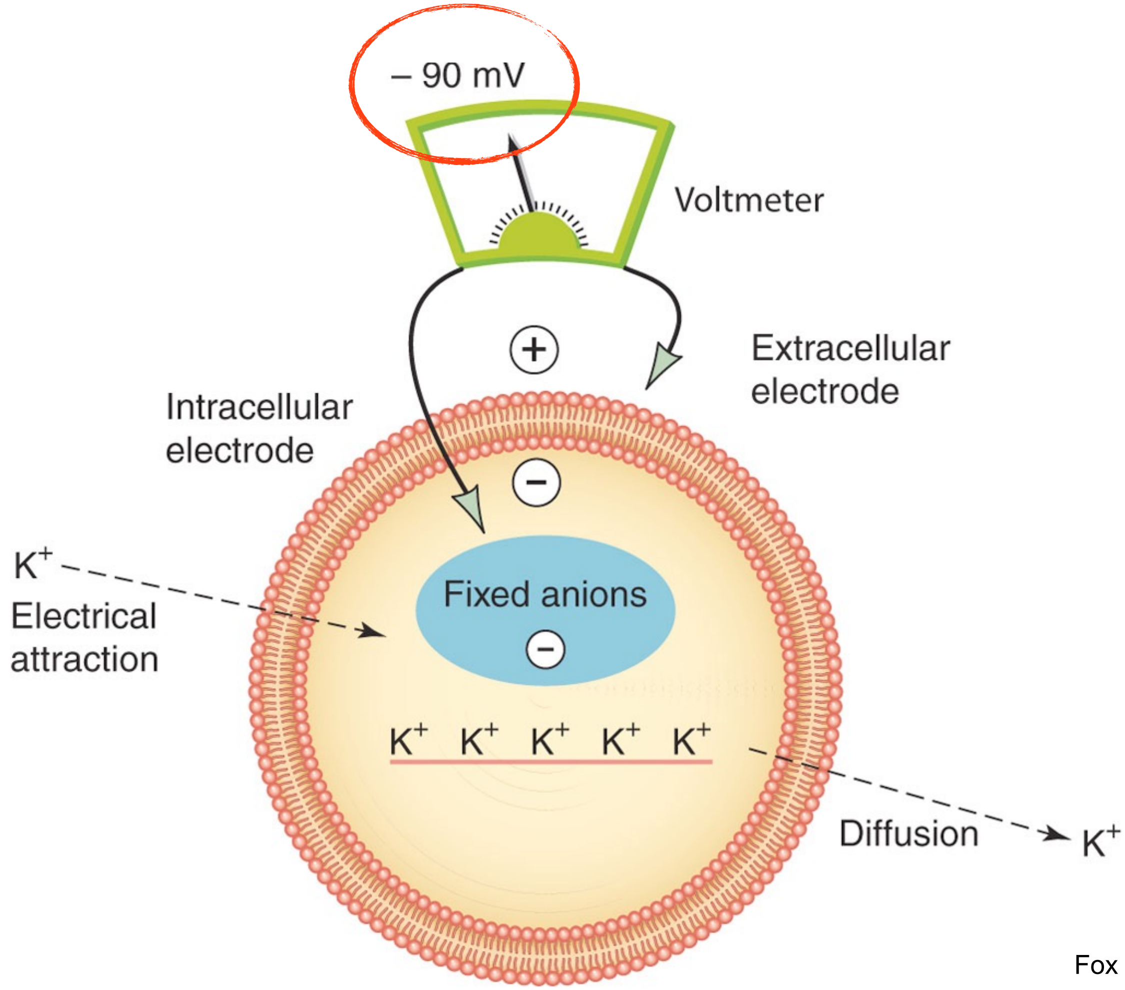
$$= 61 / +1 \cdot \log(.03)$$

$$= 61 / +1 \cdot -1.47$$

$$= -90\ mV$$

Equilibrium Potential for an ion:

