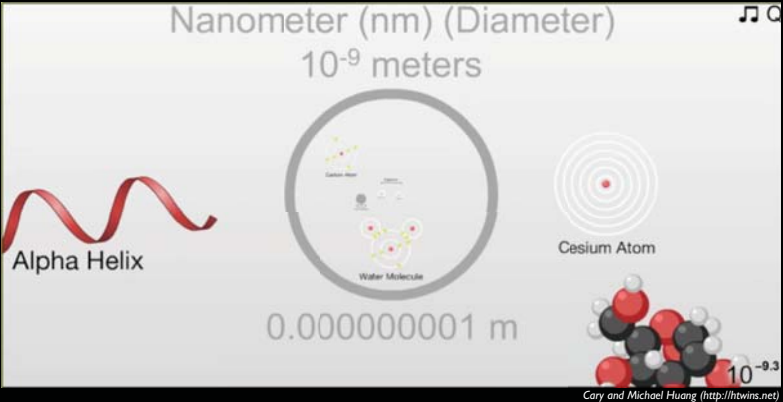


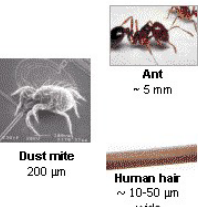
TRANSPORT PROCESSES ON THE MICROSCOPIC SCALE: DIFFUSION, BROWNIAN MOITION, OSMOSIS

MIKLÓS KELLERMAYER



Length scale of biomolecular systems

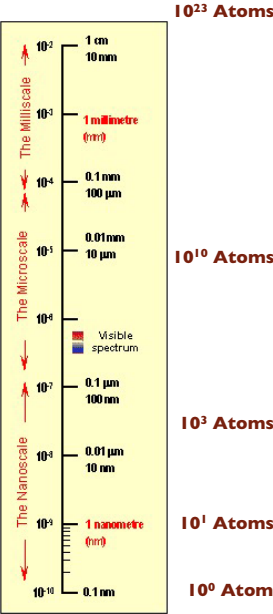
Thermodynamics



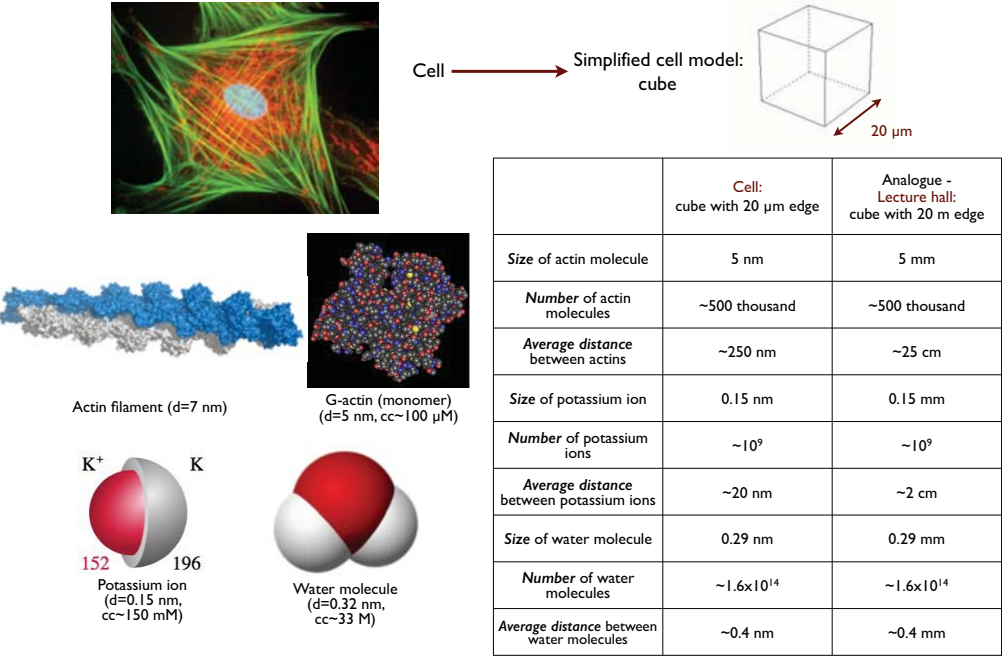
Mesoscale

Quantum chemistry

Quantum physics



Length scale of the cell



Average energy and velocity of a particle

Average kinetic energy of a particle (in thermal equilibrium): $\frac{3}{2} k_B T$ For one degree of freedom: $\frac{1}{2} k_B T$ k_B : Boltzmann's constant, T : absolute temperature, $k_B T$: "thermal energy" (4.14 pJ·nm)

