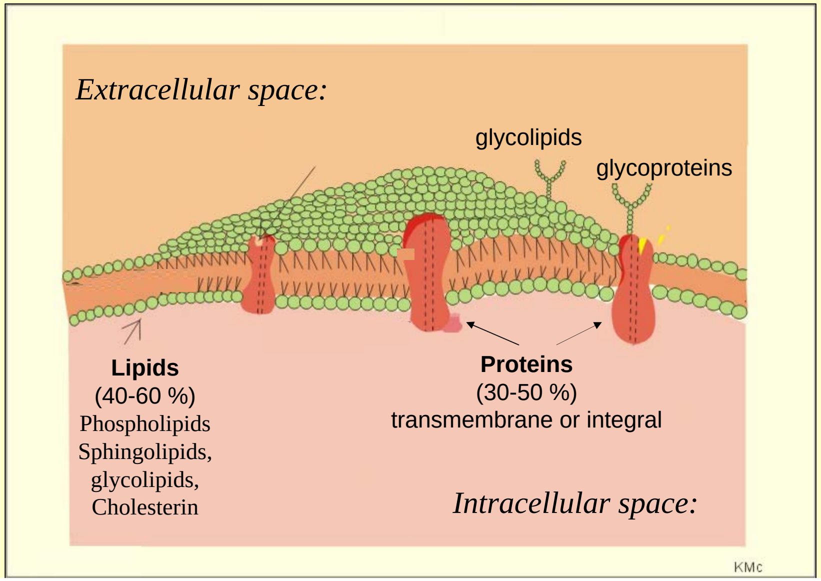
Transport across biological membranes

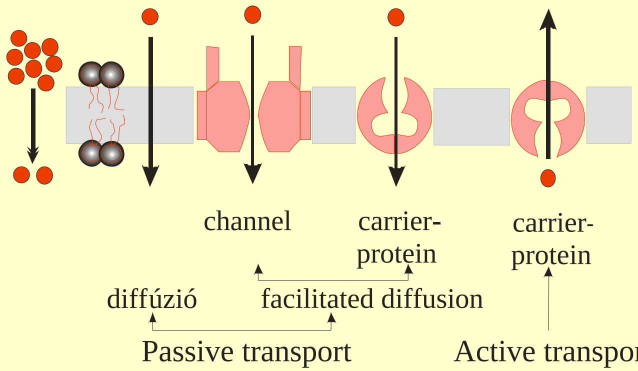
Transport in the Resting State of the Cell

Membrane structure



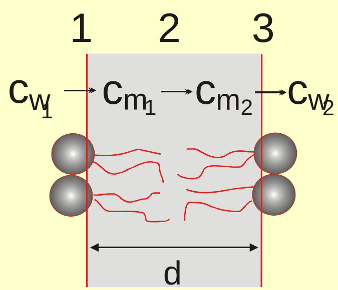
Transport types across the memebranes

Classification based on: energy consumption
molecular mechanism



Diffusion of neutral particles

Diffusion across the lipid bylayer



Assume that concentration changes linearly

Fick I.

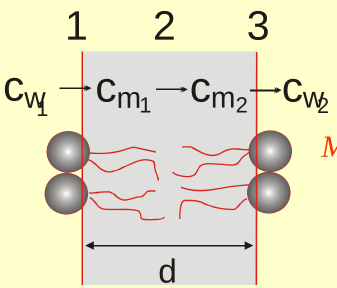
$$J_m = -D\frac{\Delta c}{\Delta x}$$

$$D_m << D$$

$$J_m = -D_m \frac{c_{m_2} - c_{m_1}}{d}$$

Diffusion of neutral particles

Diffusion across the lipid bylayer



$$J_m = -D_m \frac{c_{m_2} - c_{m_1}}{d}$$

$$J_m = -p_m (c_{m_2} - c_{m_1})$$

Membrane permeability constant [ms^{-1}]

Cannot be measured

$$\frac{C_{m1}}{C_{v1}} = \frac{C_{m2}}{C_{v2}} = K$$

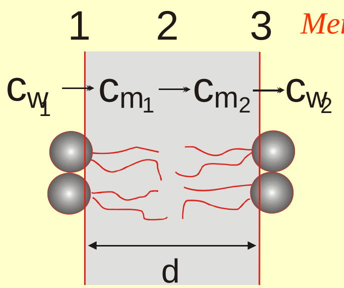
$$C_{m1} = K C_{v1}$$

Diffusion of neutral particles

Diffusion across the lipid bylayer

$$J_m = -p_m (c_{m2} - c_{m1})$$

Membrane permeability constant [ms-1]



