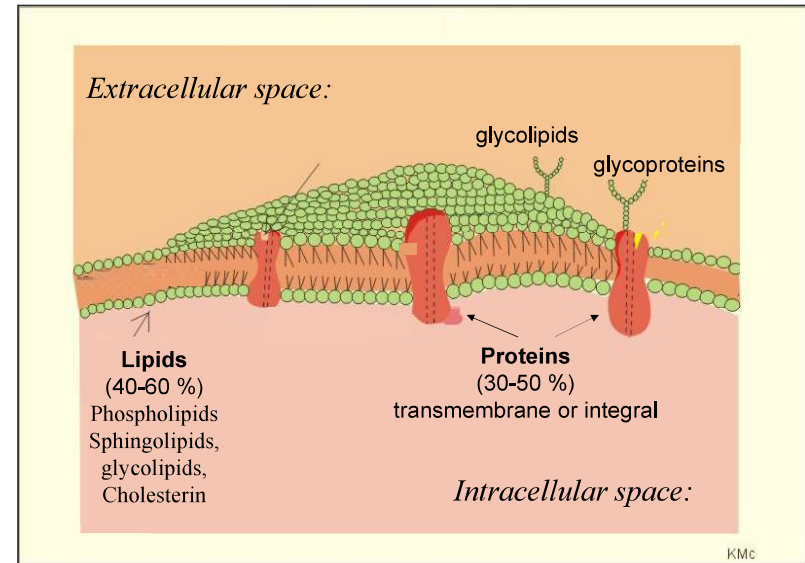


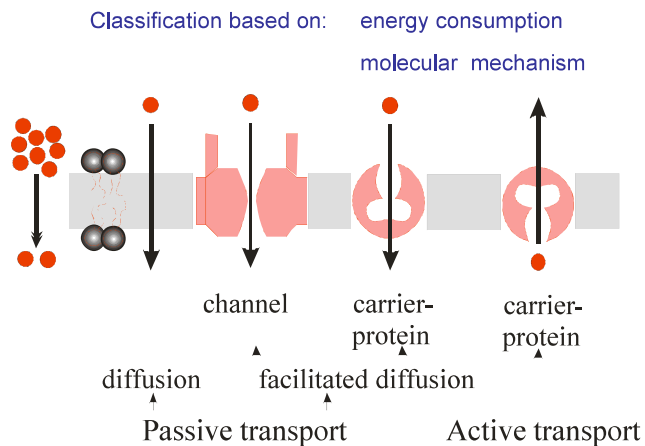
Transport across biological membranes

Transport in Resting Cell

Membrane structure

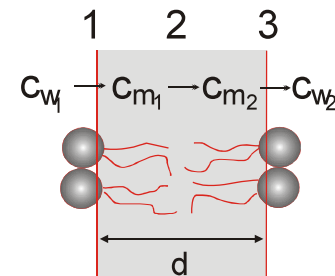


Transport types across the membranes



Diffusion of neutral particles

Diffusion across the lipid bilayer



Assume that concentration changes linearly

Fick I.

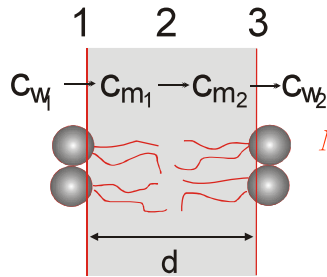
$$J_m = -D \frac{\Delta c}{\Delta x}$$

$$D_m \ll D$$

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

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⁻¹]



Cannot be measured

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

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

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

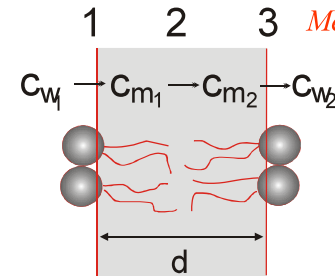
Permeability constant [ms⁻¹]

It is influenced by:

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

Diffusion of neutral particles

Diffusion across the lipid bilayer



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

Membrane permeability constant [ms⁻¹]