Voltage at which electrical force balances chemical force



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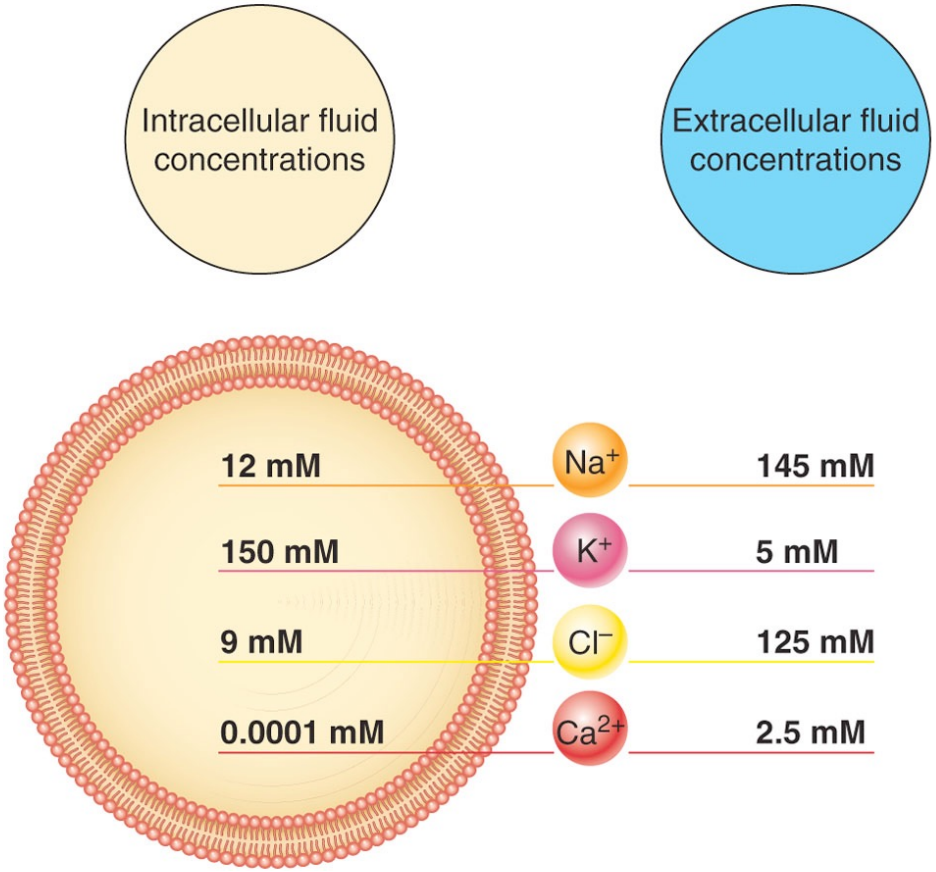
Each ion has its own Equilibrium Potential:
Depending on charge and concentrations of the ion



Fox Figure 6.26

Distribution of Ions in Mammalian Neurons

Each ion has a specific Equilibrium potential

Ion	Outside (mM)	Inside (mM)	Ratio Out : In	E_{ion} (mV)
K^+	5	150	1:30	-90 inside
Na^+	150	15	10:1	?
Cl^-	150	15	10:1	?
Ca^{++}	2.5	0.0001	10,000:1	?

chemical ← ; electrical → ; -90mV

Distribution of Ions in Mammalian Neurons

Each ion has a specific Equilibrium potential

Ion	Outside (mM)	Inside (mM)	Ratio Out : In	E_{ion} (mV)
K^+	5	150	1:30	-90
Na^+	chemical → 150 ← electrical	15 +60mV	10:1	+61
Cl^-	150	15	10:1	-61
Ca^{++}	2.5	0.0002	10,000:1	136

But how to calculate overall membrane potential?

