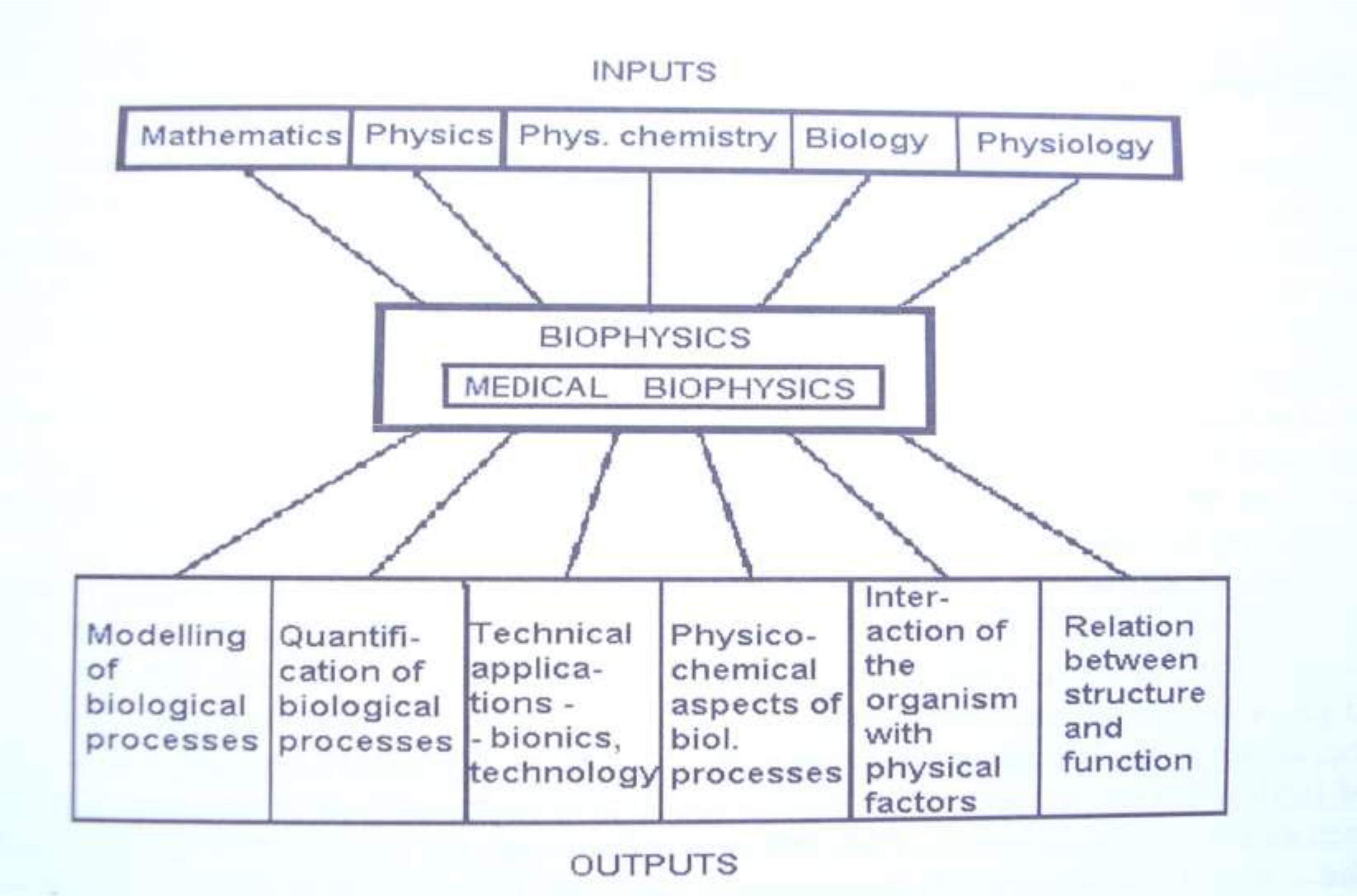
Biophysics of Cells & Transportation

Medical Biophysics - kind of Medicine Science, a part of Biophysics



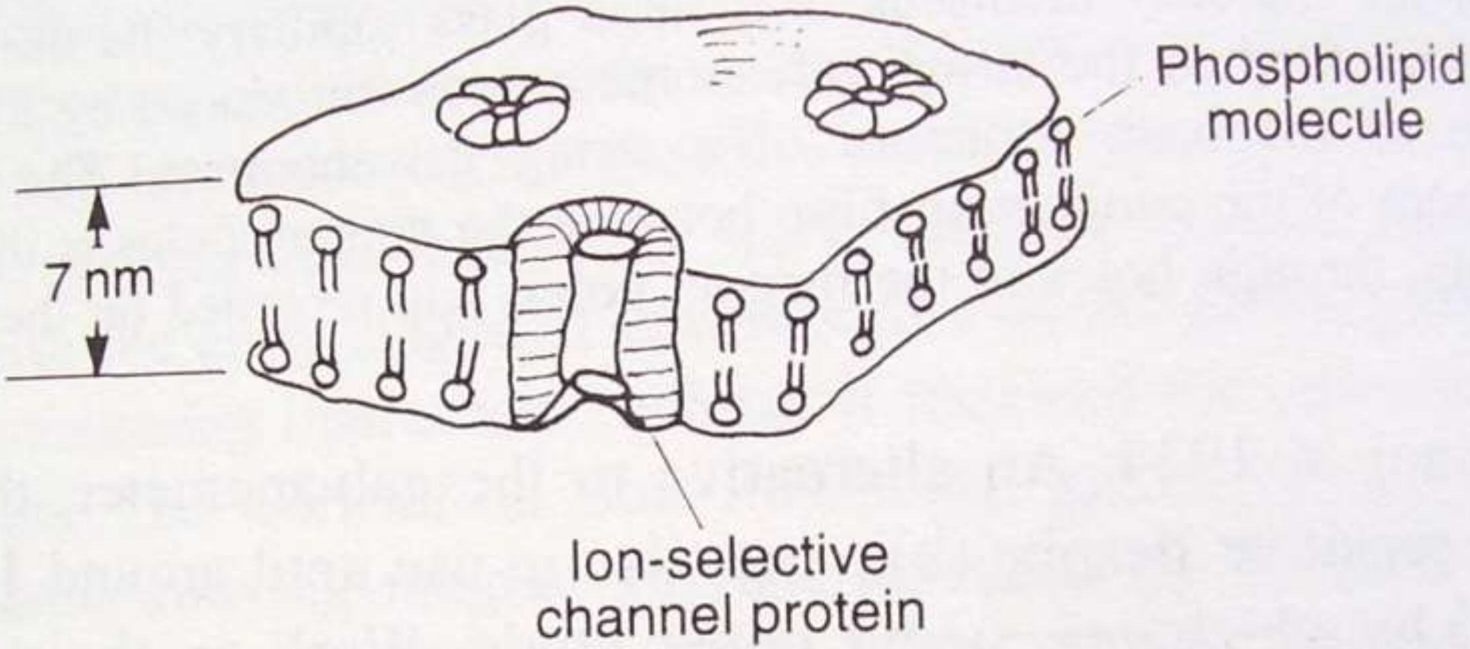
HUMAN CELL

- Definition: Cell is a basic anatomical and functional unit of the body with total number of 60.000 bilions and size from 4-120 µm (10^{-6} m). Number of cells composes tissues (206 bones ,600 muscles, thousands of nerves), number of tissues builds organs (heart, lungs, kidney..)

