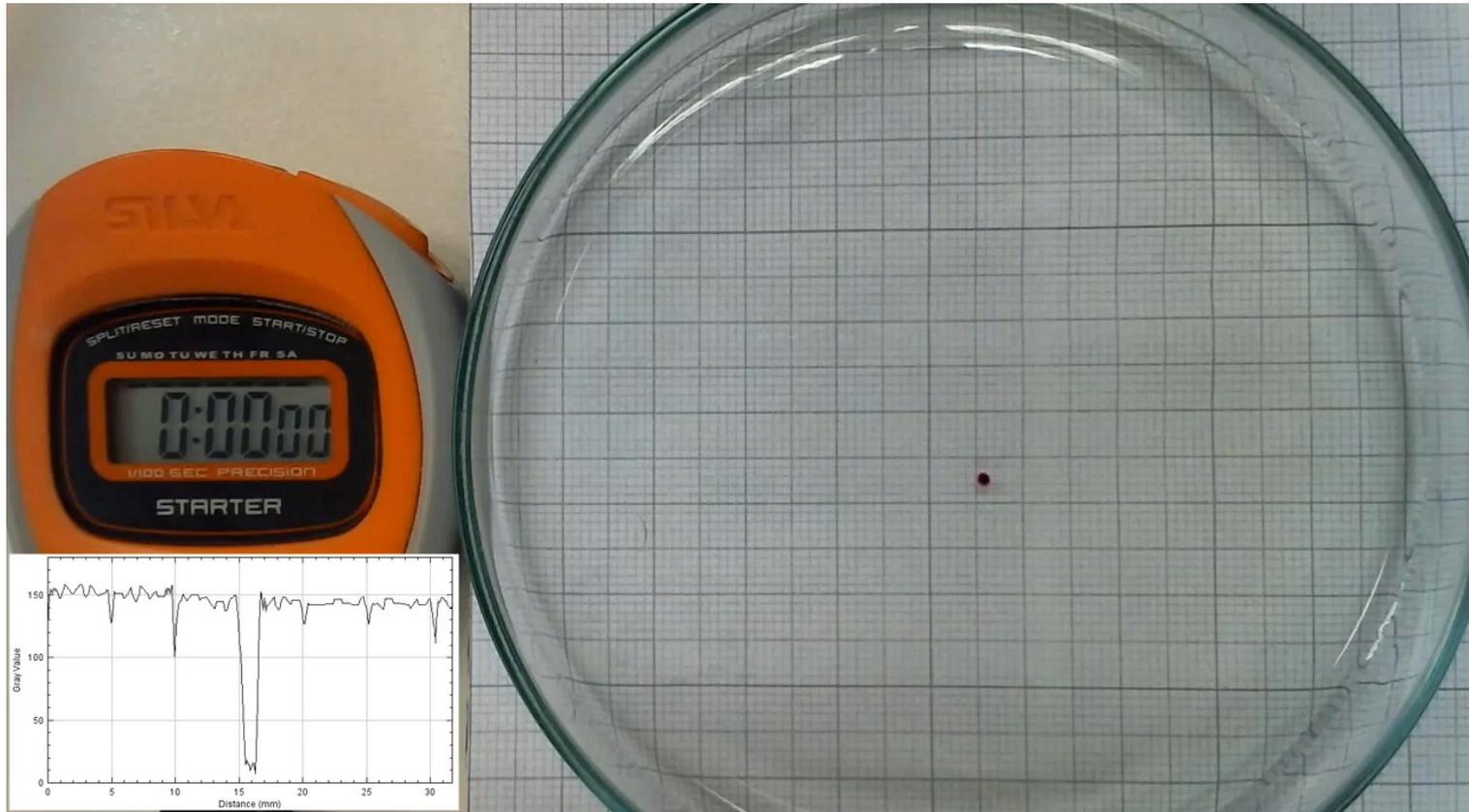


# Biophysics II

## Transport processes-2

### diffusion, osmosis



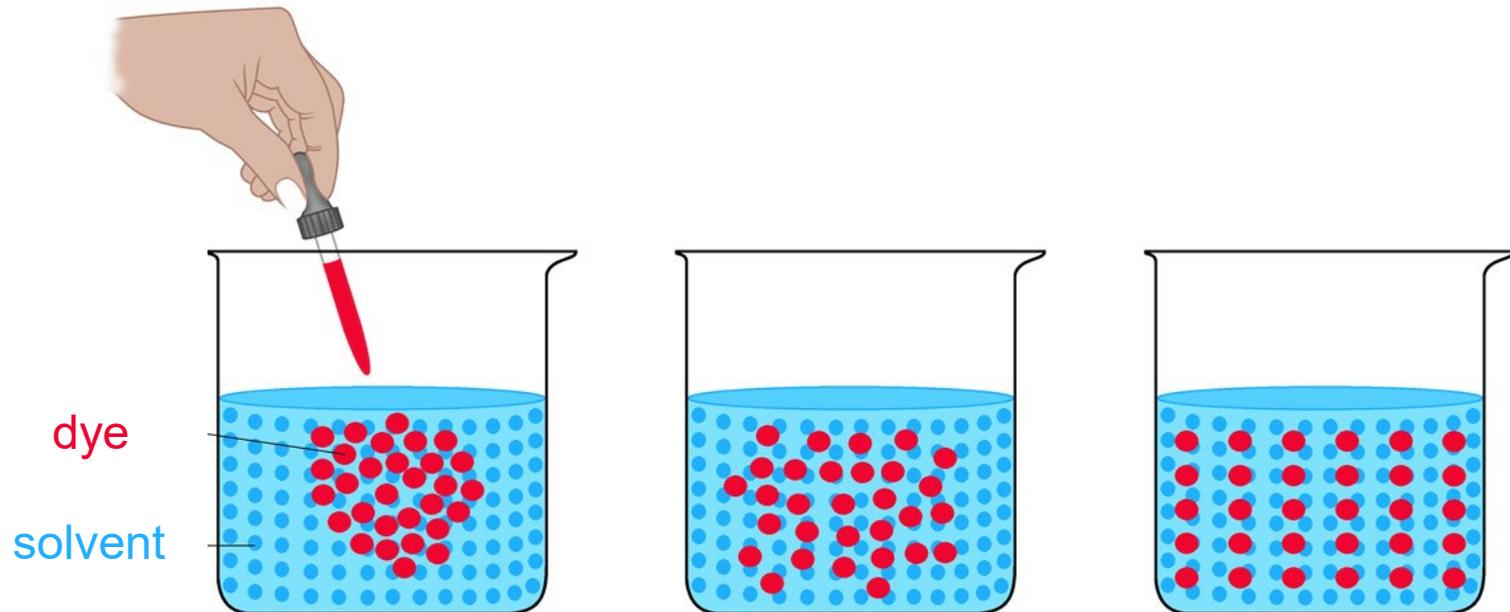
G.Schay

Diffusion = transport of materials the way that particles of fluids or gases spread to fill the available space.

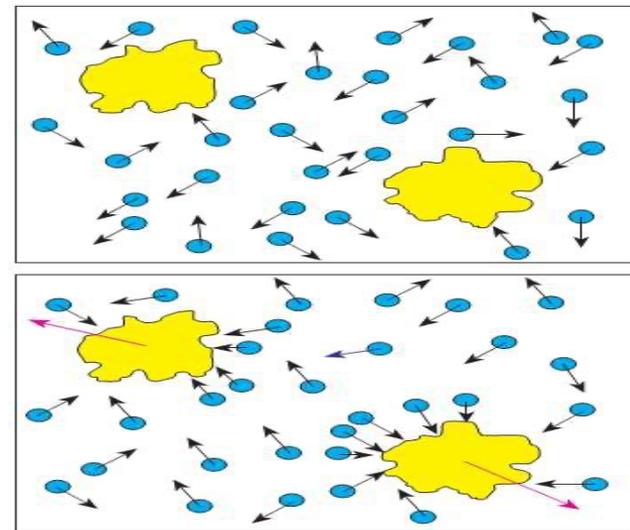
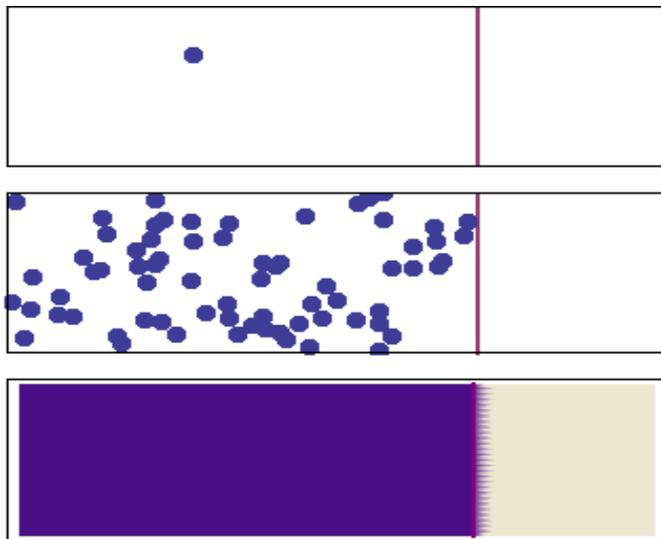
The diffusion process lasts until the initial concentration difference vanishes, particles distribute evenly.



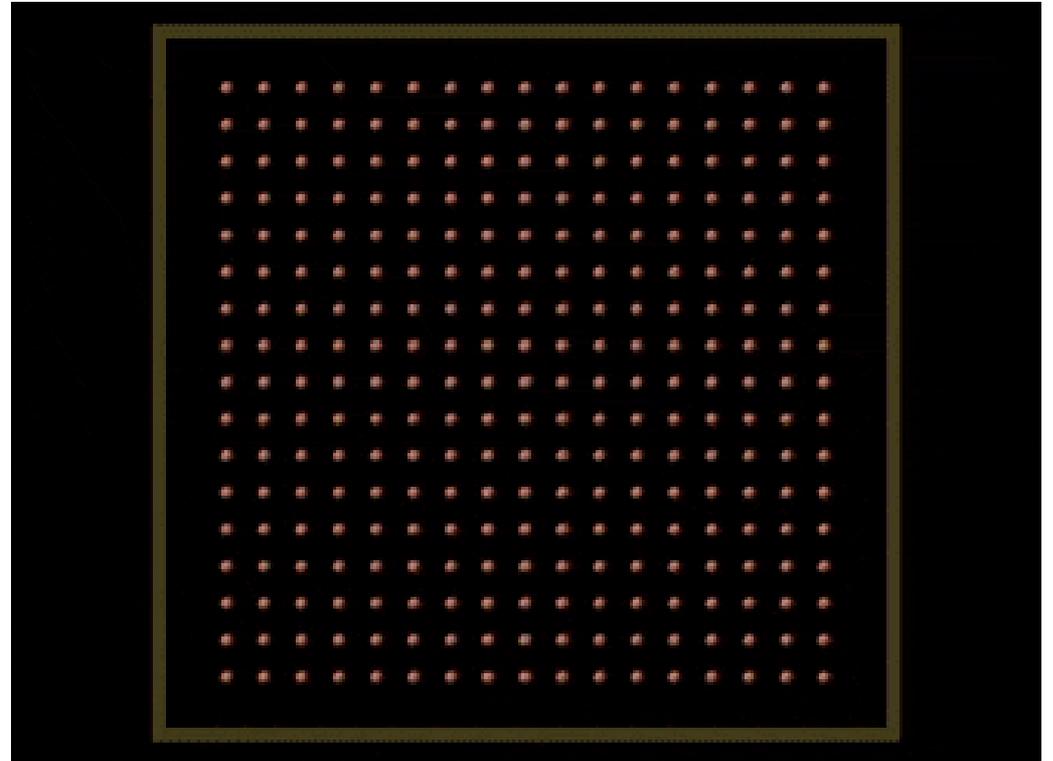
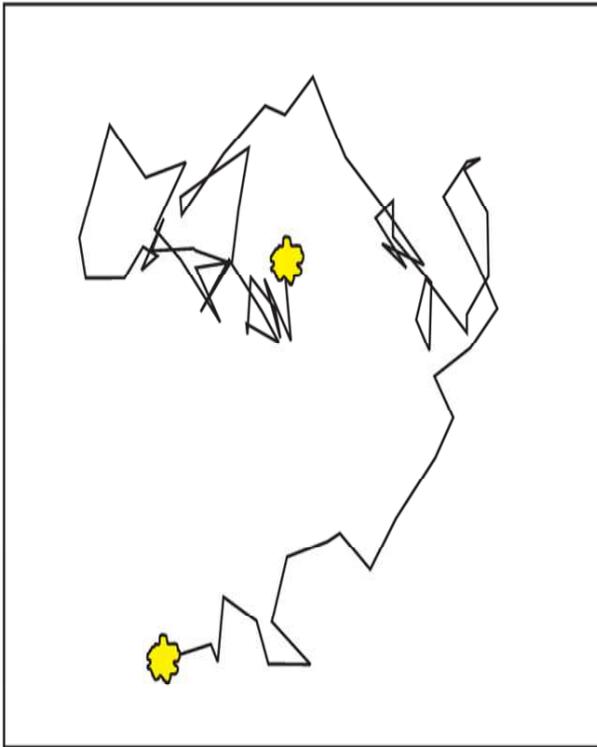
The diffusion process lasts until the initial concentration difference vanishes, particles distribute evenly.



