School of Medical Sciences

Physiology 1A

Cell Physiology lecture #4

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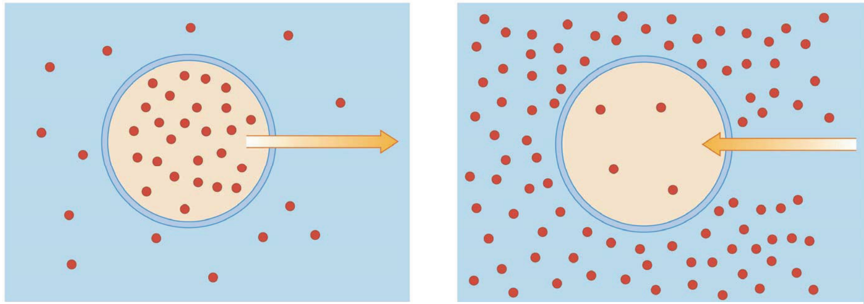
Electrical Potentials in Cells

1. Substances move down concentration gradient (a chemical force)

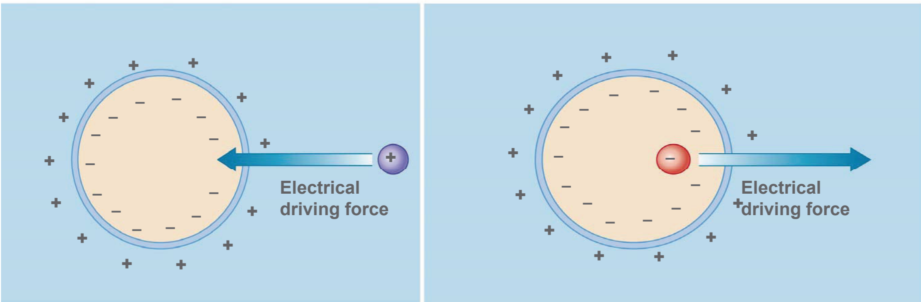


Efflux (inside to outside) **Influx (outside to inside)**

Electrical Potentials in Cells

2. Ions are charged and influenced by other charges (electrical force)

(the membrane potential influences the ions in the intra- and extra cellular solutions)



Cation influx (opposites attract) **Anion efflux (like charges repel)**

Ions move according to Electrical and Chemical Forces

➢ Chemical Force:

- Diffusion. Ions move from high to low concentration

➢ Electrical Force:

- Opposite charges attract, like charges repel

➢ A typical Cell at Rest:

- Concentration gradients for Na^+, K^+, Cl^-
- A polarized membrane (negative inside)

Why is the resting membrane potential negative?

1) In mammalian cells, there exists a concentration gradient for ions, and especially for K^+, Na^+, Ca^{2+} & Cl^-.

This provides a chemical driving force for ions to diffuse:

K^+ efflux & Na^+ influx).

TABLE 4.1 Millimolar Concentrations of Selected Solutes in Intracellular Fluid (ICF)* and Extracellular Fluid (ECF)

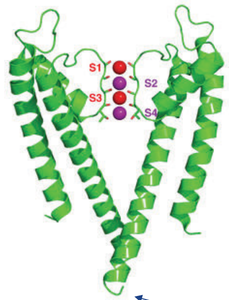
Solute	ICF (mM)	ECF (mM)
K^+	140.0	4.0
Na^+	15.0	145.0
Mg^{2+}	0.8	1.5
Ca^{2+}	$<0.001^{\dagger}$	1.8
Cl^-	4.0	115.0
HCO_3^-	10.0	25.0
P_i	40.0	2.0
Amino acids	8.0	2.0
Glucose	1.0	5.6
ATP	4.0	0.0
Protein	4.0	0.2

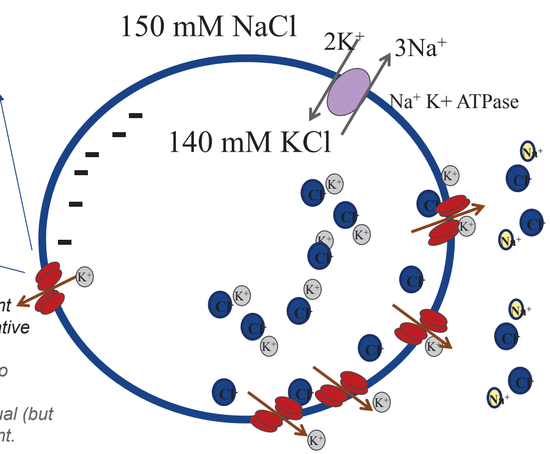
mM = millimolar

*Intracellular fluid composition varies for different cell types.