Nernst Equation for Na^+

$$E_{ion} = 61 / charge \cdot \log([ion]_{out} / [ion]_{in})$$

$$E_{Na^+} = 61 / +1 \cdot \log(150\ mM / 15\ mM)$$

$$= 61 / +1 \cdot \log(10)$$

$$= 61 / +1 \cdot 1$$

$$= +61\ mV$$

Nernst Equation for Cl^-

$$E_{ion} = 61 / charge \bullet \log([ion]_{out} / [ion]_{in})$$

$$E_{Cl^-} = 61 / -1 \bullet \log(125 \text{ mM} / 10 \text{ mM})$$

$$= 61 / -1 \bullet \log(12)$$

$$= 61 / -1 \bullet 1$$

$$= -61 \text{ mV}$$

Nernst Equation for Ca++

E_{ion} = 61 / charge • log ([ion]$_{out}$ / [ion]$_{in}$)

E_{Ca++} = 61 / +2 • log (2.5 mM / .0001 mM)

= 61 / +2 • log (25,000)

= 61 / +2 • 4.5

= 136 mV

Nernst Equations for major ions

E_{K^+} = 61 / +1 • log (5 mM / 125 mM)
= –90 mV

E_{Na^+} = 61 / +1 • log (150 mM / 15 mM)
= +61 mV

E_{Cl^-} = 61 / –1 • log (125 mM / 10 mM)
= –61 mV

$E_{Ca^{++}}$ = 61 / 2 • log (25 mM / .0002 mM)
= 136 mV

But how to calculate overall membrane potential?

Distribution of Ions in Mammalian Neurons

Each ion has a specific Equilibrium potential

Ion	Outside (mM)	Inside (mM)	Ratio Out : In	E_{ion} (mV)
K^+	5	150	1:30	-90
Na^+	150	15	10:1	+61
Cl^-	150	15	10:1	-61
Ca^{++}	2.5	0.0002	10,000:1	136

chemical

electrical -90mV

But how to calculate overall membrane potential?

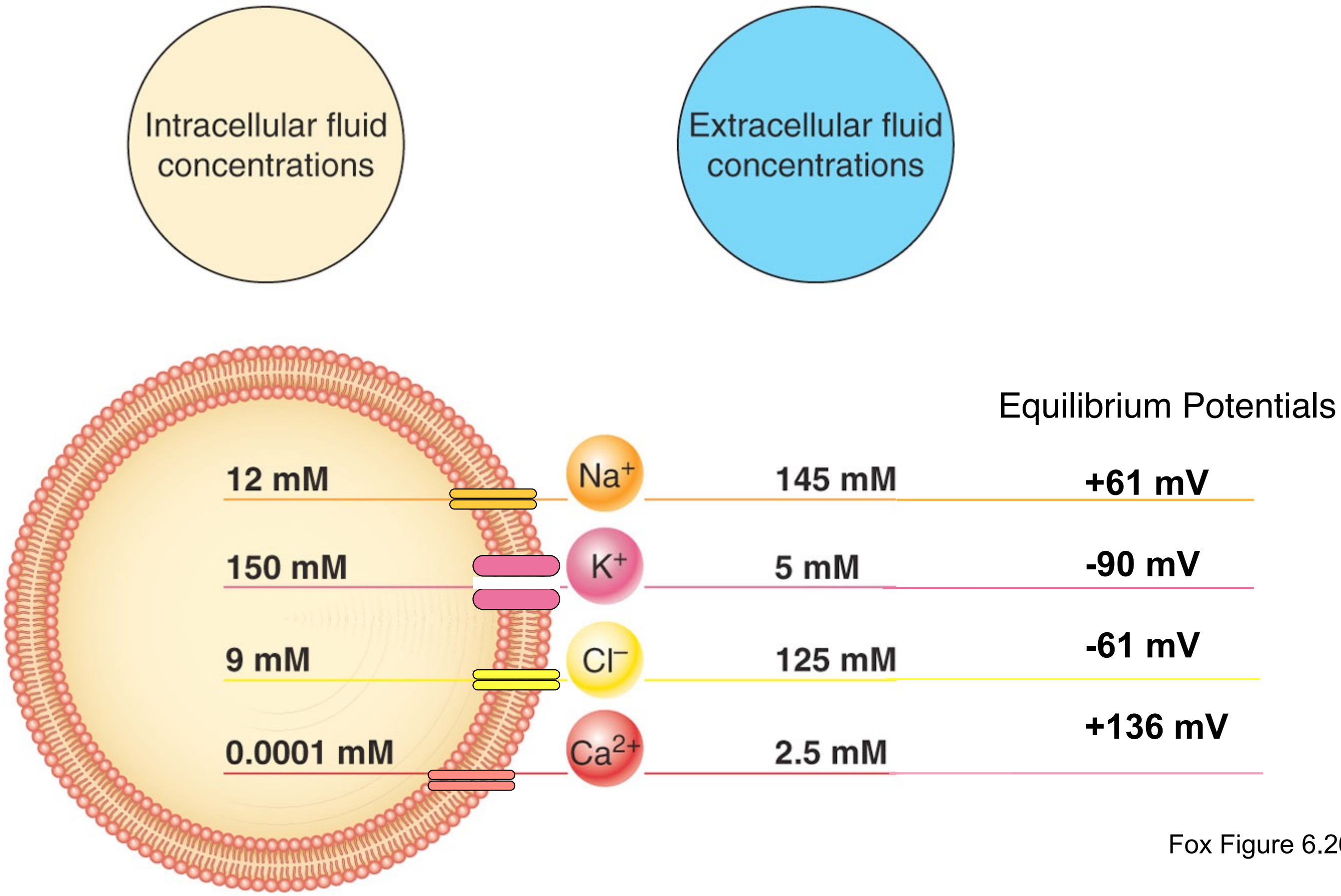
Distribution of Ions in Mammalian Neurons