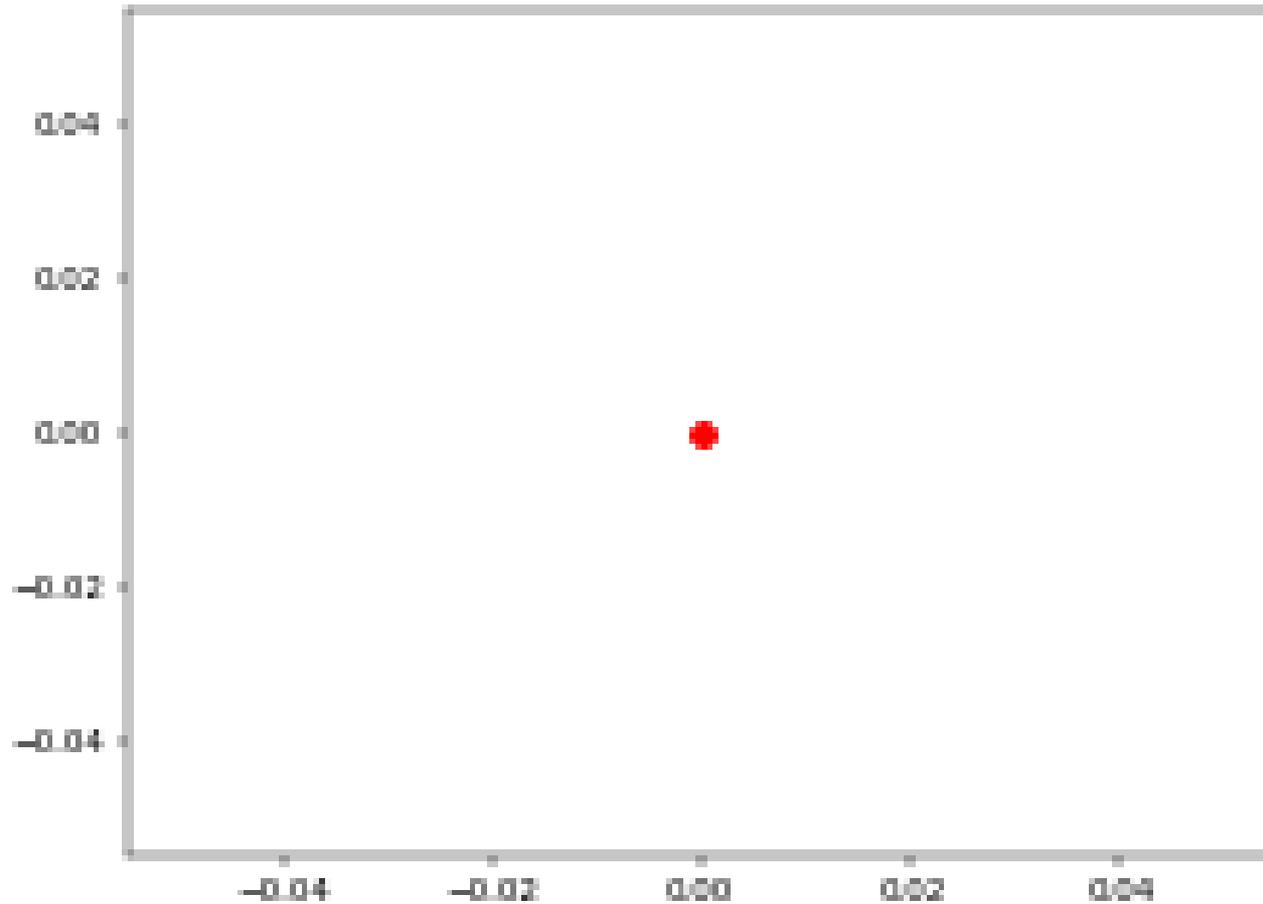
During thermal motion, particles move independently of each other, leading to their collisions. If particles are suspended in fluids or gases, they are randomly bombarded by the molecules from the surrounding and these random forces impart velocity changes to the particle. This stochastic movement called **brownian motion** was discovered by the scottish botanist Robert Brown when he investigated pollen suspensions under a microscope in 1827.



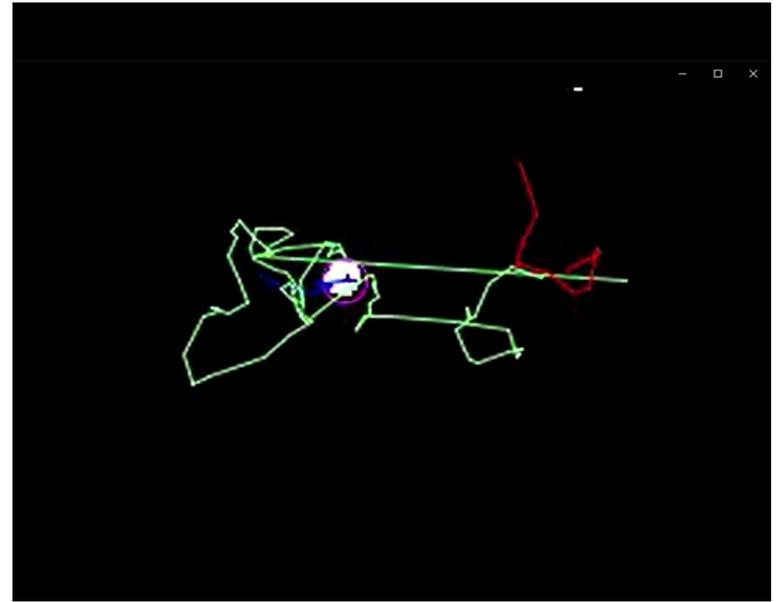
# Random walk – a model of brownian motion



the Brownian motion can be very well approximated by a random walk on a grid.



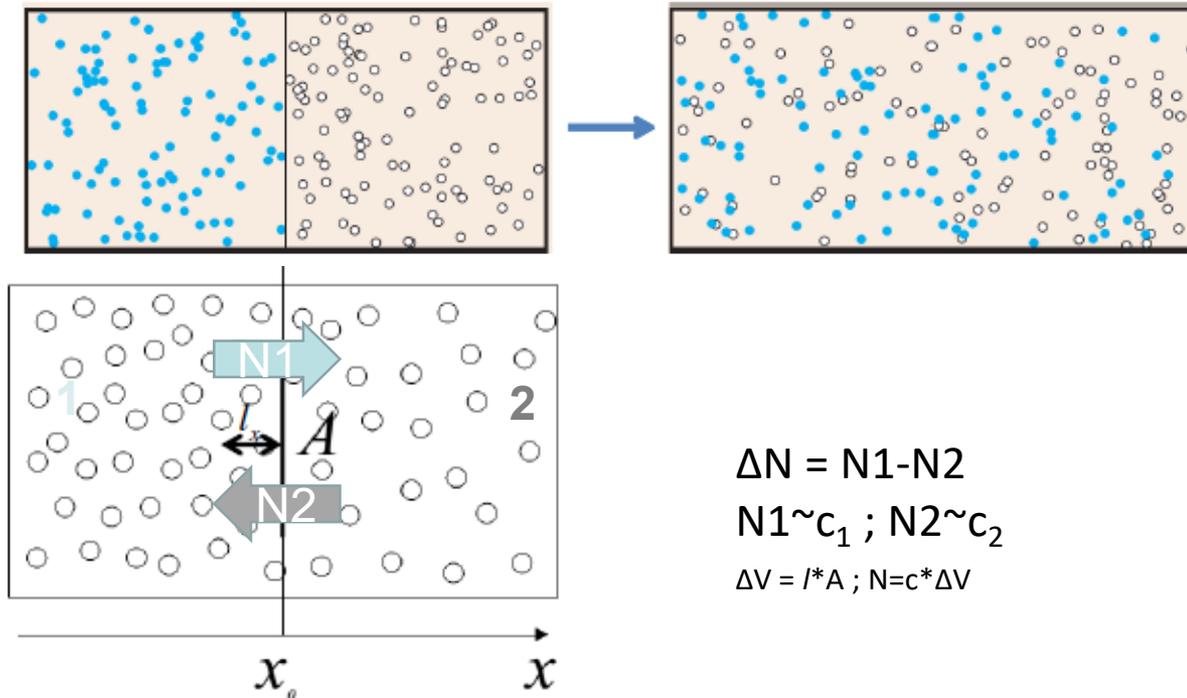
# Random walk – a model of brownian motion



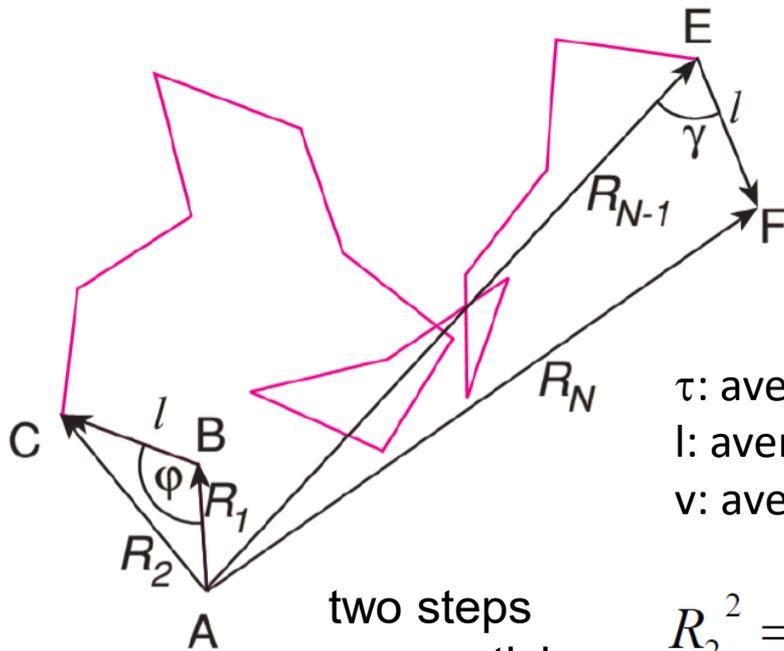
A home-made macroscopic model: vibrated poppy seeds = solvent particles, plastic ball on top = suspended particle

The change in the spatial distribution of particles because of **random thermal motion**.

In microscopic level with **net matter transport**.



**The physical driving force is the thermal motion**



$\tau$ : average time between collisions  
 $l$ : average free path length  
 $v$ : average particle velocity

two steps  
one particle

$$R_2^2 = R_1^2 + l^2 - 2 \cdot R_1 \cdot l \cdot \cos \varphi \quad (\text{cos-formula})$$

average of  $n$  particles:

$$\overline{R_2^2} = \frac{1}{n} \cdot \sum_{i=1}^n (R_1^2 + l^2 - 2 \cdot R_1 \cdot l \cdot \cos \varphi_i)$$

but  $\sum_{i=1}^n (\cos \varphi_i) = 0 \rightarrow \overline{R_2^2} = R_1^2 + l^2 = l^2 + l^2 = 2 \cdot l^2$

$$\overline{R_N^2} = N \cdot l^2$$

$$\overline{R_t} = \sqrt{N \cdot l^2} = \sqrt{\frac{t}{\tau} \cdot l \cdot l} = \sqrt{t \cdot v \cdot l}$$

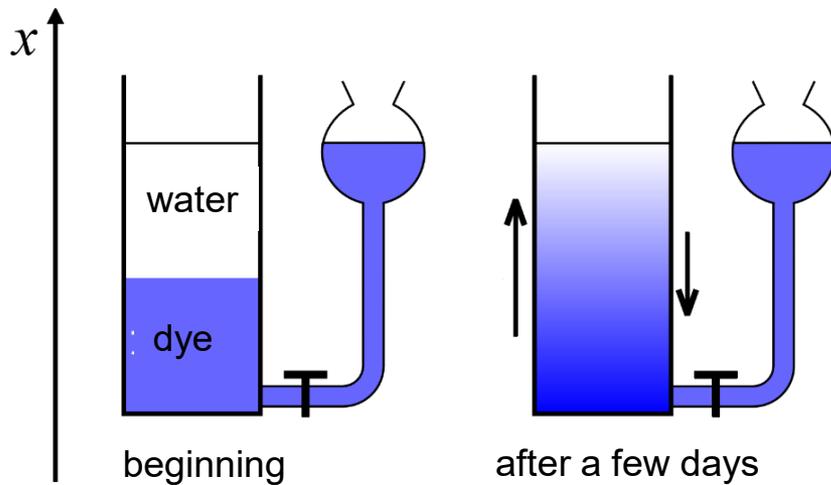
~ **D**  
[m<sup>2</sup>/s]

diffusion  
coefficient

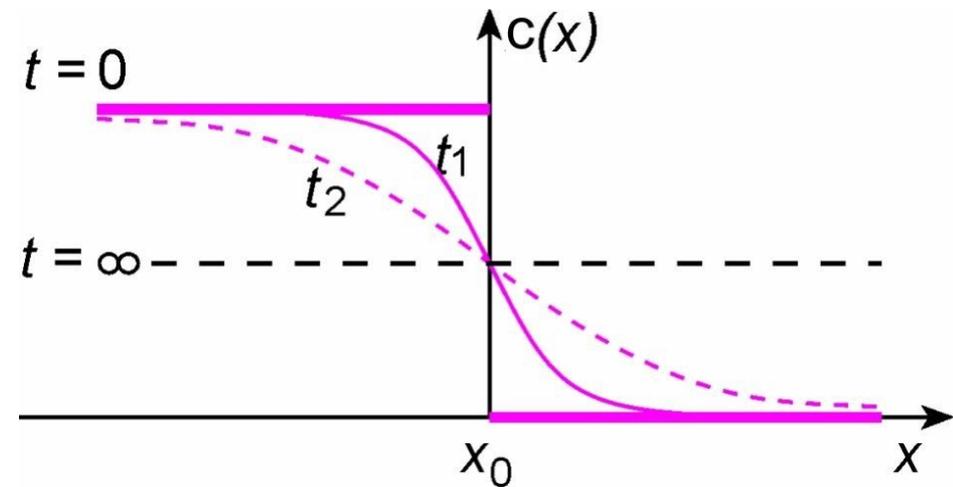
# Diffusion = material transport

Matter flow rate: 
$$I_v = \frac{\Delta v}{\Delta t}; \left[ \frac{\text{mol}}{\text{s}} \right]$$

Matter flow density (flux): 
$$J_v = \frac{\Delta I_v}{\Delta A}; \left[ \frac{\text{mol}}{\text{m}^2 \cdot \text{s}} \right]$$

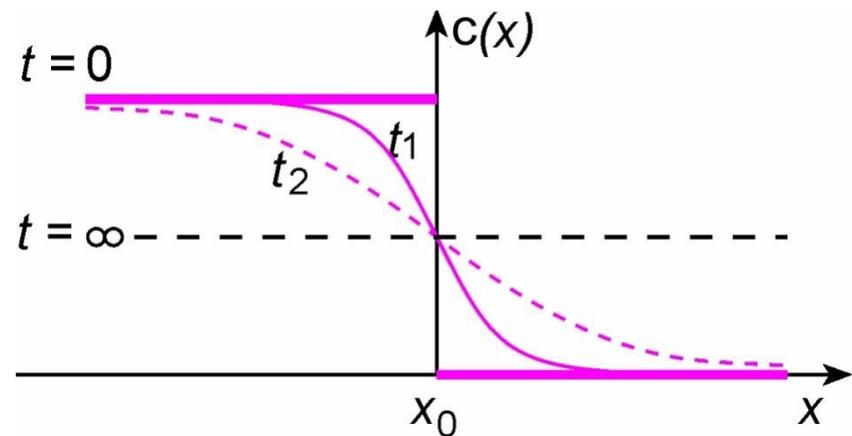
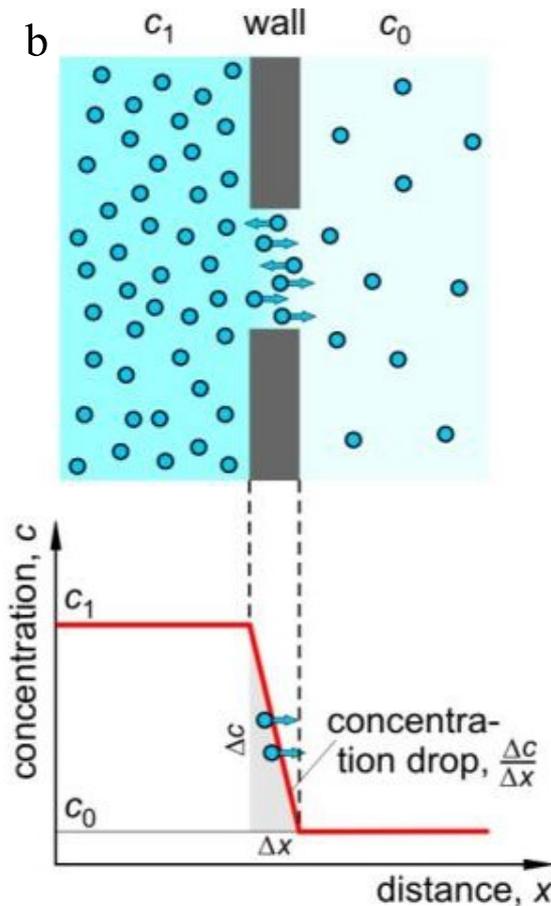


Fick's experiment



# Fick's I. law

material transport occurs always from higher concentration regions to lower concentration regions. It is a stochastic effect!