†Refers to calcium ions free in the cytosol. A significant quantity of intracellular calcium is sequestered in membrane-bound organelles and/or bound to proteins.

2. The membrane has K+-selective ion channels open, so K+ is "permeable"





Selective efflux of K+ down its gradient causes charge separation and a negative potential inside the cell. *This negative potential provides an electrical force to attract the K+ into the cell. When this electrical and chemical forces are equal (but opposite) there is no net K+ movement. This is an electrochemical equilibrium*

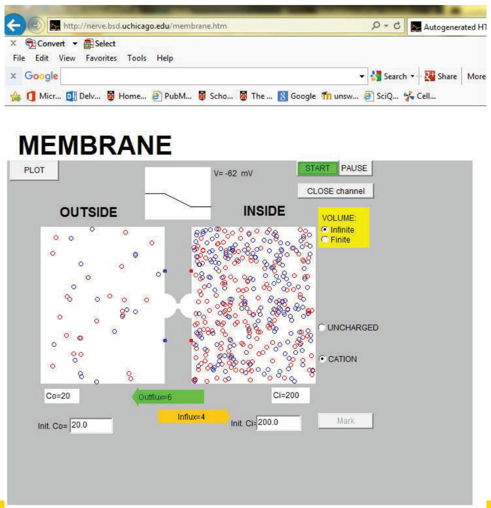
Electrochemical Equilibrium

This occurs when the chemical and electrical forces on an ion are equal:

A nice set of simulations to play with @ Francisco Bezanilla's home page :

http://nerve.bsd.uchicago.edu/

(use explorer not chrome & needs to allow JAVA to run)



Electrochemical Equilibrium

This occurs at the "Equilibrium Potential" or "Nernst Potential":

The membrane potential (V_m) at which the electrical and chemical driving forces for ion flux across the membrane are exactly equal

(to derive this equation, see p129 Stanfield)

The Nernst equation is:

$$V_m = \frac{RT}{zF} \cdot \ln\left(\frac{[X]_o}{[X]_i}\right)$$

where:

R	= the Universal Gas Constant:	= 8.3145 $VCmol^{-1}K^{-1}$,
T	= the Absolute Temperature	= 293.15 K at lab temperature of 20°C,
F	= Faraday's Constant	= 96,485 $Cmol^{-1}$,
Z	= the valency of the ion species, X	= -1 for Cl^- and +1 for Na^+, and
[X]	= the concentration of ion X (i.e. K^+ or Cl^-) in the ECF $[X]_o$ and ICF [X]i.	

Typical K+ concentrations:

$[K^+]_{outside}$ = 4 mM

$[K^+]_{inside}$ = 155 mM

If cell is only permeable to K^+ then K+ leaves until V_m = -98 mV

E_{K+} = -98 mV

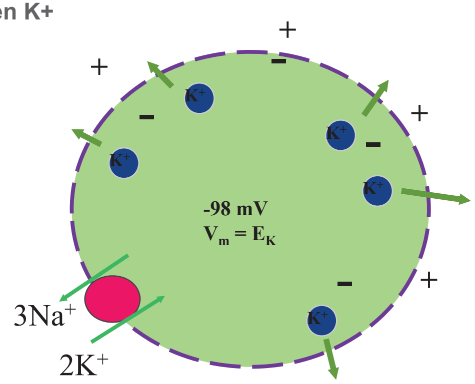
Electrical force = chemical force

"Electrochemical equilibrium"

K^+ influx (electrical force)

= K^+ efflux (chemical force)

No Net Flux



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$[K^+]_{outside}$ = 4 mM

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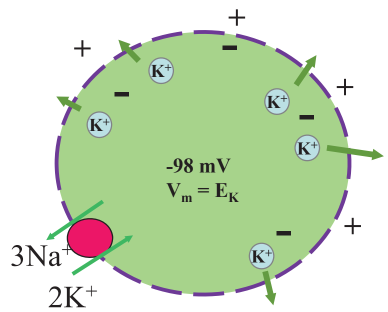


