BB 101: MODULE II
PHYSICAL BIOLOGY

Review of Lecture 3

- Life at low Reynolds number

- Thermal forces, Thermal energy and Brownian motion

- Thermal energy is comparable with other deterministic energies at molecular scales

- Boltzmann's law and some applications of Boltzmann's law

We will revisit Brownian Motion in this lecture

Diffusion Equation

- Links change of concentration in time to change of concentration in space

- Combining Fick's law and continuity equation

Fick's Law

$$\text{Flux} = J(x + \Delta x)$$
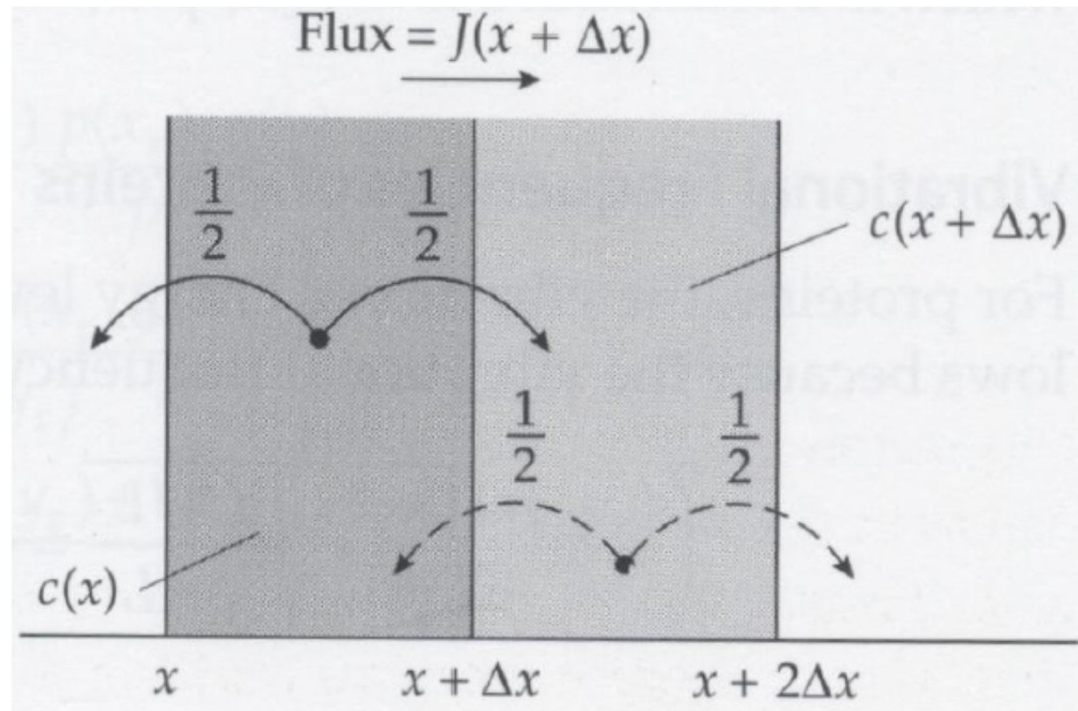
Each molecule can move by distance Δx in time Δt either to left or right

$J(x + \Delta x) \rightarrow$ Number of particles crossing plane at $x + \Delta x$ per unit time

Number of particles moved from left to right $\rightarrow \dfrac{1}{2}c(x)\Delta x$

Number of particles moved from right to left $\rightarrow \dfrac{1}{2}c(x + \Delta x)\Delta x$

