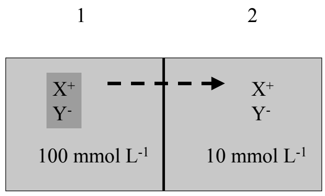
Membrane potentials

Ionic distribution across the cell membrane

Approximate concentrations of ions in millimoles/litre from a variety of cells and different animal species.

	Extracellular	Intracellular
cations:		
Na	120 - 150	10 - 15
K	2.5 - 5	140 - 160
H	3.8 x 10-5	1.3 x 10-4
anions:		
Cl	120	3 - 9
HCO3	27	8
Protein	-	150

- the unequal distribution of ions inside and outside the membrane and the semi-permeable nature of the membrane leads to the generation of a potential difference across the membrane (due to energy and concentrations gradients).



- to move a small quantity of an ion (n moles of ion X) up the concentration gradient (2 to 1) the work (Wc) required to be done is given by:

$$Wc = n.RT \ln \frac{[X1]}{[X2]}$$

R	gas constant (8.314 J deg-1 mole-1)
T	absolute temp. (oK, ≈310°K)
X1	concentration of X+ in compartment 1 (molar)
X2	concentration of X+ in compartment 2 (molar)

- electrical work (We) required to move n moles of X against electrical gradient i.e. from 1 to 2 is given by:

$$We = n.zFE$$

z	is valence.
F	Faraday's constant (96,500 coulombs mole^{-1}).
E	potential difference in volts between 1 and 2

- at equilibrium, where concentration and electrical forces acting on the ion are balanced:

$$We = Wc$$

$$n.zFE = n.RT \ln \frac{X1}{X2}$$

ie $$E = \frac{RT}{zF} \ln \frac{X1}{X2}$$

NERNST EQUATION -> expresses the potential energy difference for a particular ion (in volts) due to concentration differences across the cell membrane.

by enumerating constants: ($\ln x = 2.3 \log_{10} x$)

at 37°C $$E = \frac{RT}{zF} 2.303 \log_{10} \frac{Xo}{Xi}$$

$$= \frac{61.5}{z} \log_{10} \frac{Xo}{Xi} \text{ mv}$$

at 20°C $$E = \frac{58.2}{z} \log_{10} \frac{Xo}{Xi} \text{ mv}$$

eg for K^+ at 37°C

K^+i = 150 mM

K^+o = 5 mM

E_K = -90.84 mv

Resting potential

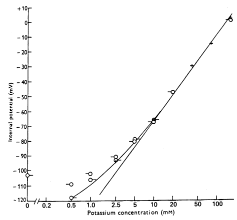
The equilibrium potential is the electrical potential (membrane voltage) required to balance the concentration potential (Nernst potential) for a particular ion.

For example: the membrane potential (E_m) that balances the concentration potential for K^+ is the equilibrium potential for K^+ such that:

$$E_m = \frac{RT}{zF} \, 2.303 \log_{10} \frac{K^+_o}{K^+_i} \text{ mv}$$

$$= E_K \text{ (Nernst potential for } K^+\text{)}$$

If the membrane was selectively permeable to only one ion (e.g. K^+), then the membrane potential will equal the Nernst potential for that ion.



At K^+ concentrations above $\approx$10 mM the equation fits the results well. Below this value E_m departs from the curve relating E_m to E_K alone.

- indication is that E_m is not solely due to K^+ permeability, but to other ions as well.

- two other principal ions: Na^+ and Cl^-.

- relative contributions to E_m depend on the relative permeabilities of the ions.

- Cl^- ions are distributed across the membrane in equilibrium with the membrane potential (i.e. $E_{Cl} = E_m$, therefore changes in Cl^- concentration do not control the steady state membrane potential).

- principle ions are therefore potassium and sodium.

- membrane is not completely impermeable to sodium, it is likely that sodium ions play some role in determining the membrane potential, along with potassium ions.

- to take account of their permeabilities - Goldman-Hodgkin-Katz equation (or referred to as Goldman equation or constant field equation).

$$E_m = \frac{RT}{F} \ln \frac{P_K (K^+)_o + P_{Na}(Na^+)_o + P_{Cl}(Cl^-)_i}{P_K (K^+)_i + P_{Na}(Na^+)_i + P_{Cl}(Cl^-)_o}$$

P_K, P_{Na} and P_{Cl} are permeability coefficients of K, Na and Cl.

Permeability coefficients (P) are measured in cm/sec and defined by:

$$P = (\mu ß/a)(RT/F)$$

where µ - mobility of ion
ß - partition coefficient between the membrane and aqueous solution
a - thickness of membrane
RTF - as above

As indicated $E_{Cl} = E_m$, the Goldman equation then simplifies to:

$$E_m = \frac{RT}{F} \ln \frac{(K^+)_o + \alpha(Na^+)_o}{(K^+)_i + \alpha(Na^+)_i}$$

$\alpha = P_{Na}/P_K$ (ie ratio of Na:K permeability).
$= 0.013$ determined using radio isotope measurements (for those interested in how this value is determined see Katz, B. Nerve, Muscle and Synapse. McGraw-Hill, New York, 1966).

Conductance (g) is an index of the ease with which charges flow (the reciprocal of resistance) and some texts use it interchangeably with permeability, such that the relation between ionic current (I) and electrical driving force is

$$I_{ion} = g_{ion} (E_m - E_{ion})$$

eg

$$I_K = g_K (E_m - E_K)$$
$$I_{Na} = g_{Na} (E_m - E_{Na})$$

- the conductance can be derived by measuring the current carried by an ion through the membrane and the membrane potential.

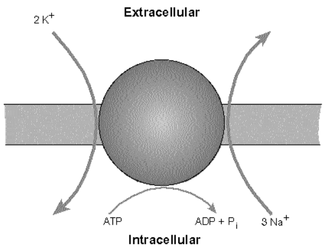
Active transport

- the membrane potential arises from the movement of K+ and Na+ down their electrochemical gradient

- there is a net movement of potassium ions out of the cell and sodium ions into the cell →on its own this would lead to potassium and sodium concentrations within the cell changing with time.

- however, these ions are in a steady state, with the internal composition of the cell remaining constant with time.

- this is achieved by an active transport mechanism, Na-K pump (or referred to as Na pump or Na-KATPase)



Steady state

==> the rate of entry of electrical charge must equal the rate of exit and that condition is only satisfied at a membrane voltage of around -70mV, where the sodium current into the cell is balanced by the potassium current out of the cell.

- the steady state principle requires that the net movement of electrical charge must be zero in a resting cell.

that is:

$$I_K + I_{Cl} + I_{Na} = 0$$

$$g_K (E_m - E_K) + g_{Cl} (E_m - E_{Cl}) + g_{Na} (E_m - E_{Na}) = 0$$

which is only satisfied when:

$$E_m = \frac{g_K E_K + g_{Cl} E_{Cl} + g_{Na} E_{Na}}{g_K + g_{Cl} + g_{Na}}$$

which shows that the resting membrane potential is a weighted average of the Nernst potentials