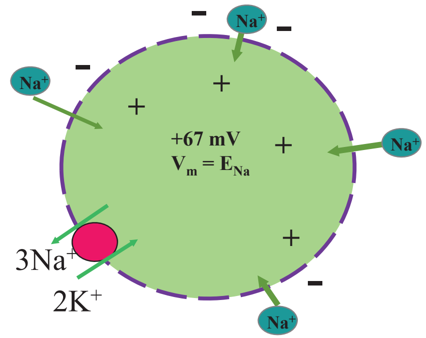
Typical Na+ concentrations:

$[Na^+]_{outside}$ = 145 mM

$[Na^+]_{inside}$ = 12 mM

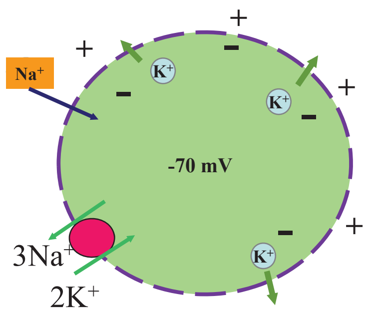
If cell is only permeable to Na^+ then Na^+ enters until V_m = +67 mV

E_{Na+} = +67 mV



By adjusting the membrane permeability to K+ and Na+, the Vm can be anywhere between E_{K+} and E_{Na+}

e.g., At a resting membrane potential of -70 mV, a small amount of K^+ efflux is balanced by a small amount of Na^+ influx. This is a "steady state" condition with no Net flux, but neither ion is at equilibrium.



- A resting nerve cell has a relative permeability of K+ and Na+ of about P_K::P_{Na} = 100
- (e.g., 100 leak K+ channels open, and 1 Na+ channel open)
- A small electrochemical force and high permeability drives small K+ efflux, while a strong electrochemical force but low permeability drives an equal Na+ influx

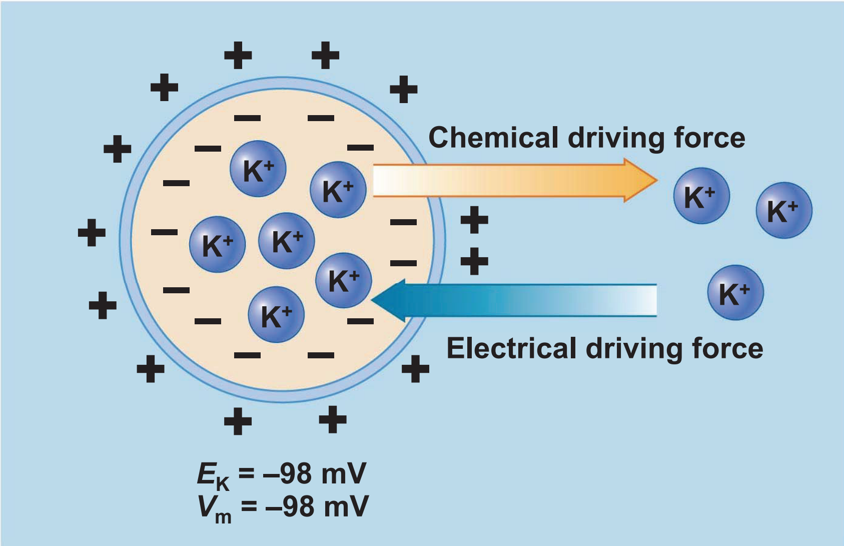
- The membrane potential always depends on the relative permeability of the physiological ions (mostly Na^+, K^+ and Cl^-)

