



SEMMELWEIS UNIVERSITY

Dept. of Biophysics and Radiation Biology,
Laboratory of Nanochemistry

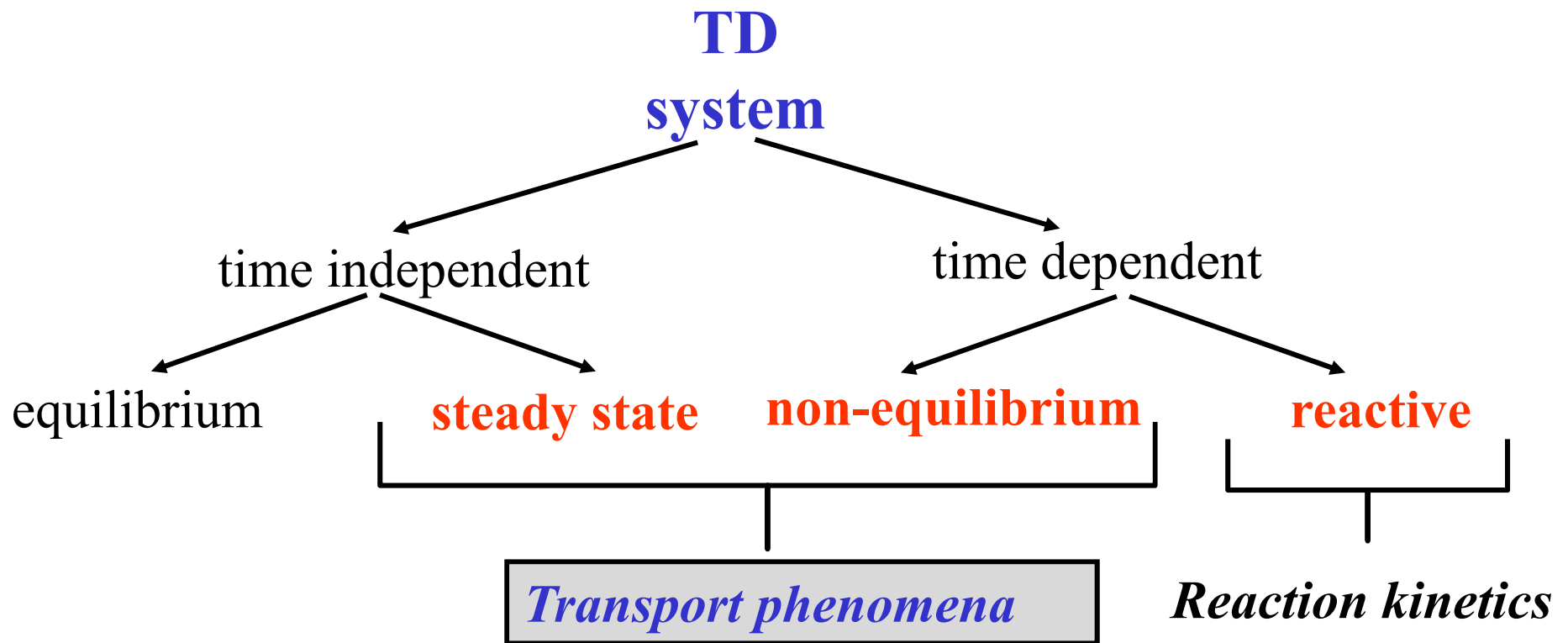


**Laboratory of
soft matters**

TRANSPORT PHENOMENA in biological systems

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Driving force: **going to equilibrium**

During spontaneous process

$$\Delta S > 0$$

$$\Delta F < 0$$

$$F = U - TS$$

$$\Delta G < 0$$

$$G = H - TS$$

TRANSPORT PHENOMENA



Sir Isac Newton
(1642-1727)



Jean-Babtiste-Joseph Fourier
(1768-1830)



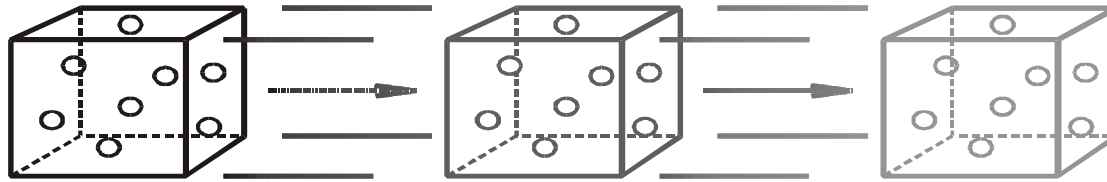
Adolf Eugen Fick
(1829-1901)



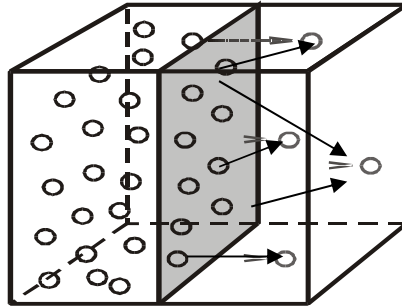
Lars Onsager)
(1903-1976)

Subject: Study of flow of energy, matter, charge and impulse from one point to another point in space.

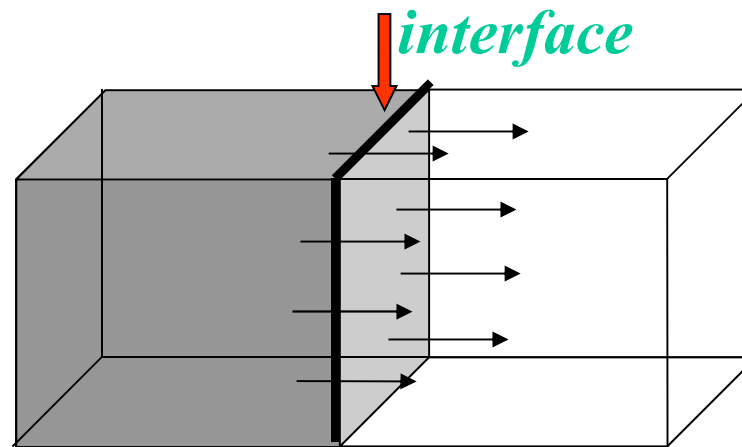
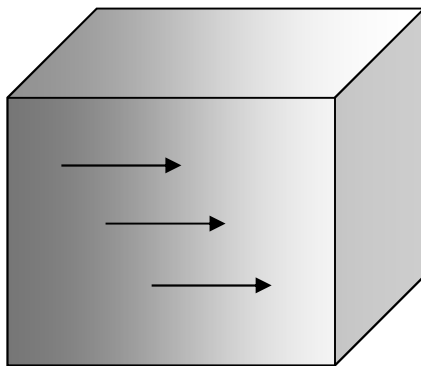
Extensive q. → **particles** (atoms, molecules and ions), carry material, energy, momentum and charge,
→ **electrons**, carry energy, momentum and charge,
→ **photons**, carry energy .



Convective transport:

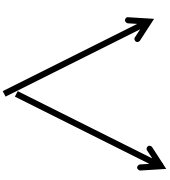


Conductive transport:



TRANSPORT PHENOMENA :

Driving force: to obtain equilibrium

Basic quantities:  current of **extensive** quantities
driving force (**intensive** quantities)

Mass flux:

$$j_n \left[\text{mol m}^{-2} \text{s}^{-1} \right]$$

Energy flux:

$$j_U \left[\text{J m}^{-2} \text{s}^{-1} \right]$$

Momentum flux:

$$j_i \left[\text{kg m}^{-1} \text{s}^{-2} \right]$$

Charge flux:

$$j_Q \left[\text{Coulomb} \cdot \text{m}^{-2} \text{s}^{-1} \right]$$

Flux: the *rate of flow of a property per unit area (current density)*

$$j = L \cdot X$$

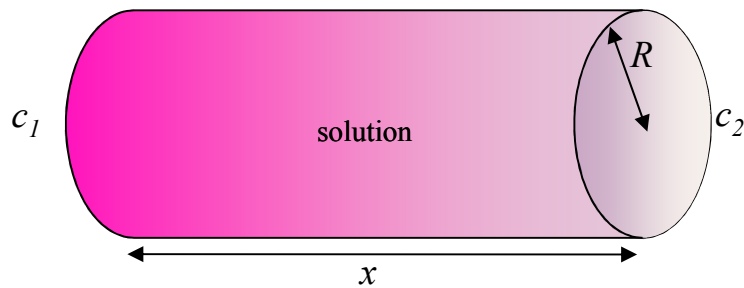
Current	Driving force (Δy)	Flux	Laws
moles	Chemical potential concentration	$j_n = -D \frac{\Delta c}{\Delta x}$	Fick
heat	temperature	$j_u = -k \frac{\Delta T}{\Delta x}$	Fourier
volume	pressure	$j_v = -\frac{R_o^2}{8\eta} \frac{\Delta p}{\Delta x}$	Hagen-Poiseuille
charge	electric potential	$j_Q = -\frac{1}{\rho} \frac{\Delta \varphi}{\Delta x}$	Ohm
momentum	velocity	$j_i = -\eta \frac{\Delta v_y}{\Delta x}$	Newton

↓

$$\tau = \eta \frac{\Delta v_y}{\Delta x}$$

Material transport (diffusion)

Thermodynamic current	Relevant intensive variable (its difference maintains current)	Current density	Physical law
Material transport (diffusion)	Chemical potential (μ)	$J_n = -D \frac{\Delta c}{\Delta x}$	Fick

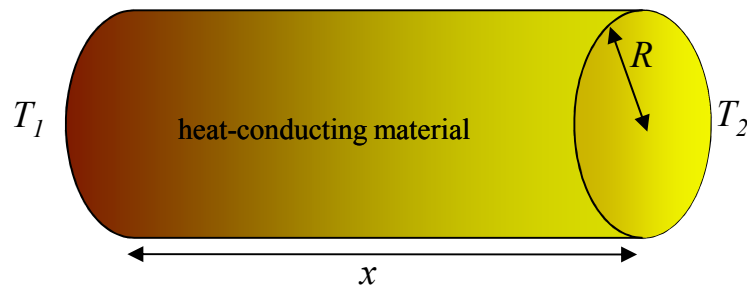


m = amount of material transported
 t = time
 R = tube radius
 x = length
 $(\Delta c/\Delta x = \text{concentration gradient, maintained by } c_1 - c_2)$
 A = cross-sectional area of tube
 J_n = heat current density
 D = diffusion coefficient

$$\frac{m}{tA} = J_n = -D \frac{\Delta c}{\Delta x}$$

Heat flow

Thermodynamic current	Relevant intensive variable (its difference maintains current)	Current density	Physical law
Heat flow	Temperature (T)	$j_u = -k \frac{\Delta T}{\Delta x}$	Fourier



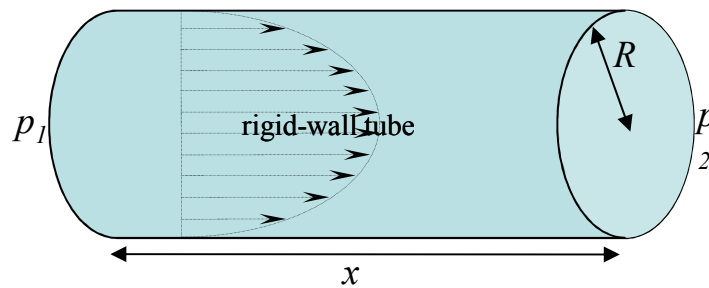
$$\frac{Q}{A \cdot t} = j_u = -k \frac{\Delta T}{\Delta x}$$

Q = heat
 t = time
 R = tube radius
 x = length
 $(\Delta T/\Delta x = \text{temperature gradient, maintained by } T_1 - T_2)$
 A = cross-sectional area of tube
 J_E = heat current density
 k = coefficient of heat conductance

$$A = R^2 \pi$$

Volume flow

Thermodynamic current	Relevant intensive variable (its difference maintains current)	Current density	Physical law
Volumetric flow	Pressure (p)	$J_V = -\frac{R^2}{8\eta} \frac{\Delta p}{\Delta x}$	Hagen-Poiseuille



V = volume
 t = time
 R = tube radius
 η = viscosity
 p = pressure
 x = tube length
 $(\Delta p/\Delta x)$ = pressure gradient, maintained by p_1-p_2
 A = cross-sectional area of tube
 J_V = flow intensity

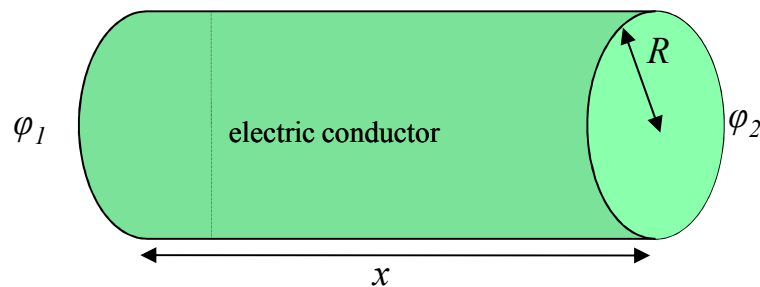
$$\frac{V}{t} = \frac{R^4 \pi}{8\eta} \frac{\Delta p}{\Delta x}$$

$$A = R^2 \pi$$

$$J_V = \frac{V}{tA} = \frac{R^2}{8\eta} \frac{\Delta p}{\Delta x}$$

Electric current

Thermodynamic current	Relevant intensive variable (its difference maintains current)	Current density	Physical law
Electric current	Electric potential (φ)	$J_Q = -\frac{1}{\rho} \frac{\Delta\varphi}{\Delta x}$	Ohm