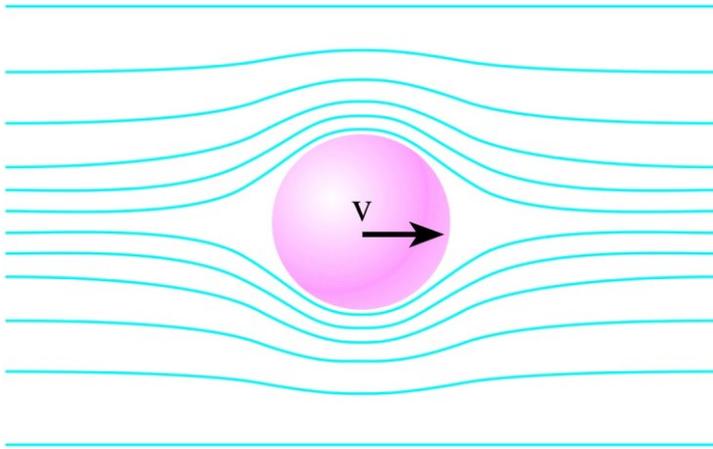


$$J_v = -D \frac{\Delta c}{\Delta x}$$

Matter flow density is linearly proportional with the concentration gradient.

$$[D] = \text{m}^2/\text{s}$$

# Diffusion coefficient for spherical particles: Einstein-Stokes relationship



$$D = u \cdot kT \text{ (Einstein)}$$
$$u = v/F \text{ (mobility)}$$

*for spheres:*

$$F = 6\pi\eta r v \text{ (Stokes)}$$

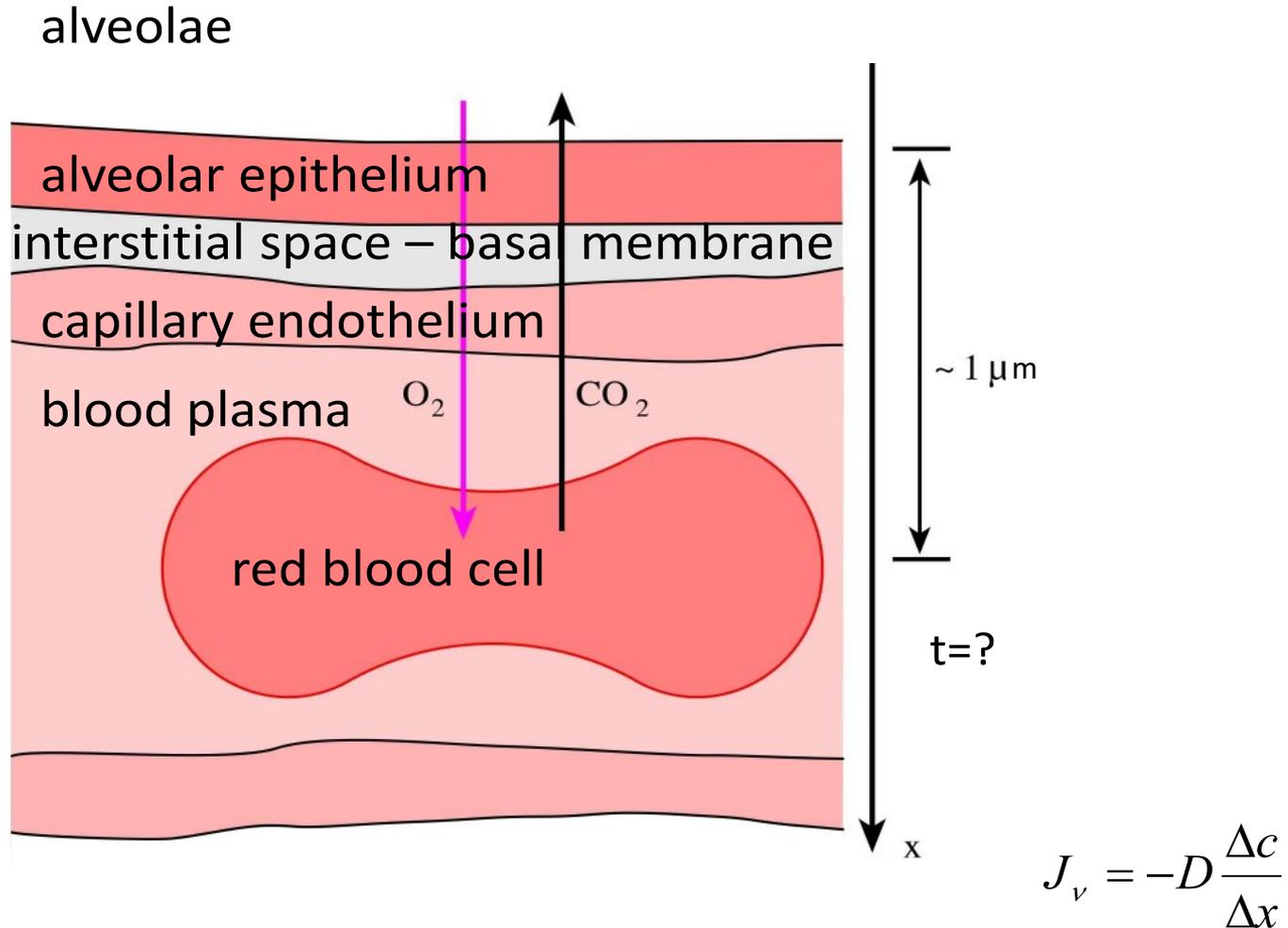
$$D = \frac{kT}{6\pi\eta r}$$

nonlinear temperature-dependence!

# A few typical diffusion coefficient values

diffusing particle (molecular weight)	medium	$D$ (m <sup>2</sup> /s)
H <sub>2</sub> (2)	air	$6.4 \cdot 10^{-5}$
O <sub>2</sub> (32)	air	$2 \cdot 10^{-5}$
CO <sub>2</sub> (44)	air	$1.8 \cdot 10^{-5}$
H <sub>2</sub> O (18)	water	$2.2 \cdot 10^{-9}$
O <sub>2</sub> (32)	water	$1.9 \cdot 10^{-9}$
Glycine (75)	water	$0.9 \cdot 10^{-9}$
Serum albumine (69 000)	water	$6 \cdot 10^{-11}$
Tropomyosine (93 000)	water	$2.2 \cdot 10^{-11}$
Tobacco mosaic virus (40 000 000)	water	$4.6 \cdot 10^{-12}$

# Can O<sub>2</sub>/CO<sub>2</sub> exchange happen by diffusion?

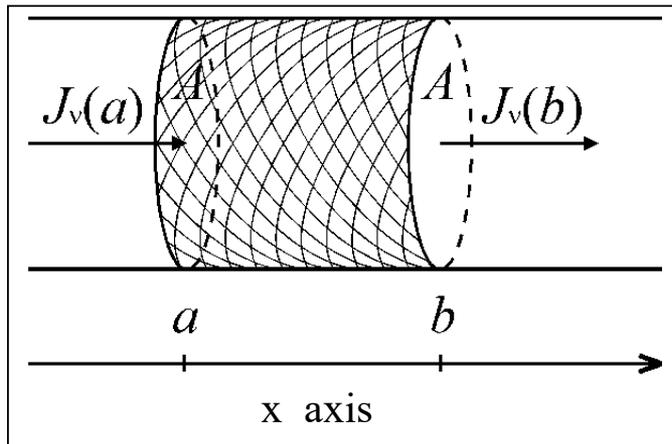


$D(\text{O}_2) \sim 2 \cdot 10^{-9} \text{ m}^2/\text{s}$ ,  $D(\text{CO}_2) \sim 6 \cdot 10^{-9} \text{ m}^2/\text{s}$ ,  
mean travel time of RBC in lung capillaries  $\sim 0,5 \text{ s}$

average distance covered (3 dimension):  $\sqrt{3Dt} = \sqrt{3 * 0.5\text{s} * 6 \cdot 10^{-9}\text{m}^2\text{s}^{-1}} = 95 \mu\text{m}$

# How fast is the material transport by diffusion? Generalized equation of continuity.

$$J_v(a)A\Delta t - J_v(b)A\Delta t = 0$$



Let  $J_v(a) > J_v(b)$

If there is a net material influx into the space enclosed by a and b, then this amount of material has to appear as the net concentration increase in the given volume during influx.

$$c = \frac{\Delta v}{\Delta V}$$

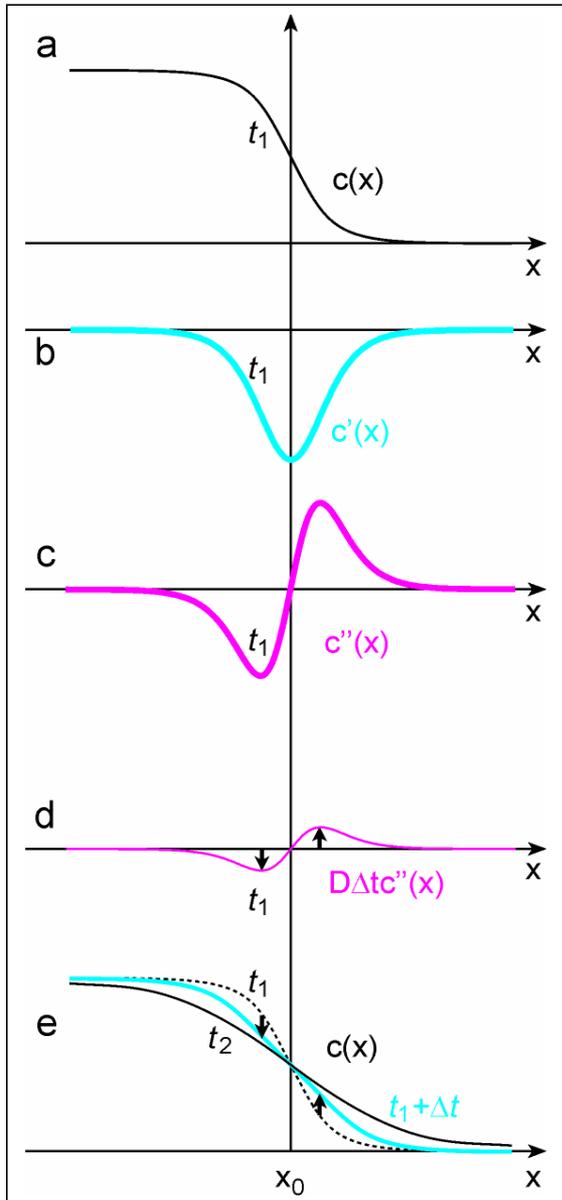
Let  $a=x$  and  $b=x+\Delta x$  be sufficiently close to each other:

$$[J_v(x) - J_v(x + \Delta x)]A\Delta t = [c(t + \Delta t) - c(t)]A\Delta x$$

$$A\Delta x = \Delta V$$

$$-\frac{\Delta J_v}{\Delta x} = \frac{\Delta c}{\Delta t}$$

# Fick's II. law



$$-\frac{\Delta J_v}{\Delta x} = \frac{\Delta c}{\Delta t} \qquad J_v = -D \frac{\Delta c}{\Delta x}$$

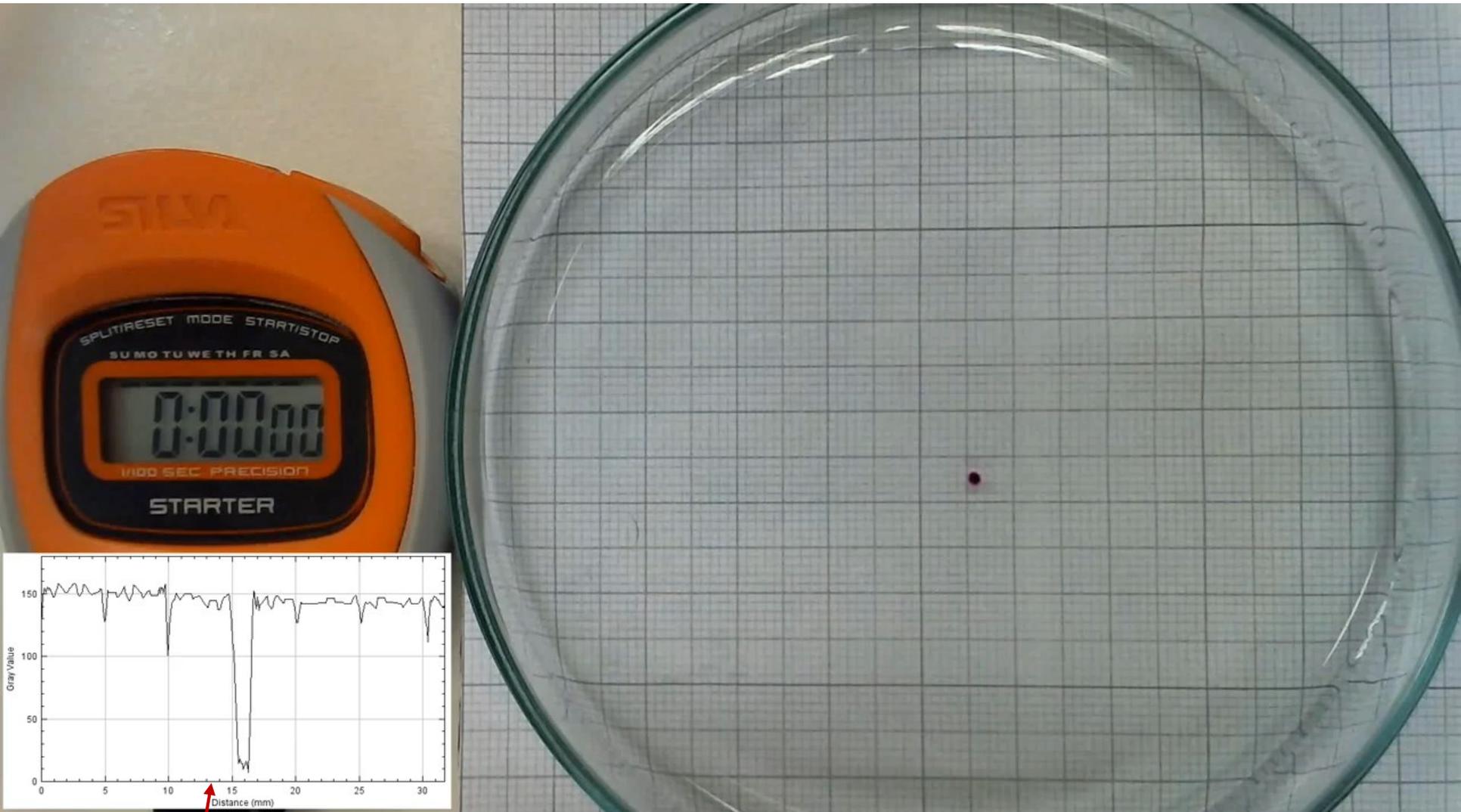
$$D \frac{\Delta \left( \frac{\Delta c}{\Delta x} \right)}{\Delta x} = \frac{\Delta c}{\Delta t}$$