- Typical signs of living cell: own meta-bolism, excitability, reproduction

- Composition: Cytoskeleton -surface membrane,cytoplasm, organelles (for details see our videos at Practical Sessions also look a book of Biology)

SURFACE MEMBRANE



(b) Cut-away view of a segment of neuron membrane showing the arrangement of phospholipid molecules and ion-selective channel proteins.

Surface Membrane of RBC

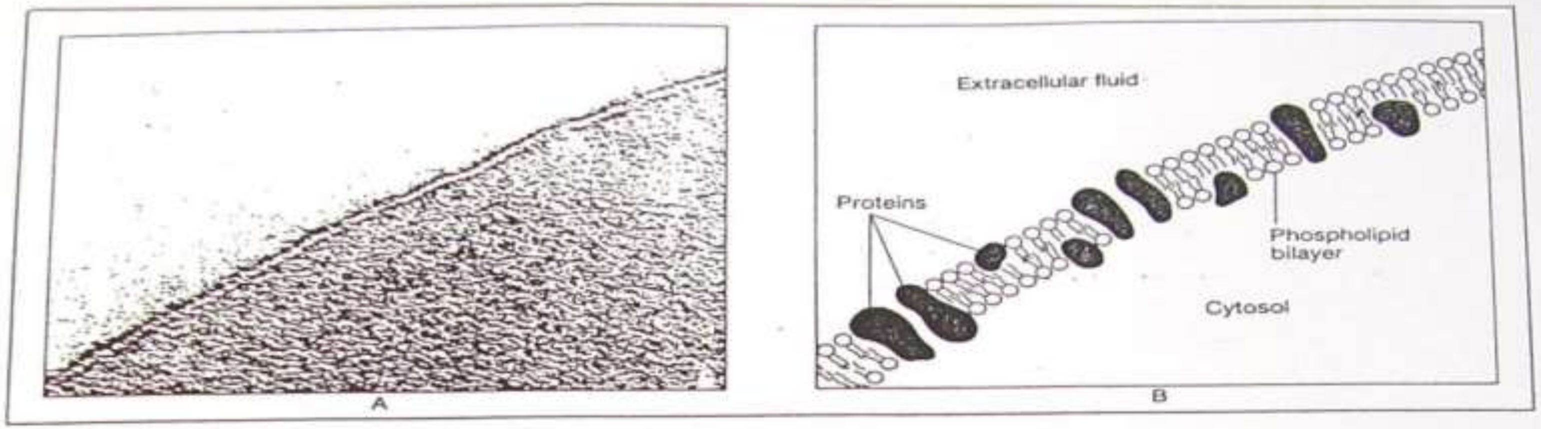


FIGURE 3-6 (A) Electron micrograph of a human red-cell plasma membrane. [*From J. D. Robertson in Michael Locke (ed.), "Cell Membranes in Development," Academic Press, Inc., New York, 1964.*] (B) Arrangement of the proteins and lipids in the membrane.

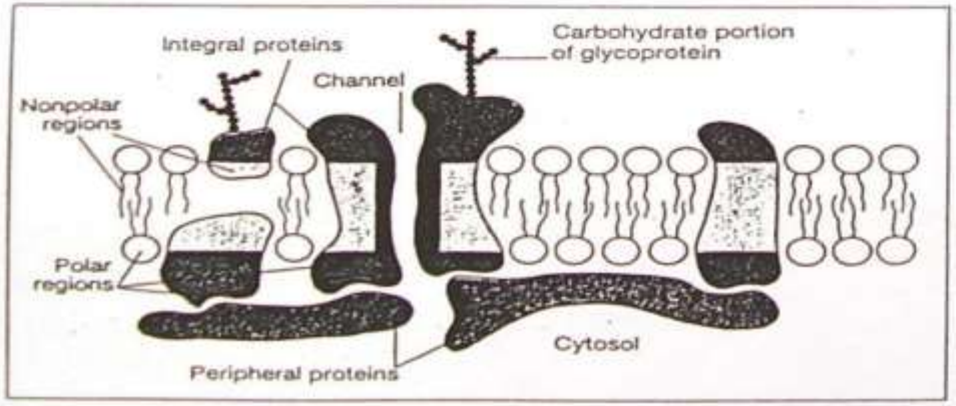


FIGURE 3-7 Arrangement of integral and peripheral membrane proteins in association with the biomolecular layer of phospholipids. Dark blue areas indicate the polar regions of proteins.

Surface Membrane (SM)

- *Intracellular SM-* covers subcellular structures (e.g.Nucleus, Golgi complex, Mitochondria)
- *Plasmatic SM* - covers the surface of each cell
- Functions: semipermeability, division, protec-tion, integrative roles, transport of ions, source of enzymes, storage of electric charges, etc.
- Composition: SM is Phospholipid bilayer- 45%

Hydrophilic heads (*consisting of phosphates*-soluble in water)

Hydrophobic tails (consisiting of *hydrocarbon fatty acids*-insoluble in water- 45%) . Proteins bilayer (peripheral, integral) - 50% , + Sugar + Cholesterol (5%)

Heads are (+) electrically charged and directed towards the membrane exterior, tails are *charged* negatively (–), being oriented to membrane interior

Transport Membrane Mechanisms

- are responsible for movement of water and solutes across the cell membrane
- are of vital importance for cell metabo-lism, for production of cell electricity i.e. (resting and action membrane potentials)
- Types: PASSIVE - it does not need deli-very of a free energy. (Simple and Facilita-ted Diffusion, Osmosis, Filtration).

  ACTIVE - free energy from ATP is needed and must be delivered (Na-Kpump, Ca-pump, H-pump, exo/ endo-cytosis, and phagocytosis)