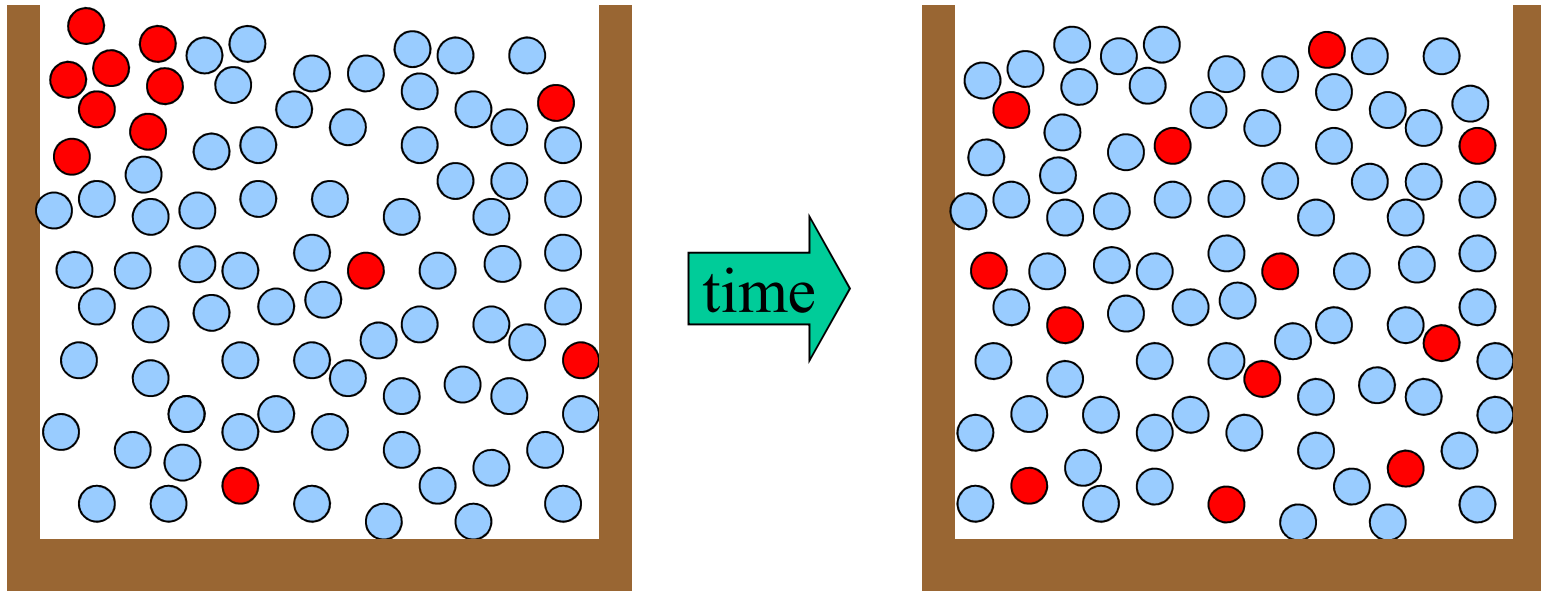


q = electric charge
 t = time
 R = tube radius
 φ = electric potential
 x = length of conductor
 $(\Delta\varphi/\Delta x = \text{potential gradient (voltage), maintained by } \varphi_1 - \varphi_2)$
 A = cross-sectional area of tube
 J_Q = electric current

$$\frac{q}{tA} = J_Q = -\frac{1}{\rho} \frac{\Delta\varphi}{\Delta x}$$

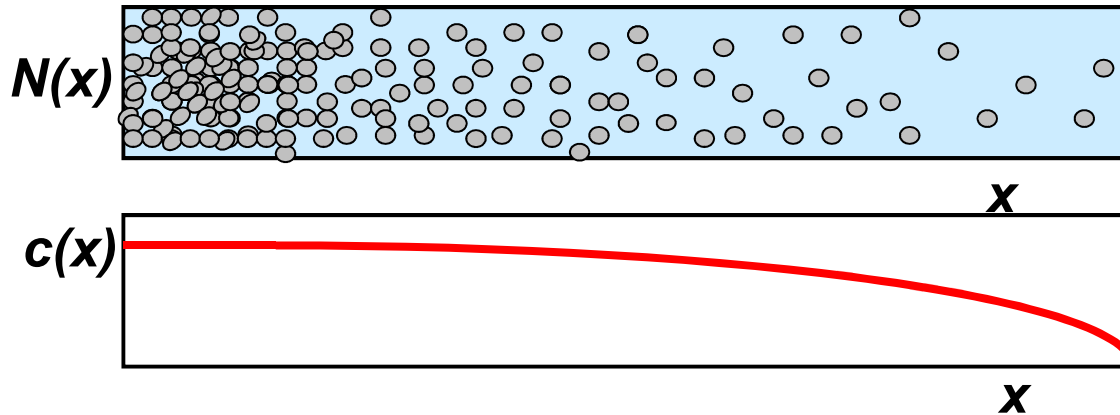
Diffusion

- Spontaneous mixing,
- **concentration-equilibration** driven by molecular (*thermal*) motion of particles.



Theory of diffusion: Fick's laws

Microscopic and **macroscopic** descriptions



solution:

$$c(x, t)$$
$$c(\mathbf{r}, t)$$

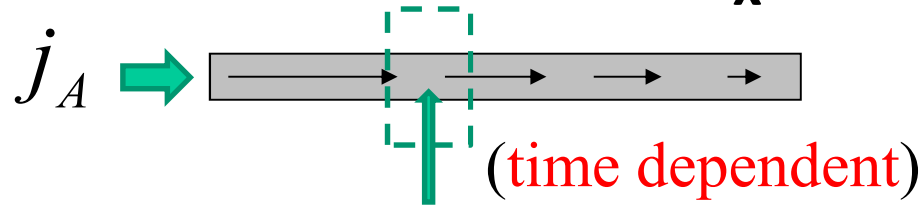
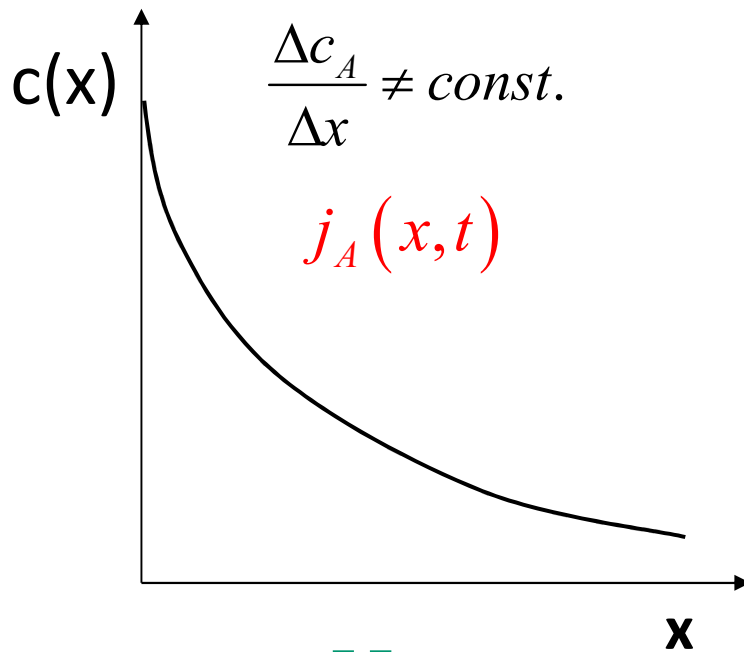
Fick's I. law:

$$j_A = -D \cdot \frac{\Delta c_A}{\Delta x}$$

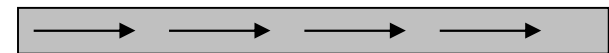
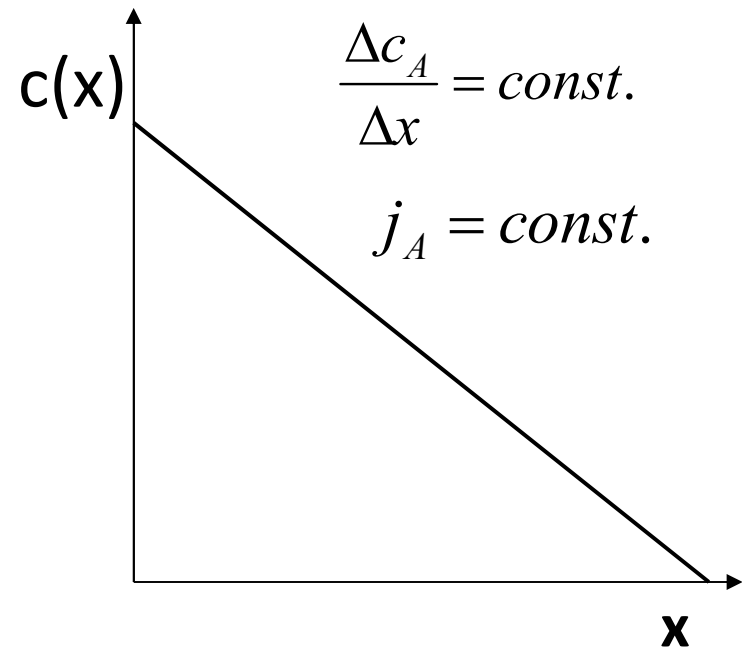
- diffusional flow is proportional to the slope of concentration-position dependence,
- materials flow from higher concentration to lower concentration,
- $D > 0$

The real driving force: $\frac{\Delta \mu_A}{\Delta x}$

$$j_A = -D \cdot \frac{\Delta c_A}{\Delta x}$$



$$\frac{\Delta J_A}{\Delta x} = -\frac{\Delta c_A}{\Delta t}$$



Steady-state diffusion
(time independent)

$$\frac{\Delta J_A}{\Delta x} = 0 \quad \rightarrow \quad \frac{\Delta c_A}{\Delta t} = 0$$

Fick's II. law = conservation of mass + Fick's I. law

Provides: time dependence of concentration

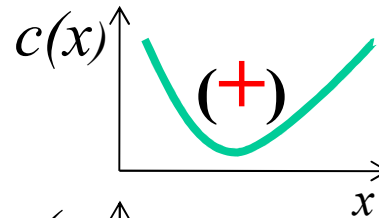
$$\left. \frac{\Delta c}{\Delta t} \right| = D \cdot \text{curvature of } c(x) \text{ function} \quad D > 0$$

Diffusion
coefficient

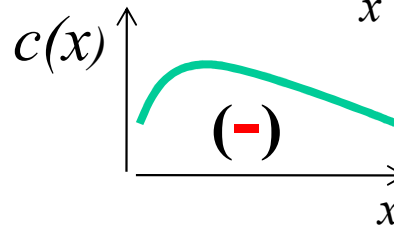
$$\left(\frac{d^2 c}{dx^2} \right)$$

$$\frac{dc}{dt} = D \cdot \frac{d^2 c}{dx^2}$$

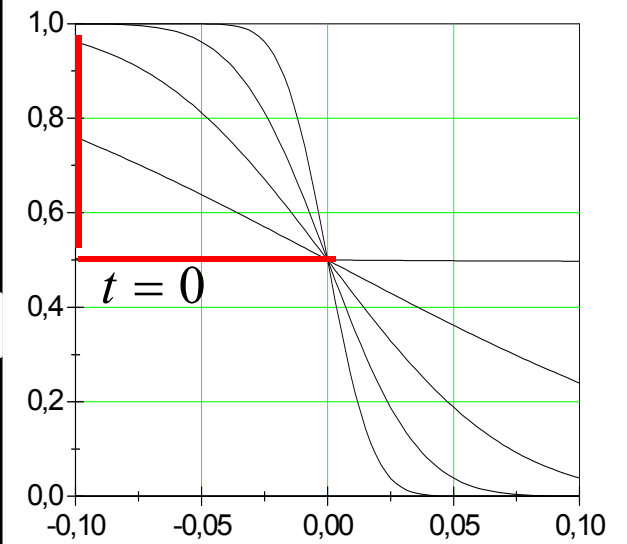
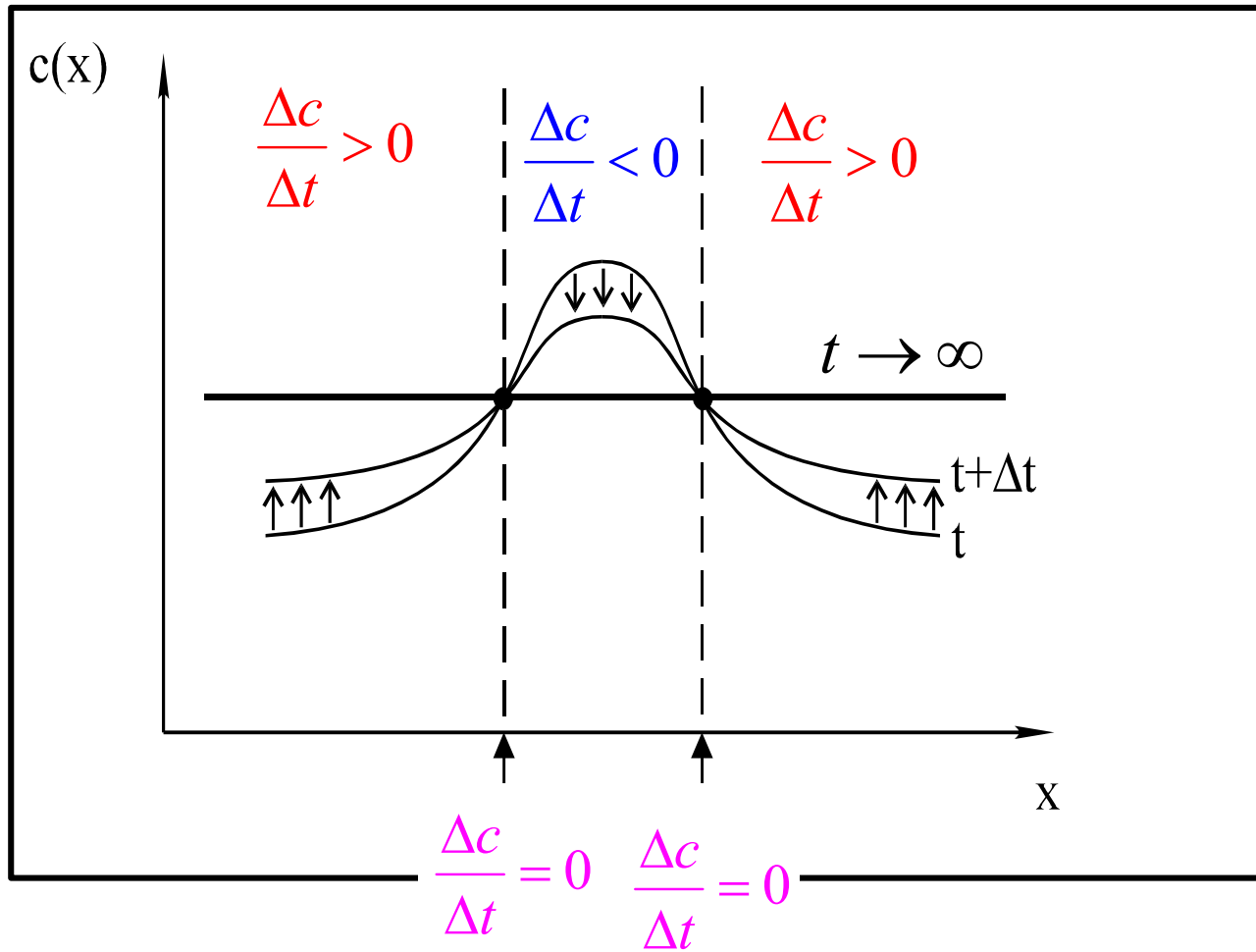
curvature
 ↗ convex (+)
 ↘ concave (-)



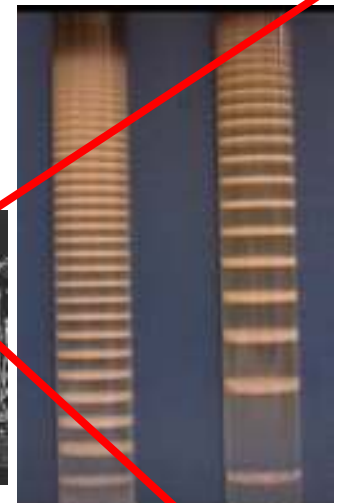
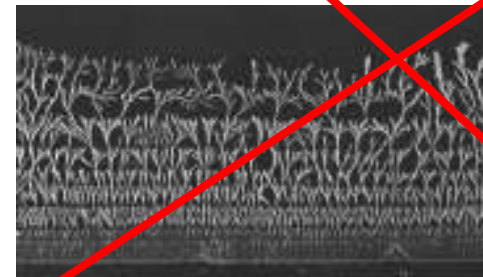
$$\frac{\Delta c}{\Delta t} > 0$$



$$\frac{\Delta c}{\Delta t} < 0$$



Diffusion is against pattern formation!