Cannot be measured

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

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

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

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

Permeability vs hydrophobicity

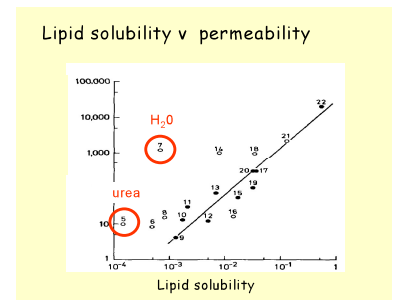
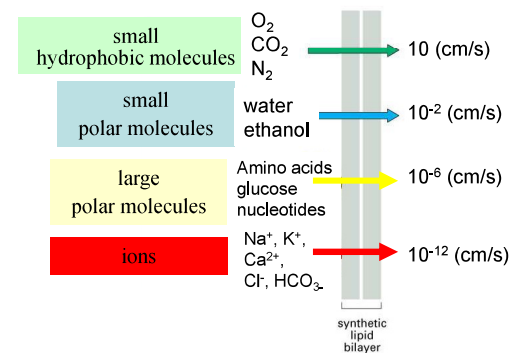


Figure 12-2 Essential Cell Biology, 2/e, © 2004 Garland Science

Diffusion of ions

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

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

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

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

$$D = u k T$$

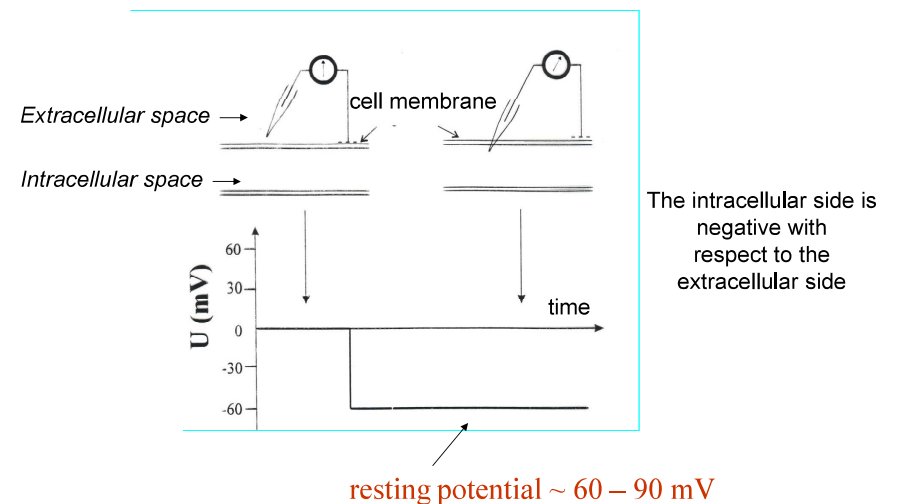
$$J_k = -u_k k T \left(\frac{\Delta c_k}{\Delta x} + c_k \frac{z_k F}{RT} \frac{\Delta \phi}{\Delta x} \right)$$

flux of k -th ion

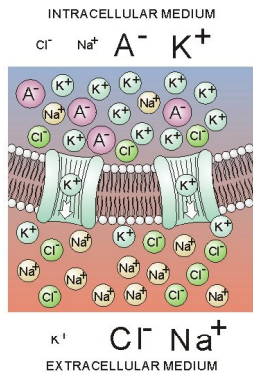
Basic principles of electrophysiology

Interpretation by transport phenomena

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



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

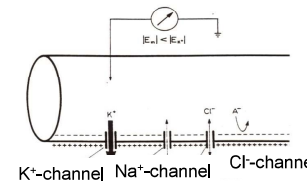
Interpretation of the membrane potential

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,

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

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

$$D_k = dp_k$$

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

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

Electrodifusion 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_{measured}	-62	-92
U_{GHK}	-61,3	-89,2