Explanation:

$$c(t) + D\Delta t \frac{\Delta \left( \frac{\Delta c}{\Delta x} \right)}{\Delta x} = c(t + \Delta t)$$

$$c(t) + c'' D\Delta t = c(t + \Delta t)$$

# Time-laps video of $\text{KMnO}_4$ diffusion on agar gel



$$w = 6 \cdot \sqrt{2 \cdot D \cdot t}$$

# How fast is the material transport by diffusion?

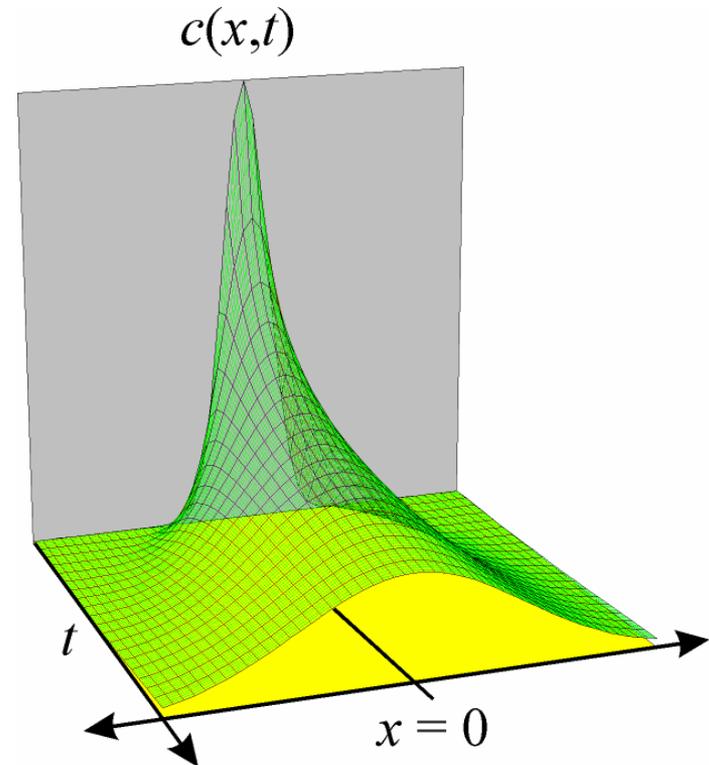
graphical representation of  $c(x,t)$

$$c(x,t) = \frac{c_0}{\sqrt{2\pi}\sigma(t)} e^{-\frac{x^2}{2[\sigma(t)]^2}}$$

$$\sigma(t) \sim \sqrt{2Dt}$$

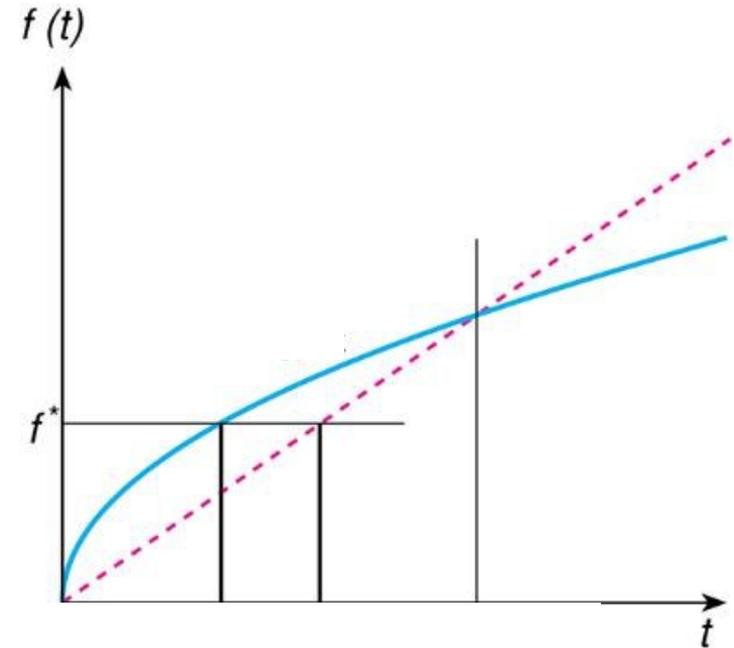
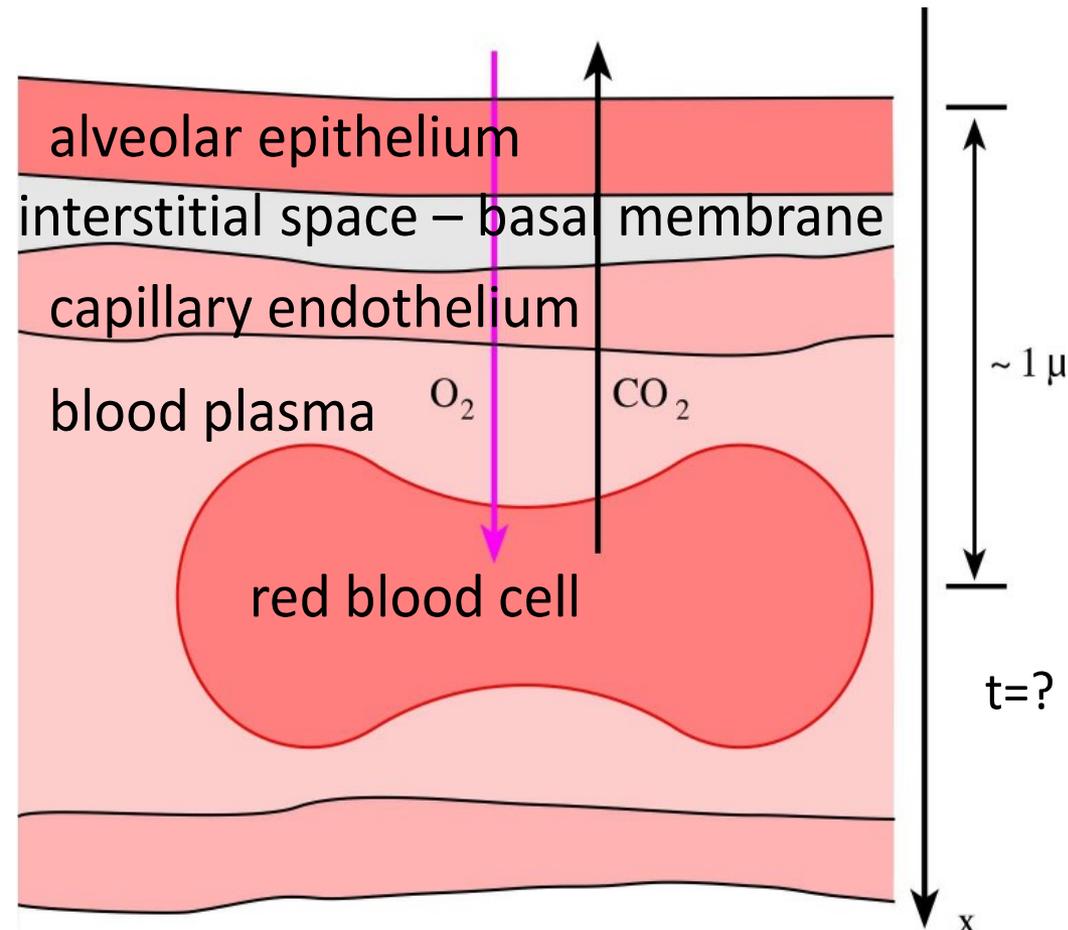
$$R_{\text{mean}} = \sqrt{6 \cdot D \cdot t}$$

$$t = R_{\text{mean}}^2 / 6D$$



# Can O<sub>2</sub>/CO<sub>2</sub> exchange happen by diffusion?

alveolae



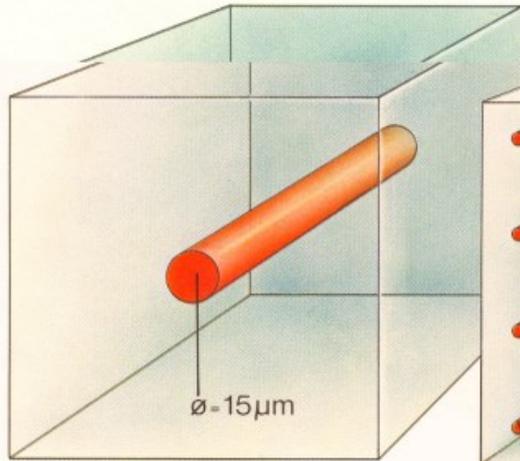
*Diffusion is fast up to  $\sim 100 \mu\text{m}$ , but it slows down over longer distances!*

$D(\text{O}_2) \sim 2 \cdot 10^{-9} \text{ m}^2/\text{s}$ ,  $D(\text{CO}_2) \sim 6 \cdot 10^{-9} \text{ m}^2/\text{s}$ ,  
 mean travel time of RBC in lung capillaries  $\sim 0,5 \text{ s}$

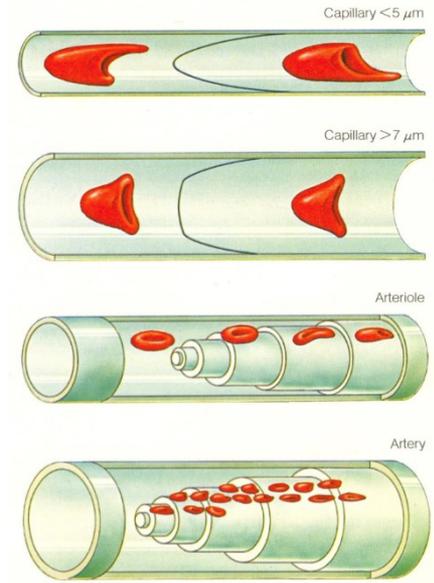
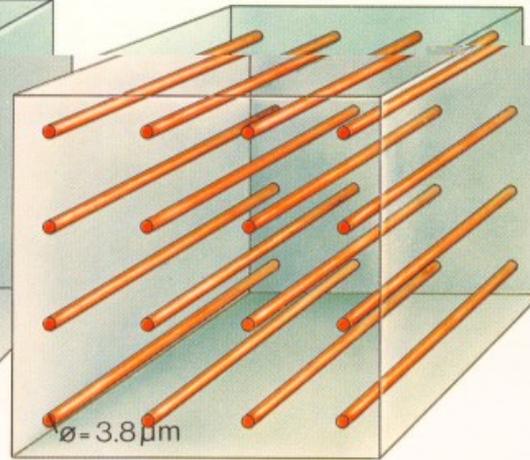
$$t = R_{\text{mean}}^2 / 6D \quad \rightarrow \quad t_{\text{O}_2}^{1\mu\text{m}} \sim 500 \text{ us}, \quad t_{\text{CO}_2}^{1\mu\text{m}} \sim 80 \text{ us}$$