Simple Diffusion through cell membrane

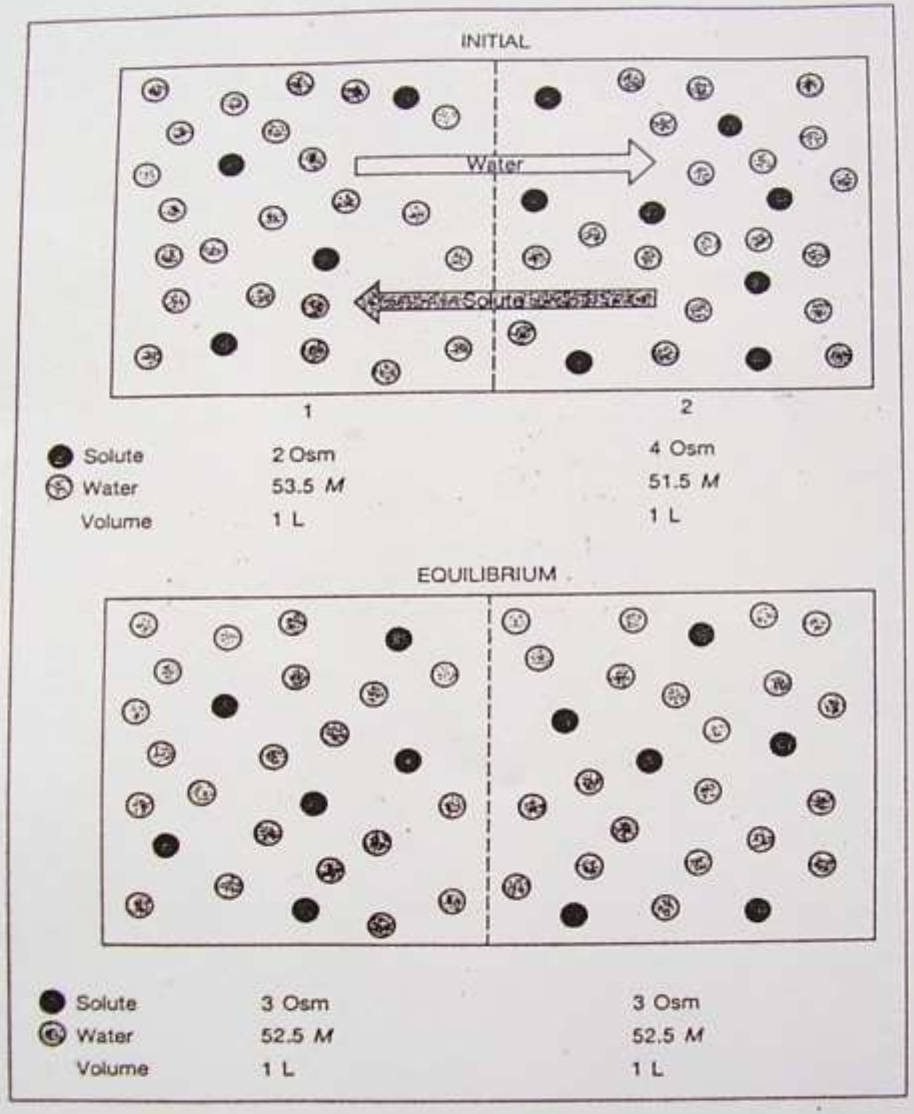


FIGURE 6-20 The net diffusion of water and solute in opposite directions across membrane permeable to both leads to diffusion equilibrium with no change in the volume of either compartment.

Simple Diffusion

- is a kind of passive membrane transport of $H_2 0$, solutes, or gases (O_2, CO_2) from the space with a higher concentration towards the space with lower one (along the concentration gra-dient), untill the equilibrium is established. Total volume of solution does not change in both of spaces.

- Rate of diffusion:Fick Law: J = - d . conc.grad. [d- koeficient of diffusion]

Generally: diffusion depends - linearly on a conc. gradient, solubility of a matter, and on ambient temperature Nonlinearly depends on a size of particles

- Types of diffusion: Simple, Facilitated, Through the protein channels

Scheme of Facilitated Diffusion

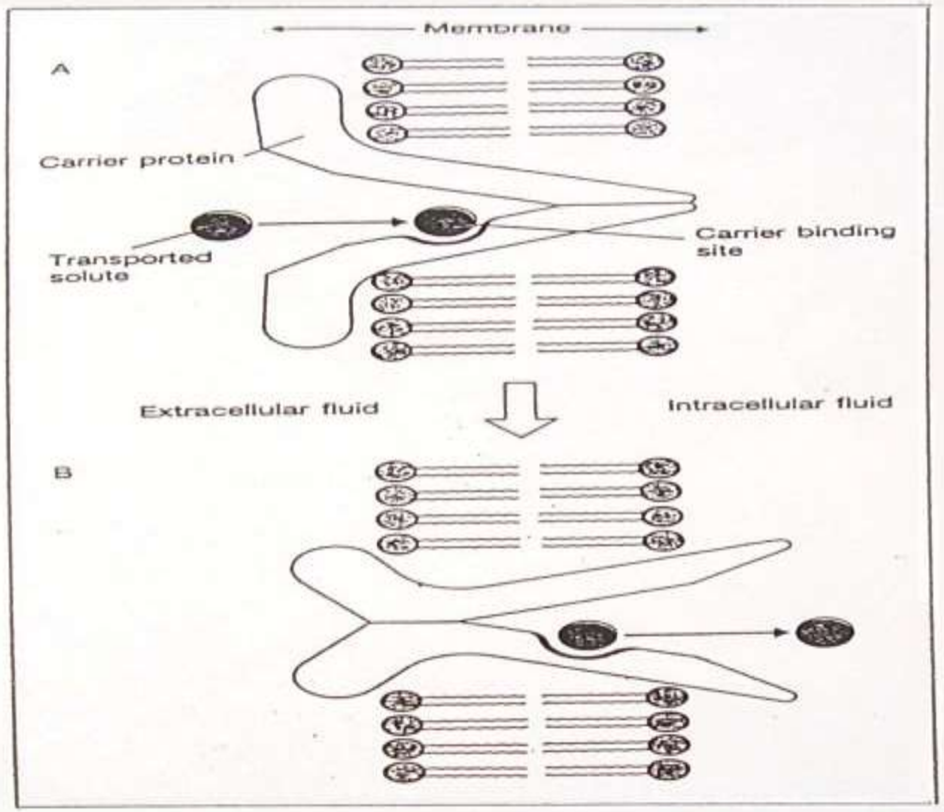


FIGURE 6-9 Carrier-mediated transport. When the carrier protein is in conformation A, its solute-binding site is exposed to solute in the extracellular fluid. When the carrier protein changes its conformation from A to B, the solute-binding site becomes exposed to the intracellular fluid. These changes in carrier conformation move a solute molecule that is bound to the carrier-binding site through the membrane.

Facilitated Diffusion

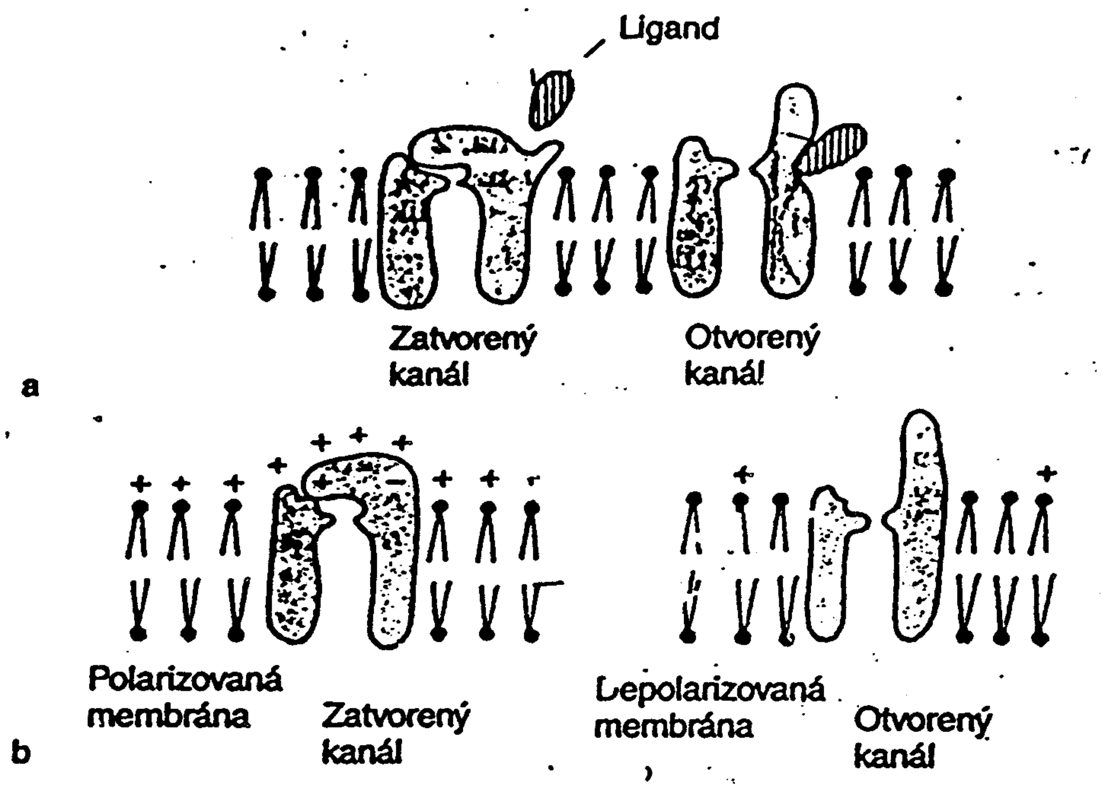
- is a passive transport mechanism of bigger molecules (e.g.aminoacids),along a concentration gradient, when substance binds to a protein carrier
- the carrier is protein placed within the membrane and undergoes a process of conformation (is a change of its chemistry)
- after *binding* of molecule and *conformation,* the carrier shifts (turns around) and finally releases substance on an opposite site of a cell membrane

Diffusion through the protein (ion selective) channels

- is a passive transport of ions Na^{+}, K^{+}, Ca^{2+}, Cl^{-} ,or low molecular soluble sub-stances through the protein channels within the membrane, along the concen-tration gradient

- Protein channels are :1.“voltage“gated - they are open or closed (gating) due to a membrane electricity,or 2.„ligand“gated-when e.g. a hormone binds to a channel, thus opening it.