Multiple Choice

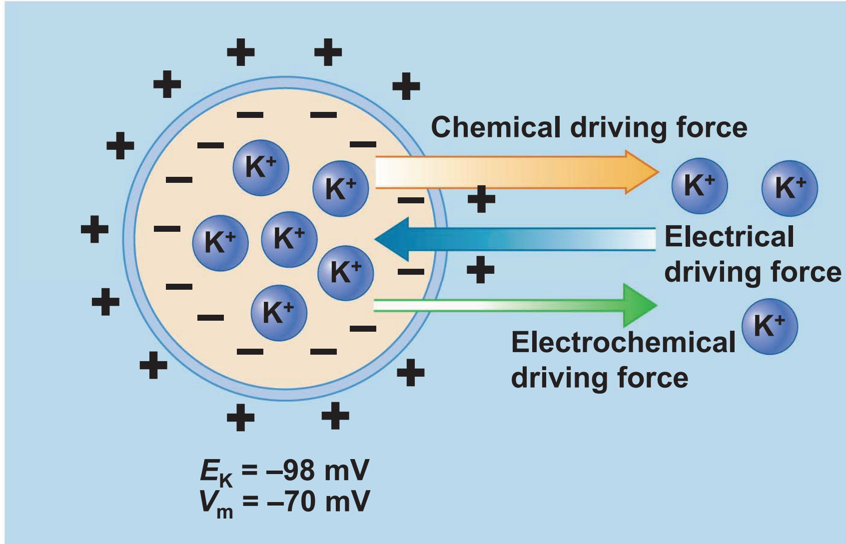
If the K+ equilibrium potential is -98mV, and the membrane potential is steady at -70 mV, which of the following is true (may be more than 1)

- There will be a continuous efflux of K+
- The intracellular K+ concentration will decrease towards 100 mM
- If more K+ channels are opened, the membrane ppotential doesnt change
- This is all very confusing
- No Na+ ions move across the membrane as the cell is at rest

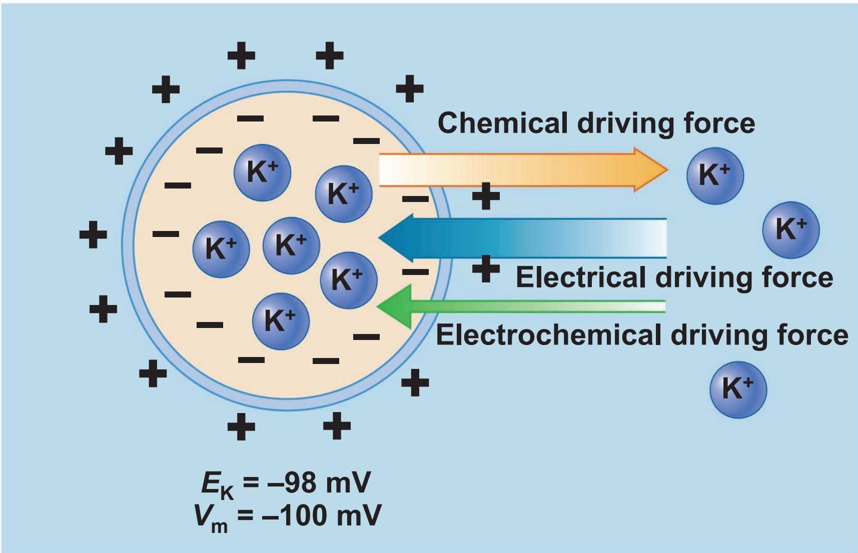
Electrochemical Equilibrium. Electrical force for K+ influx = chemical force for K+ efflux. No Net Flux



At resting membrane potential. Electrical force for K^+ influx < chemical force for K^+ efflux. K^+ Efflux

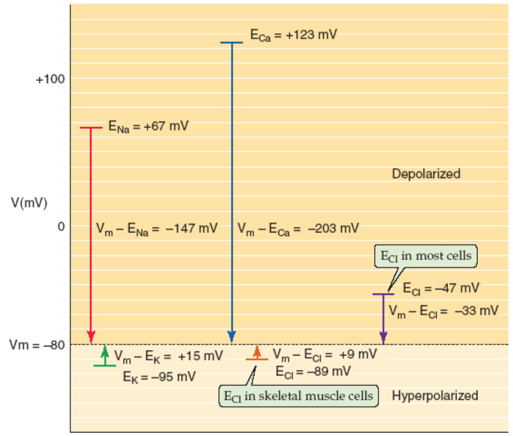


At a very negative membrane potential. Electrical force for K^+ influx > chemical force for K^+ efflux. K^+ Influx



The electrochemical forces for ions in physiological conditions when a cell is at rest

- The difference between the equilibrium potential (E_x) and the membrane potential (V_m) is the driving force for movement of ion x