# Red blood cells are elastic, deformable bodies

**Schematic diagram of capillary formation in cold-blooded animals**

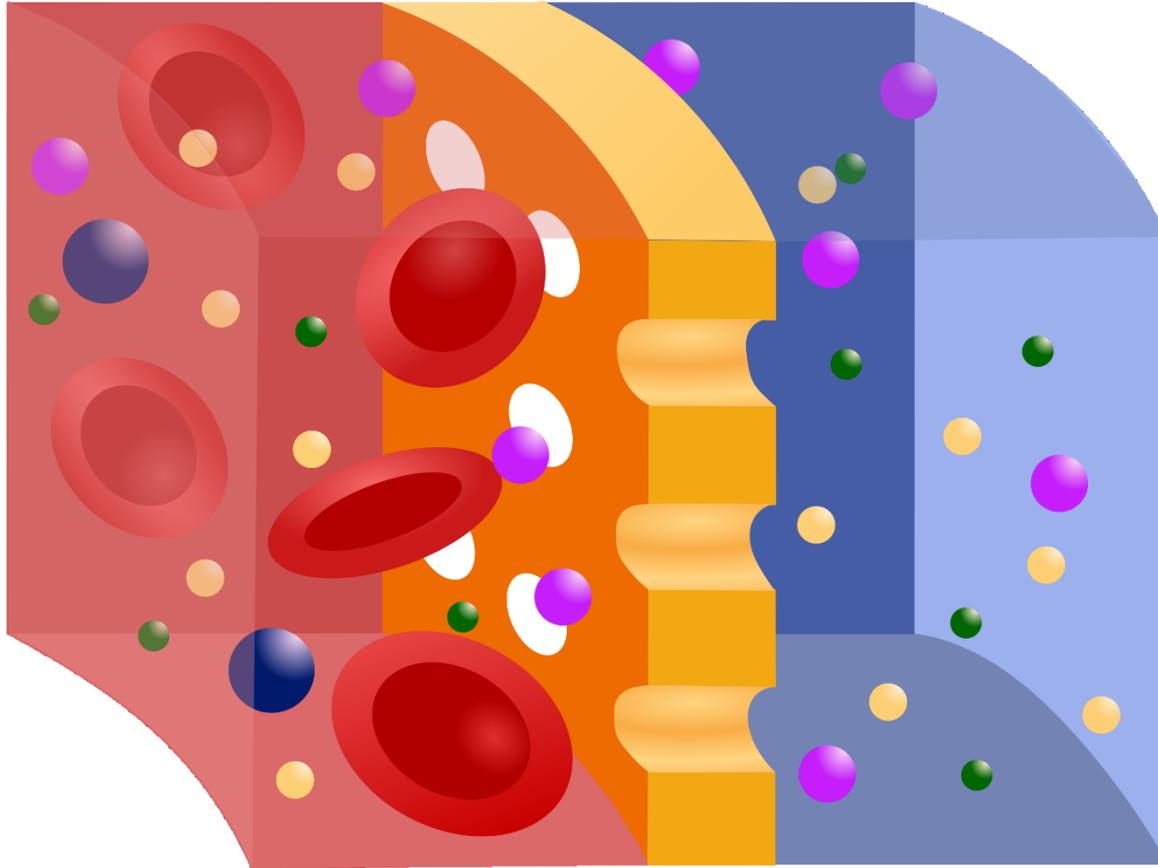


**Schematic diagram of capillary formation in mammals**



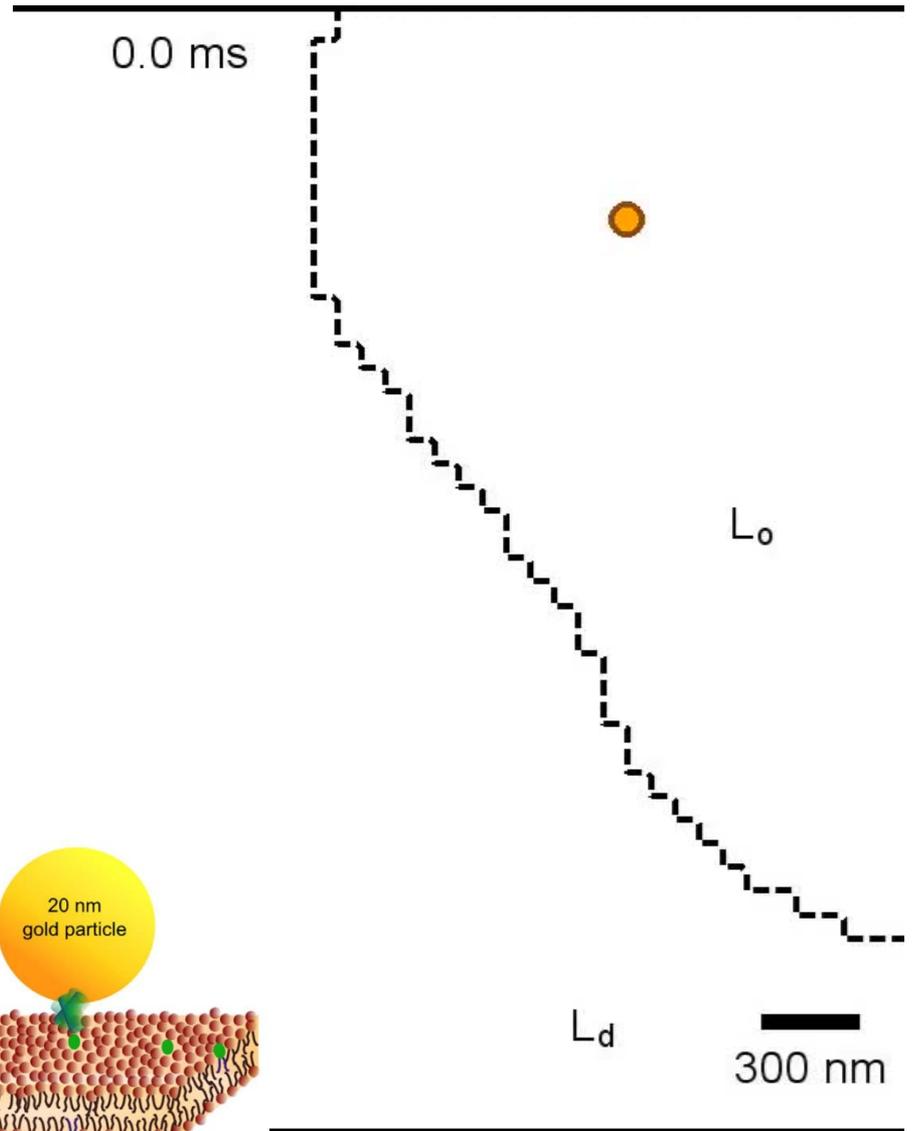
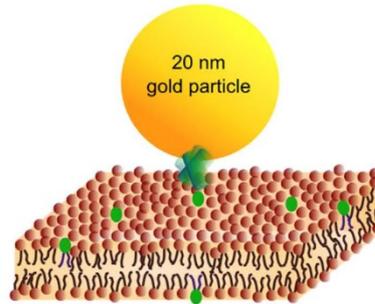
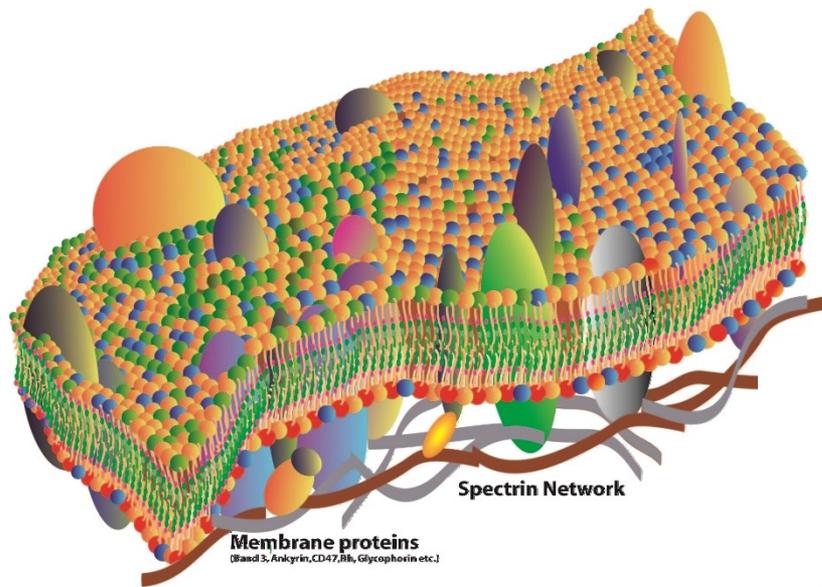
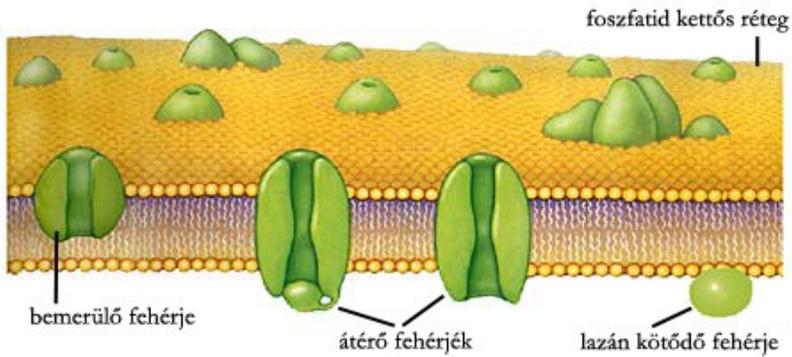
Evolutionary advantage in mammals: the reduction in capillary diameter leading to increased number of capillaries resulted in a significant reduction of distances for diffusion – tissue with high metabolic activity becomes possible!

# Hemodialysis



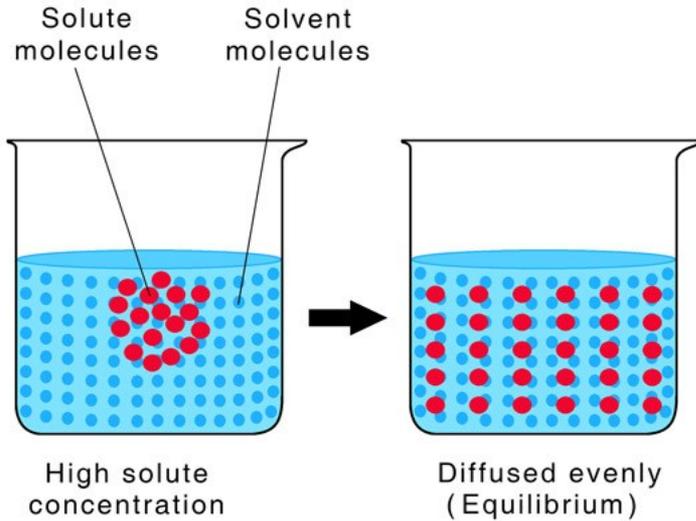
In renal failor, secreted molecules can be diffused out from blood through a semipermeable membrane into a dialysis buffer.

# Lateral diffusion in membranes



# Diffusion

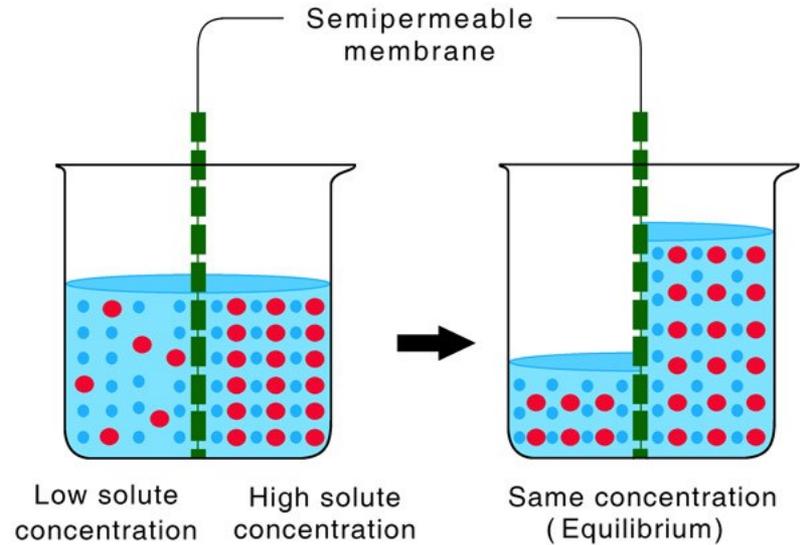
Solute molecules move from high to low concentration