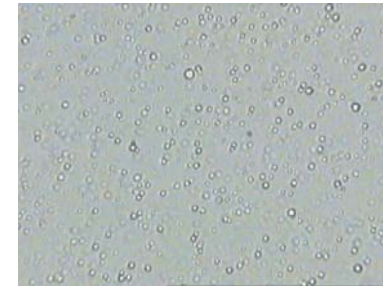
average kinetic energy of a particle with mass m along the x-axis: $\left\langle \frac{1}{2} m v_x^2 \right\rangle = \frac{1}{2} k_B T \rightarrow$ Average velocity: $\sqrt{\langle v_x^2 \rangle} = \sqrt{\frac{k_B T}{m}}$

Particle	Mass (kg)	Velocity (m/s)	Time for passing the cell (μs)*
G-actin (43 kDa)	7.2×10^{-23}	~8	~2.5
Potassium ion (39 Da)	6.5×10^{-26}	~240	~0.08
Water molecule (18 Da)	3×10^{-26}	~374	~0.05

*constant-velocity linear motion in vacuum

Thermally driven particle experiences random collisions on its path

Phenomenon of Brownian motion

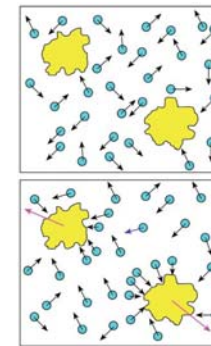


Fat droplets suspended in milk (0.5-3 μm)



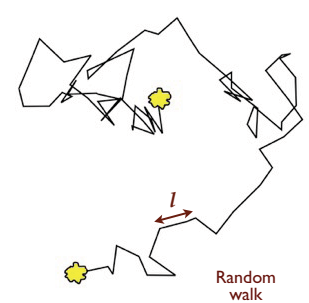
Robert Brown (botanist, 1773-1858)

Explanation of Brownian motion



Movement of microscopic particle is the result of random collisions with (solvent and other) molecules.

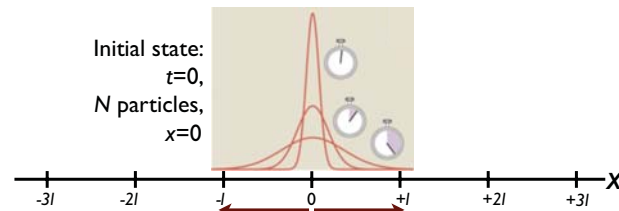
Trajectory of Brownian motion



l = mean free path (average distance between consecutive collisions)
 v = average velocity of thermally propelled particle

Diffusion: transport process driven by thermal motion; spreading.

One-dimensional random walk



Rules:

1. Each particle steps right or left once every τ seconds with velocity $\pm v_x$, a distance $l = \pm v_x \tau$. The distance covered after the n th step may be calculated as:

$$x_i(n) = x_i(n-1) \pm l$$

2. Probability of stepping right = probability of stepping left = $1/2$. Particles have no memory (consecutive steps are independent).
 3. Particles do not interact with each other (or with the solvent).

Observations:

1. Average position of the particles does not change!

$$\langle x(n) \rangle = \frac{1}{N} \sum_{i=1}^N [x_i(n-1) \pm l]$$

2. Particle spreading is proportional the square root of time!

$$\langle x^2(n) \rangle = \frac{1}{N} \sum_{i=1}^N [x_i^2(n-1) \pm 2l x_i(n-1) + l^2] = \langle x_i^2(n-1) \rangle + l^2$$

Spreading increases by l^2 in every step: $\langle x^2(n) \rangle = n l^2$

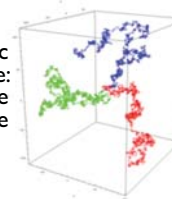
Since n is proportional to time, $n = t/\tau$: $\langle x^2(t) \rangle = \left(\frac{l^2}{\tau} \right) t$