Fick's Law

$$J(x + \Delta x).\, \Delta t = -\frac{1}{2}[c(x + \Delta x) - c(x)\,]\Delta x$$

$$J(x + \Delta x) = -\frac{1}{2}\frac{\Delta x^{\,2}}{\Delta t}\frac{[c(x + \Delta x) - c(x)\,]}{\Delta x}$$
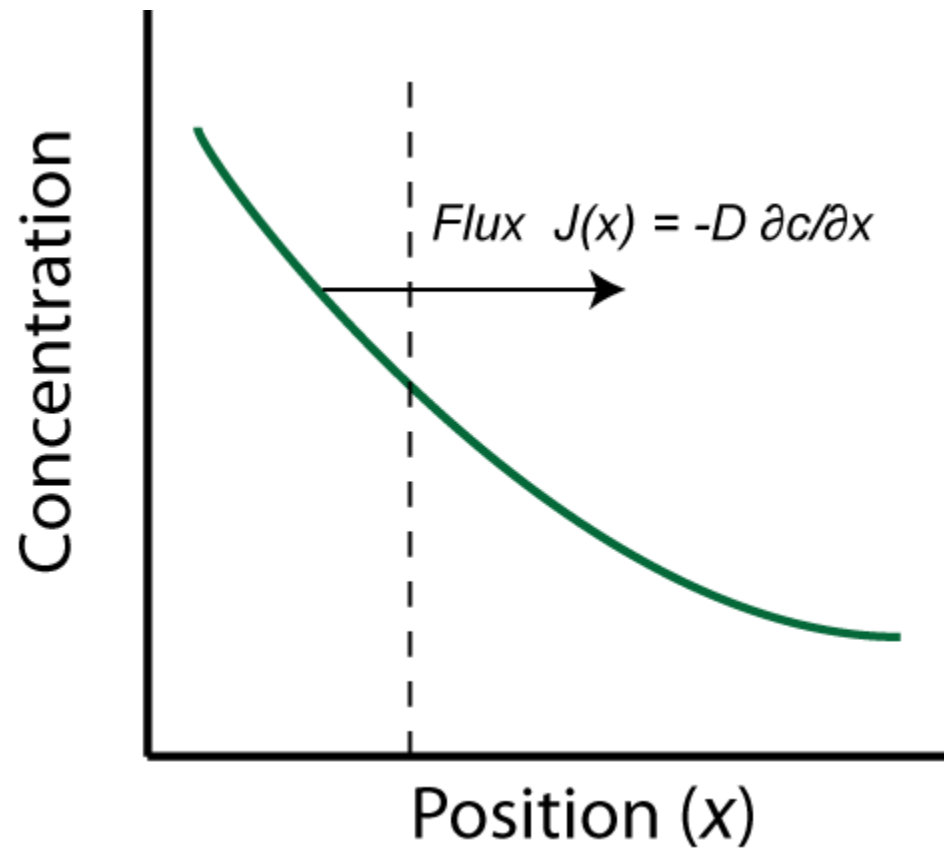
$$Taking\ limit\quad \Delta x \to 0$$

$$\boxed{Flux\ \ J(x) = -D\frac{\partial c}{\partial x}}$$
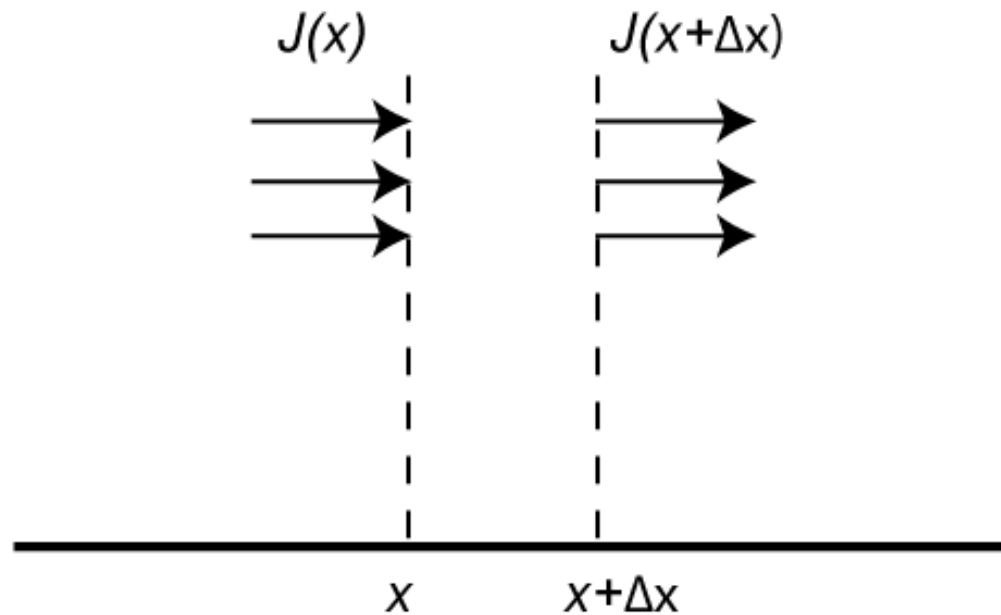
$$where\ D = \frac{1}{2}\frac{\Delta x^{\,2}}{\Delta t}$$