„Voltage“ and „ligand“ gated protein (ion selective) channels



Obr. 5. Schematické znázornenie dvoch typov iónových kanálov
a) kanál otváraný naviazaním ligandu (ligand gating), b) kanál otváraný elektricky (voltage gating)

Filtration

- is a passive transport of water and small particles from a space with higher *hyd-rostatic pressure* to a space with lower one
- the power that drives Filtration is Pressure gradient of a hydrostatic pressure (not a concentration gradient !)
- examples: filtration and resorption in capillary loop or in kidneys

Osmosis

- is kind of passive transport through the semipermeable cell membrane, when only water moves from a space with lower concentration (lower osmotic pressure) to a space with higher concentration (higher osmotic pressure), till to equilibrium.Total volume of solution in both compartments will change.

Simply –water wants to dilute more concentrated solution (Van Hoff´s Law)

- normal osmolarity 300 mOsm/l- isotonic solution with blood plasma (e.g. 0.9 % NaCl, or 5% of glucose) Below 0.9%- hypotonic solution

Above 0.9% - hypertonic solution

- example: Osmotic fragility of RBC (see practicals)

OSMOSIS – scheme

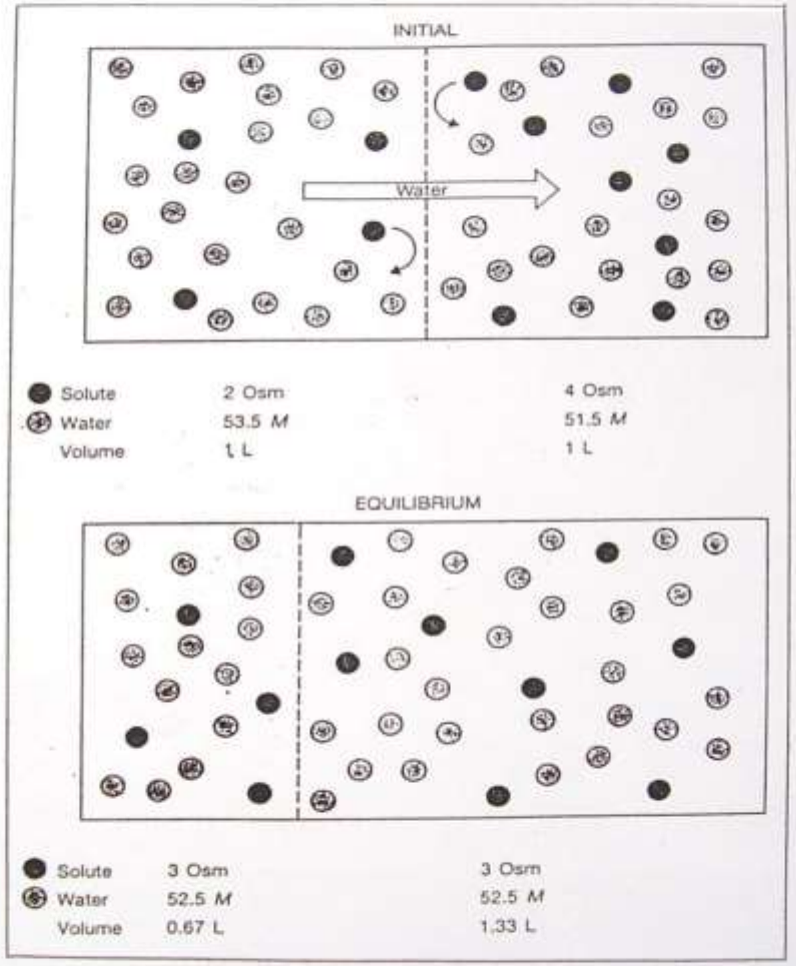


FIGURE 6-21 The movement of water across a membrane that is permeable to water but not permeable to solute leads to an equilibrium state in which there is a change in the volumes of the two compartments due to the net transfer of water (0.33 L in this case) from compartment 1 to 2. (The membrane in this example stretches as the volume of compartment 2 increases so that no significant change in intracellular pressure occurs.)

Changes in size of RBC due to osmosis
(HAEMOLYSIS)

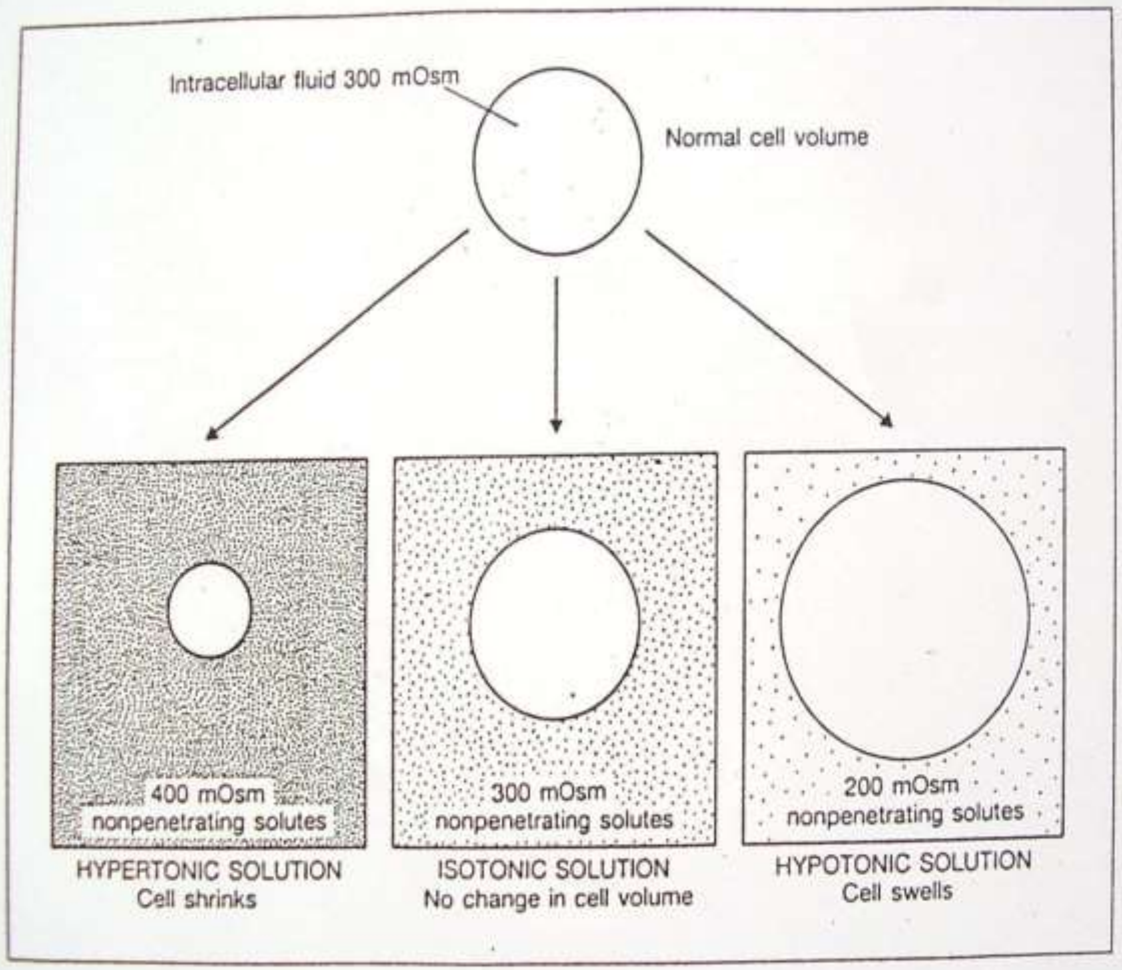


FIGURE 6-22 Changes in cell volume produced by hypotonic, isotonic, and hypertonic solutions.