Let us define a "diffusion coefficient": $D = \frac{l^2}{2\tau}$

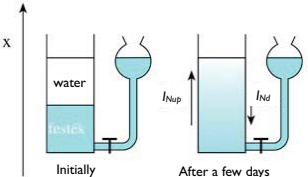
$$\langle x^2 \rangle = 2Dt \quad \text{és} \quad \sqrt{\langle x^2 \rangle} = \sqrt{2Dt}$$

Result of diffusion: particles explore the available space entirely

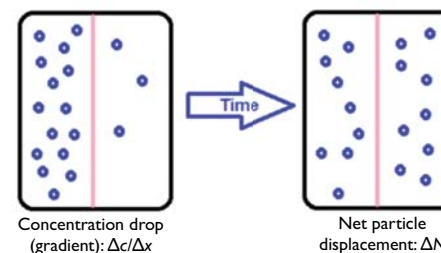
microscopic consequence: exploring the volume



macroscopic consequence: concentration equilibration



At the boundary (A):



Particle flux:

$$I_N = \frac{\Delta N}{\Delta t} = \frac{1}{6} v A \left(-2l \frac{\Delta n}{\Delta x} \right) = -\frac{1}{3} v l A \frac{\Delta n}{\Delta x}$$

particle-number difference at the boundary across the dimension of mean free path (l)

$$\text{Matter flow rate: } I_v = -\frac{1}{3} v l A \frac{\Delta c}{\Delta x}$$

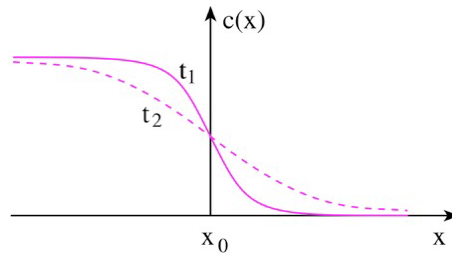
Let us define the diffusion coefficient (a bit differently): $D = \frac{1}{3} v l$

$$\text{Matter flow density - flux (Fick's First Law): } \frac{I_v}{A} = J_v = -D \frac{\Delta c}{\Delta x}$$

In reality, the shape of the concentration gradient changes with time

Fick's Second Law

Concentration drop decreases with time (boundary becomes "smeared")



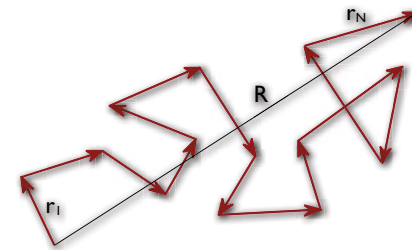
Spatial and temporal variation in concentration:

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

If we the spatial distribution of concentration (c) at a given time-point t, [c(x,t)], then we may calculate it after Δt as well.

Relationship between random walk and diffusion

Brownian movement - "random walk"



$$\langle R^2 \rangle = Nl^2 = Ll$$

R = displacement
N = number of unit vectors (steps)
l = $|\vec{r}_i|$ = mean free path
r_i = unit step
Nl = L = total distance

Mean particle velocity: $v = \frac{l}{\tau}$

Full walk time: $t = N\tau$

Diffusion coefficient: $D = \frac{1}{3}vl$

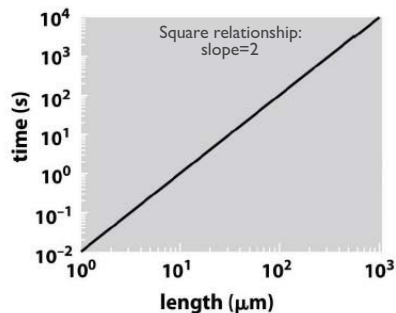
$$\langle R \rangle = \sqrt{Nl^2} = \sqrt{\frac{t}{\tau}}l^2 = \sqrt{tvl} = \sqrt{3Dt}$$

Meaning of diffusion coefficient (m²/s): molecular mobility

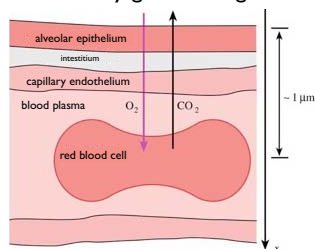
Diffusion coefficient for spherical particle: $D = \frac{k_B T}{6\pi\eta r}$