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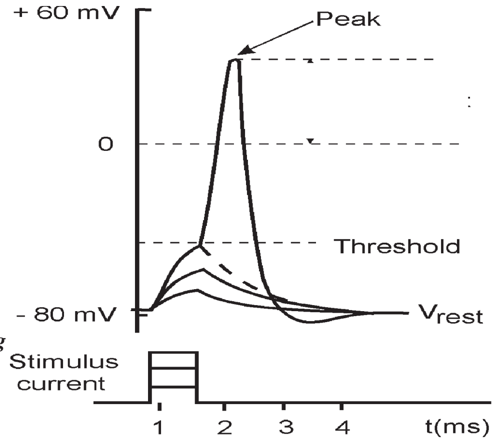
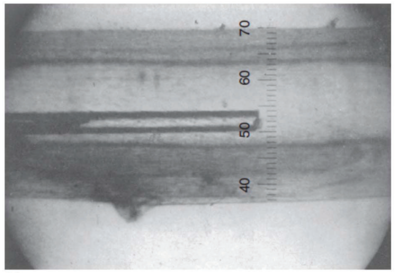
The nerve action potential….

1. *Concept of Threshold*
2. *Features / Phases*
3. *Ionic Currents involved*
4. *Ion Channels involved*
5. *Molecular Physiology*
6. *Voltage-dependent Gating*



The nerve action potential….
Underlying ionic Currents.

- *The 1st nerve action potential recording, from inside the giant axon of a squid*

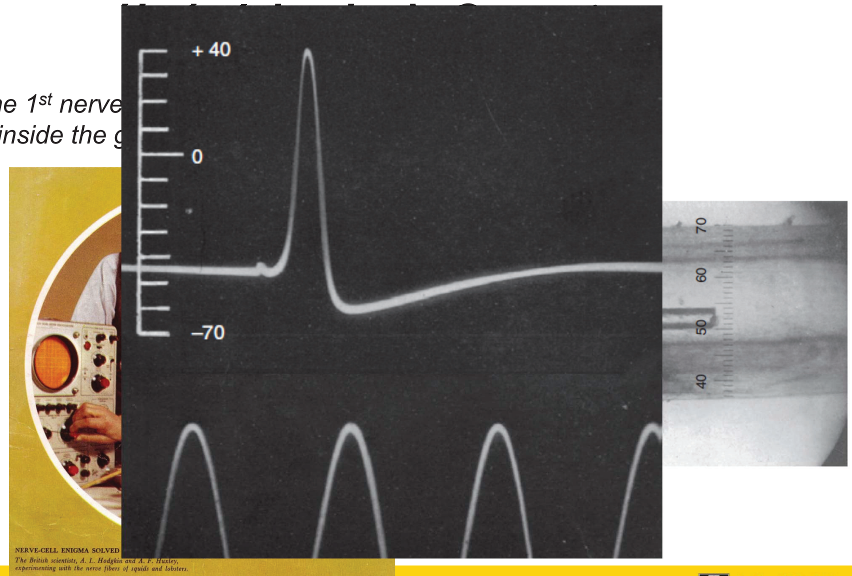


See also https://www.youtube.com/watch?v=k48jXzFGMc8 for video of this early experiment

Hodgkin & Huxley, Nature, 1939, J Physiol., 1945

The nerve action potential….

- *The 1st nerve*
from inside the g



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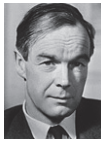
The nerve action potential….
Underlying ionic Currents.

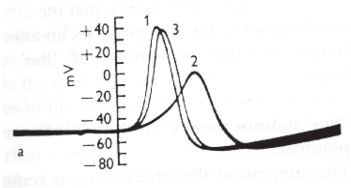


Sir Alan Hodgkin
Nobel Prize1963

Sir Bernard Katz
Nobel Prize1971

- *One of the 1st Action Potential experiments….*

J. Physiology, 1949



1 = control,
2 = low Na^+ in the sea water,
3 = wash / recovery response

Conclusion?:

The nerve action potential….
Underlying ionic Currents.

1. Inward Na^+ current, → **Rapid depolarization**
   - *Na^+ influx*

2. Outward K^+ current → **Slow repolarization**
   - *K^+ efflux*

The nerve action potential….
Underlying ionic Currents and the Channels involved.

1. Inward Na^+ current, → **Rapid depolarization**
   - *Na^+ influx*
   - *Fast, voltage gated channels*

2. Outward K^+ current → **Slow repolarization**
   - *K^+ efflux*
   - *Slow, voltage gated channels*