ACTIVE MEMBRANE TRANSPORTS

- transport of molecules among cells against the concentration, or electric gradients,

- a delivery of free energy from ATP is crucial.

- Classification: ***Primary active transport*** through the selective ions channels. Pumps : Na^{+}- K^{+} pump (in all cells), Ca^{2+}- pump (in muscle cells), H^{+}- proton pump (in cells of stomach producing HCl)

Secondary active transport

when a substance (e.g. glucose) binds on ion (Na^{+}), then this complex (Na^{+} glucose) is carried through the membrane actively (the *glucose-Na^{+} contransport*), exo-/endo, phagocytosis

Na^+-K^+ pump (Na^+- K^+ ATPase)

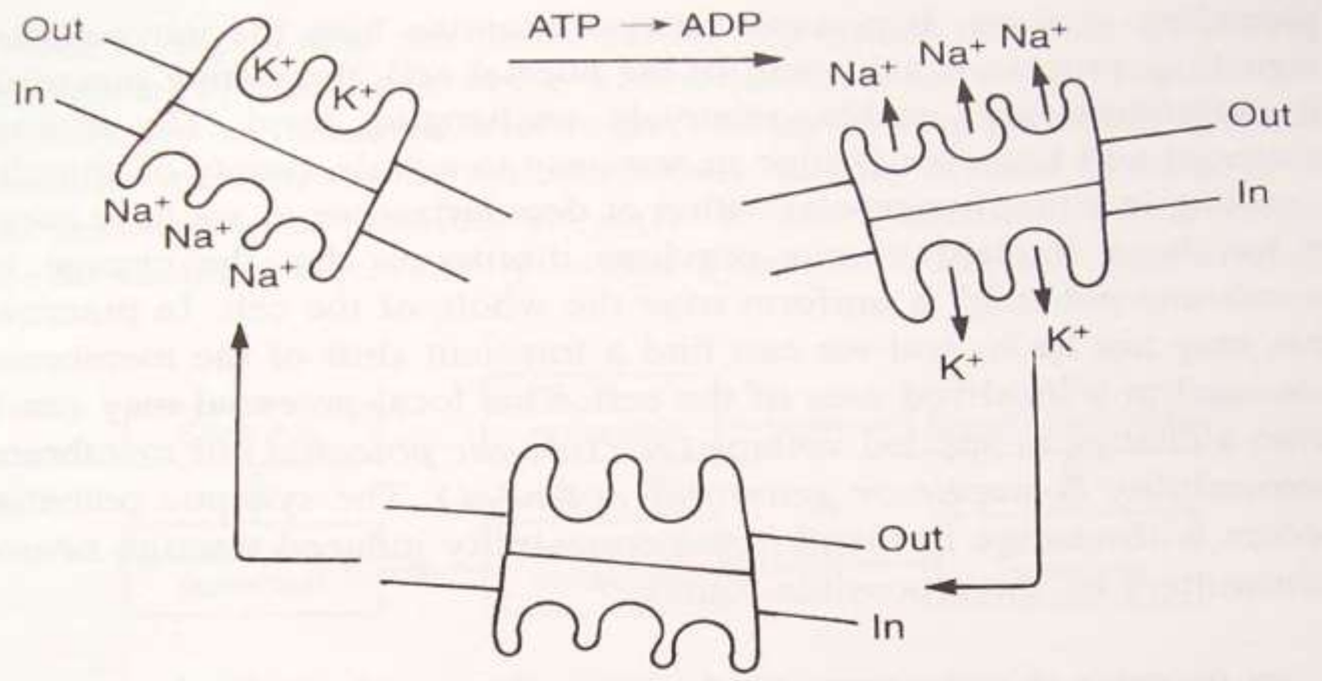
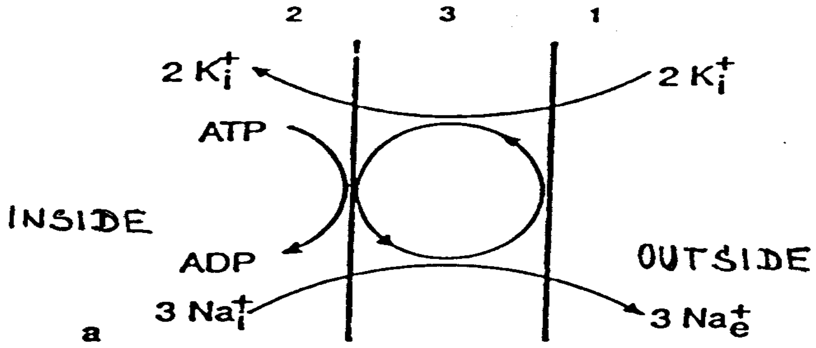
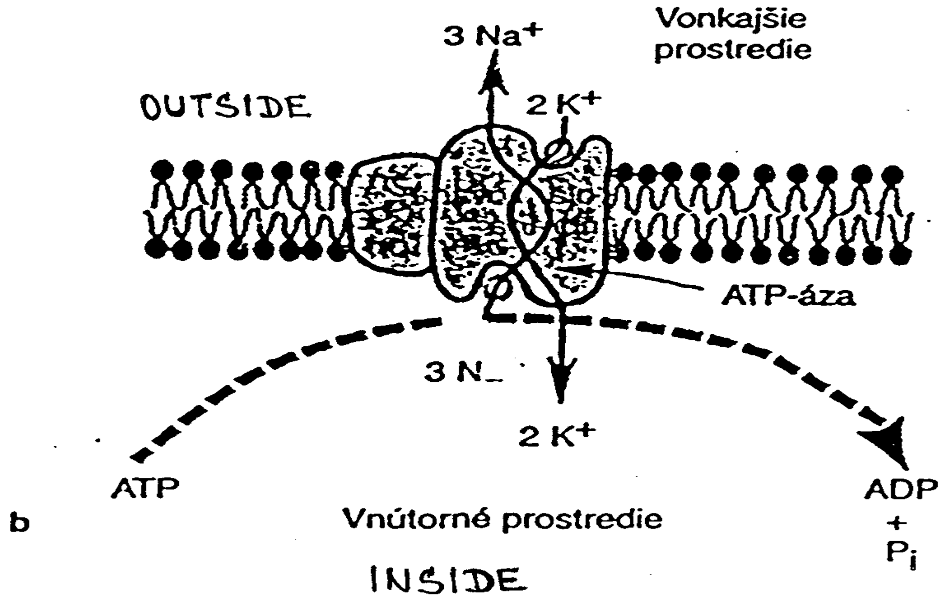


Figure 2.19 The sodium–potassium 'pump' responsible for the restoration of the sodium and potassium ion concentrations in a neuron. The idealized 'pump' molecule is here depicted as rotating about an axis in the neuron membrane and transporting three sodium ions out of the neuron for every two potassium ions transported inwards. In operation the 'pump' causes the neuron to hyperpolarize.