Relates diffusive flux to concentration gradient

Fick's Law

Continuity Equation

$J(x)$ $J(x+\Delta x)$

x $x+\Delta x$

If inflow=outflow then concentration at x doesn't change with time

However, if inflow ≠ outflow then concentration at x will change with time

Continuity Equation

$$\Delta c = \frac{A.J(x).\Delta t - A.J(x + \Delta x).\Delta t}{A.\Delta x} = -\frac{[J(x + \Delta x) - J(x)].\Delta t}{\Delta x}$$

Dividing both sides by Δt and taking limit $\Delta t \rightarrow 0$

$$\boxed{\frac{\partial c}{\partial t} = -\frac{\partial J}{\partial x}}$$

$$\boxed{\frac{\partial c(x,t)}{\partial t} = -\frac{\partial J(x,t)}{\partial x}}$$

Diffusion Equation

Combine Fick's Law and Continuity Equation

$$\frac{\partial c(x,t)}{\partial t} = D\,\frac{\partial^2 c(x,t)}{\partial x^2}$$
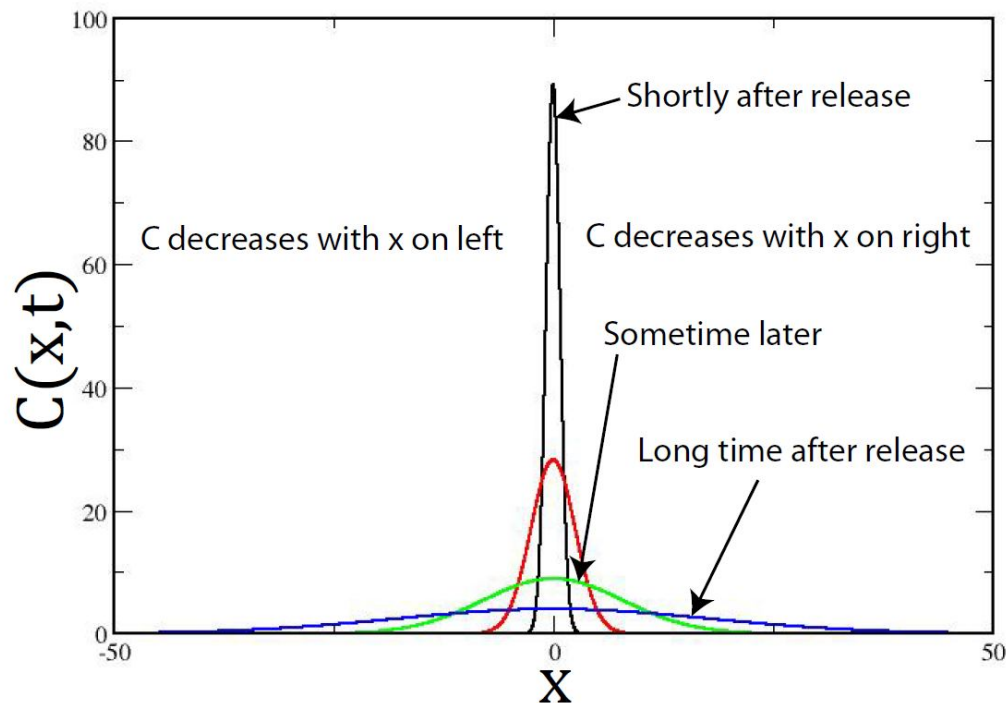
Solution of diffusion equation for given initial condition and boundary conditions is beyond the scope of this course