Each ion has a specific Equilibrium potential

Ion	Outside (mM)	Inside (mM)	Ratio Out : In	E_{ion} (mV)
K^{+}	5	150	1:30	-90
Na^{+}	150	chemical → 15 ← electrical +60mV	10:1	+61
Cl^{-}	150	15	10:1	-61
Ca^{++}	2.5	0.0002	10,000:1	136

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

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 nerve cell,

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

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

Remember: cell actively controls concentrations of Na^+ & K^+

Na+/K+ ATPase pumps keep high K^+, low Na^+ inside the cell

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

Calculating the overall Membrane Potential (V_m)

Membrane potential (V_m) or RMP

The cell's overall membrane potential (V_m) is a combination of the E_{ion} of all the ions that can permeate the membrane, with a greater contribution for the ions with the greatest permeability (i.e. with the most open ion channels).

The **Goldman Equation** finds the compromise membrane potential accounting for each **permeant** ion.

V_m approaches the Equilibrium Potential of the most permeable ion.

For neurons and most cells, the most permeable ion is K+.

So, the membrane potential V_m at -70 mV is close to E_{K+} at -90 mV.

Need to understand that V_m is dependent on most permeable ion, but don't need to memorize the Goldman equation.

Permeability of Ions in Mammalian Neurons

	Outside	Inside (mM)	E_{ion}	Permeab.
K^+	5	150	-90	1.0
Na^+	150	15	+61	0.04
Cl^-	125	10	-61	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 finds the compromise membrane potential accounting for each **permeant** ion.

$$V_{membrane} = 61 \log \frac{P_K[K^+]_o + P_{Na}[Na^+]_o + P_{Cl}[Cl^-]_i}{P_K[K^+]_i + P_{Na}[Na^+]_i + P_{Cl}[Cl^-]_o}$$