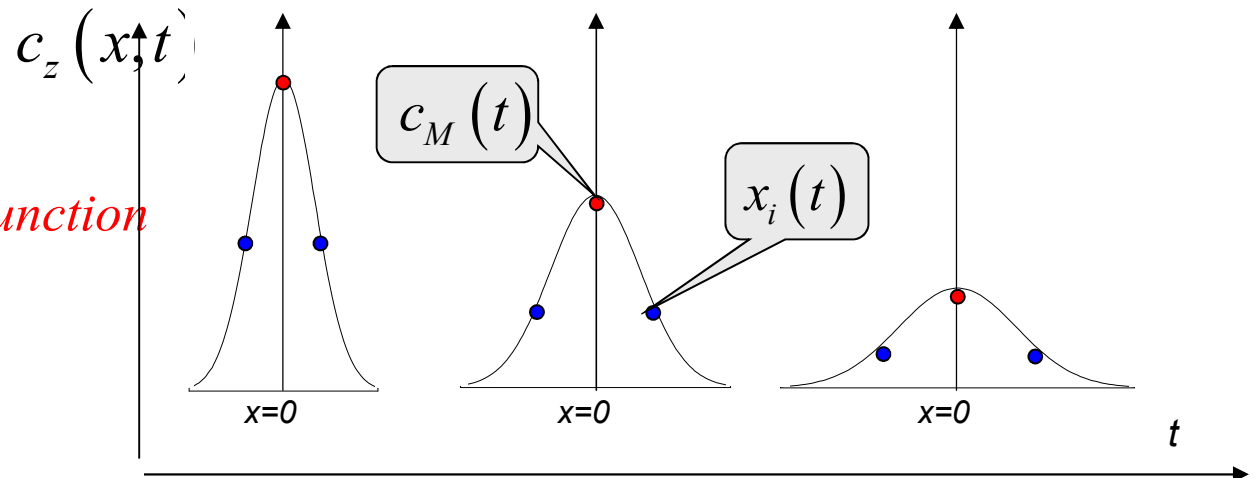


One dimensional free diffusion.

$$\left. \frac{\Delta c}{\Delta t} \right|_x = D \cdot \text{curvature of } c(x) \text{ function}$$

↓

$$\frac{\Delta c}{\Delta t} < 0$$



$$c_M(t) = \frac{c_o \delta_x}{(4\pi D)^{1/2}} \cdot t^{-1/2}$$

$$x_i(t) = \sqrt{2D} \cdot t^{1/2}$$

Characteristic quantities of diffusion scale with the square root of time!

Steady state diffusion (equal solubilities)

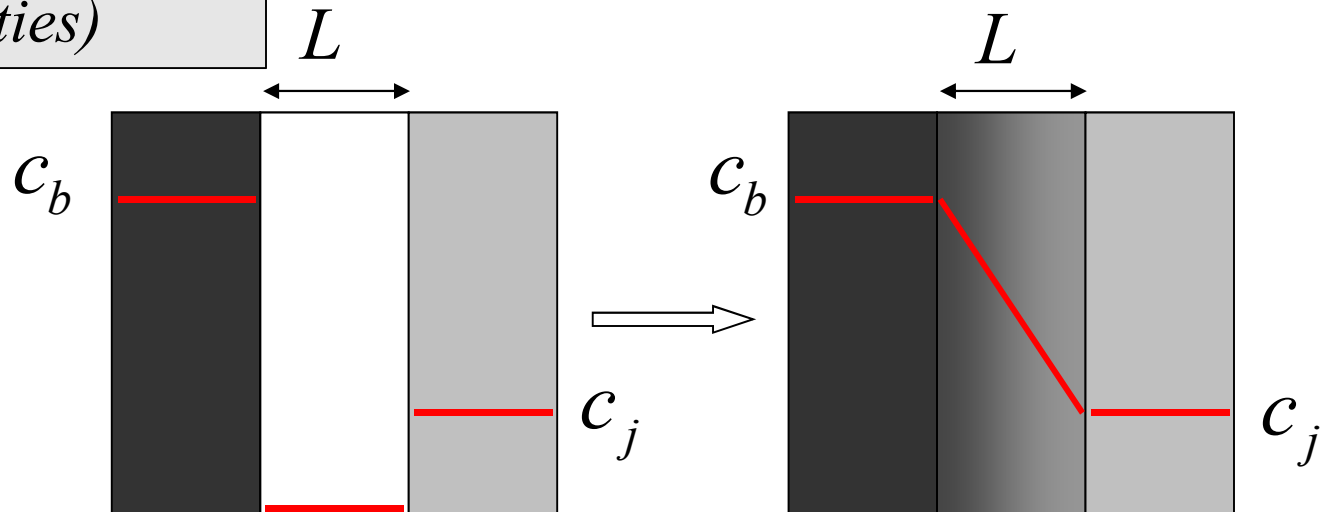
$$j_n = \text{const.}$$

$$\frac{\Delta c}{\Delta x} = \text{const.}$$

$$\frac{\Delta c}{\Delta x} = \frac{c_j - c_b}{L}$$

$$j_n = -D \frac{\Delta c}{L}$$

$$P_{erm} = \frac{j_n}{\Delta c} = \frac{D}{L}$$



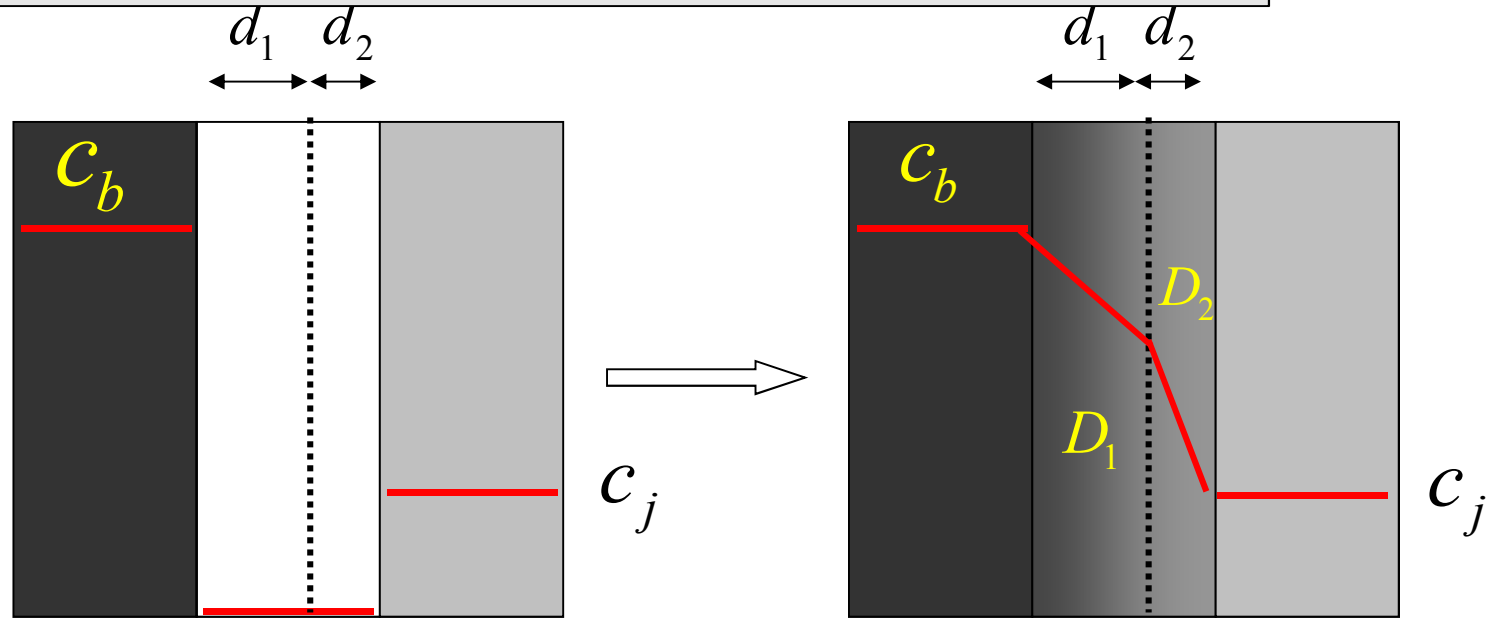
Initial conditions: $c(0, x) = 0$ if $0 < x < L$ és $c(0, L) = c_j$ $c(0, 0) = c_b$

Boundary conditions $c(t, 0) = c_b$ and $c(t, L) = c_j$

$$c(x) = -\frac{c_b - c_j}{L} x + c_b$$

Membran permeability: material current density due to unit concentration difference. Depends on the thickness of the membrane. It can be measured.

Steady state diffusion between phases



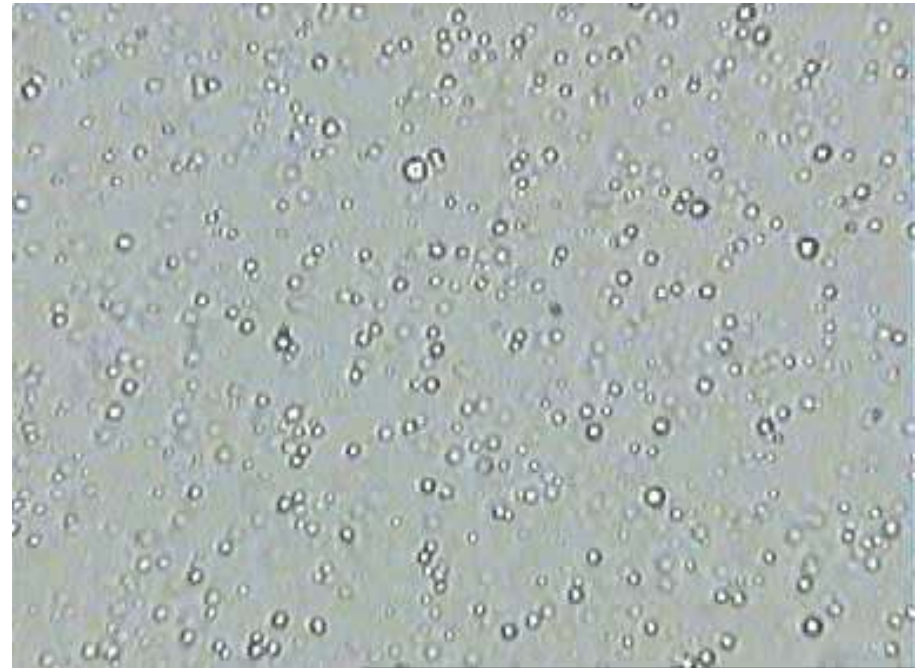
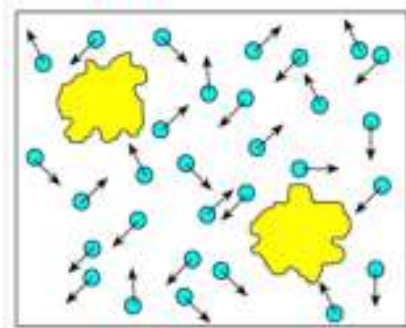
$$j_n = -D_1 \frac{\Delta c}{d_1} = -D_2 \frac{\Delta c}{d_2} = \text{const.} \quad \Rightarrow \quad D_1 > D_2$$

The **slope** of concentration – position dependence is inversionally proportional to the magnitude of diffusion coefficient.

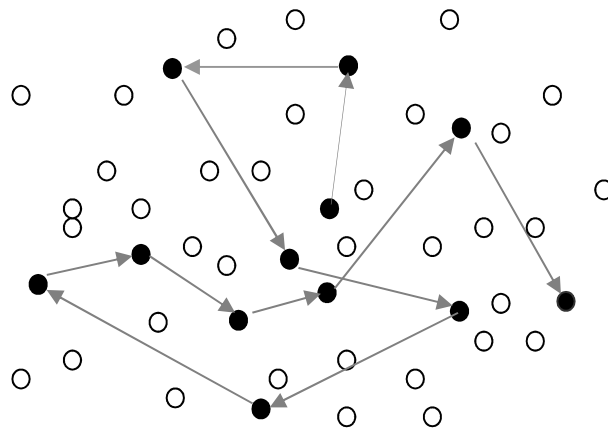
Microscopic manifestation of diffusion: Brownian movement



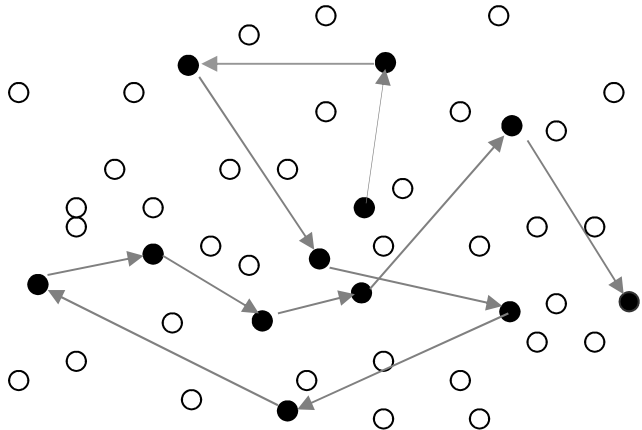
Robert Brown
(1773-1858)




Fat droplets in milk (size: 0.5 - 3 μm)



Molecular theory of diffusion: **random walk**

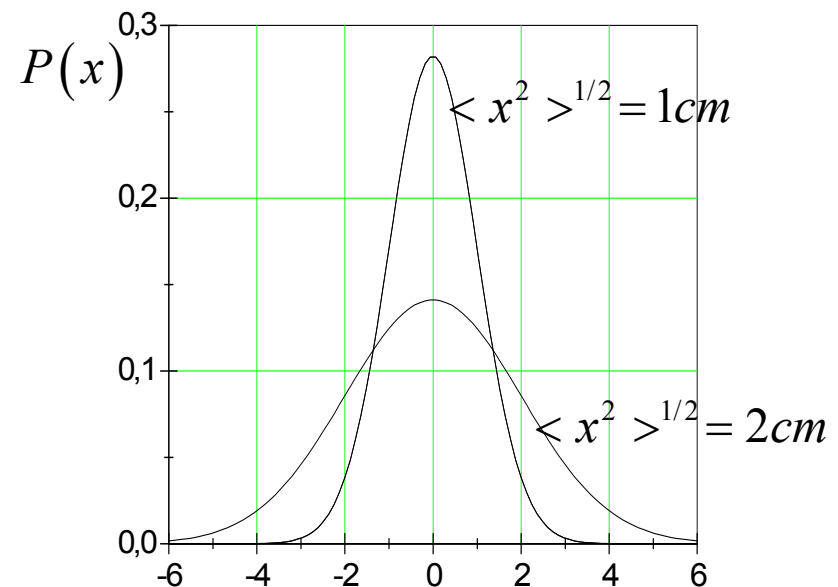


1 dimensional	$\langle x^2 \rangle = 2 D t$
2D	$\langle \sigma^2 \rangle = 4 D t$
3D	$\langle r^2 \rangle = 6 D t$

Brownian movement,  random walk

$$D = \frac{k_B T}{\xi} = \frac{k_B T}{6\pi\eta R}$$

Stokes-Einstein equation



Diffusion of ions

There is no individual diffusion coefficients of any ion!