Cannot be measured

$$\frac{C_{m1}}{C_{v1}} = \frac{C_{m2}}{C_{v2}} = K$$

$$C_{m1} = K C_{v1}$$

$$J_m = -p_m K (c_{v2} - c_{v1})$$

$$J_m = -p (c_{v2} - c_{v1})$$

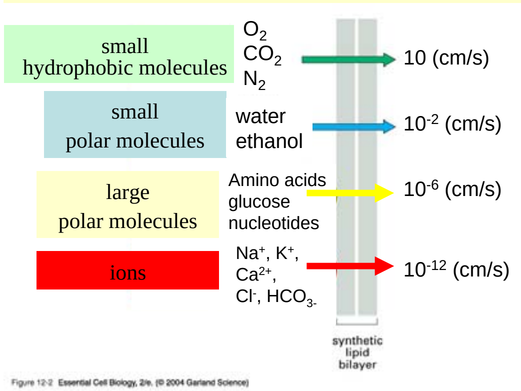
$J_m = -\mathbf{p}(C_{v2} - C_{v1})$

Permeability constant [ms^{-1}]

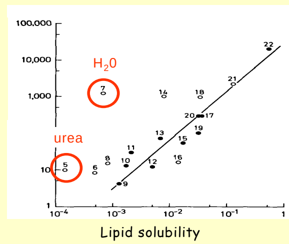
It is influenced by:

- diffusion coefficient within the membrane
- thickness of the membrane
- partition coefficient

Permeability vs hydrophobicity



Lipid solubility v permeability



Diffusion of ions

Fick I. $J_m = -D\frac{\Delta c}{\Delta x}$

chemical potential
and
electric potential
together

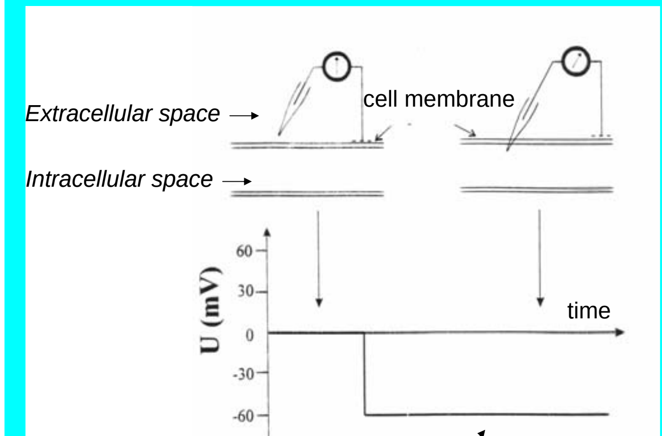
$$J_k = -D_k\left(\frac{\Delta c_k}{\Delta x} + c_k\frac{z_k F}{RT}\frac{\Delta\varphi}{\Delta x}\right)$$

flux of *k*-th ion

Basic principles of electrophysiology

Interpretation by transport phenomenon

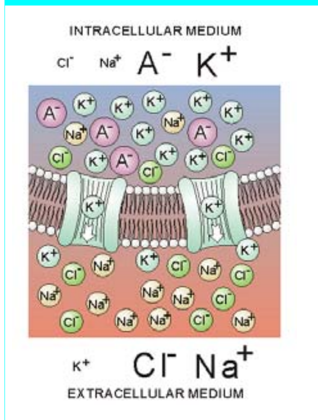
Observation 1: There is an electric potential difference between extra- and intracellular space



The intracellular side is negative with respect to the extracellular side

resting potential ~ 60 – 90 mV

Observation 2: Inhomogeneous ion distribution



Cell type	$C_{Intracellular}$ (mmol/l)			$C_{Extracellular}$ (mmol/l)		
	$[Na^+]_i$	$[K^+]_i$	$[Cl^-]_i$	$[Na^+]_e$	$[K^+]_e$	$[Cl^-]_e$
Squid axon	72	**345**	61	**455**	10	540
Frog muscle	20	**139**	3,8	**120**	2,5	120
Rat muscle	12	**180**	3,8	**150**	4,5	110

Interpretation of the membrane potential

Model 1

Constant ion distribution in resting state

↓

No transport (?)