Einstein-Stokes formula:
k_B = Boltzmann's constant
T = absolute temperature
η = viscosity
r = radius of particle

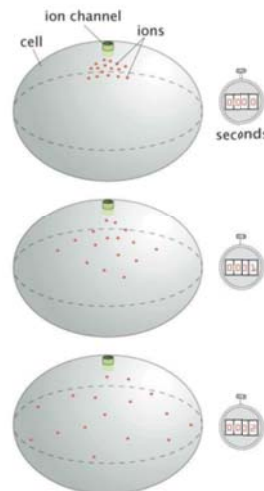
Diffusion-driven transport is fast only on short spatial scales



Pulmonary gas exchange:

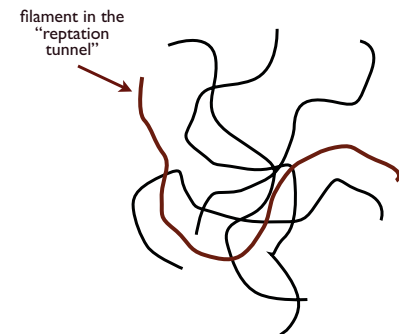


Ion distribution in the cell

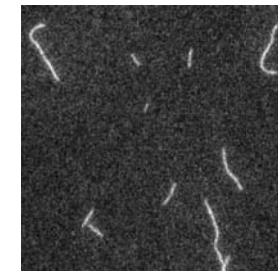


Special case of diffusion: reptation

Reptation: "snake-like" diffusion within a polymer network (Reptilia)

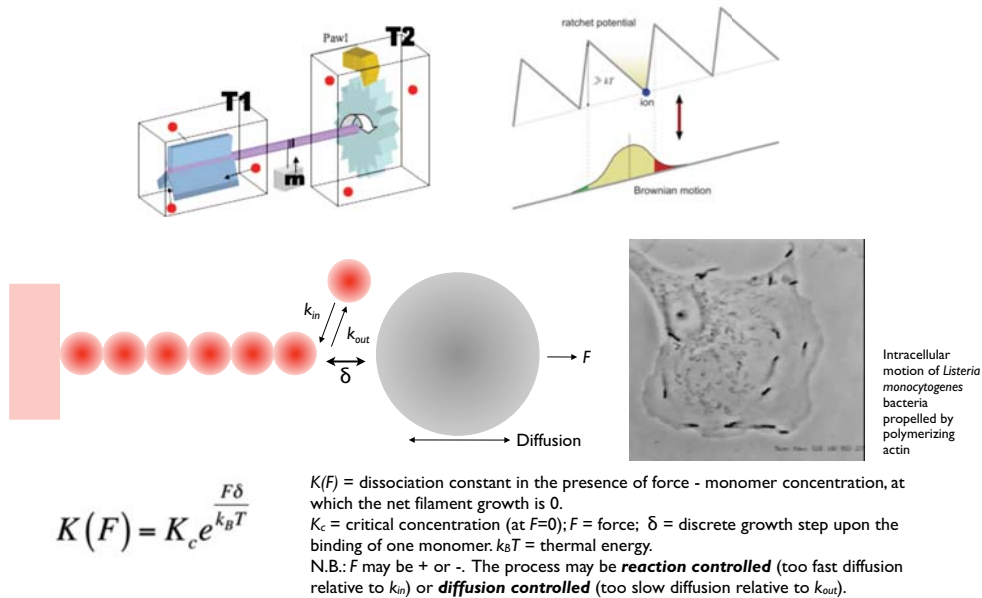


polymer matrix: "entanglement"



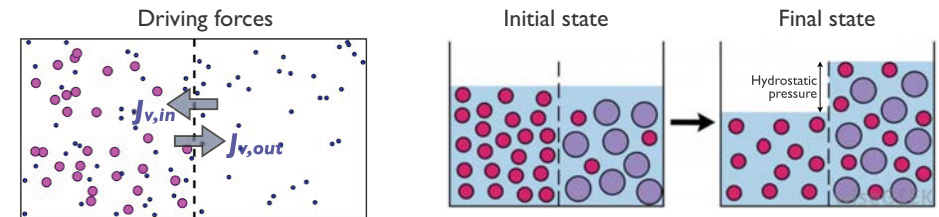
Actin filaments in methylcellulose matrix.
"unidirectional diffusion"