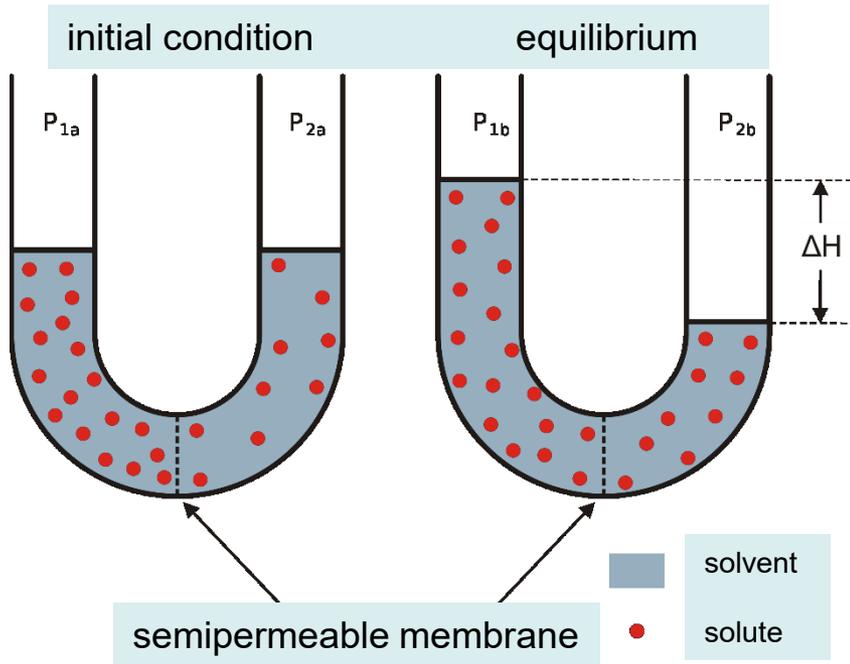
VS

# Osmosis

Solvent molecules move from low to high solute concentration



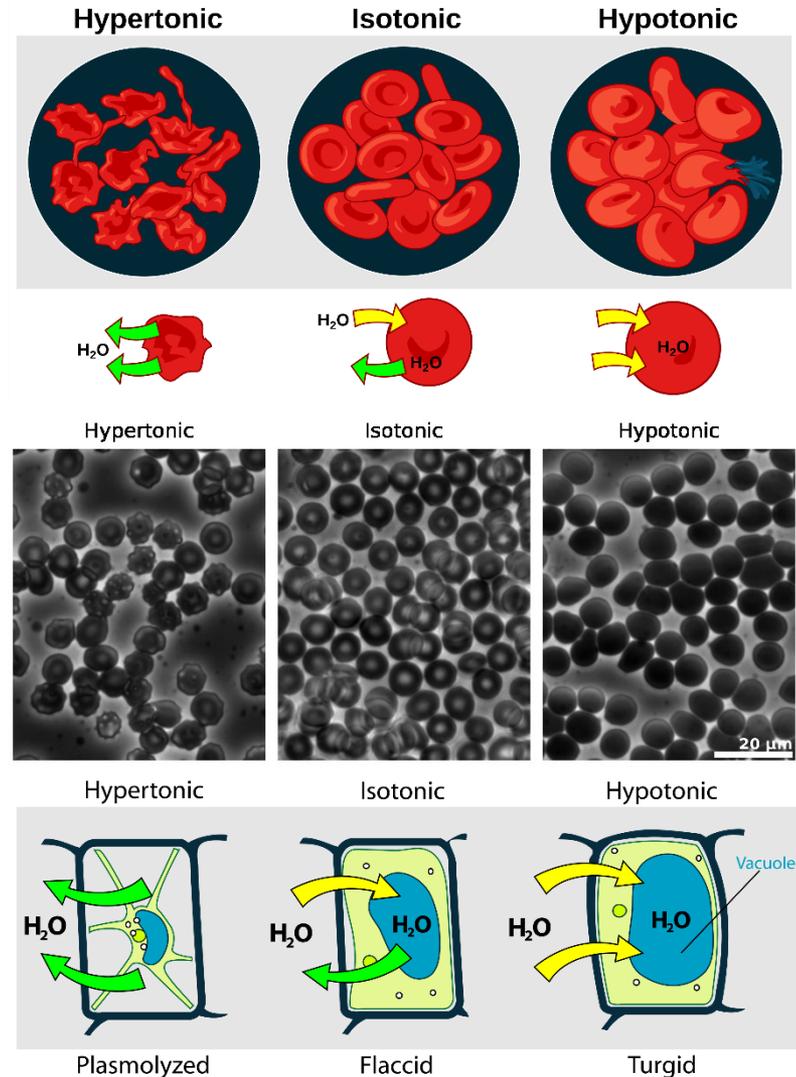
# Osmosis: van't Hoff's law



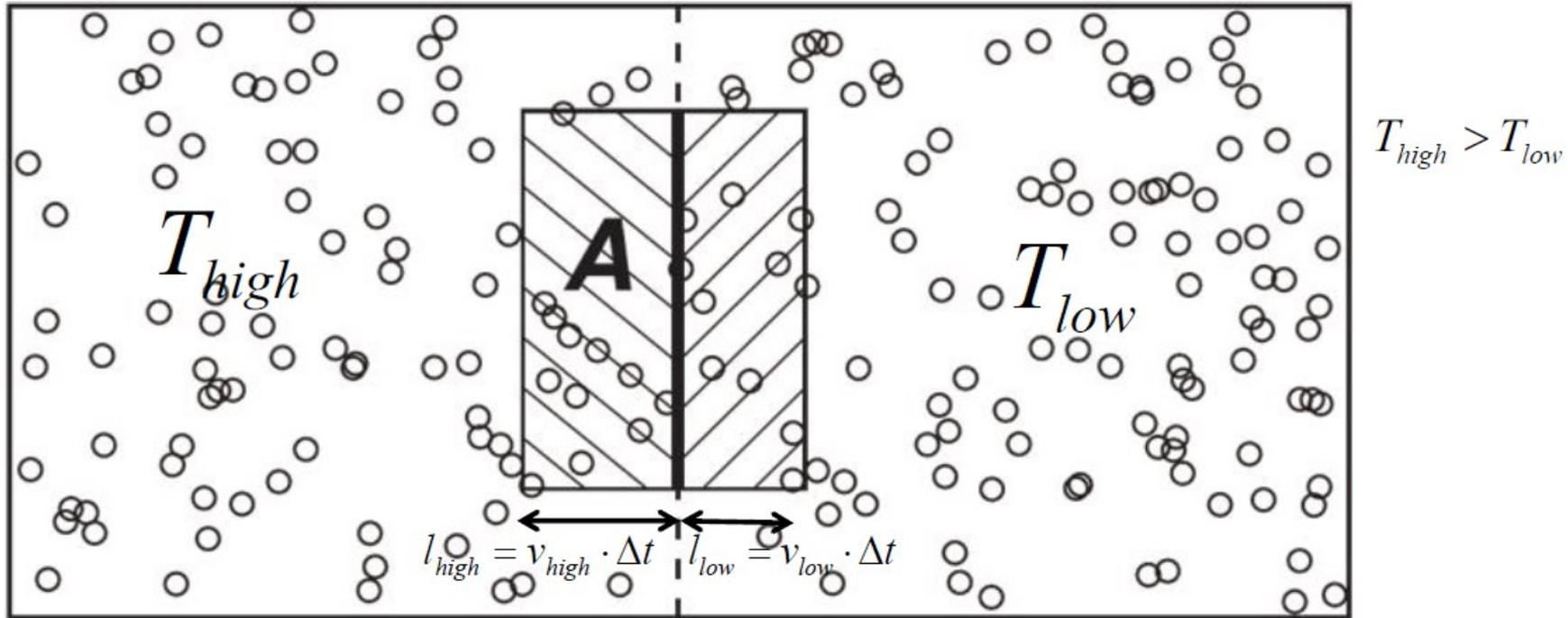
$$\pi = cRT$$

$c$ : osmolarity = total number of particles (dissociation!)  
 -blood plasma ~ 300 mOsm/l

isotonic (physiologic) salt solution: 0,9% (w/v) NaCl

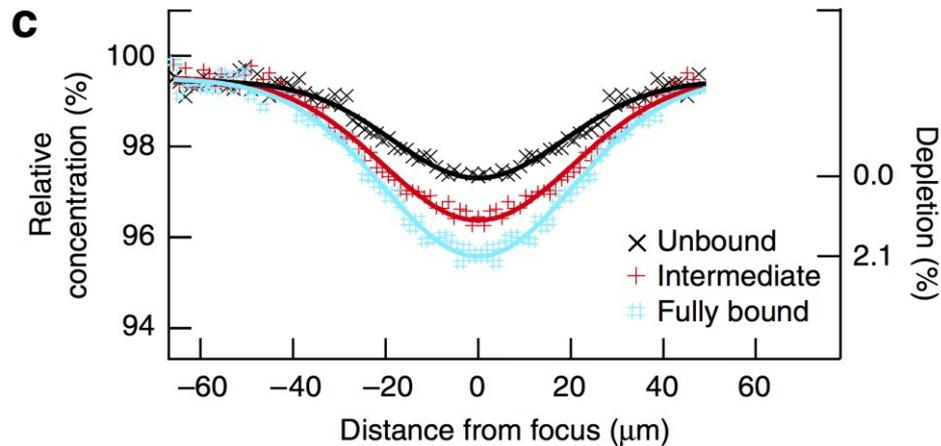
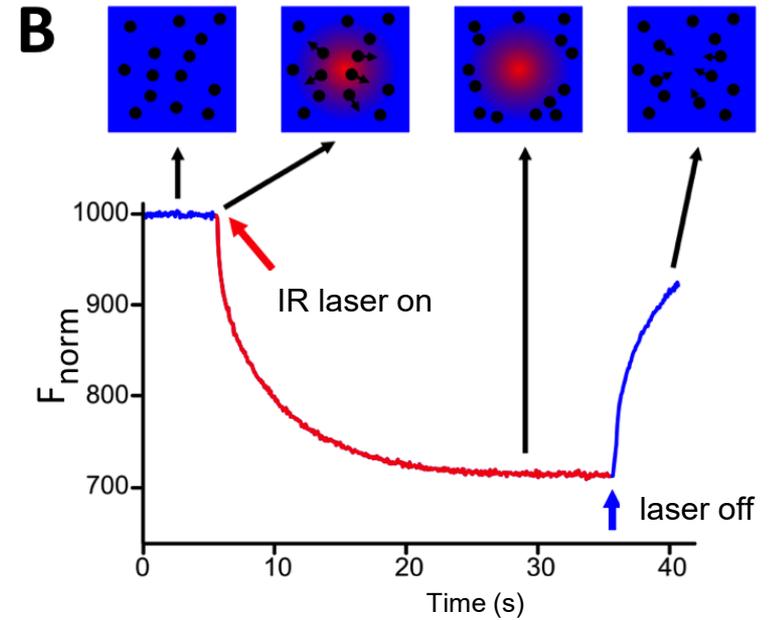
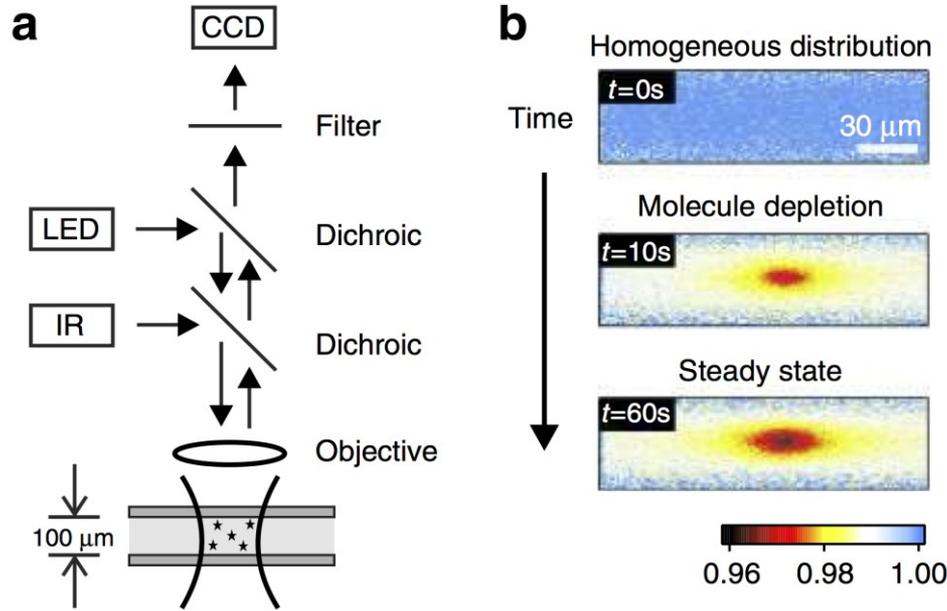


# Thermodiffusion



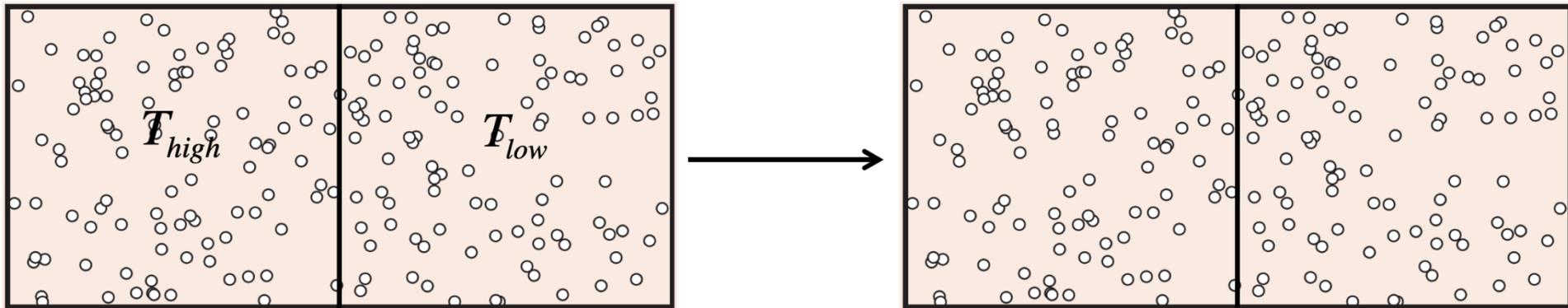
$$\Delta N = N_{high} - N_{low} = \frac{1}{2} \cdot n \cdot \Delta t \cdot A \cdot v_{high} - \frac{1}{2} \cdot n \cdot \Delta t \cdot A \cdot v_{low}$$

# Thermodiffusion: Ludwig-Soret effect



$$J_v = -L_T \cdot \frac{\Delta T}{\Delta x}$$

# Heat conduction: Fourier's law



$$T_{high} > T_{low}$$

$$\Delta N = N_{high} - N_{low} = 0$$

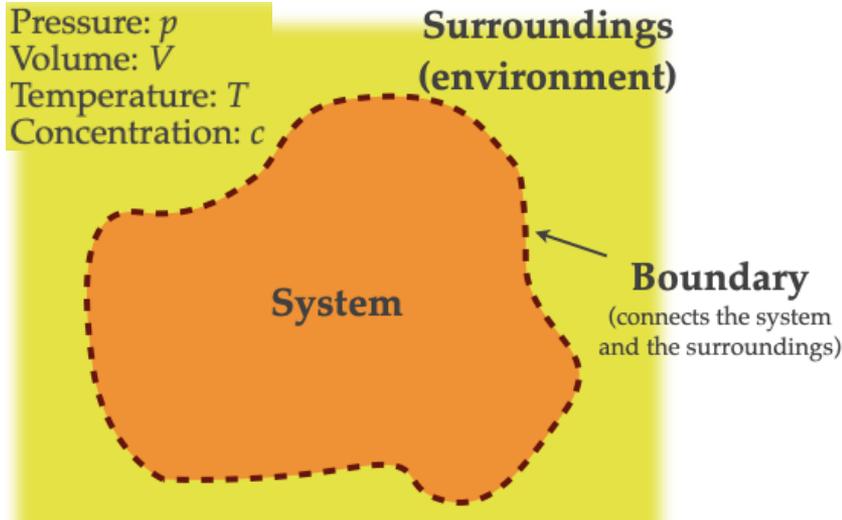
$$N_{high} = N_{low}$$

$$\bar{\varepsilon} = \frac{3}{2} \cdot k \cdot T$$

Energy flow density

$$J_v = \frac{\Delta E}{A \cdot \Delta t} = \frac{N_{high} \cdot \frac{3}{2} \cdot k \cdot (T_{high} - T_{low})}{A \cdot \Delta t} = -\lambda \cdot \frac{\Delta T}{\Delta x}$$

# Generalization: Onsager-relations

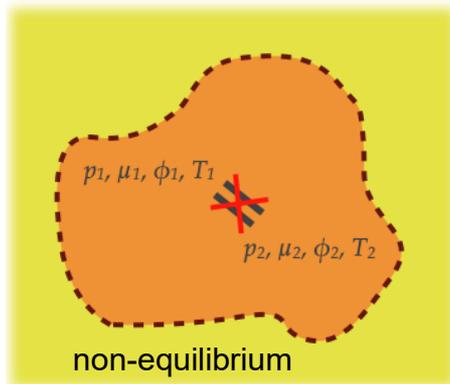


Macroscopic characterization:  
*state variables* - explicitly determine the *state* of the system

Equilibrium = homogenous distribution of intensive variables!

Extensive variable	Intensive variable
Volume ( $V$ )	Pressure ( $p$ )
Matter ( $n$ )	Chemical potential ( $\mu$ )
Charge ( $Q$ )	Electric potential ( $\phi$ )
Entropy (disorder, $S$ )	Temperature ( $T$ )

- *Extensive* variables: their value is proportional to the size of the system
- *Intensive* variables: their value is independent of the size of the system



Onsager-relation:  $J_{ext.} = L_{cond} * X_{int\_grad}$

$J_{ext.}$ : flow density of extensive quantity (eg.  $J_{matter}$ )

$X_{int\_grad}$ : gradient of intensive quantity (eg.  $\frac{\Delta c}{\Delta x}$ )

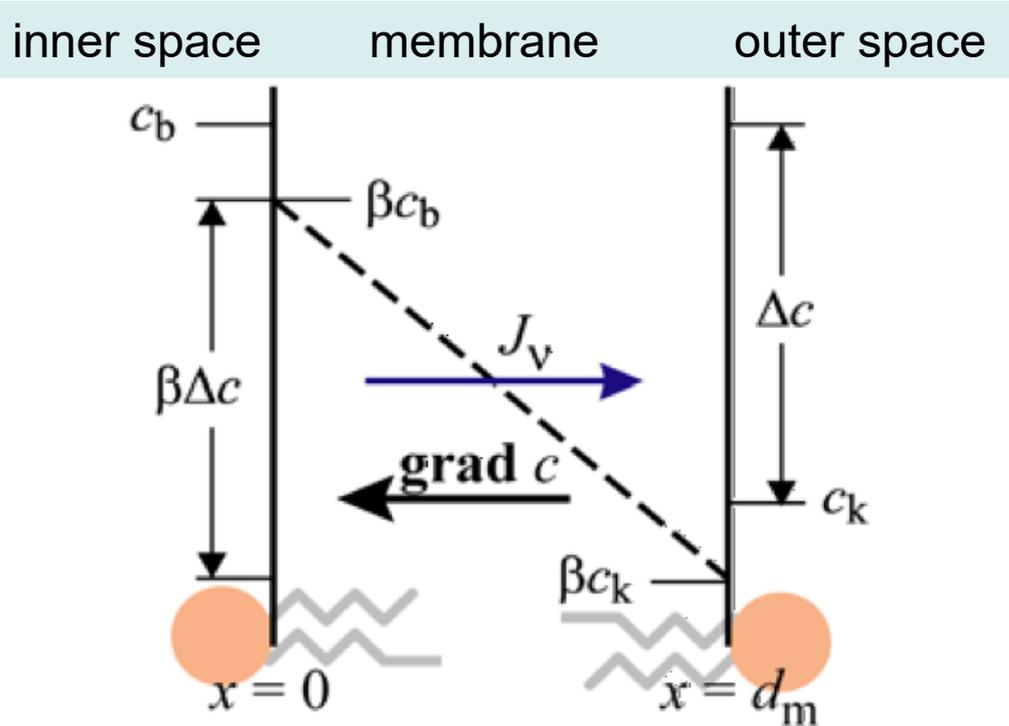
$L_{cond}$ : conductivity coefficient (eg.  $D$ )

# Generalization: Onsager-relations

Thermodynamic current	Relevant intensive variable (its difference maintains current)	Current density	Physical law
Heat flow	Temperature ( $T$ )	$J_E = -\lambda \frac{\Delta T}{\Delta x}$	Fourier
Volumetric flow	Pressure ( $p$ )	$J_V = -\frac{R^2}{8\eta} \frac{\Delta p}{\Delta x}$	Hagen-Poiseuille
Electric current	Electric potential ( $\phi$ )	$J_Q = -\frac{1}{\rho} \frac{\Delta \phi}{\Delta x}$	Ohm
Material transport (diffusion)	Chemical potential ( $\mu$ )	$J_n = -D \frac{\Delta c}{\Delta x}$	Fick

In a non-equilibrium system thermodynamic flows emerge to restore the equilibrium = the homogeneity of the intensive variables (irreversible processes).