↓

<u>Assume that</u> (1) the system is in ***equilibrium***

that is

no electrochemical potential difference

$$\mu^{II}_{e,i} - \mu^{I}_{e,i} = 0$$

$$\mu^{II}_{e,i} - \mu^{I}_{e,i} = 0$$

↓

$$\mu_0 + RT\ln c_i^I + zF\varphi_i^I = \mu_0 + RT\ln c_i^{II} + zF\varphi_i^{II}$$

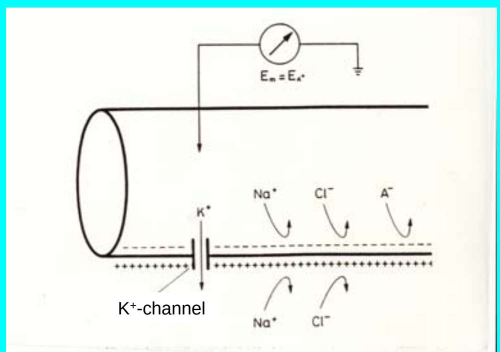
↓

Equilibrium potential → $\varphi_i^I - \varphi_i^{II} = \frac{RT}{zF}\ln\frac{c_i^I}{c_i^{II}}$

Nernst-equation

<u>Assume</u> (2) unlimited ***K^+*** -ra permeability

(3) zero ***Na^+*** permeability



Donnan model – Equilibrium model

- No electrochemical potential difference between extra- and intracellular medium
- The membrane is permeable only for K^+ (and Cl^-)
- The cell with its extracellular region is thermodynamically closed system

↓

equilibrium potential ≡ resting potential

$$\varphi_e - \varphi_i = \frac{RT}{F}\ln\frac{[K^+]_i}{[K^+]_e}$$

$$\varphi_e - \varphi_i = \frac{RT}{F} \ln \frac{[K^+]_i}{[K^+]_e}$$

Data from the equilibrium approach do not agree with the experiments

Tissue	Resting potential (mV)	
	calculated	measured
Squid axon	*91*	62
Frog muscle	*103*	92
Rat muscle	*92,9*	92

Calculations based on other ions

potential (mV)	Squid axon	Rat muscle
$U_{measured}$	**-62**	**-92**
U_{0K+}	-91	-103
U_{0Na+}	+47	+46
U_{0Cl-}	-56	-88

There is no good agreement

Interpretation of the membrane potential

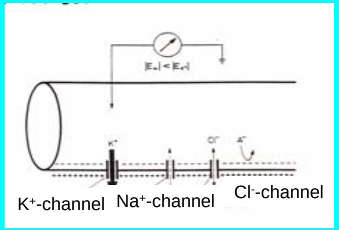
Model 2

1. Assume that the system is *not in* ***equilibrium***

that is

transport is forced across the membrane

2. Take into consideration the real permeability of the membrane



the membrane is represented by specific ion-permeabilities

Electrodiffusion model - transport across the membrane

$$\sum J_k = 0$$

k: Na, K, Cl, ….

$$\Sigma J = J_{K^+} + J_{Na^+} + J_{Cl^-} = 0$$

$$J_k = -D_k \left(\frac{\Delta c_k}{\Delta x} + c_k \frac{z_k F}{RT} \frac{\Delta \varphi}{\Delta x} \right)$$

$$D_k = d p_k$$

$$\boxed{\varphi_e - \varphi_i = -\frac{RT}{F} \ln \frac{\Sigma p_k^+ c_{ke}^+ + \Sigma p_k^- c_{ki}^-}{\Sigma p_k^+ c_{ki}^+ + \Sigma p_k^- c_{ke}^-}}$$

Electrodiffusion model

Goldman – Hodgkin – Katz formula

$$\boxed{\varphi_e - \varphi_i = -\frac{RT}{F}\ln\frac{\Sigma p_k^+ c_{ke}^+ + \Sigma p_k^- c_{ki}^-}{\Sigma p_k^+ c_{ki}^+ + \Sigma p_k^- c_{ke}^-}}$$

c_k: ion-concentration
p_k: permeability constant
e: extracellular
i: intracellular

Electrodiffusion model

Goldman – Hodgkin – Katz formula

$$\boxed{\varphi_e - \varphi_i = -\frac{RT}{F}\ln\frac{\Sigma p_k^+ c_{ke}^+ + \Sigma p_k^- c_{ki}^-}{\Sigma p_k^+ c_{ki}^+ + \Sigma p_k^- c_{ke}^-}}$$

potential (mV)	Squid axon	Rat muscle
$U_{measured}$	**-62**	**-92**
U_{GHK}	-61,3	-89,2

