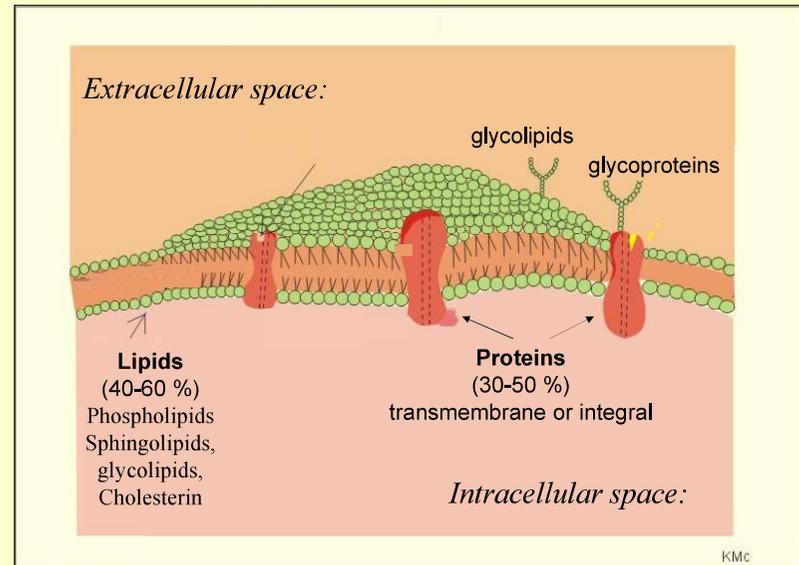


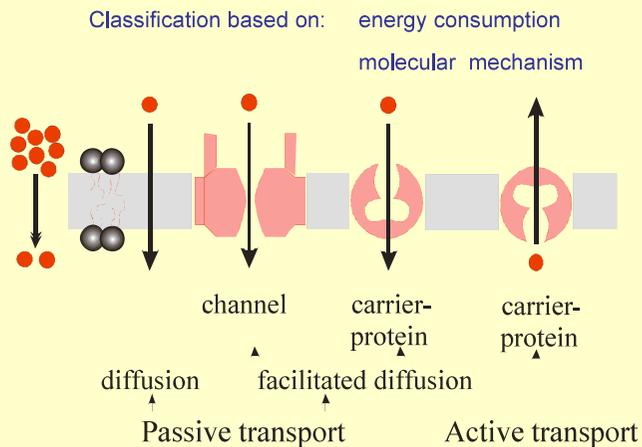
# Transport across biological membranes

Transport in Resting Cell

## Membrane structure

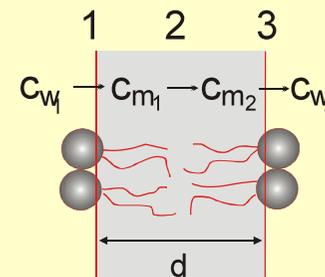


## Transport types across the membranes



## Diffusion of neutral particles

Diffusion across the lipid bilayer



Assume that concentration changes linearly

Fick I.

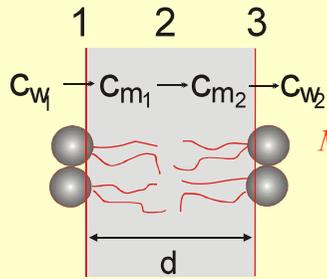
$$J_m = -D \frac{\Delta c}{\Delta x}$$

$$D_m \ll D$$

$$J_m = -D_m \frac{c_{m2} - c_{m1}}{d}$$

# Diffusion of neutral particles

Diffusion across the lipid bilayer



$$J_m = -D_m \frac{C_{m2} - C_{m1}}{d}$$

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

Membrane permeability constant [ms<sup>-1</sup>]