$$j_i = -D_i \cdot \left(\frac{\Delta c_i}{\Delta x} + c_i \frac{z_i F}{RT} \frac{\Delta \psi}{\Delta x} \right) \quad \text{Nernst-Planck equation}$$

$$c_- = c_+ \quad \frac{\Delta c_-}{\Delta x} = \frac{\Delta c_+}{\Delta x} \quad j_+ = j_- \quad \leftarrow \text{Due to electroneutrality}$$

$$j_+ = -\frac{2D_+D_-}{D_+ + D_-} \cdot \frac{\Delta c_+}{\Delta x} = -D_{\pm} \cdot \frac{\Delta c_+}{\Delta x}$$



$$D_{\pm} = \frac{D_+D_- (c_+z_+^2 + c_-z_-^2)}{D_+c_+z_+^2 + D_-c_-z_-^2}$$

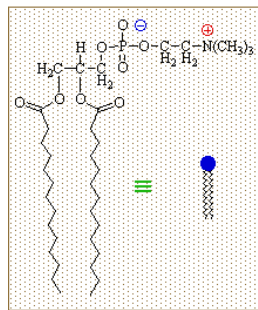
$$D_{\pm} = \frac{2}{\frac{1}{D_+} + \frac{1}{D_-}}$$



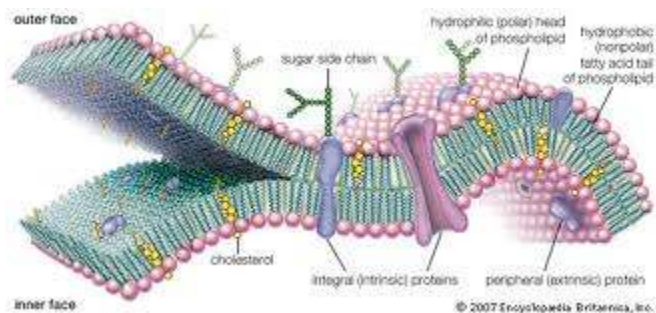
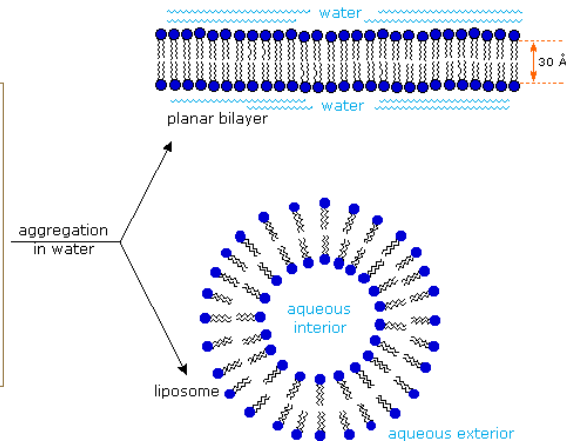
(1:1)
electrolite

Membranes

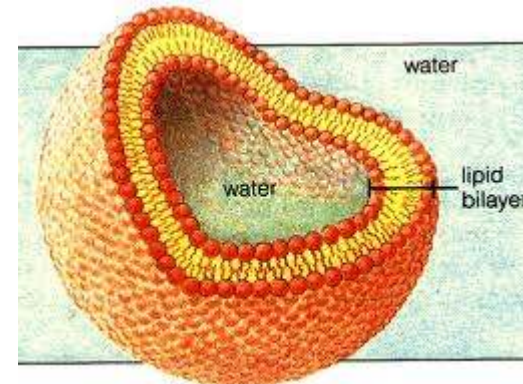
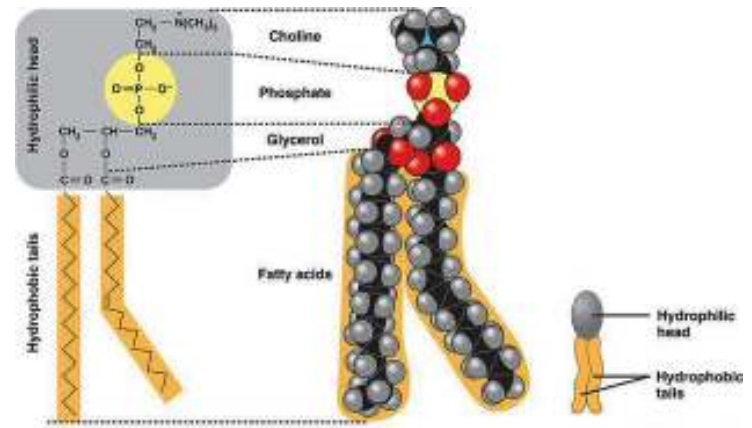
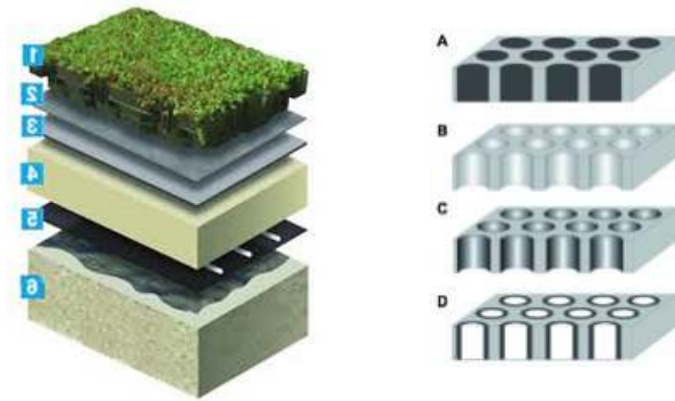
membranes \swarrow synthetic
 \searrow biological



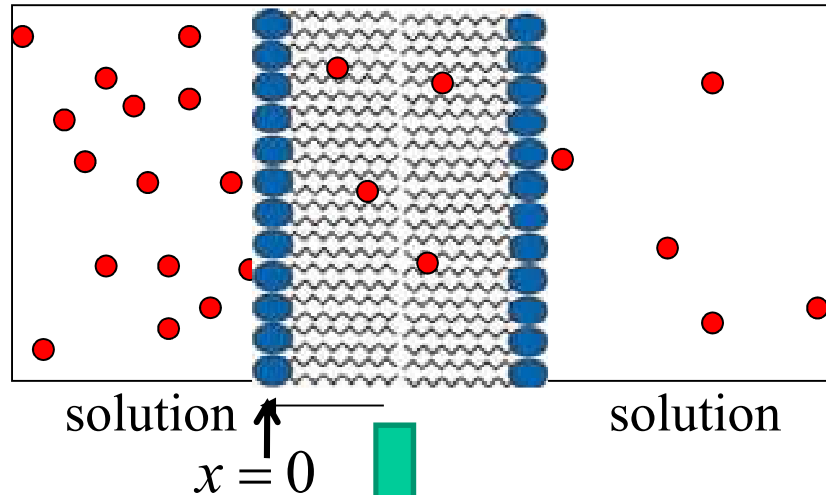
phospholipid



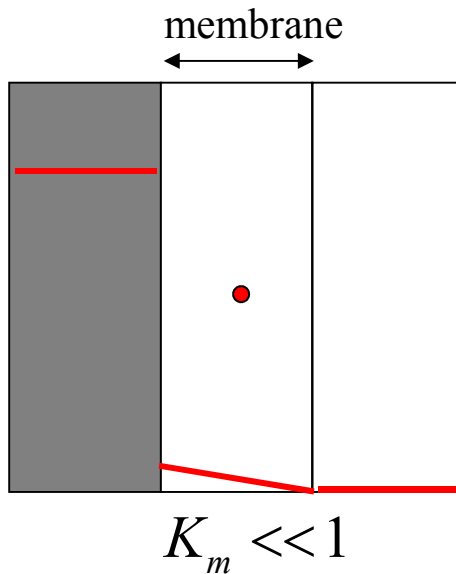
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Steady state diffusion and partition between phases.



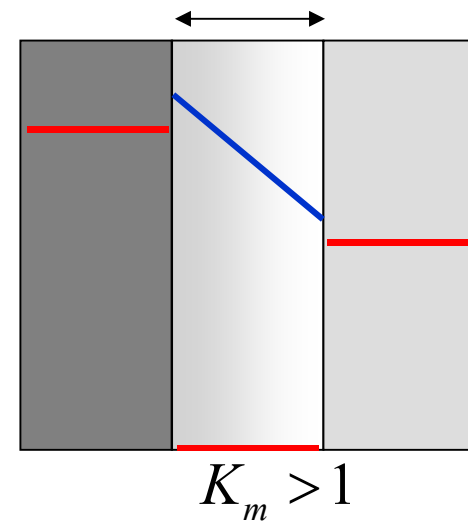
Different solubility K_m



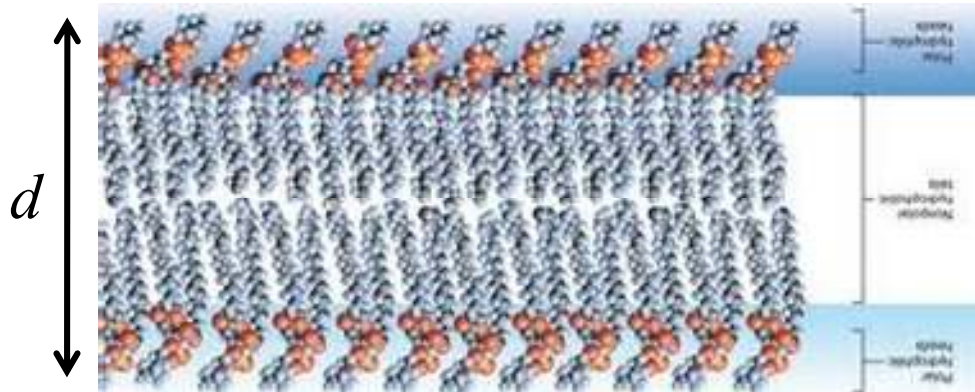
$$K_m = \frac{c_{dh}}{c_d} \text{ Partition coefficient}$$

$$c_m(x=0) = K_m \cdot c_o(x=0)$$

$$c(x) = -K_m \frac{c_b - c_j}{d} x + K_m \cdot c_b$$



Membrane permeability: P_{erm}

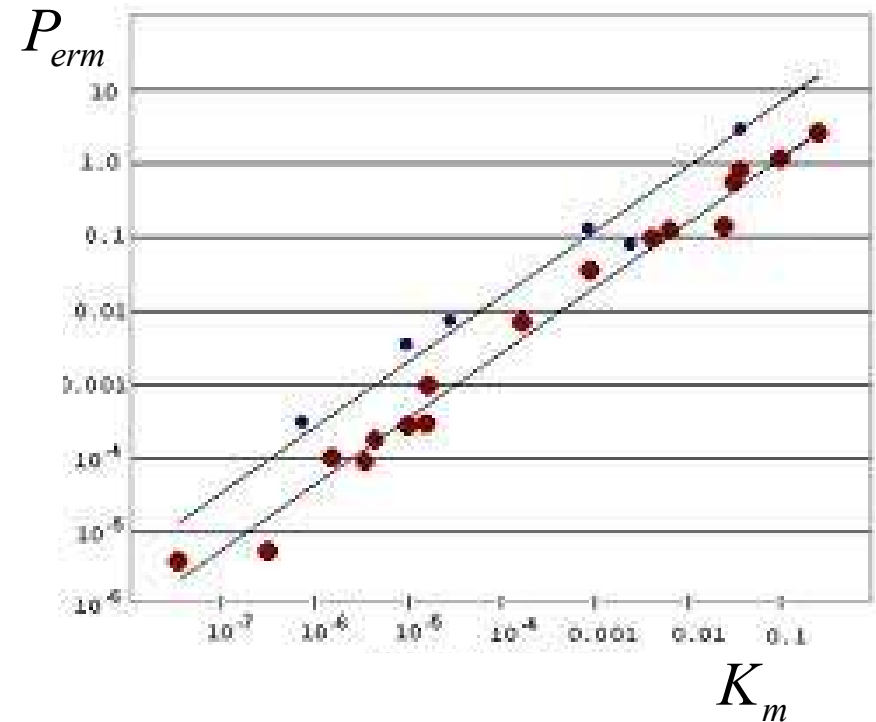


$$j_n = -D \frac{\Delta c}{\Delta x} \quad \frac{\Delta c}{\Delta x} = \frac{K_m (c_j - c_b)}{d} = -\frac{K_m \Delta c}{d}$$

$$P_{erm} = \frac{j_n}{\Delta c} = \frac{K_m D}{d}$$

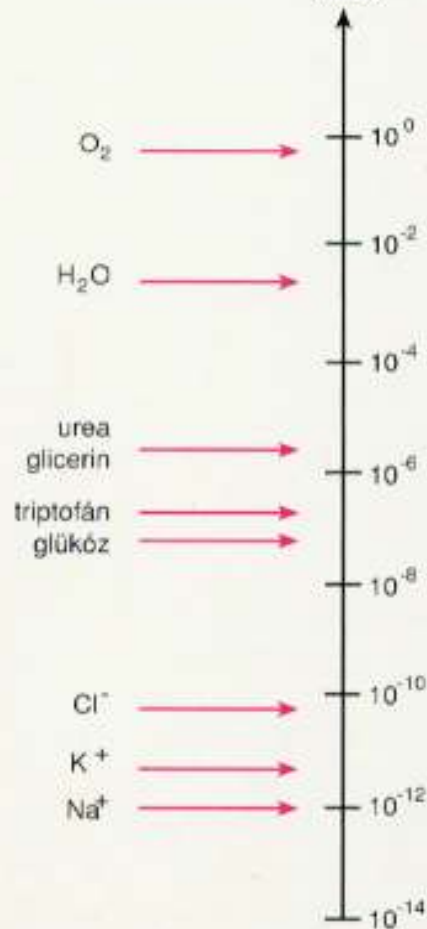
K_m : partition coefficient

$$P_{erm} \propto K_m \cdot D$$



Dependence of permeability on the partition coefficient of solute.