Good agreement with experimental results

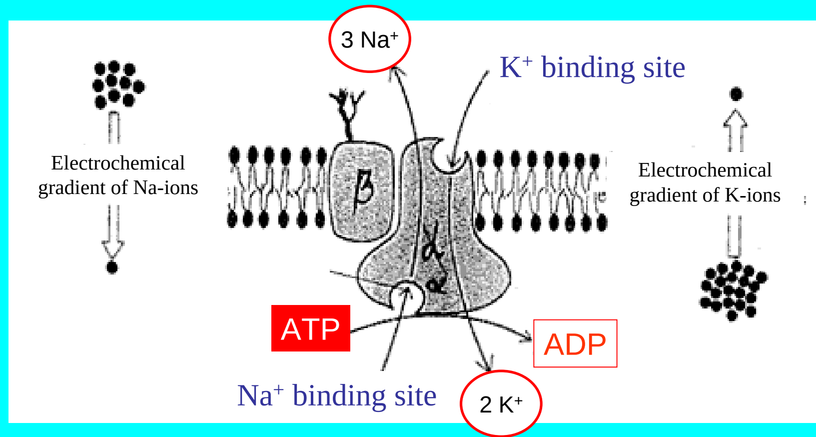
Electrodiffusion model

- Resting U_m depends on the concentration gradients and on the relative permeabilities to Na, K and Cl.
- The GHK equation describes a steady-state condition, not electrochemical equilibrium.
- There is net flux of individual ions, but no net charge movement.
- The cell must supply energy to maintain its ionic gradients.

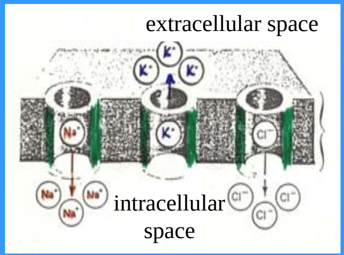
Na – K pump

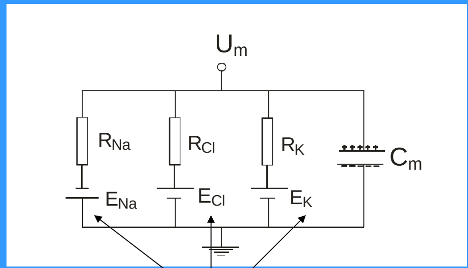
antiporter

The condition for stationary flow is maintained by the active transport



Equivalent circuit model

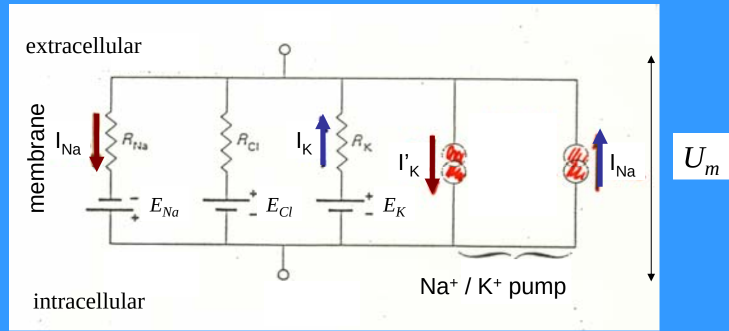




Nernst-potential of ions

Ion-selective channels modeled by electromotive force and conductivity

Na^+ /K^+ pump restores the ion distribution



Ohm's law: $\boxed{I_k=1/R_k(U_m-E_k)}$

Calculation of resting potential according to the equivalent circuit model

$I_k=1/R_k(U_m-E_k)$

E_k – Nernst-potential of ions

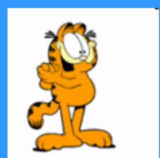
$\Sigma I_k=I_{ion}=0$

$\Sigma I_k=I_{Na}+I_K+I_{Cl}=0$

$$g_K\,(U_m-E_K) + g_{Na}\,(U_m-E_{Na}) = 0$$

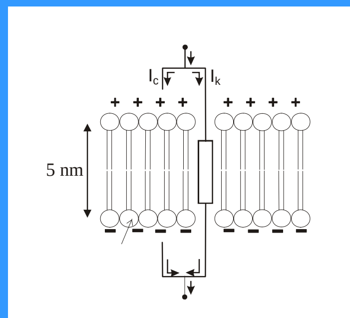
$$U_m = \frac{(U_{0K}\,x g_K) + (U_{0Na}\,x g_{Na})}{g_K + g_{Na}}$$

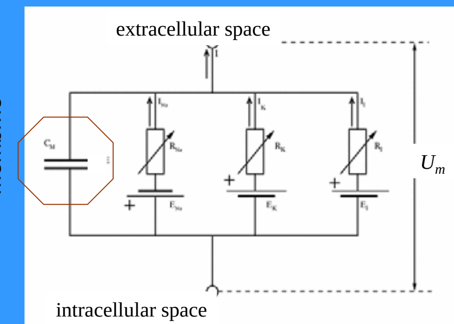
Calculation e.g.: $U_m = \frac{(-100\times 5)+(50\times 1)}{5+1} = -75$ [mV]



Capacitive property of the membrane

Capacitance ~10^{-6} F/cm²





$$I_m = I_{ion} + I_c$$

Ion current

Capacitive current

$$I_c = C_m \frac{\Delta U_m}{\Delta t}$$