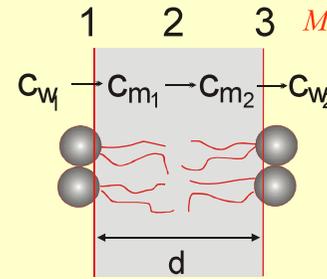
Cannot be measured

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

$$C_{m1} = KC_{v1}$$

# Diffusion of neutral particles

Diffusion across the lipid bilayer



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

Membrane permeability constant [ms<sup>-1</sup>]



Cannot be measured

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

$$C_{m1} = KC_{v1}$$

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

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

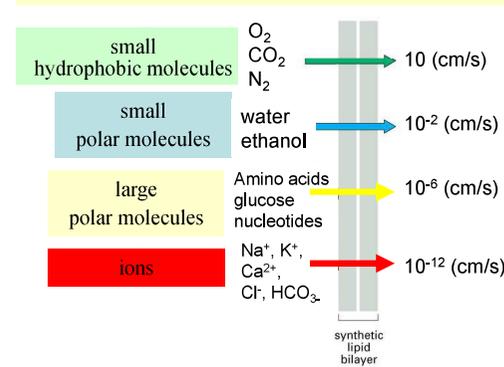
$$J_m = -p(C_{v2} - C_{v1})$$

Permeability constant [ms<sup>-1</sup>]

It is influenced by:

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

## Permeability vs hydrophobicity



Lipid solubility v permeability

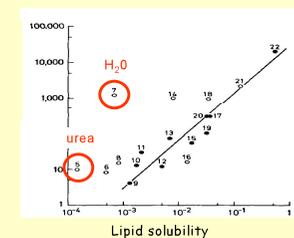


Figure 10-2 Essential Cell Biology, 2/e. © 2004 Garland Science

## Diffusion of ions

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

chemical potential  
and  
electric potential  
together

$$J_k = L_k X_k = -L_k \frac{\Delta \mu_{ek}}{\Delta x}$$

flux of  $k$ -th ion

## Diffusion of ions

$$J_k = L_k X_k = -L_k \frac{\Delta \mu_{ek}}{\Delta x}$$

$$\frac{\Delta \mu_{ek}}{\Delta x} = \frac{\Delta \mu_k}{\Delta x} + z_k F \frac{\Delta \phi}{\Delta x} \quad \text{és} \quad L_k = c_k \frac{D_k}{RT}$$

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

$$D = u k T$$

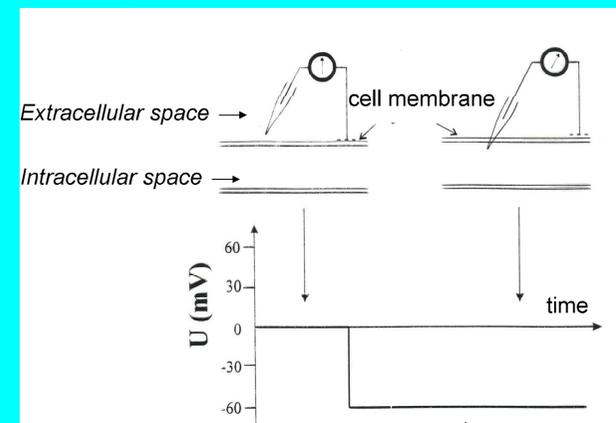
$$J_k = -u_k k T \left( \frac{\Delta c_k}{\Delta x} + c_k \frac{z_k F}{RT} \frac{\Delta \phi}{\Delta x} \right)$$

flux of  $k$ -th ion

## Basic principles of electrophysiology

### Interpretation by transport phenomena

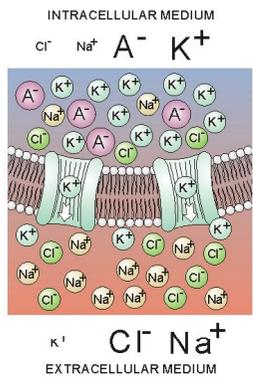
**Observation 1:** There is an electric potential difference between extra- and intracellular space



The intracellular side is negative with respect to the extracellular side

resting potential  $\sim 60 - 90$  mV

## Observation 2: Inhomogeneous ion distribution



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

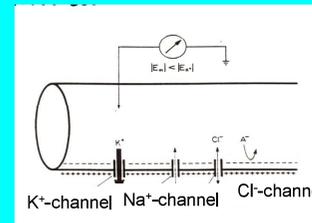
## Interpretation of the membrane potential

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, ...