Permeability / $cm \cdot s^{-1}$



$$P_{erm} = \frac{j_n}{\Delta c} = \frac{K_m D}{d}$$

$$P_{erm} \propto D$$

In water at 25 °C.

material	Molecular mass	R/nm	$10^9 D / m^2 s^{-1}$
water	18	0.15	2.0
oxygen	32	0.2	2.1
carbamide	60	0.4	1.38
glucose	180	0.5	0.7
hemoglobin	68000	3.1	0.069
collagen	345000	31	0.007
virus		50	5.0 $cm^2 s^{-1}$
bacteria		1000	0.5 $cm^2 s^{-1}$
cell		10000	0.05 $cm^2 s^{-1}$

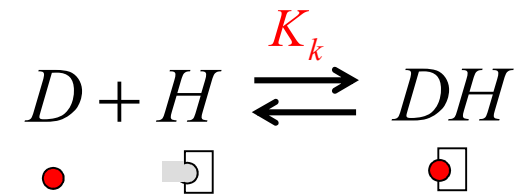
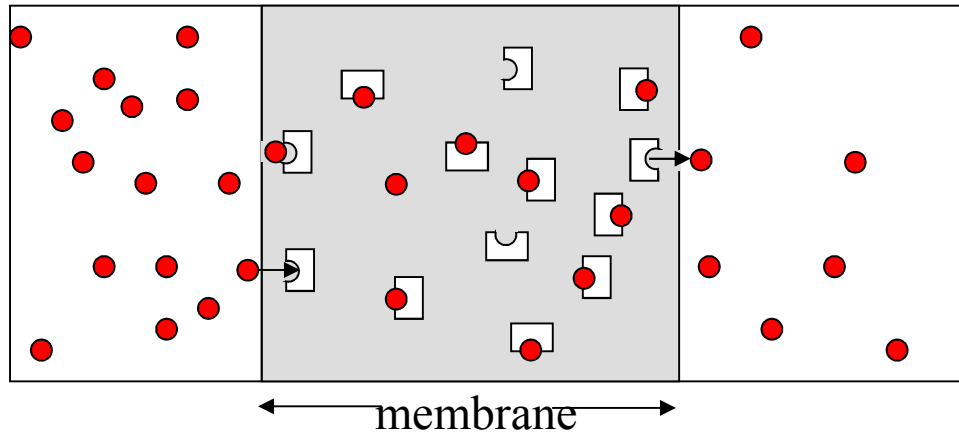
$$D = \frac{k_B T}{6\pi\eta R}$$

$$D\eta = \frac{k_B T}{6\pi} \cdot \frac{1}{R}$$

Stokes –Einstein formula

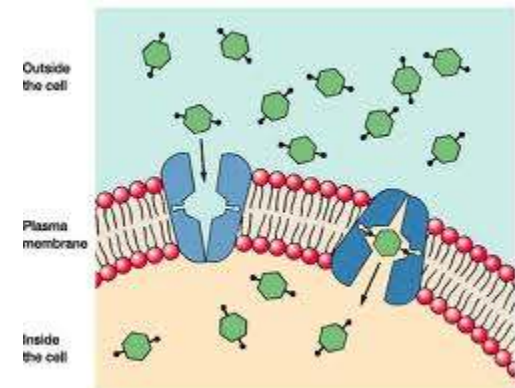
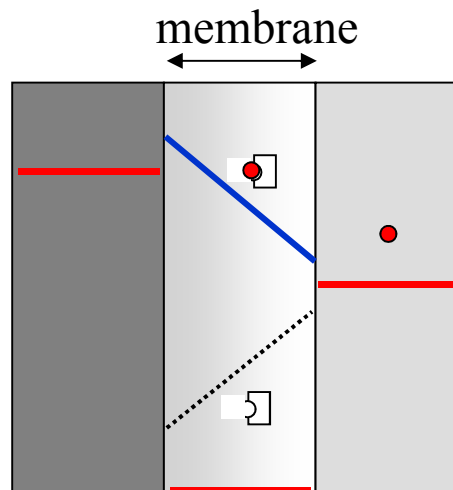
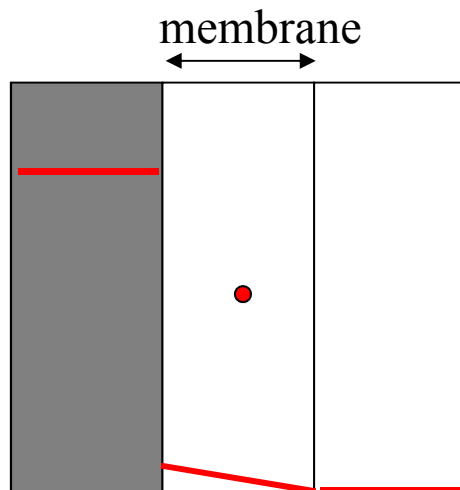
Facilitate diffusion

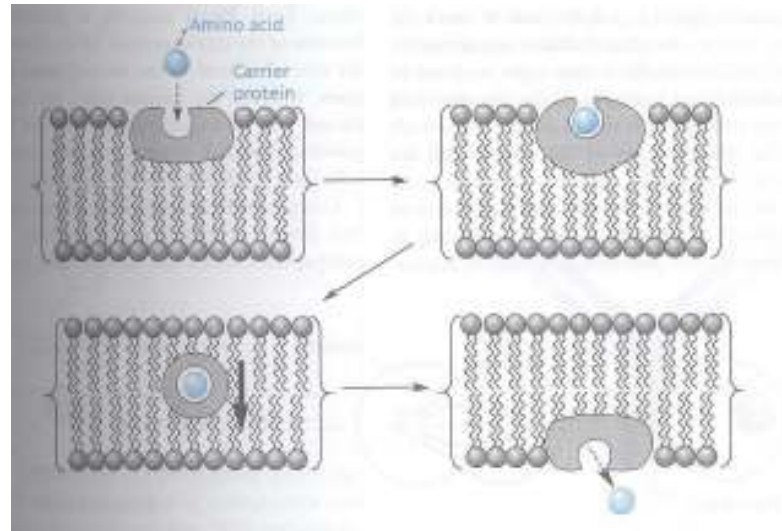
• molecule □ complexing ◻ molecule-complex



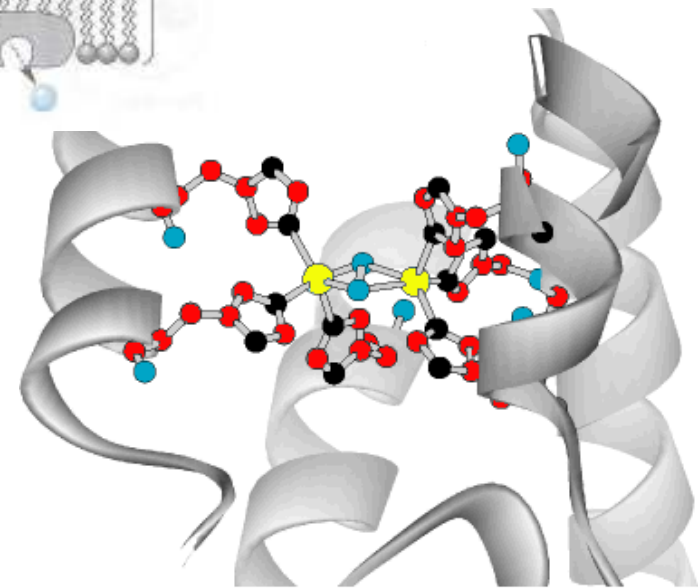
$$K_k = \frac{[DH]}{[D][H]}$$

$$c_{dh}(x=0) = K_k \cdot c_d(x=0) \cdot c_h(x=0)$$





3-ketoacyl-(acyl-carrier-protein)

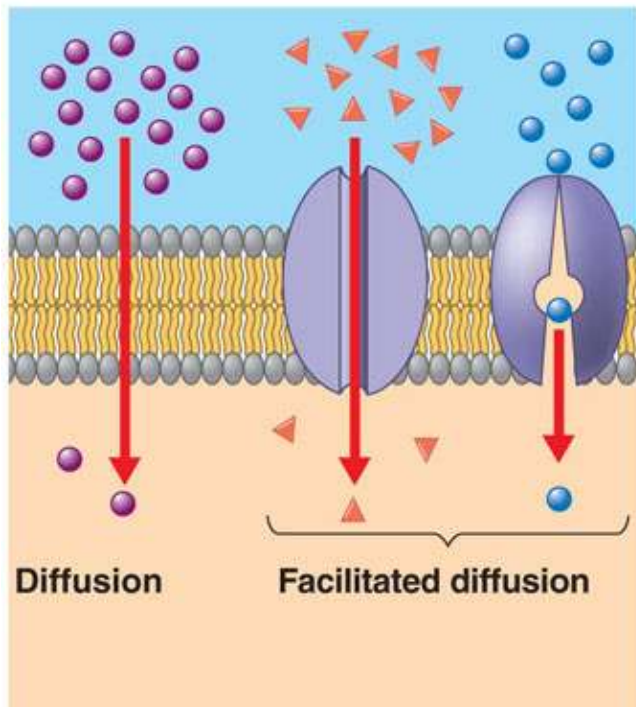


Key:
 ● carbon ● oxygen ● copper ● nitrogen

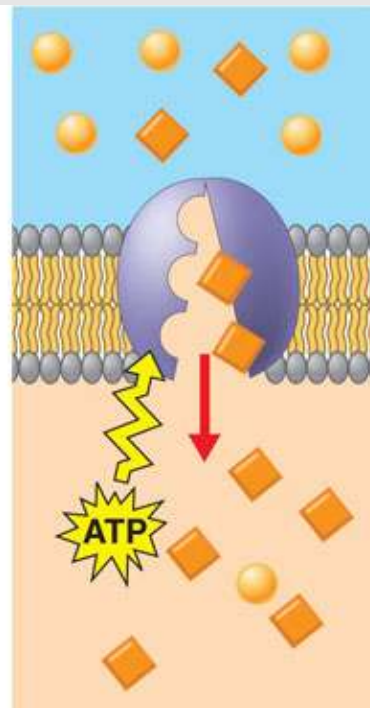
active place of oxyhemocyanin
 protein that carries oxygen

Active and passive transport phenomena

Passive transport



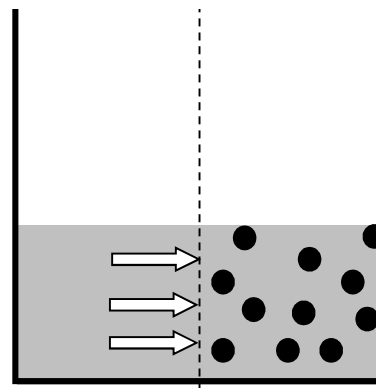
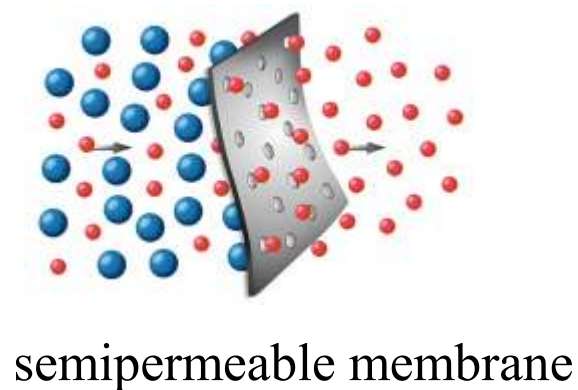
Active transport



← Opposit direction of Fick's law.
(sodium – potassium pump)

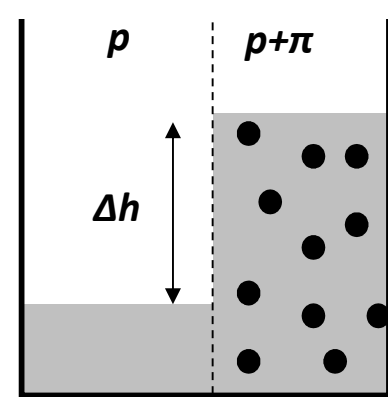
According to Fick's laws.

Convective and conductive mass transport in solutions:
osmosis: diffusion-driven process between two compartments separated by semipermeable membrane (solvent diffusion).



osmosis

$$\Delta h(t) \rightarrow \Delta h_{\max}$$



Osmosis: one-directional solvent transport by diffusion.