Na^+- K^+ pump – scheme



Obr. 6. Model sodíkovo-draslíkovej pumpy
a) schéma činnosti (1 – vonkajšia strana, 2 – vnútorná strana, 3 – membrána), b) schéma štruktúry sodíkovo-draslíkovej pumpy



Na^+-K^+ pump (Na^+- K^+- ATP-ase)

- It is an enzyme, placed within the cell membrane (number $=10^6$ molecules within a membrane of one neuron)
- it carries 3 ions of Na^+ from inside to outside, and at the same time, 2 K^+ from outside to inside of the cell
- It can exchange max. 200 Na^+ and 133 K^+ / sec. (maximal capacity of pump)
- It requires delivery of *free energy* (from ATP)
- It is important for renewal of electric charges on body cells

Exocytosis, Endocytosis (Phagocytosis)

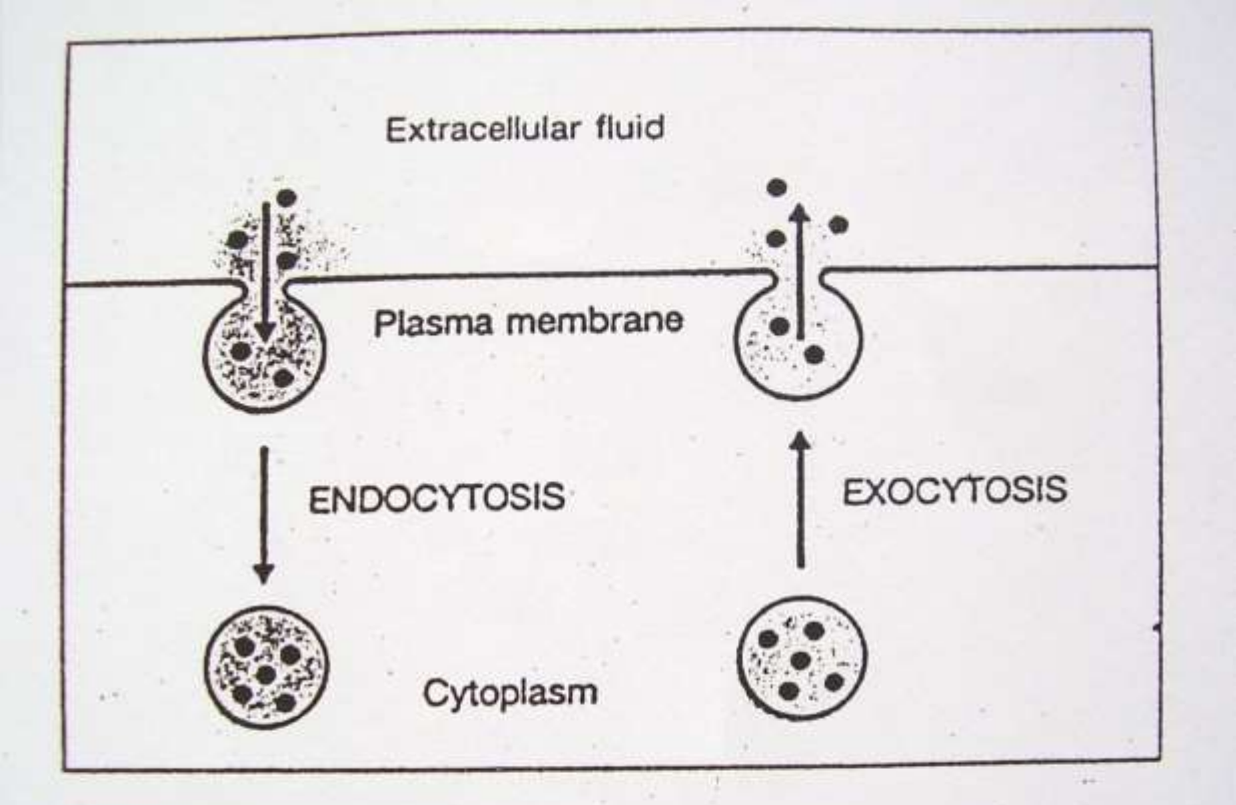


FIGURE 6-23 Endocytosis and exocytosis.

ACTIVE membrane transports.:

Exocytosis and Endocytosis.

- Exocytosis - “*cell vomiting*“ is a release of larger molecules by the protrusion of a cellular membrane, under delivery of energy and Ca^{2+} ions
- Endocytosis –“*cell eating*“ is an uptake of molecules by a cellular membrane, e.g. ingestion of bacteria by leukocytes (phagocytosis). It needs a delivery of energy, too.

Resting membrane potential (RMP)

- It is an electric potential difference measured between (+) charged cell exterior and (–) charged cell interior. Its value is negative and equals to a Sum of Equilibrium Potentials of all 3 ions (K^+, Na^+, Cl^-).
- is a result of membrane semipermeability i.e. different leakage of cell membrane for 3 main ions (K^+, Na^+, Cl^-).
- permeability of cell membrane for ions at *rest* is:

  $K^+ : Na^+ : Cl^- = 1 : 0.04 : 0.45$

  $K^+ : Na^+ : Cl^- = 100 : 4 : 45$ (%)
- Value of RMP for nerve cells is: -70 mV, sceletal muscle:– 90 mV, heart muscle:- 80mV, smooth muscle: -50 mV (non-stabile)

Mahidol University
Faculty of Science

60 YEARS MAHIDOL UNIVERSITY SCIENCE

Equilibrium Potential (EP) is a value of electrical voltage that just stops the passive diffusion of ions (K^+ ,Na^+ ,Cl^-) along their concentration gradients

Cell Inside (-) charged   Cell Outside(+) cha.

(because PROTEINS inside) (because Na^+ outside)