Good agreement with experimental results



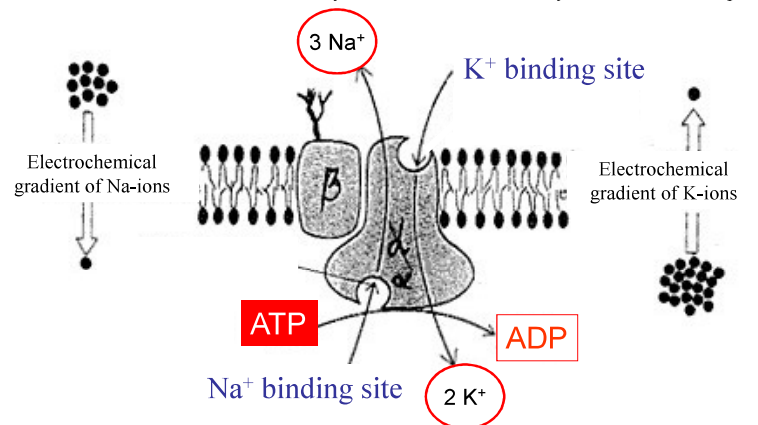
Electrodifusion model

- 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

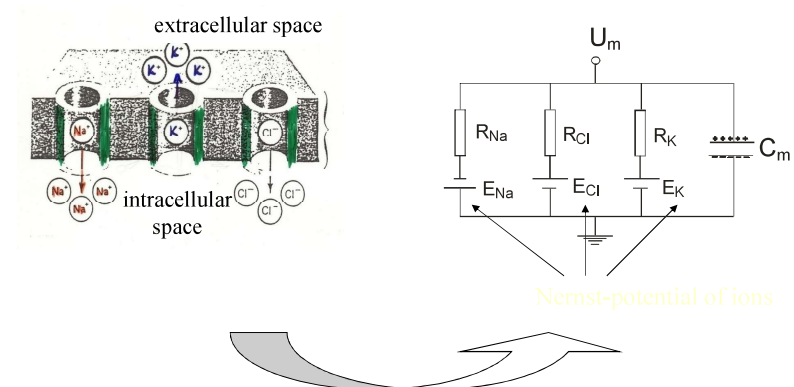
antiporter

The condition for stationary flow is maintained by the active transport



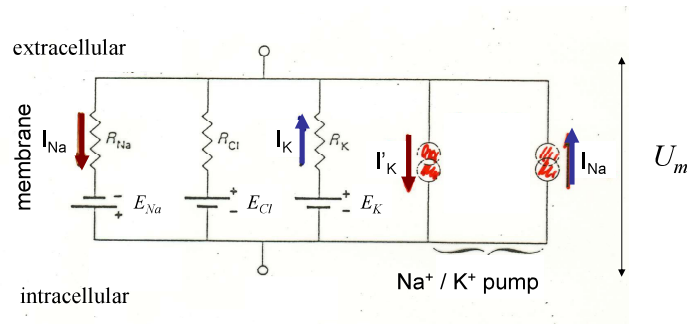
Interpretation of the membrane potential 2

Equivalent circuit model



Ionselective channels modeled by electromotive force and conductivity

Na⁺ /K⁺ pump restores the ion distribution



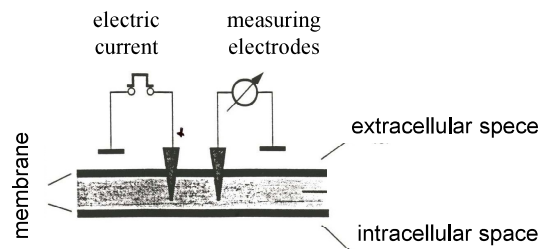
Ohm's law:

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

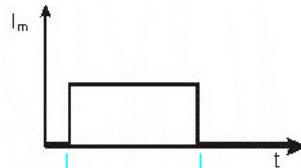
Alteration of resting membrane potential