For dilute solutions

$$\pi_{id}(x_2) = \frac{RT}{V_1} x_2$$

$$\pi_{id} = \frac{RT}{M_2} c_2$$

molar volume of solvent

mole fraction of solute

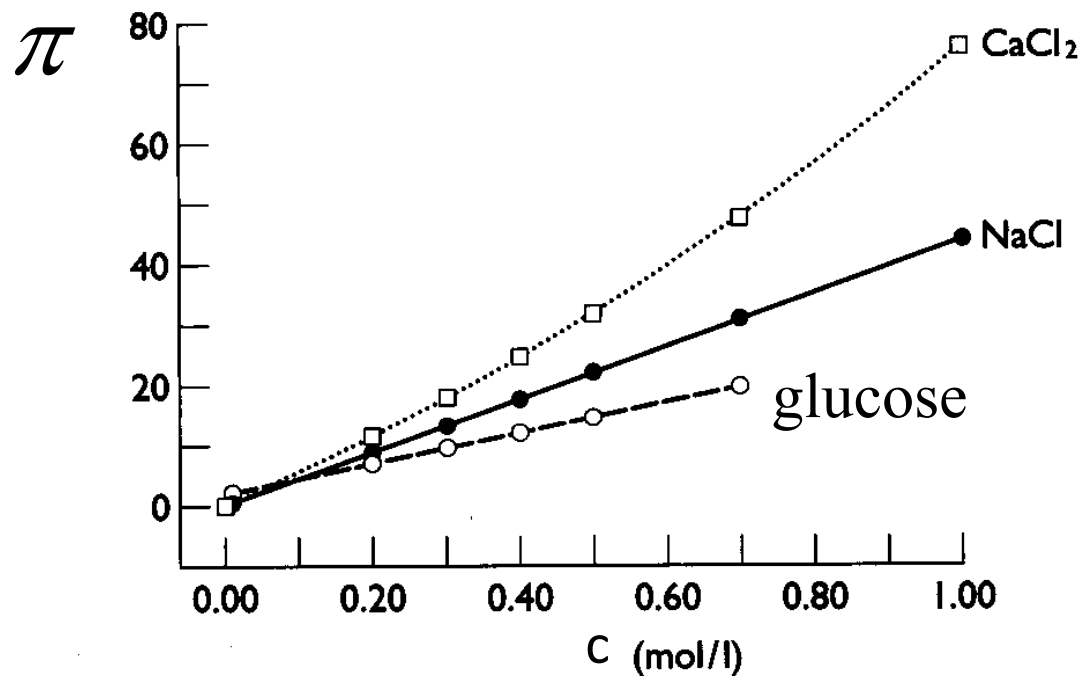
Osmosis: **colligative property**

$$n = n_0 \alpha \nu + n_0 (1 - \alpha) = n_0 [1 + \alpha(\nu - 1)]$$

$$\pi = \frac{RT}{M_2} c_2 \cdot i$$

$$i = [1 + \alpha(\nu - 1)]$$

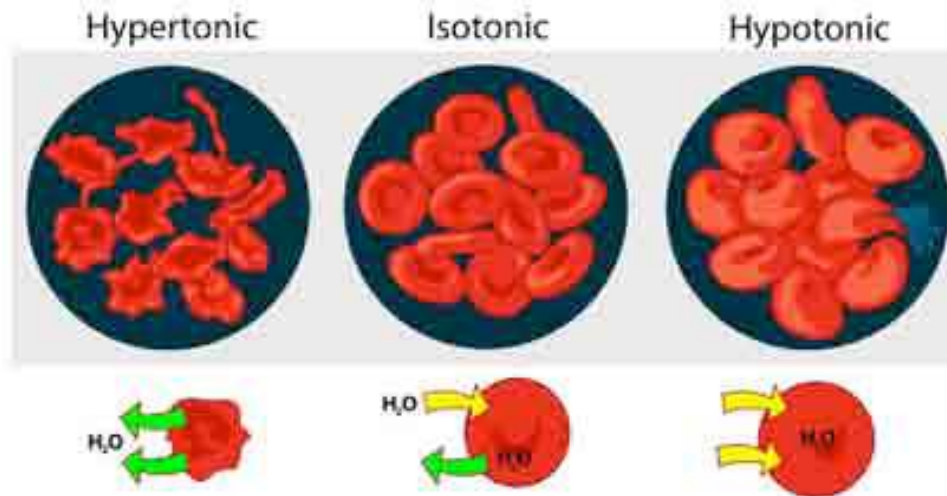
degree of dissociation



Isotonic solution: osmotic pressure inside and outside are equal

Hypertonic solution: water ← cell

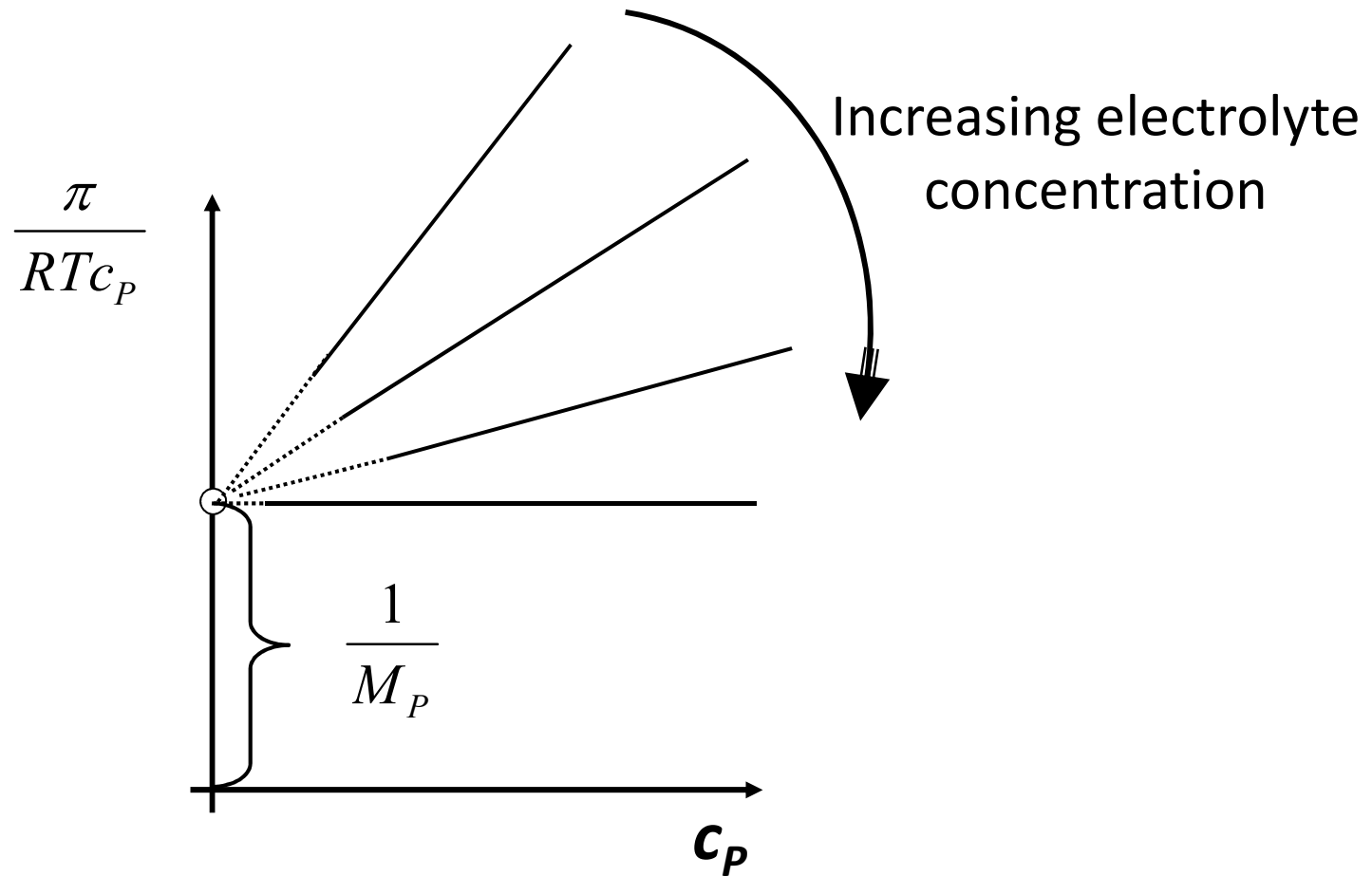
Hypotonic solution: water → cell



Isotonic solution
with blood and cell
liquid

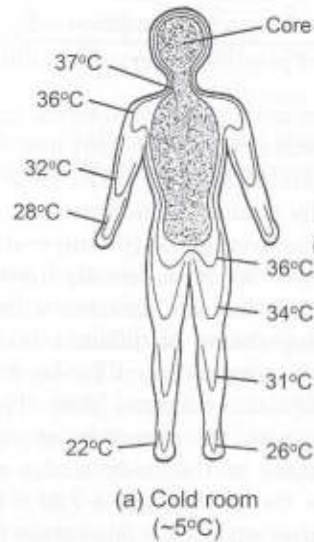
3.8 m%-os Na-citrate solution,
5.5 m%-os glucose solution,
0.87 m%-os NaCl solution.

Concentration dependence of osmotic pressure of polyelectrolyte solution



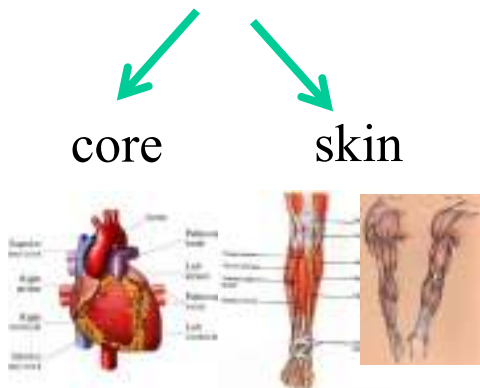
Transport of internal energy (**heat flow**).

Source of body heat



<i>brain</i>	25%
<i>heart</i>	15%
<i>muscle</i>	25%
<i>viscera</i>	25%
<i>kidney</i>	6%
<i>skin</i>	4%

Temperature distribution in body is not uniform.



$$Q_{loss} = Q_{radiation} + Q_{convective} + Q_{conductive} + Q_{evaporation} + Q_{respiration}$$

↑
Loss body heat

54-60 %

25 %

7 %

14 %

*Energy flux
(unit surface area)*

Loss of body heat by radiation



Wien's law: $R = \varepsilon \sigma T^4$ ε : emission

Stefan-Boltzmann const.: $\sigma = 5,67 \cdot 10^{-8} \text{ W} / \text{m}^2 \text{K}^4$

$$-\frac{\Delta Q_{rad}}{\Delta t} = R \cdot A_s = \varepsilon \sigma T^4 \cdot A_s$$

$A_s = 1,85 \text{ m}^2$ Average surface area

$\varepsilon \cong 1$ for human skin

$$\frac{\Delta Q_{sugározó}}{\Delta t} = \frac{\Delta Q}{\Delta t} \Big|_{loss} - \frac{\Delta Q}{\Delta t} \Big|_{harvest}$$

$$R = \varepsilon \sigma \left(T_{body}^4 - T_{environment}^4 \right)$$

$$\varepsilon_1 = \varepsilon_2 = \varepsilon$$

material	emission
human skin	0.95 – 0.99
wood	0.99
concrete	0.95
brick	0.92



Convective heat flow (1)

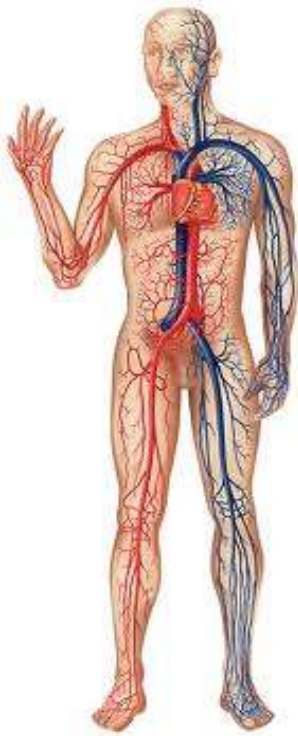
$$-\frac{1}{A_s} \frac{\Delta Q_{conv.}}{\Delta t} = h_c \cdot (T_{skin} - T_{air})$$

h_c : convective heat transfer coefficient

$W / m^2 C^o$

Wind speed [m/s]	$h_c [W / m^2 C^o]$
0,1	2,6
0,6	6,4
2,0	11,7
4,0	16,6

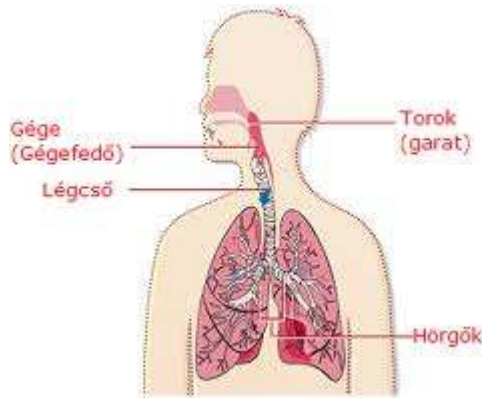
In wind: $h_c = 10,45 - v + 10v^{1/2}$ v : speed of wind in m/sec
(crude approximation)



Convection inside body (2)

(between different parts of body and blood)

$$-\frac{1}{A_s} \frac{\Delta Q_{\text{bloodflow}}}{\Delta t} = h_c \cdot (T_{\text{blood}} - T_{\text{bodypart}})$$



Heat loss by evaporation (1) (respiration)

Inhalation and exhalation volume: 500 ml

Frequency of inhalation and exhalation: 12 – 14 /min



$$I_{air} = \frac{\Delta V_l}{\Delta t} \approx 0,1 \quad l \cdot s^{-1}$$

$$-\frac{\Delta Q}{\Delta t} = \rho_l c_{p,l} (T_{ex} - T_{in}) \frac{\Delta V_{air}}{\Delta t}$$



V_{sweating}

Heat loss by sweating (2)

Heat of evaporation of
water: $\Delta h_{\text{parolgas}} = 2,25 \text{ kJ} / \text{g}$

$$-\frac{\Delta Q}{\Delta t} = \Delta h_{\text{evap}} \cdot \left(\rho_{\text{water}}^{\text{expired}} - \rho_{\text{water}}^{\text{inspired}} \right) \frac{\Delta V_{\text{water}}}{\Delta t}$$

Conductive heat flow: **Fourier laws**

$$j_Q = -k_T \frac{\Delta T}{\Delta x}$$

$$\frac{\Delta T}{\Delta t} = \alpha \cdot \text{curvature of } T(x) \text{ function}$$

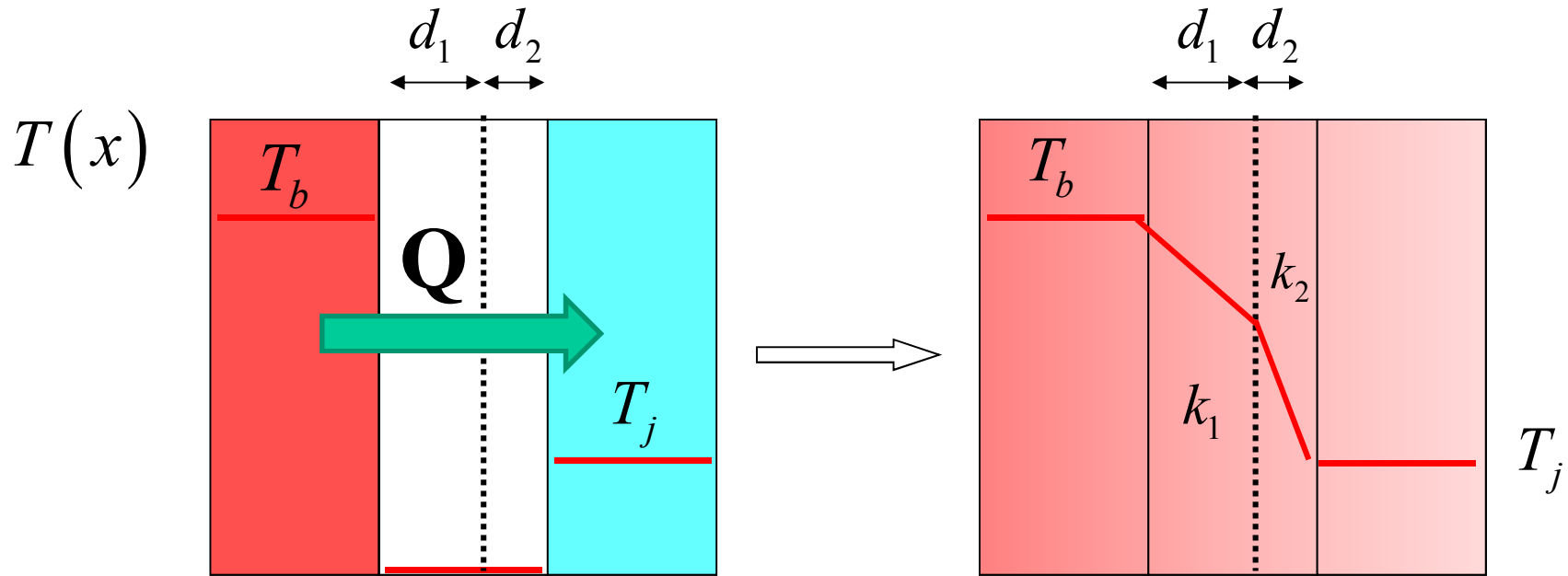
$$\alpha = \frac{k_T}{\rho \cdot C_p}$$

$$\frac{dT}{dt} = \alpha \frac{d^2 T}{dx^2}$$

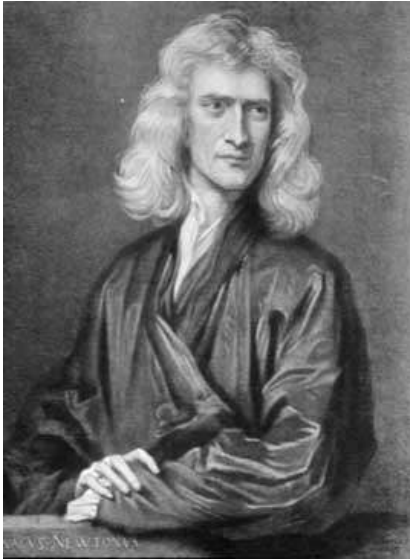
anyag	T/K	$k_T / Wm^{-1}K^{-1}$	α / m^2s^{-1}	$c_p / kJkg^{-1}K^{-1}$
levegő	300	0,025	$2,11 \cdot 10^{-5}$	1,006
víz	300	0,609	$1,5 \cdot 10^{-7}$	4,186
zsír	298	0,21	$0,69 \cdot 10^{-7}$	3,258
vér	298	0,642	$1,76 \cdot 10^{-7}$	3,889
bőr	310	0,442	$1,19 \cdot 10^{-7}$	3,471

$$\frac{\Delta Q_{\text{conductive}}}{\Delta t} = -k_T \cdot A_s \cdot \frac{\Delta T}{\Delta x}$$

Steady state heat conduction between phases



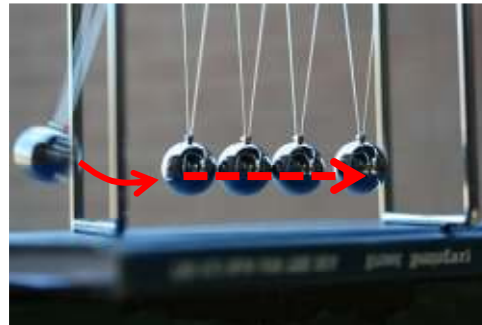
$$j_U = -k_1 \frac{\Delta T}{d_1} = -k_2 \frac{\Delta T}{d_2} = \text{const.} \quad \Rightarrow \quad k_1 > k_2$$



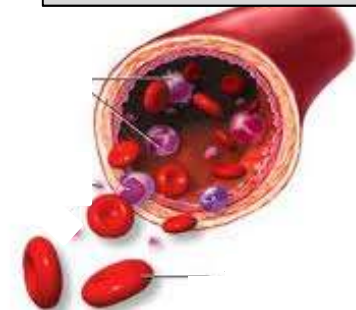
Sir Isaac Newton (1642-1727)

RHEOLOGY

(*conductive transport of **momentum***)



Hemorheology



What is Rheology?