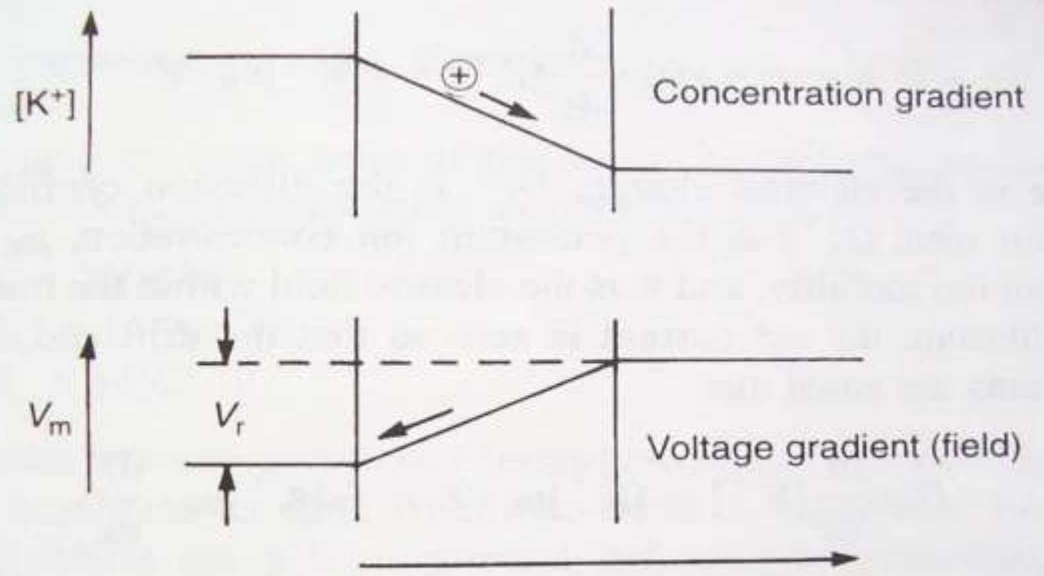
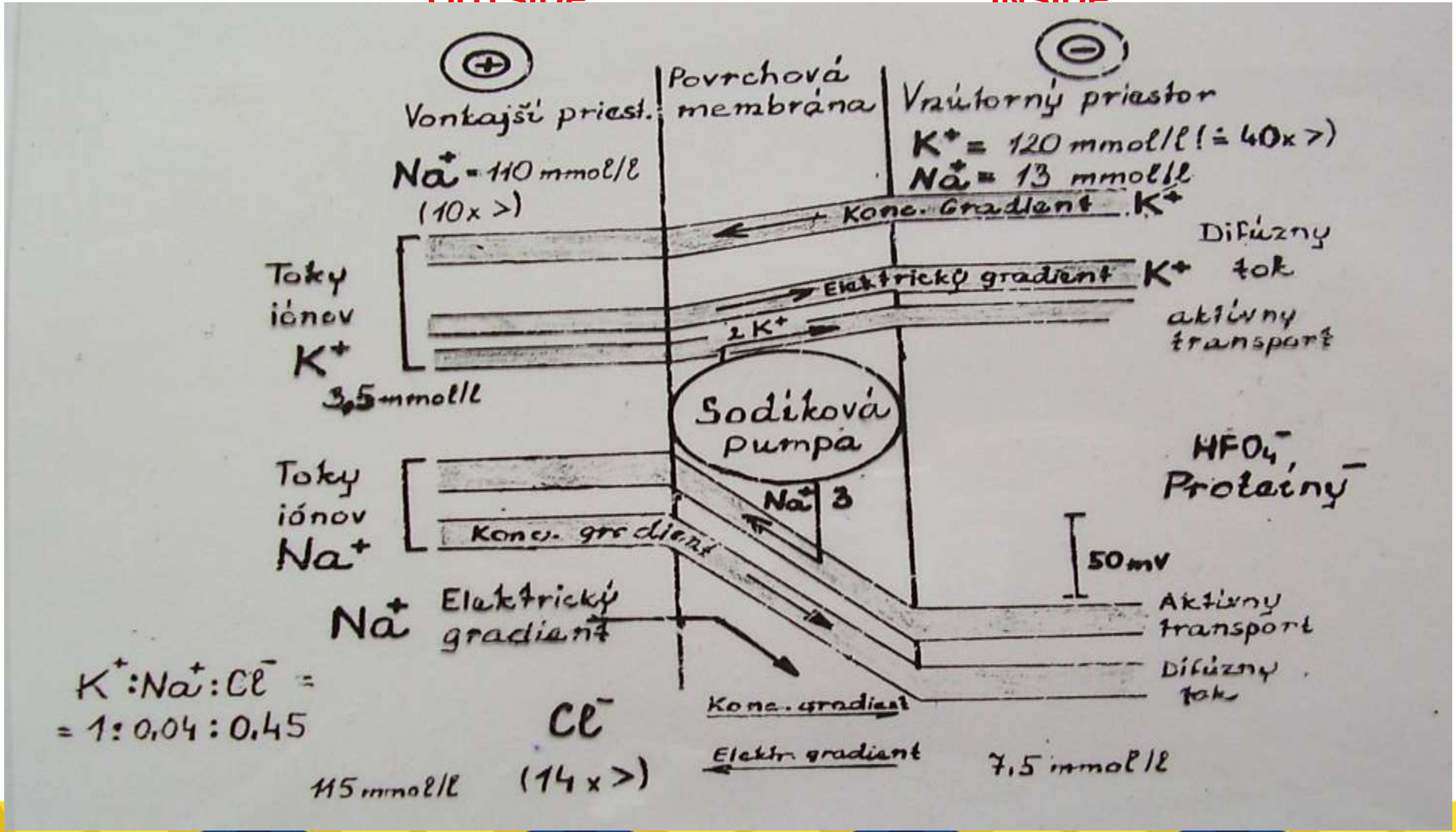


Figure 2.5 Origin of resting potential across cell membrane, a balance between the diffusion driven transport of ions down the concentration gradient and the opposing drift of ions in the voltage gradient resulting from ion transport.

Concentration and electrical gradients of K^+, Na^+, Cl^- ions

OUTSIDE INSIDE



Nernst formula

Each ion has its own *Equilibrium Potential* (mV) which can be counted:

(Nernst counted it only for K^+)

<u>Nernst equation</u> for calculation of the equilibrium potential:

$$E = \frac{R \cdot T}{z \cdot F} \cdot \ln \frac{[C]e}{[C]i},$$

where E is the equilibrium potential,
R is the gas constant (8314,4 $mV \cdot C \cdot mol^{-1} \cdot K^{-1}$),
T is the absolute temperature (at 37°C = 310,15 K),
z is the valence ($Na^+ = 1$, $K^+ = 1$, $Cl^- = -1$),
F is the Faraday constant (9,64846 . 10^4 C . mol^{-1})
$\ln \frac{[C]e}{[C]i}$ is the natural logarithm of the concentration ratio of an ion outside the cell [C]e and inside the cell [C]i, (ln A = 2,303 log A).

In mammalian spinal motor neuron, the K^+ concentration inside the cell is 150,0 mmol/l H_2O and outside the cell is 5,5 mmol/l H_2O. The equilibrium potential for potassium ions can be calculated from the Nernst equation, as follows:

$$E_K = \frac{R \cdot T}{z \cdot F} \cdot \ln \frac{[K^+]e}{[K^+]i}$$

$$E_K = \frac{8314{,}4 \cdot 310{,}15}{1 \cdot 9{,}6485 \cdot 10^4} \cdot 2{,}303 \cdot \log \frac{5{,}5}{150}$$

$$E_K = 61{,}5 \cdot \log \frac{5{,}5}{150} = 61{,}5 \cdot (0{,}74 - 2{,}18) = -61{,}5 \cdot 1{,}44$$

$$E_K = -88{,}6 \text{ mV}$$

Goldman´s Equation

Sumation of all Equilibrium potentials (for K, Na, Cl) results in a *real value* of Resting Membrane Potential (e.g. V_m = -70 mV for neuronal cells) Goldmann counted it for all 3 ions (their concentrations outside and inside) + the permeabilities of membrane for 3 ions

<u>**Goldman equation**</u> for calculation of the membrane potential considers both the distribution of K^+, Na^+ and Cl^- and the permeability of the membrane to each of these ions in the resting cell:

$$V_m = \frac{R \cdot T}{F} \cdot \ln \frac{P_{K^+}[K^+]e + P_{Na^+}[Na^+]e + P_{Cl^-}[Cl^-]i}{P_{K^+}[K^+]i + P_{Na^+}[Na^+]i + P_{Cl^-}[Cl^-]e},$$

where V_m is the membrane potential, and

P_{K^+}, P_{Na^+} and P_{Cl^-} are the permeabilities to K^+, Na^+ and Cl^-.