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

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

$$D_k = dp_k$$

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

## Electrodiffusion model

Goldman – Hodgkin – Katz formula

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

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

## Electrodiffusion model

Goldman – Hodgkin – Katz formula

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

potential (mV)	Squid axon	Rat muscle
$U_{\text{measured}}$	<b>-62</b>	<b>-92</b>
$U_{\text{GHK}}$	-61,3	-89,2

Good agreement with experimental results



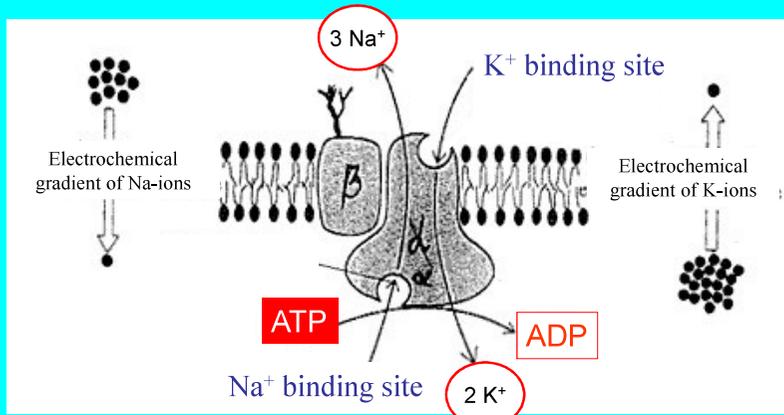
## Electrodiffusion model

- 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

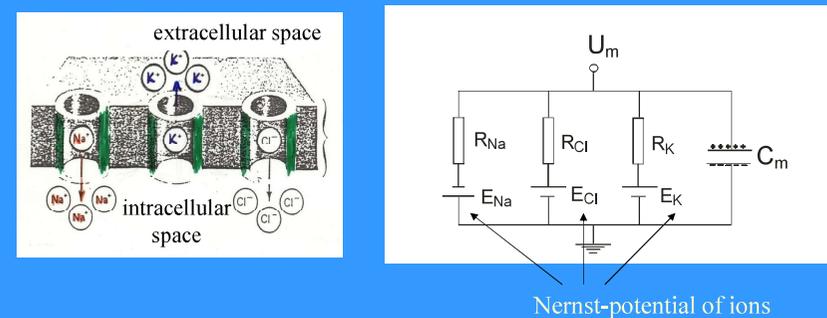
antiporter

The condition for stationary flow is maintained by the active transport



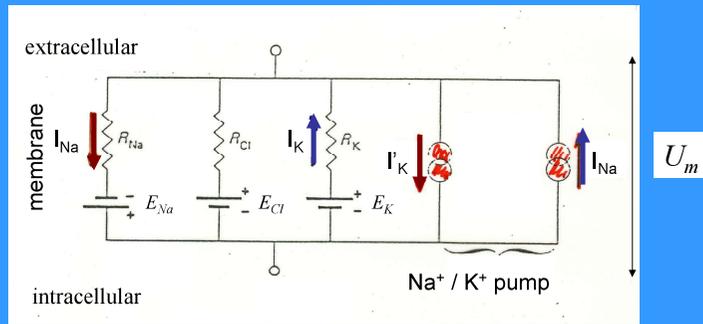
## Interpretation of the membrane potential 2

### Equivalent circuit model



Inselective channels modeled by electromotive force and conductivity

# Na<sup>+</sup> /K<sup>+</sup> pump restores the ion distribution



Ohm's law:

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