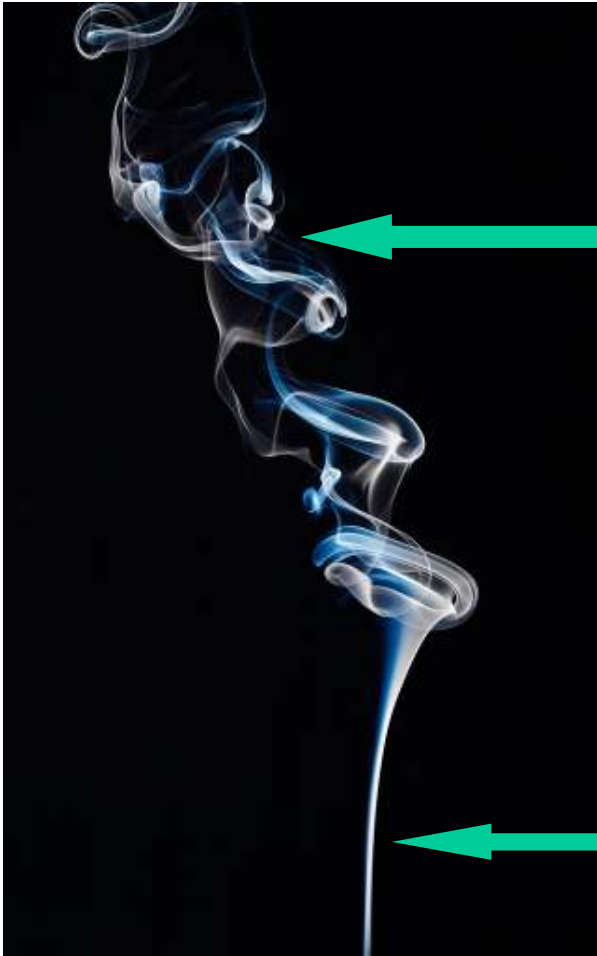
Knowledge of physical properties of fluids associated with their **deformation and flow**.

Rheology is the field of science that deals with viscosity.

The science of **deformation and flow** of matter. Rheological descriptions usually refer to the **property of viscosity** and departures from Newton's law of viscosity.

Rheology, a branch of mechanics, is the study of those properties of materials which determine their **response to mechanical force**.

Laminar and turbulent flow



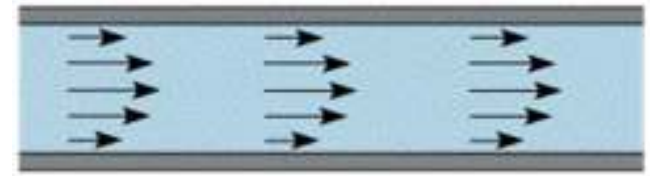
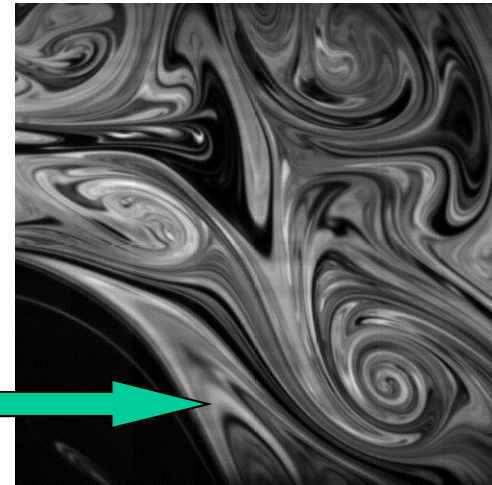
turbulent

$$R_e = \frac{vd\rho}{\eta}$$

$$v_{kr} = R_e \cdot \frac{\eta}{\rho \cdot d}$$

laminar

$$R_e < 2100(?)$$



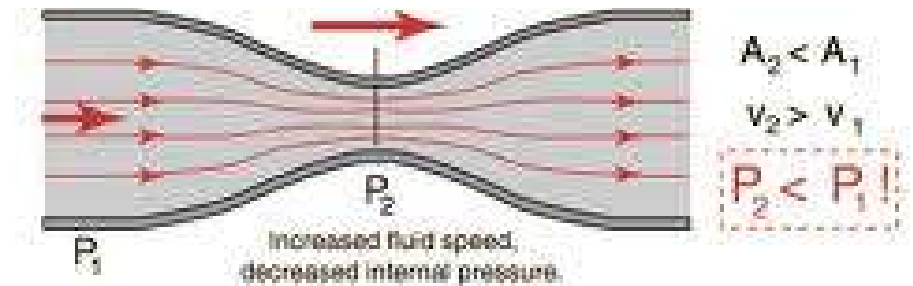
Flow

laminar,
turbulent,
compressible,
incompressible,
„dry”,
viscous,
steady,
pulsatile,
rotary.



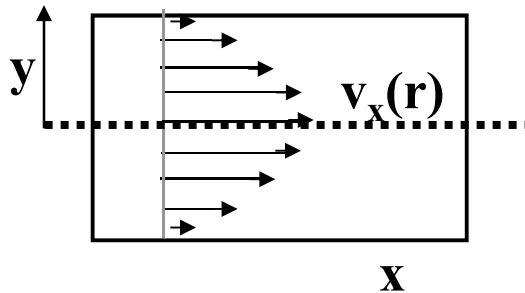
Bernoulli's law

$$p + \frac{1}{2} \rho v_x^2 + \rho gh = konst.$$



The blood flow in the circulation system is laminar except the blood forced out from the heart (turbulent).

Foundation of rheology: **Newton's law**



$$j_i = -\eta \frac{\Delta v_x}{\Delta y}$$

*Relationship between
the momentum flux
and velocity gradient.*



$$\tau = \eta \frac{\Delta v_x}{\Delta y}$$

*Relationship between the
shear stress and velocity
gradient*

Shear stress:

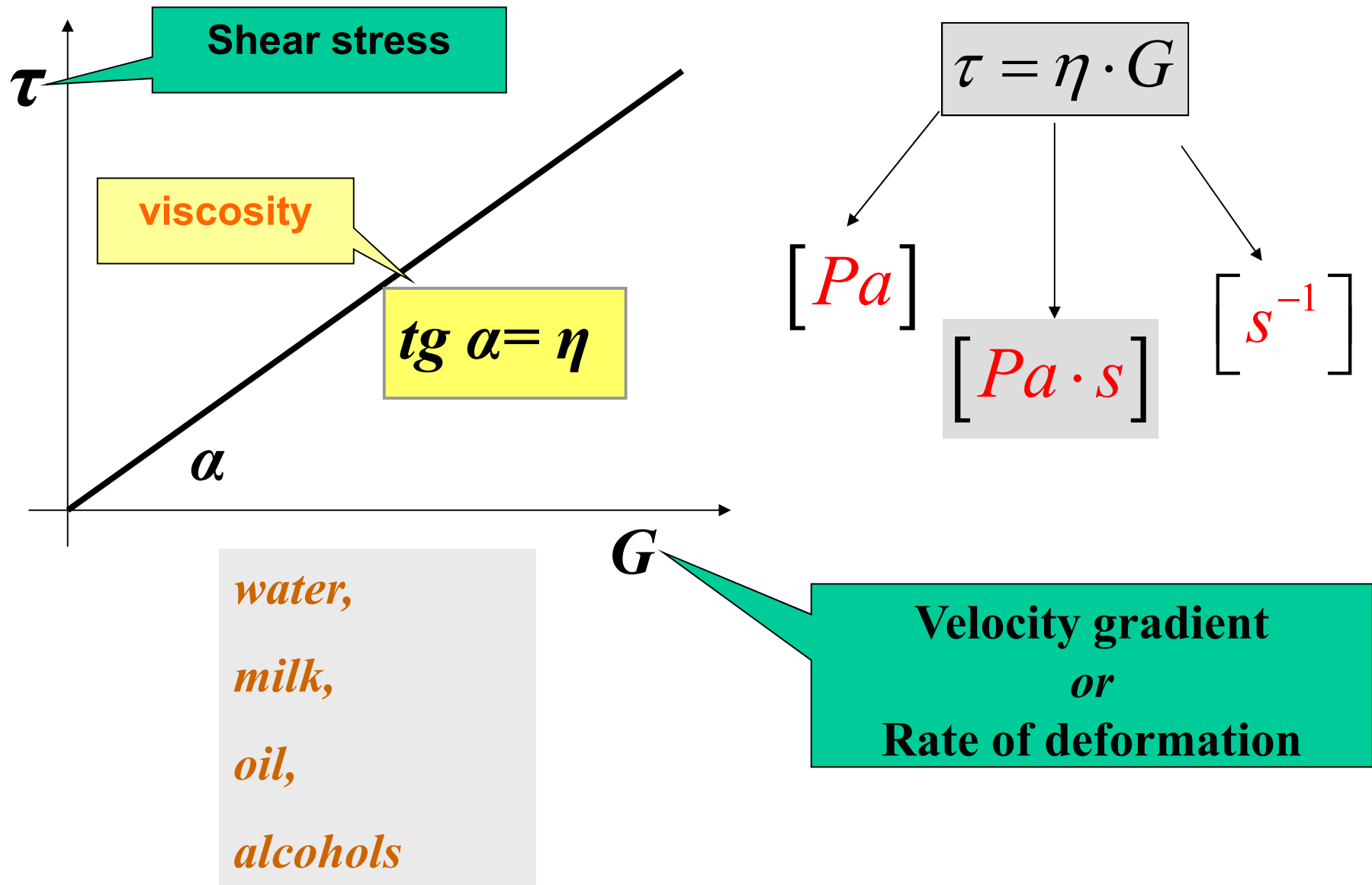
$$\tau = \frac{F}{A_S}$$



Velocity gradient:

$$G = \frac{\Delta v_x}{\Delta y} = \frac{\Delta v_x}{r}$$

Flow curve of a newtonian liquid

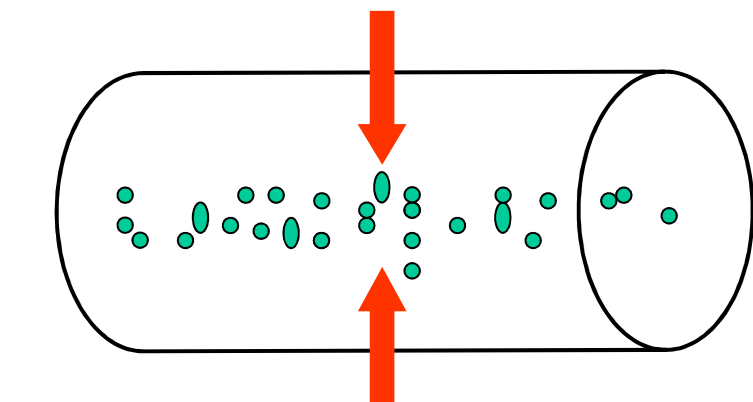
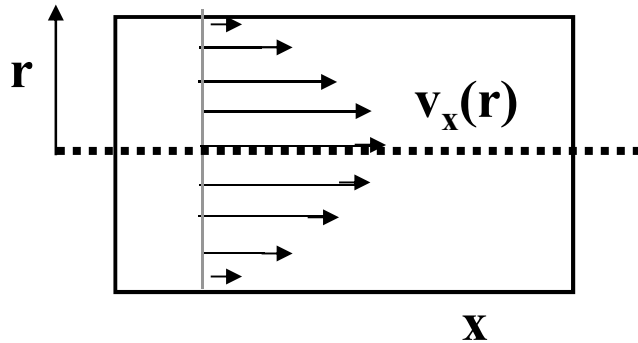


liquid	T/ °C	viscosity /$mPa \cdot s$
water	20	1,0
glycerol	20	1500
n-pentane	20	0,23

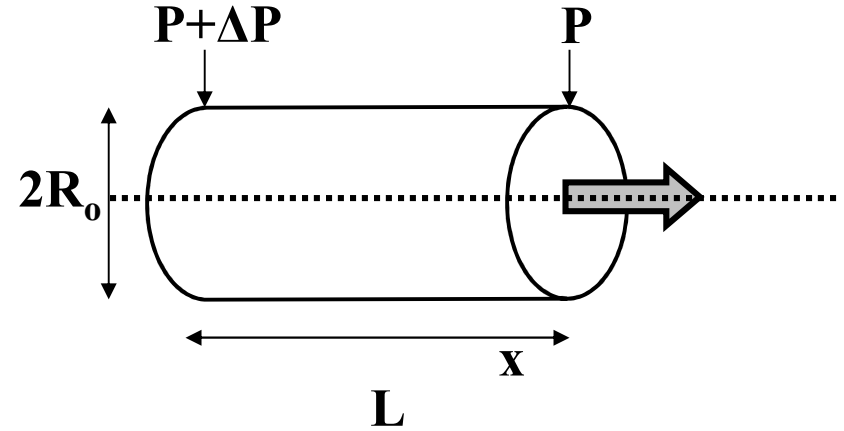
Bio-liquid	T/ °C	viscosity /$mPa \cdot s$
blood	37	4 (non newtonian)
Blood plasma	37	1,5
tear	37	0,73 – 0,97
air	18	0,018
cerebrospinal fluid	20	1,02

Flow of Newtonian liquid in tube or capillary

Parabolic velocity profile



$$p + \frac{1}{2} \rho v_x^2 + \rho gh = \text{const} \quad \text{Bernoulli's law}$$

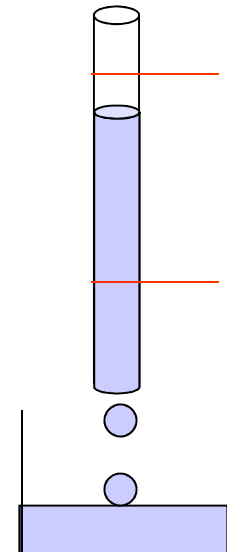


$$v_z(r) = \frac{\Delta P R_0^2}{4L\eta} \cdot \left(1 - \frac{r^2}{R_0^2} \right)$$