However, we will look at the solution in a very special case

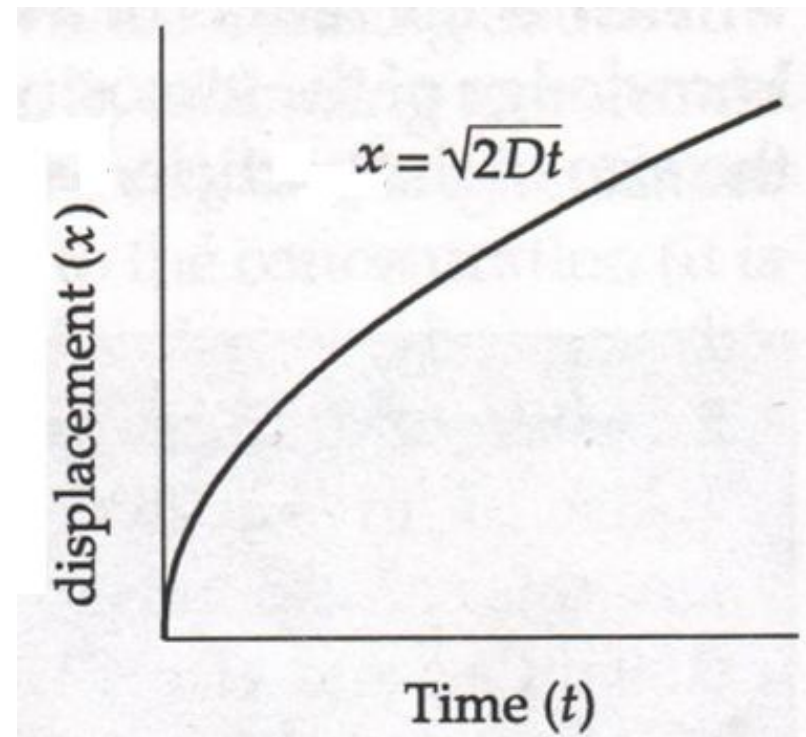**Free diffusion from a point source**

Free diffusion from a point source

$$c(x,t) = \frac{c_0}{\sqrt{}} e^{-\frac{x^2}{4Dt}}$$

Shortly after release

C decreases with x on left   C decreases with x on right

Sometime later

Long time after release

1D Diffusion
$< x^2 >=$

$x = \sqrt{2Dt}$

3D Diffusion
$< r^2 >=$

Characteristics of diffusion

Figure Source: Mechanics of Motor Proteins and the Cytoskeleton, Jonathan Howard

Need for Active Transport

Times for one-dimensional diffusion in aqueous solution

Object	1 μm	100 μm	10 mm	1 m
K^+	0.25 ms	2.5 s	2.5×10^4 s (7 hrs)	2.5×10^8 s (8 years)
Protein	5 ms	50 s (~1 min.)	5×10^5 s (6 days)	5×10^9 s (150 years)
Organelle	1 s	10^4 s (~3 hr.)	10^8 s (3 years)	10^{12} s (30 millennia)

Note: K^+: Radius ~0.1 nm, $T = 25°C$, $D \cong 2000$ μm²/s.
Protein: Radius = 3 nm, viscosity = 0.6915 mPa·s⁻¹, $T = 37°C$, $D \cong 100$ μm²/s.
Organelle: Radius = 500 nm, viscosity = 0.8904 mPa·s⁻¹, $T = 25°C$, $D \cong 0.5$ μm²/s.

Diffusion is not efficient mechanism for transporting cargo over large distances and hence molecular motor active transport is essential

Watch the video "A Day in the Life of a Motor Protein" on following link:

https://www.youtube.com/watch?v=tMKIPDBRJ1E

Figure Source: Mechanics of Motor Proteins and the Cytoskeleton, Jonathan Howard

Einstein and Einstein Relation

1. **Photoelectric Effect (March 1905)**
Title: "On a Heuristic Point of View Concerning the Production and Transformation of Light" ("Über einen die Erzeugung und Verwandlung des Lichtes betreffenden heuristischen Gesichtspunkt")
(*Annalen der Physik* 17:132-148)
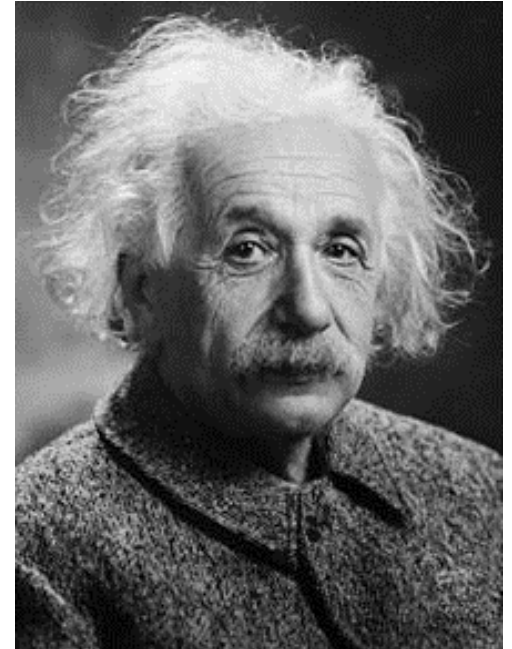
2. **Brownian Motion (May 1905)**
Title: "On the Movement of Small Particles Suspended in Stationary Liquids Required by the Molecular-Kinetic Theory of Heat" ("Über die von der molekularkinetischen Theorie der Wärme geforderte Bewegung von in ruhenden Flüssigkeiten suspendierten Teilchen")
(*Annalen der Physik* 17:549-560)