# Diffusion across membranes



$\beta$  – partition coefficient

$$\beta = c_m(0)/c_b = c_m(d_m)/c_k$$

Fick I. law:

$$J = -D \Delta c / \Delta x$$

$$= -D_m (c_k^m - c_b^m) / d_m$$

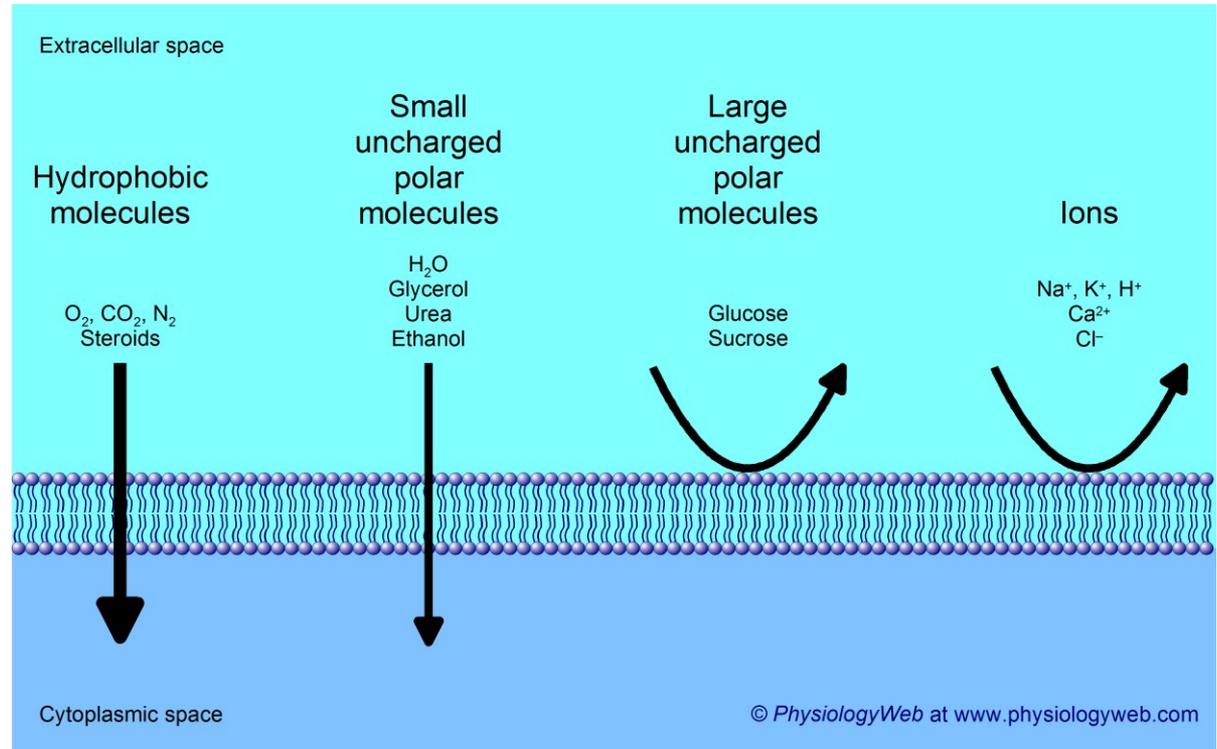
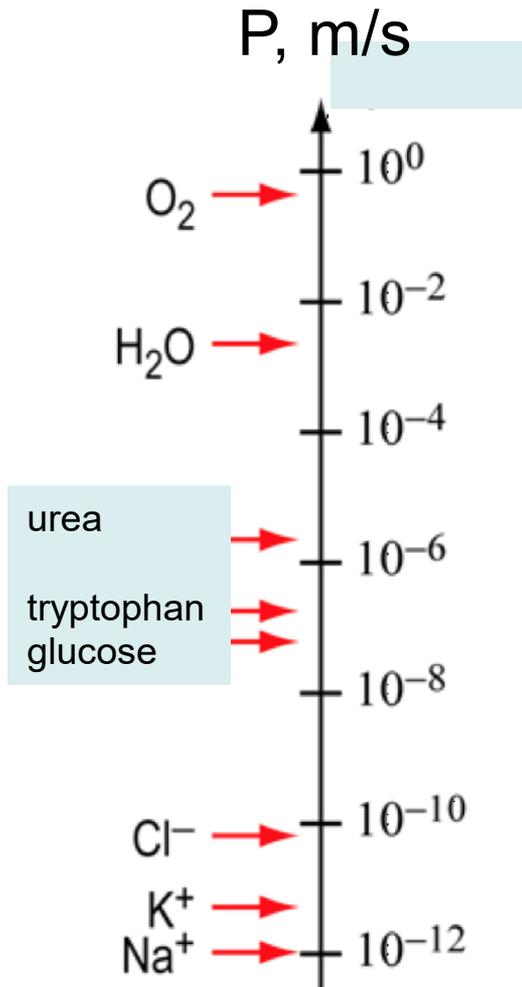
$$= -P_m \Delta c_m$$

$$= -P_m \beta \Delta c = -P \Delta c$$

$P$ : permeability coefficient

$$[P] = \text{m/s}$$

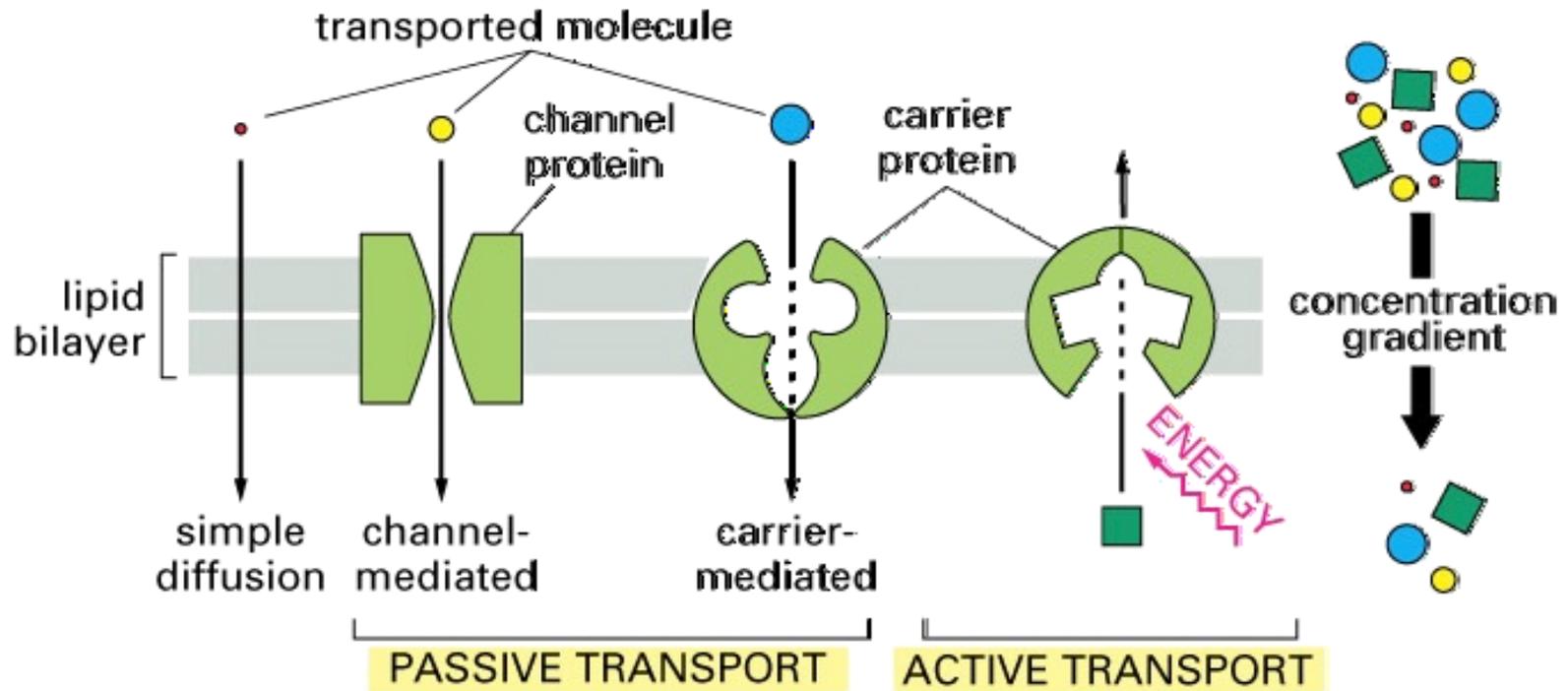
# Diffusion across membranes



$Na^+$  ions:  $P = 10^{-12} \text{ m/s} = 10^{-3} \text{ nm/s}$ , so it takes  $\sim 2\text{h}$  to get across a 5 nm membrane!

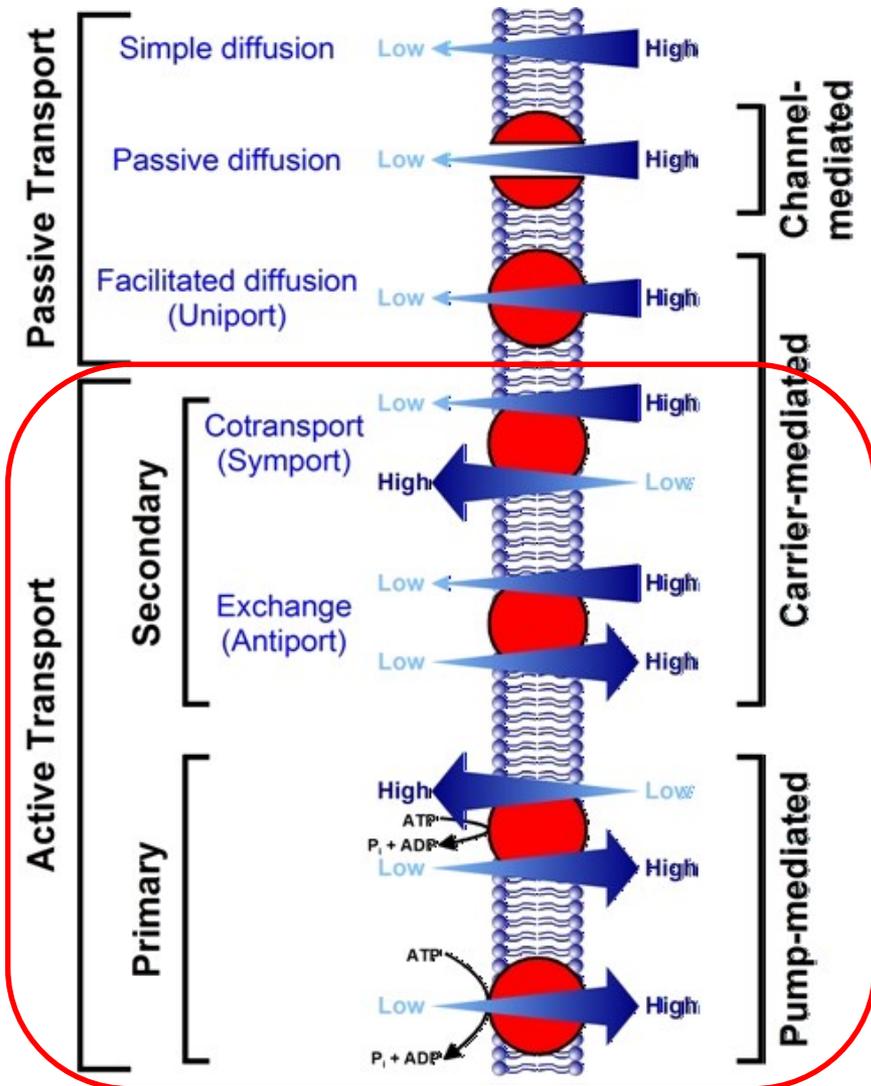
The phospholipid bilayer is practically impermeable for small ions and larger charged molecules!