Special case of diffusion: Brownian ratchet



A special case of diffusion: osmosis

One-directional **solvent** transport by diffusion



$J_{v,in}$ driving force: solvent concentration difference

$J_{v,out}$ driving force: pressure difference

Osmotic equilibrium: $J_{v,in} = J_{v,out}$

Osmotic pressure: $p_{osmosis} = cRT$

Importance of osmosis: cell swelling, edema, hemodialysis.

van't Hoff's Law:
 c = concentration of solute
 R = universal gas constant
 T = absolute temperature

Mechanisms of osmosis

van't Hoff's gas-law mechanism

Universal gas law: $pV = RT$

$$p = \frac{1}{V} RT$$

Osmotic pressure: $p_{osm} = \pi = cRT$

p = pressure
 V = volume
 R = gas constant (8,3 J/mol.K)
 T = absolute temperature
 c = molar concentration of solute

Example:

What is the osmotic pressure of a 0.1 M (0.1 mol/dm³) sucrose solution?

$\pi = 8.3 \text{ (J/mol.K)} \times 293 \text{ (K)} \times 0.1 \text{ (mol/dm}^3\text{)} = 243 \text{ kPa} \sim 2.4 \text{ atm.}$

Note: the formula applies to dilute solutions.

Importance of osmosis

Properties of the semipermeable membrane: **reflexion coefficient** (σ)

For a perfect semipermeable membrane:

$$\Delta P = \Delta \pi \quad \text{and} \quad \sigma = \frac{\Delta P}{\Delta \pi} = 1$$

In reality:

$$\Delta P < \Delta \pi \quad \text{and} \quad \sigma = \frac{\Delta P}{\Delta \pi} < 1$$

$$0 < \sigma < 1$$

Osmotic work:

$$-L = nRT \ln \frac{c_1}{c_2} = nRT \ln \frac{\pi_1}{\pi_2}$$

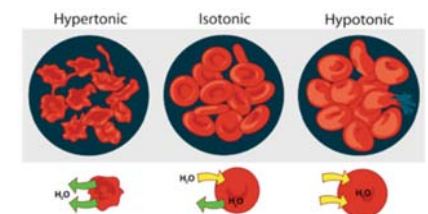
R = gas constant
 n = total number of moles of solute
 c_1 = initial molarity of solution
 c_2 = final molarity of solution (after equilibration)
 π_1 = initial osmotic pressure
 π_2 = final osmotic pressure (after equilibration)

Equivalent osmotic pressure (osmotic concentration): concentration of non-electrolyte solution in equilibrium with a heterogeneous solution system.

Units: mmol/kg = mOsmol/kg = mOsm

Osmolarity of blood plasma ~ 300 mOsm.

Oncotic pressure: colloid osmotic pressure. Osmotic pressure of a solution of colloidal macromolecules.



Thermodynamic currents

- If there are inequalities in the intensive variables at different locations within the system, thermodynamic currents arise.
- Thermodynamic currents aim at the restoration of equilibrium.

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 (φ)	$J_Q = -\frac{1}{\rho} \frac{\Delta \varphi}{\Delta x}$	Ohm
Material transport (diffusion)	Chemical potential (μ)	$J_n = -D \frac{\Delta c}{\Delta x}$	Fick

Onsager's linear function

- Lars Onsager (1903-1976), Nobel prize (1968)
- General relationship between transport processes.

$$J = LX$$

Flow intensity of transported extensive variable (thermodynamic current, J) $J = \frac{\Delta x_{ext}}{A \Delta t}$	=	Coefficient of conductance (thermodynamic coefficient, L)	x	Change in intensive variable ("gradient", thermodynamic force, X) $X = -\frac{\Delta y_{int}}{\Delta x}$
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A thermodynamic current may be evoked by several different intensive variables. E.g., thermodiffusion (material transport evoked by temperature gradient).

$$J_1 = L_{11}X_1 + L_{12}X_2 \quad J_2 = L_{21}X_1 + L_{22}X_2$$

L_{11}, L_{22} = "linear" coefficients of conductance

L_{12}, L_{21} = "cross" coefficients of conductance