P_X = relative permeability of ion X

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

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

Goldman Equation

K+ Na+ Cl-

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

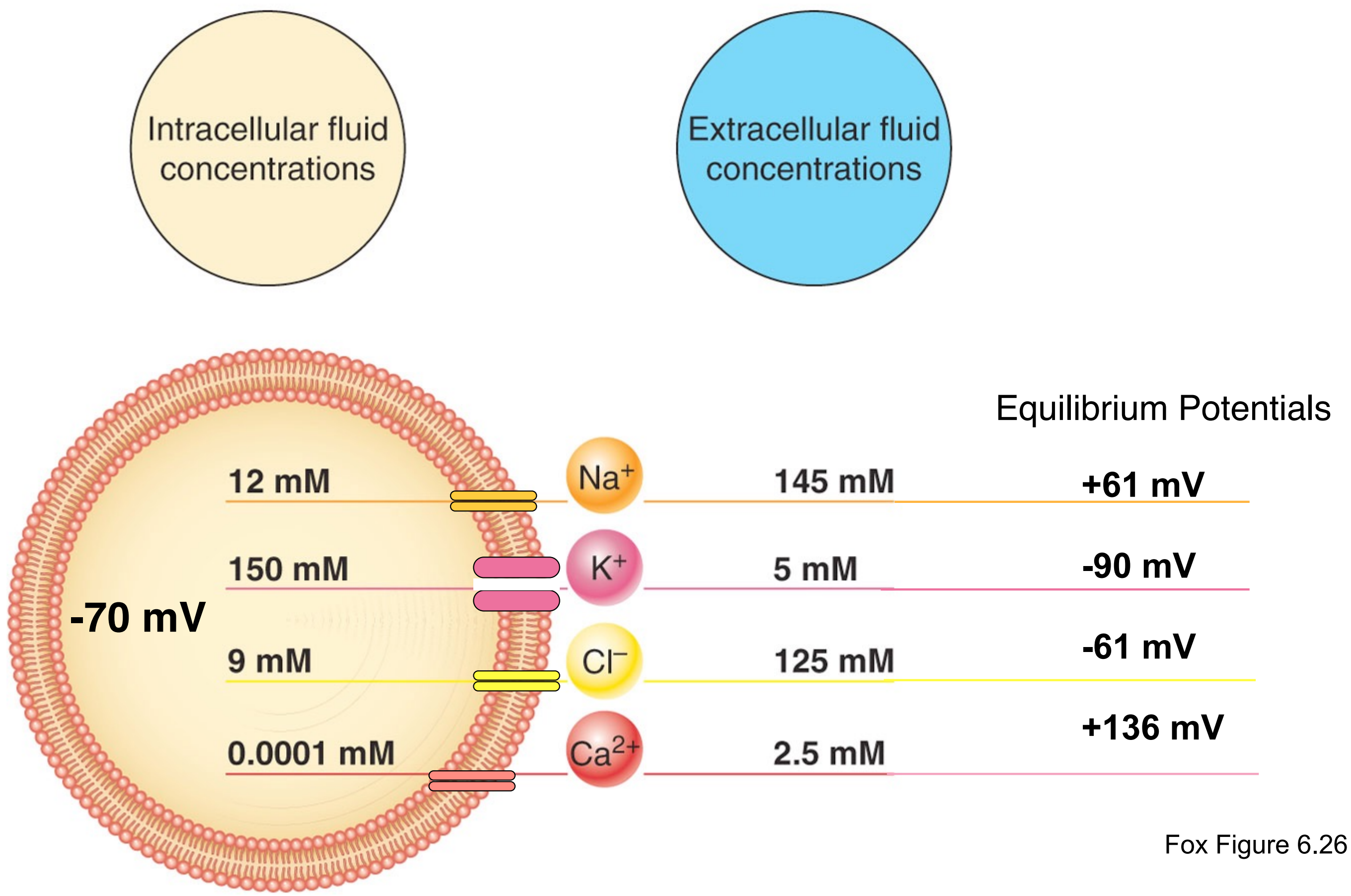
V_m= -70 mV

V_m approaches the Equilibrium Potential of the most permeable ion.

Need to understand that Vm is dependent on most permeable ion, but don't need to memorize the Goldman equation.

Membrane Potential (V_m) for a cell:

Voltage at which electrical forces balance chemical forces for <u>all</u> ions, depending on permeability of the ions.