# Transport across biological membranes



- free diffusion is limited to small non-polar molecules
- the transport mechanism can be channel-mediated or carrier-mediated
- based on its energy requirement, the transport can be passive or active

# Transport across biological membranes

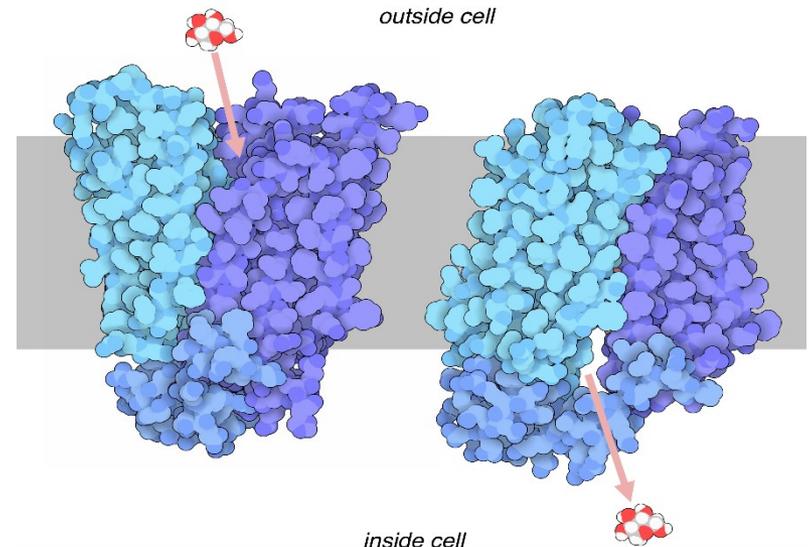
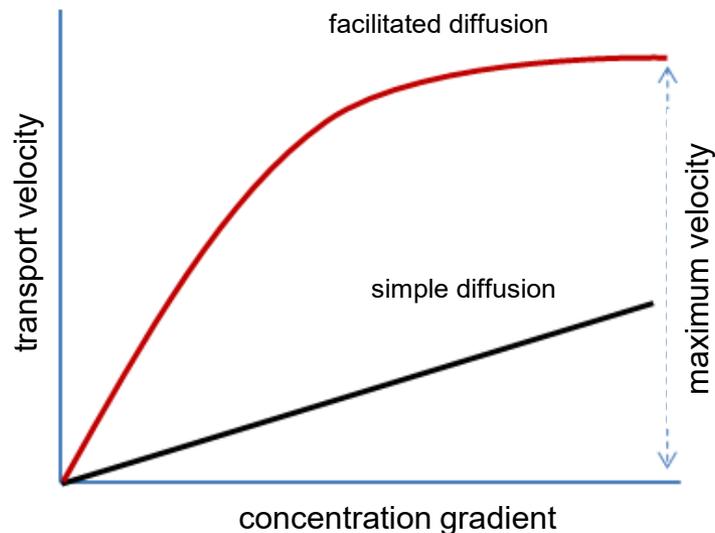
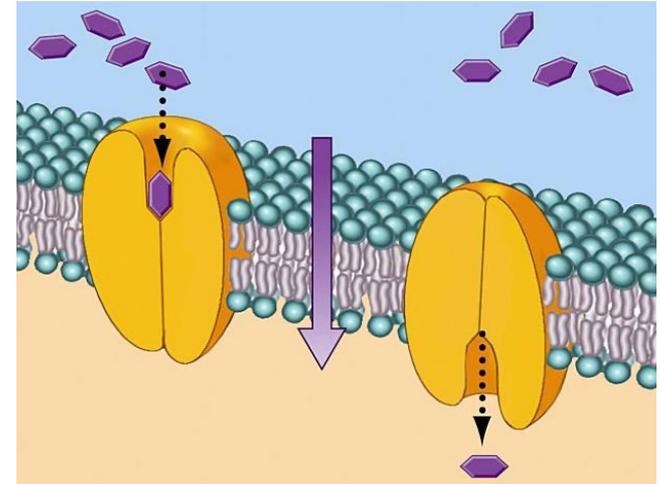


- in passive transport processes materials can move according to the concentration gradient, its flux depends on the size, shape, and polarity of the molecule as well as on the temperature (gases, steroids, alcohol, water)

- in active transport materials move against concentration gradient, either utilizing directly the energy of ATP (primary active transport), or utilizing a chemical gradient built up by a primary transporter (secondary active transport), this can be further classified as symport or antiport

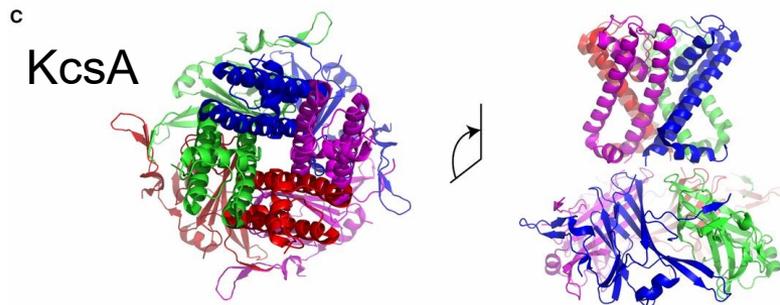
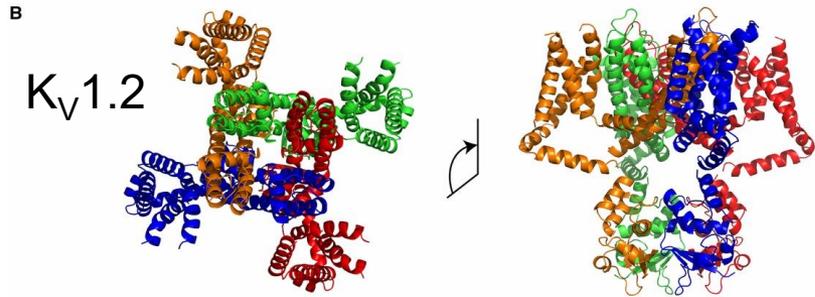
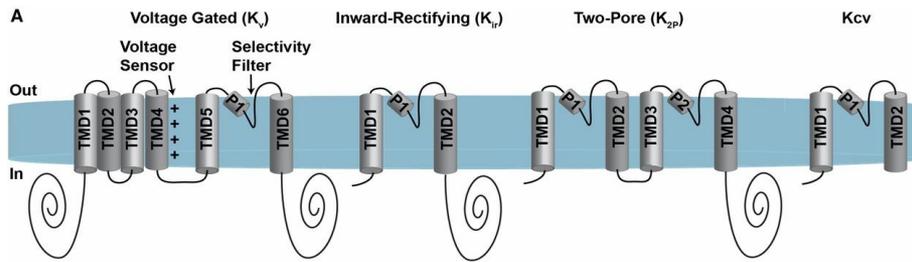
# Facilitated diffusion

- utilizing a carrier protein, which binding site has access both on the extracellular and on the intracellular sides
- at a given concentration gradient the transport velocity is higher in the case of facilitated diffusion
- it follows Michalis-Menten kinetics, saturatable and can be selectively inhibited (example: "GLUT" glucose transporters)



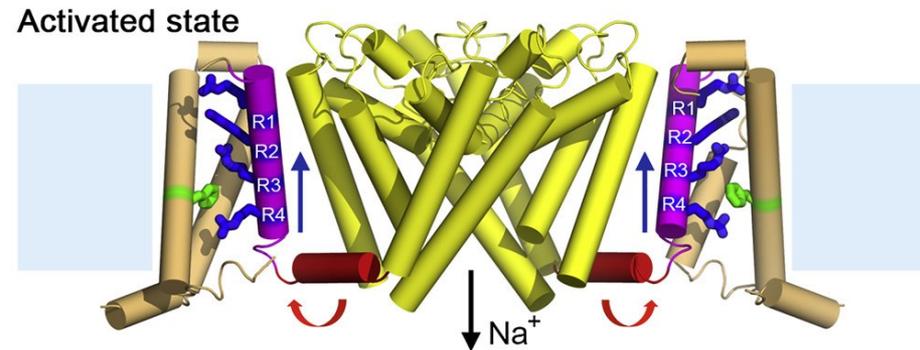
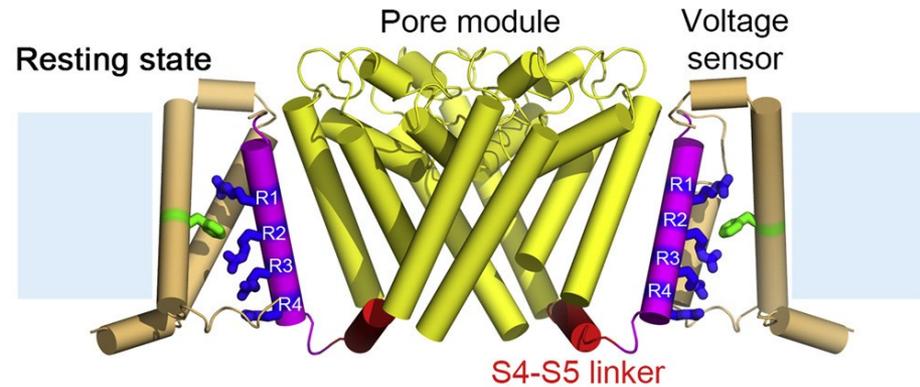
# Ion channels

multisubunit transmembrane proteins, selective for given ions, their open/closed states are governed either by regulatory molecules (e.g. neurotransmitters, hormones) or by change in membrane potential



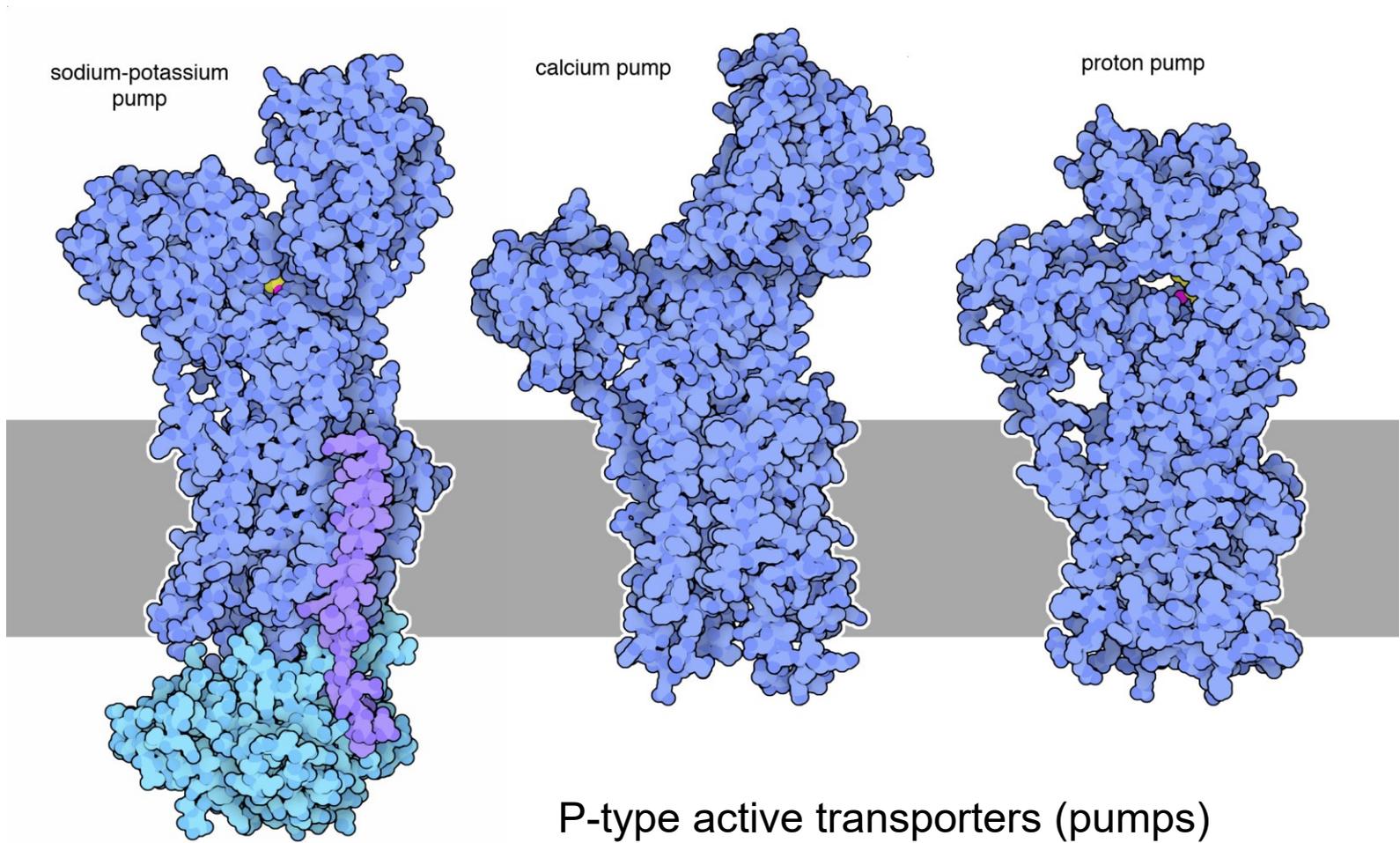
$K^+$  channels

Resting State Structure of a Voltage-gated  $Na^+$  Channel Defines the Gating Mechanism

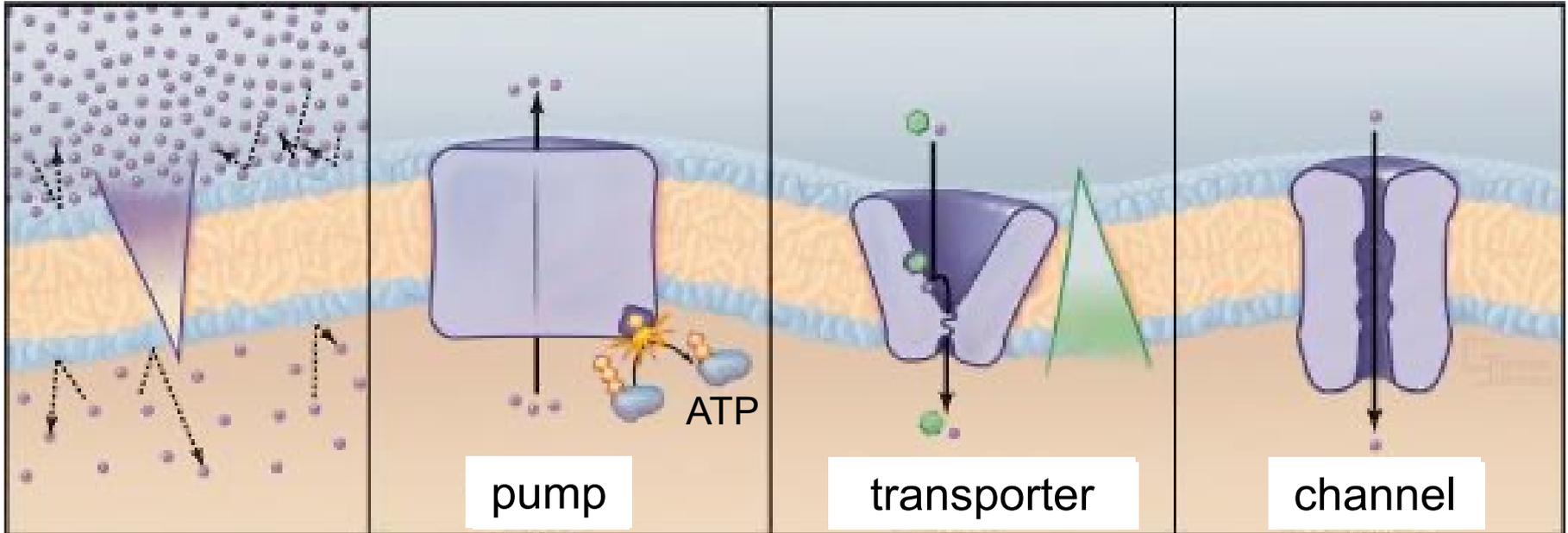


voltage-gated  $Na^+$  channel

# Active transporters



# Comparison of Transporters



pump

transporter

channel

specificity

maximal

medium

low

rate (ion/s)

slow (100)

medium (1000)

fast ( $10^6$ )

conc. gradient

against

along

along

energy need

yes

no

no

transported ion/  
conformation change

~1

~1

many

Related Chapters:

*Damjanovich, Fidy, Szöllösi: Medical Biophysics*

III./2.

2.1

2.2

III./3.

3.1

3.2

*Practicals: Diffusion*