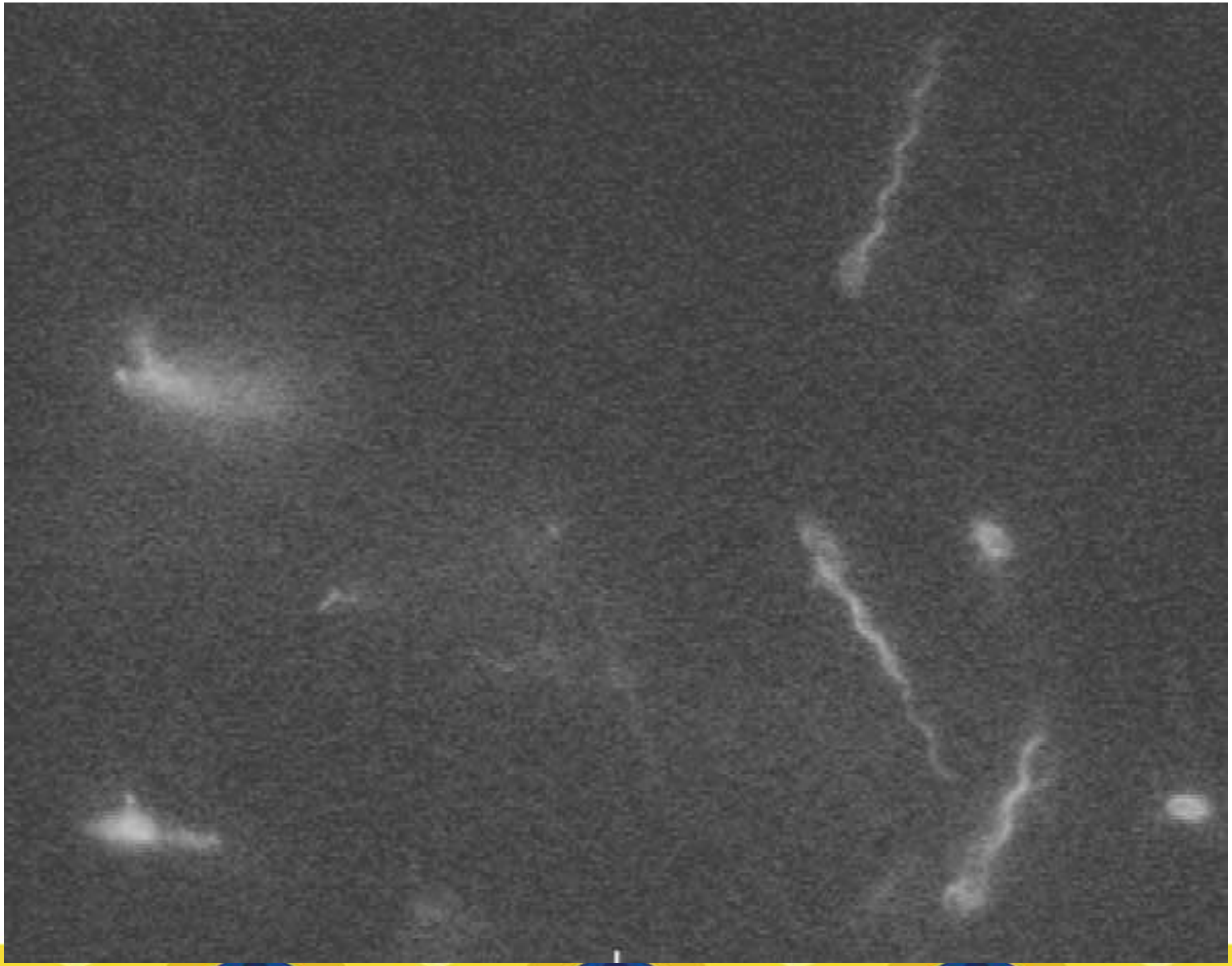
(P_{K^+} : P_{Na^+} : P_{Cl^-} = 1 : 0,04 : 0,45)

Some of the physics cells have to deal with:

Random walks, diffusion and Brownian motion

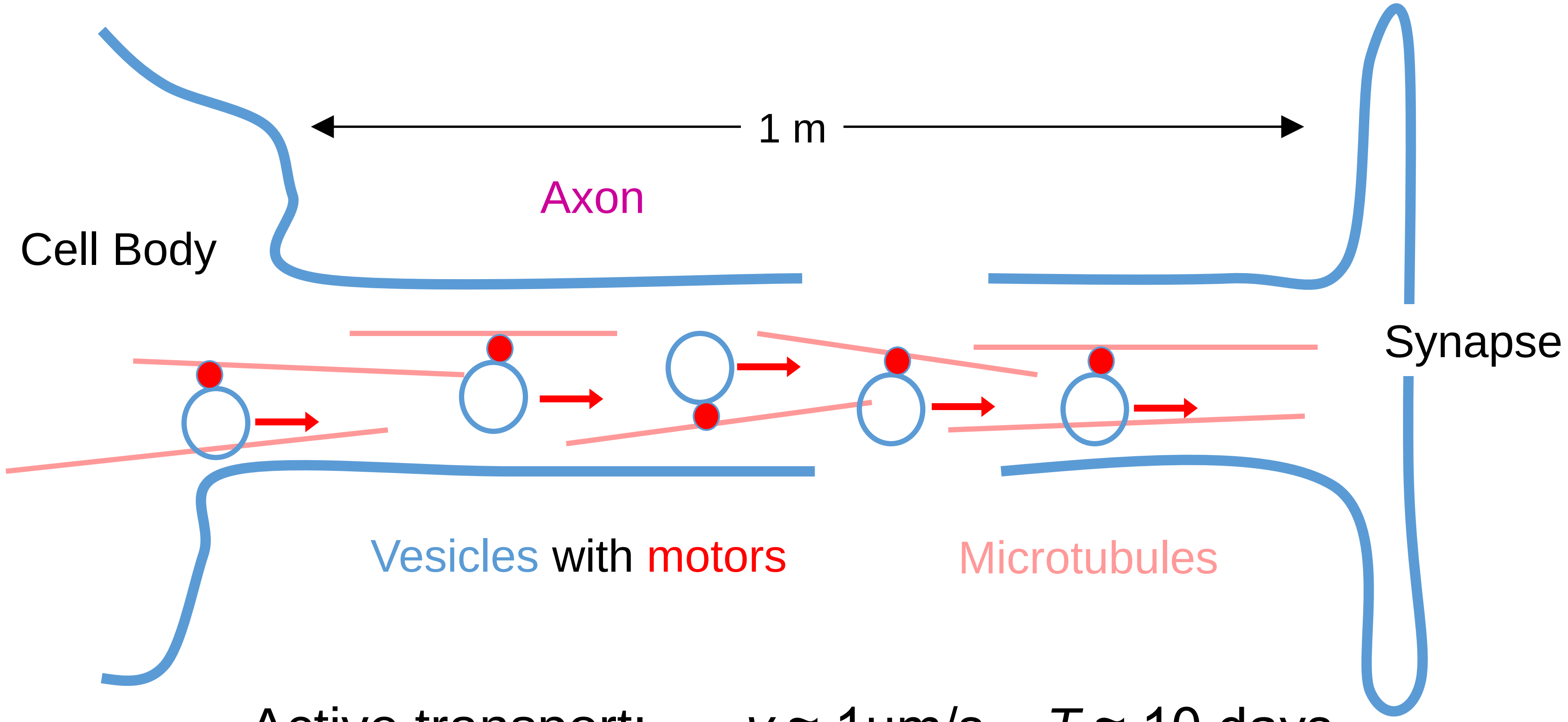
Bacterial motility, E. coli

from Howard Berg lab, courtesy Linda Turner



2D random walk, 18050 steps

Intracellular Transport on Cytoskeletal Tracks



Active transport: $v \approx 1\mu m/s$, $T \approx 10$ days

Diffusion: $T = x^2/6D \approx 26{,}000$ years