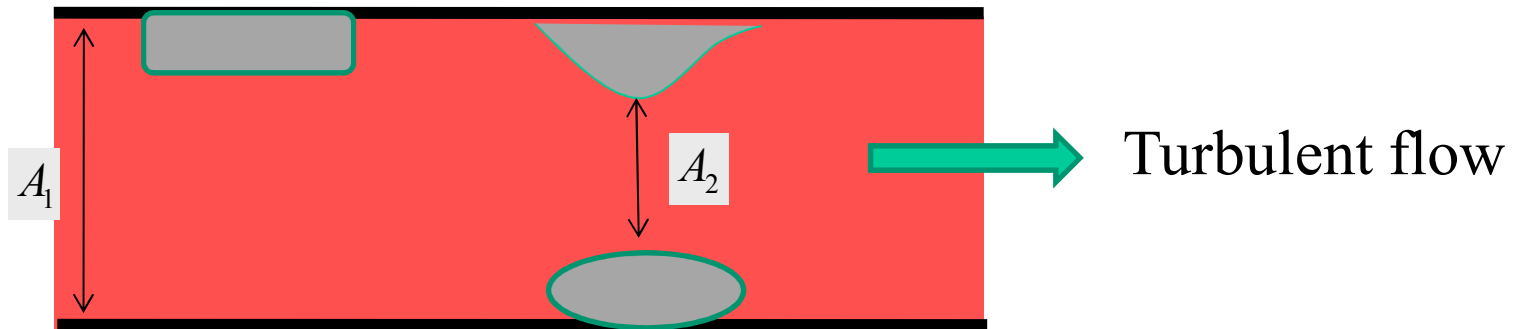
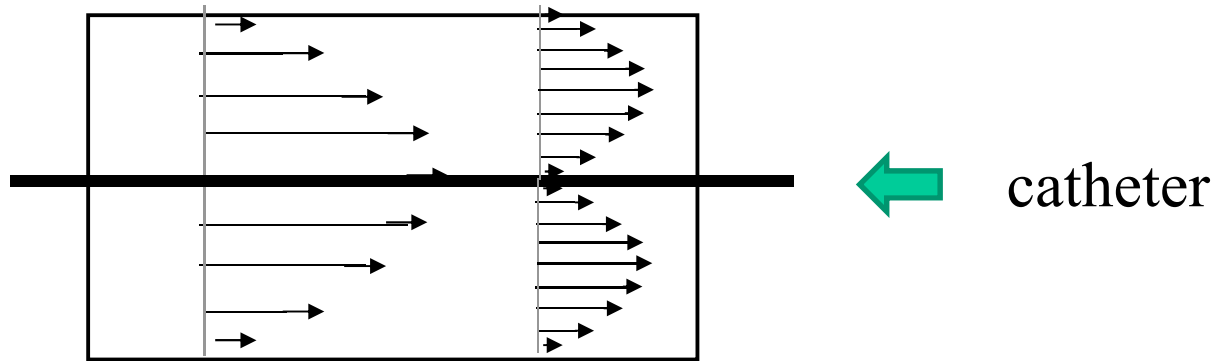
Hagen-Poiseuille's law

$$I_V = \frac{\pi \cdot R_o^4}{8\eta} \cdot \frac{\Delta P}{L}$$

Volume current

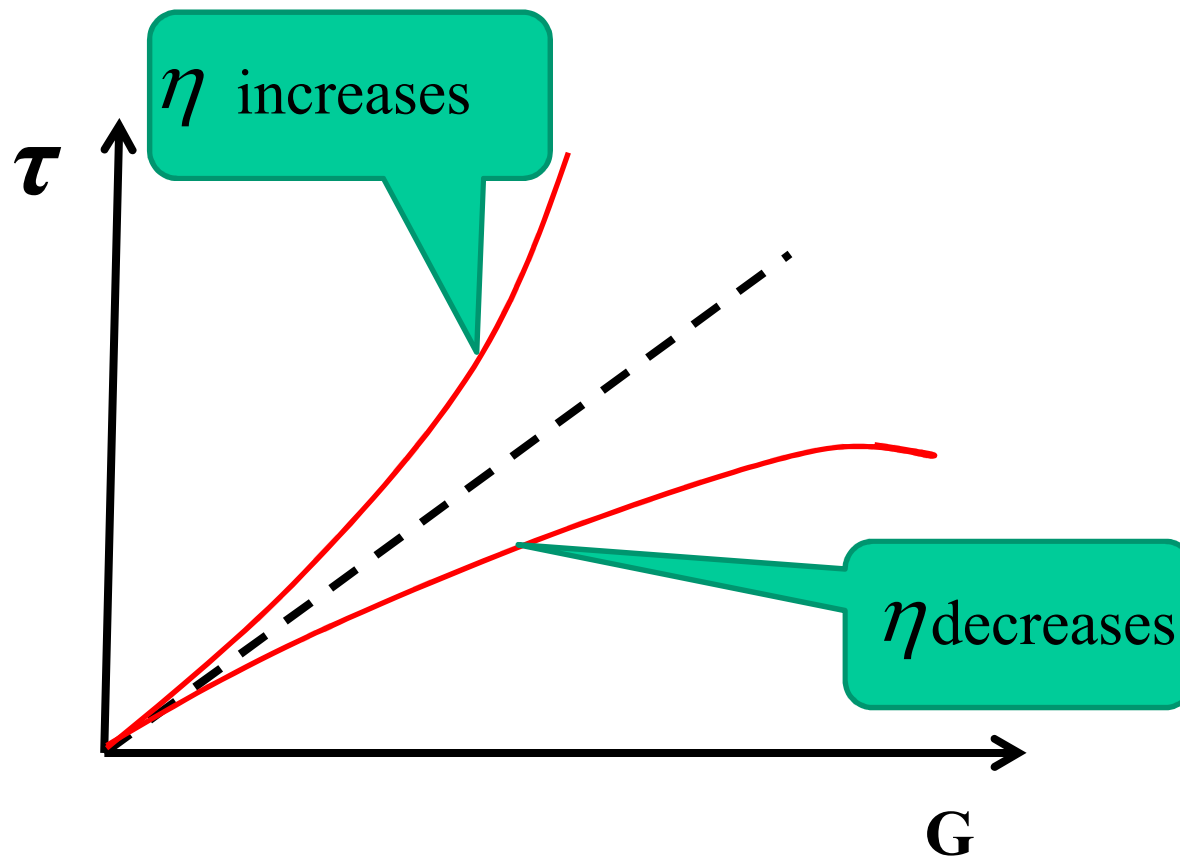


Velocity profile modified by catheter



Non-Newtonian liquids

- Viscosity depends on the shear rate.



Blood circulation



$$I_V = \frac{\pi \cdot R_o^4}{8\eta L} \cdot \Delta P = \frac{1}{R_{res}} \cdot \Delta P$$

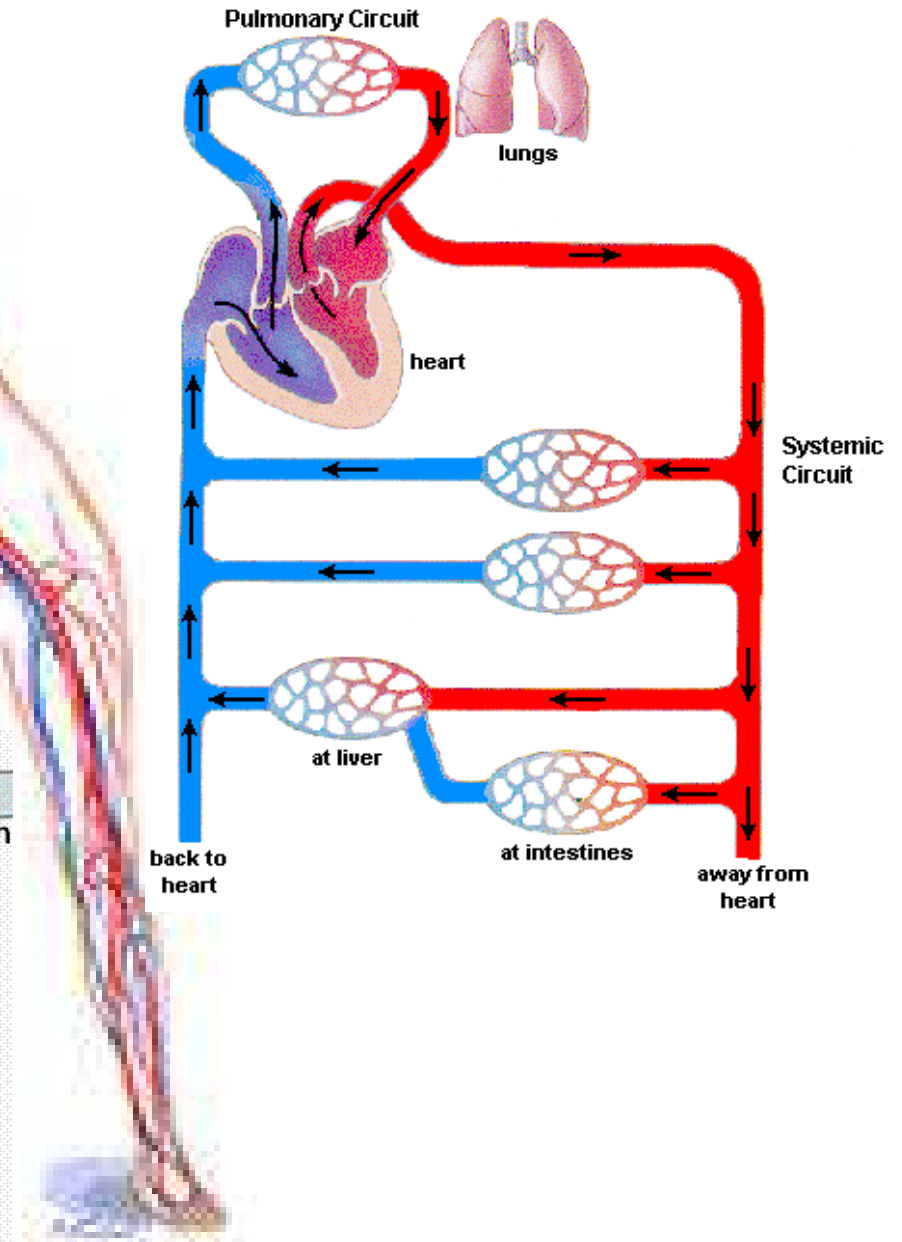
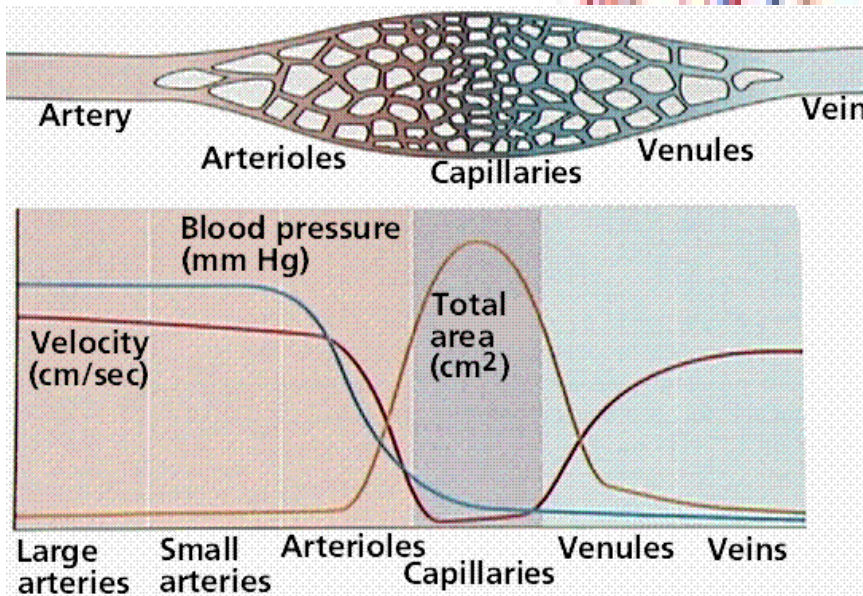
$$R_{res} (serial) = \sum_i R_{res,i}$$

$$R_{res} (parallel) = \sum_i \frac{1}{R_{res,i}}$$

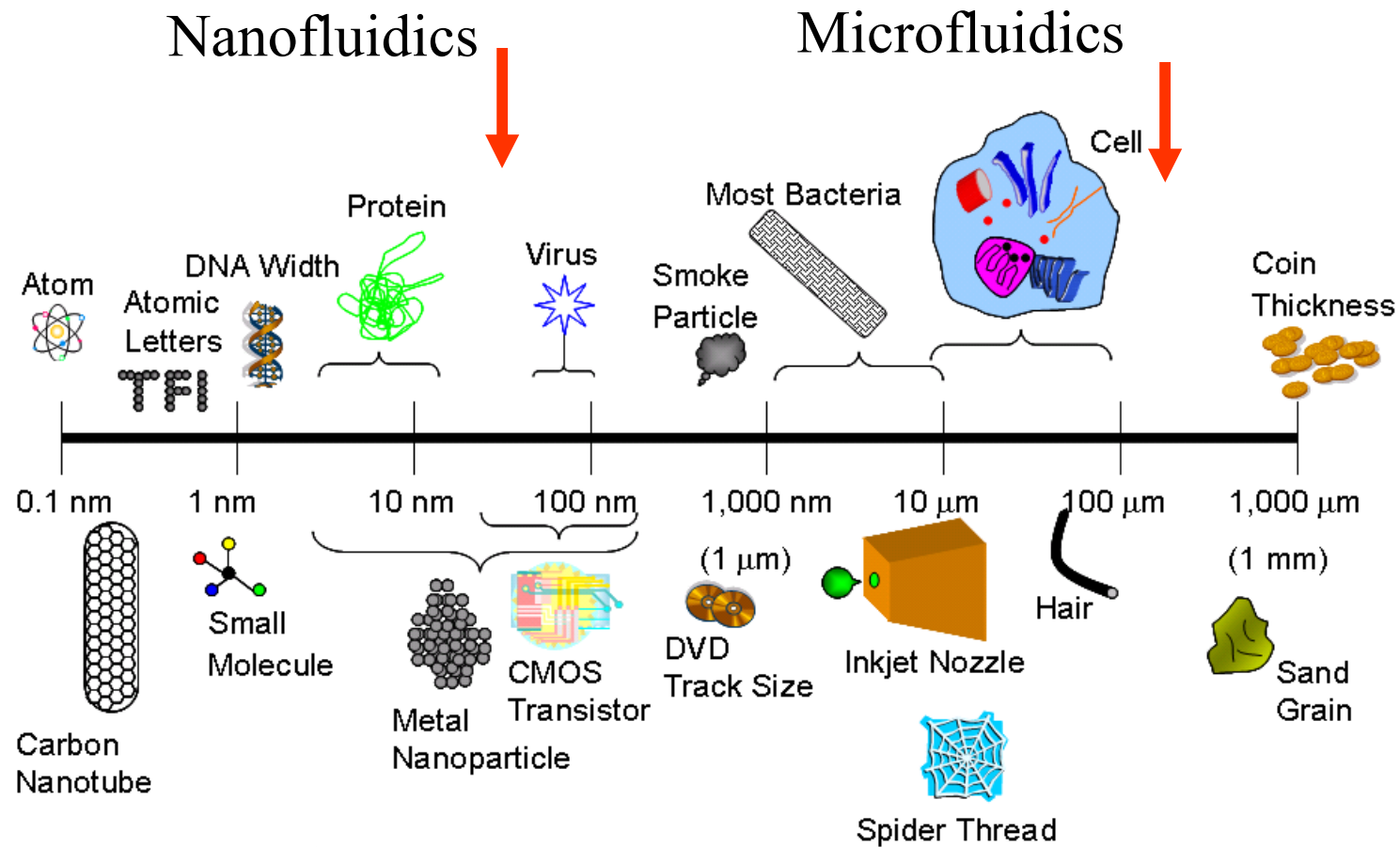
	diameter cm	length cm	Branching points	Flow velocity. cm/s
aorta	2,4	40	1	23
artery	0,4	15	160	5
capillary	0,0007	0,07	$1,2 \cdot 10^{10}$	0,022
vein	0,5	15	200	2,5

Nature Uses Microfluidics!

Pump, valves,
manifold,
functional “chips”,
reagents



Microfluidics compared to some important objects



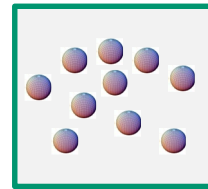
Viscosity of dilute suspensions

Newtonian flow behaviour,

Einstein-law



$$[\eta] = 2.5\Phi$$



$$\eta = \eta_o (1 + 2.5\Phi)$$

Volume
fraction

Stokes-Einstein law:

$$D = \frac{k_B T}{6\pi\eta a_r}$$