1. "passive" electric properties of the membrane

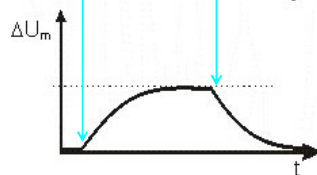
Observation



Inward current

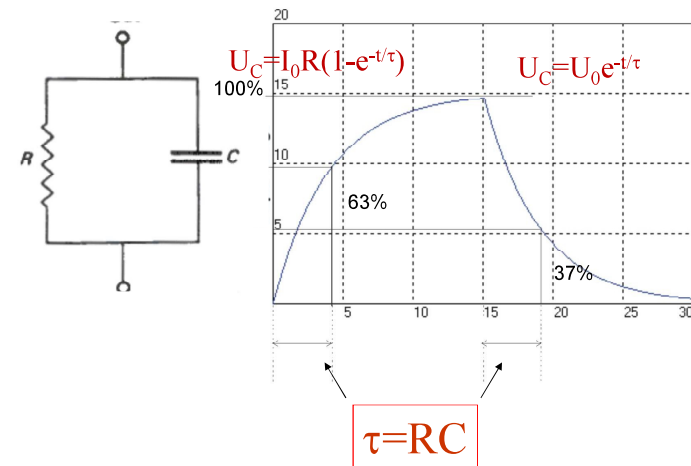


Depolarization of the membrane

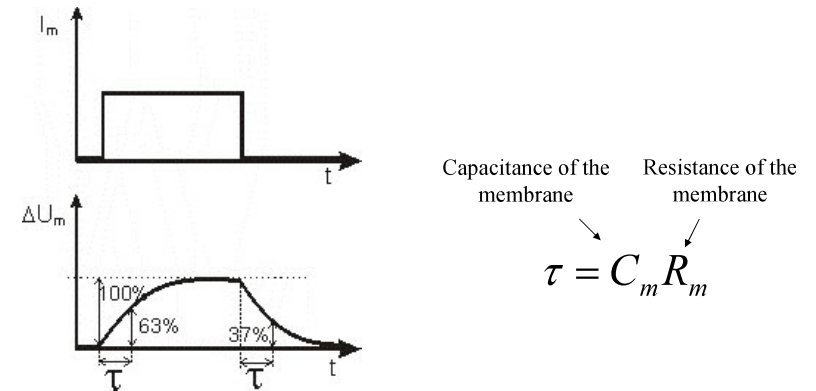
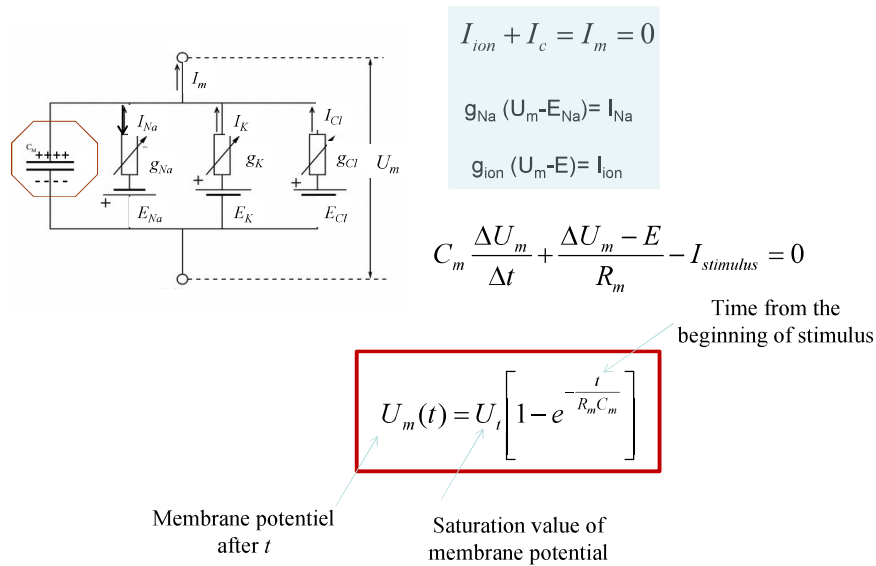


What is it like?

Charge and discharge of RC-circuit



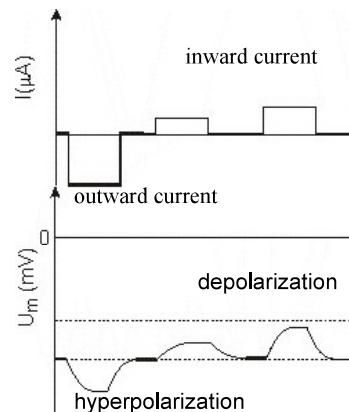
Interpretation with equivalent circuit model:



τ : time constant of membrane

- the time required for the membrane potential to reach 63% of its saturation value
- during which the membrane potential decreases to the e-th of its original value