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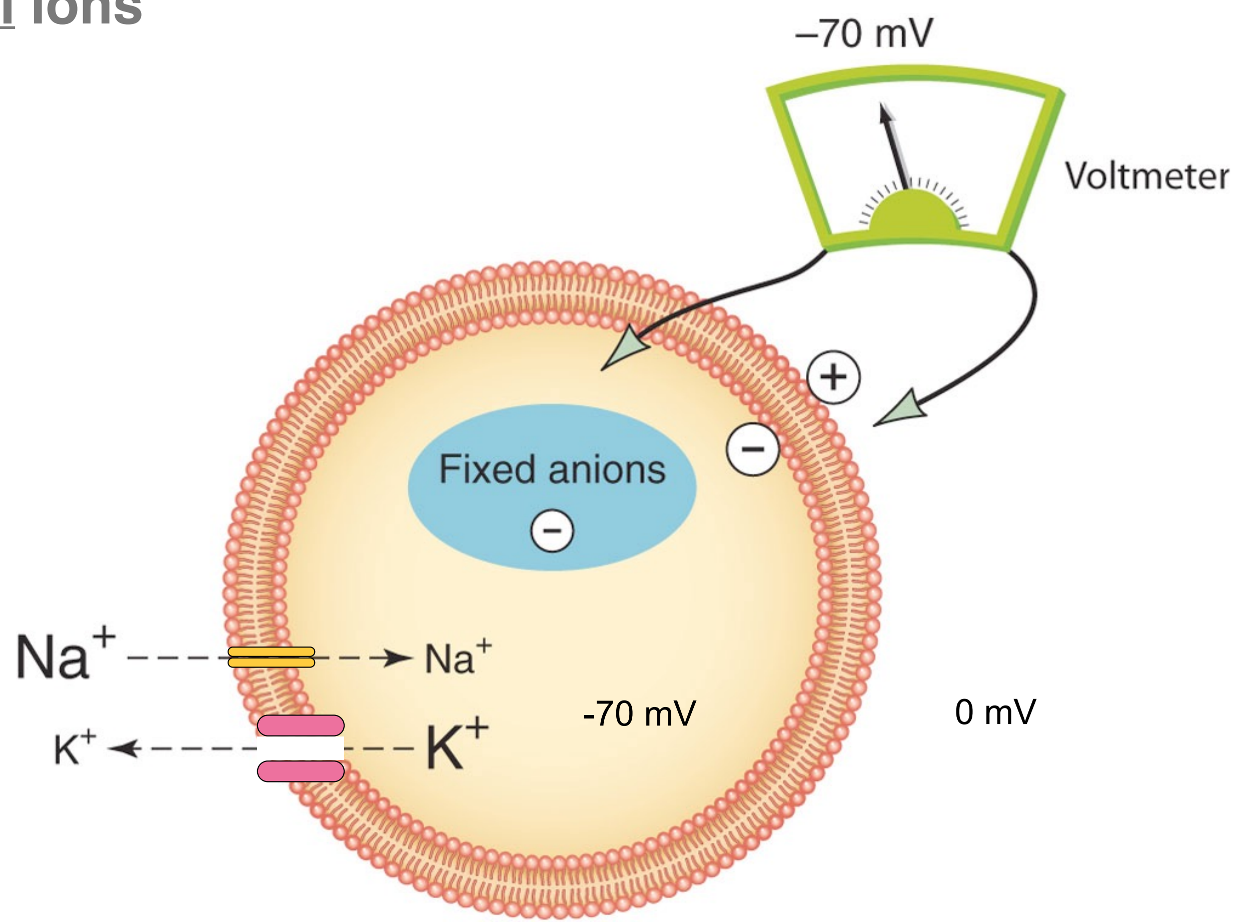
Membrane Potential (V_m) for a cell:

Voltage at which electrical forces balance chemical forces for all ions



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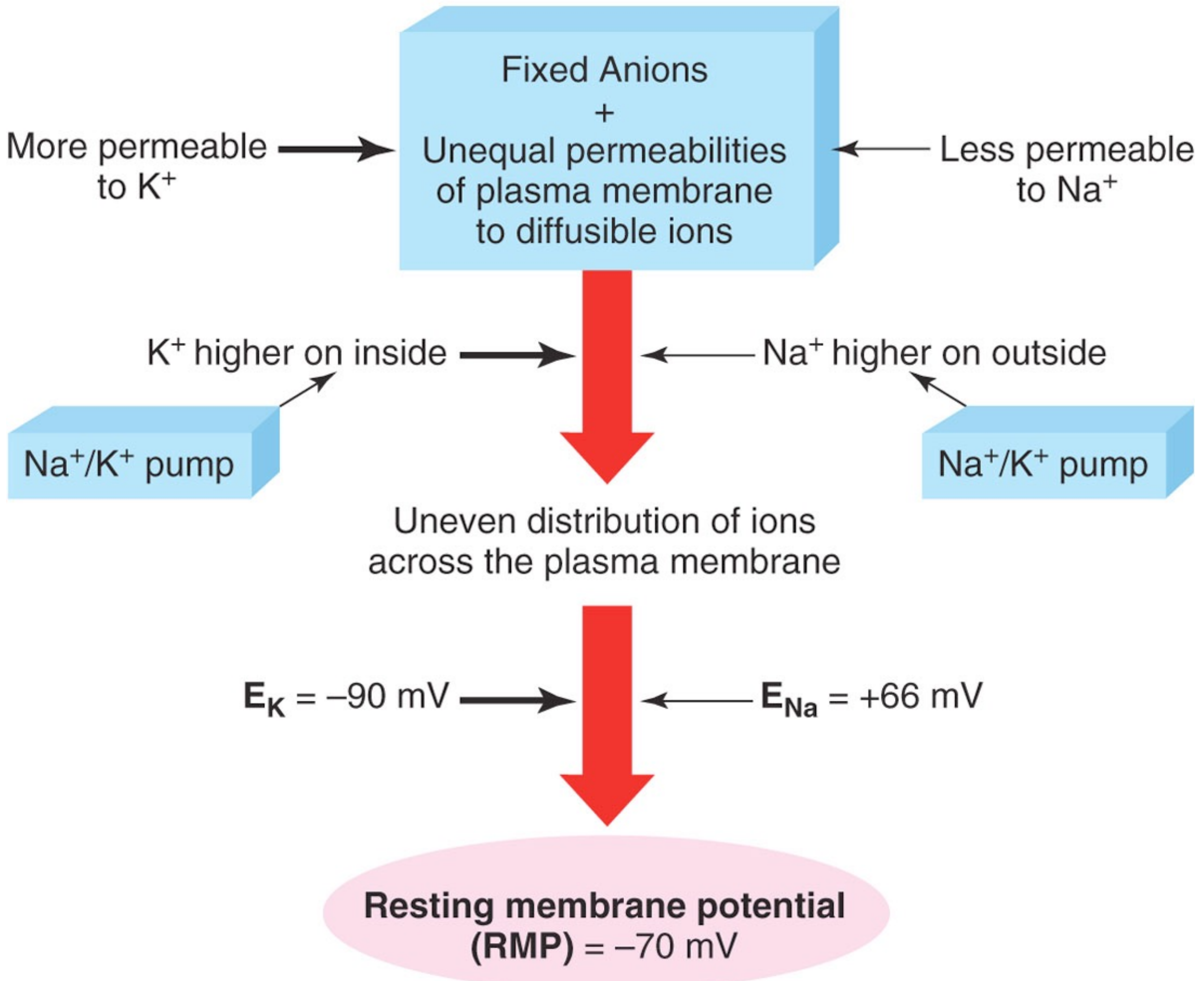
Contributions to Membrane Potential



Fox Figure 6.28

Distribution of Ions in Mammalian Neurons

	Outside	Inside (mM)	E_{ion}	Permab.
K^+	5	150	-90	1.0
Na^+	150	15	+61	0.04
Cl^-	125	10	-61	0.045

V_m= -70 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	+61	0.04
Cl^-	100	10	-61	0.045

$V_m = +0$ mV