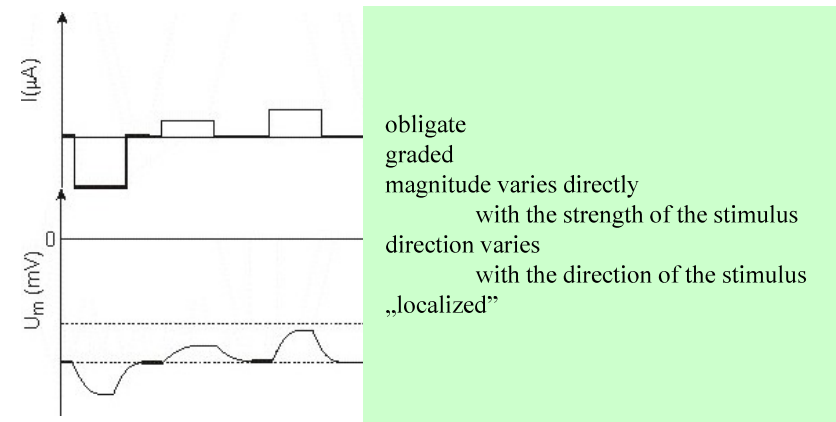
$$U_m(t) = U_t \left[1 - e^{-\frac{t}{R_m C_m}} \right]$$



U_t is proportional to the stimulating current

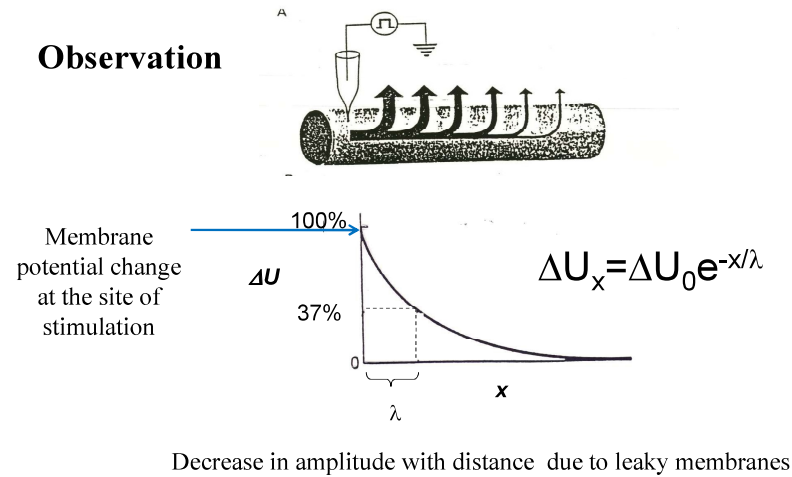
The rate of the change depends on U_t

Local changes of membrane potential



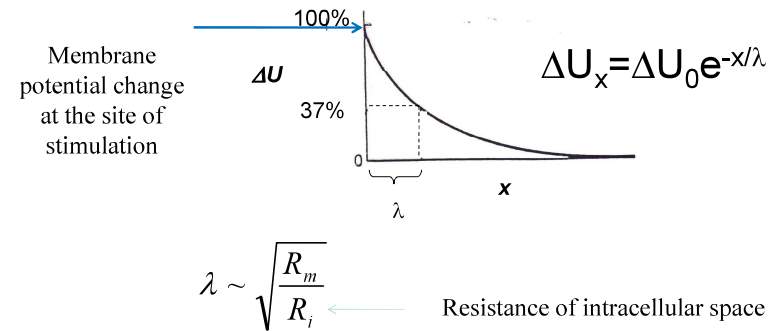
The local changes are not isolated from the neighborhood

Observation



λ : space constant of the membrane:

distance in which the maximal value of induced membrane potential change decreases to its e-th value



Local changes of resting membrane potential can be induced

- by electric current pulses
- by adequate stimulus at receptor cells
- by neurotransmitters at postsynaptic membrane
 - excitatory inhibitory postsynaptic potential - depolarization
 - inhibitory postsynaptic potential - hyperpolarization

Significance of the local changes of resting membrane potential

- Sensory function
- Impulse conduction
- Signal transduction