3. Special Relativity (June 1905)
Title: "On the Electrodynamics of Moving Bodies" ("Zur Elektrodynamik begetter Körper") (*Annalen der Physik* 17:891-921)

4. **Special Relativity: E=mc² (September 1905)**
Title: "Does the Inertia of a Body Depend upon its Energy Content?" ("Ist die Trägheit eines Körpers von seinem Energieinhalt abhängig?")
(*Annalen der Physik* 18:639-641)

Figure Source: http://en.wikipedia.org/wiki/Albert_Einstein#mediaviewer/File:Albert_Einstein_Head.jpg
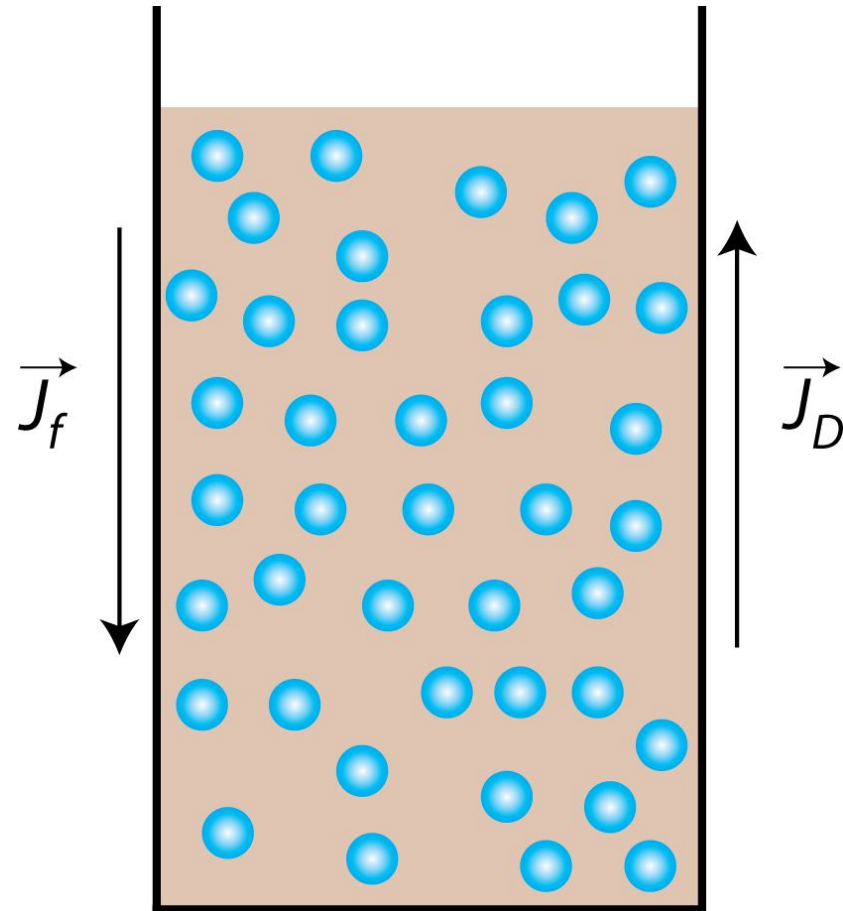
Einstein Relation

Consider that suspended particles are experiencing an external force f

In equilibrium, flux due to external force f will be balanced by the flux due to diffusion

Now, flux due to external force f

$$\vec{J_f} = C\vec{v} = \frac{C\vec{f}}{6\pi\eta r} = -\frac{Cf}{6\pi\eta r}\hat{i}$$

Einstein Relation

Concentration profile is given by $C = C_0 e^{-\frac{fx}{k_B T}}$
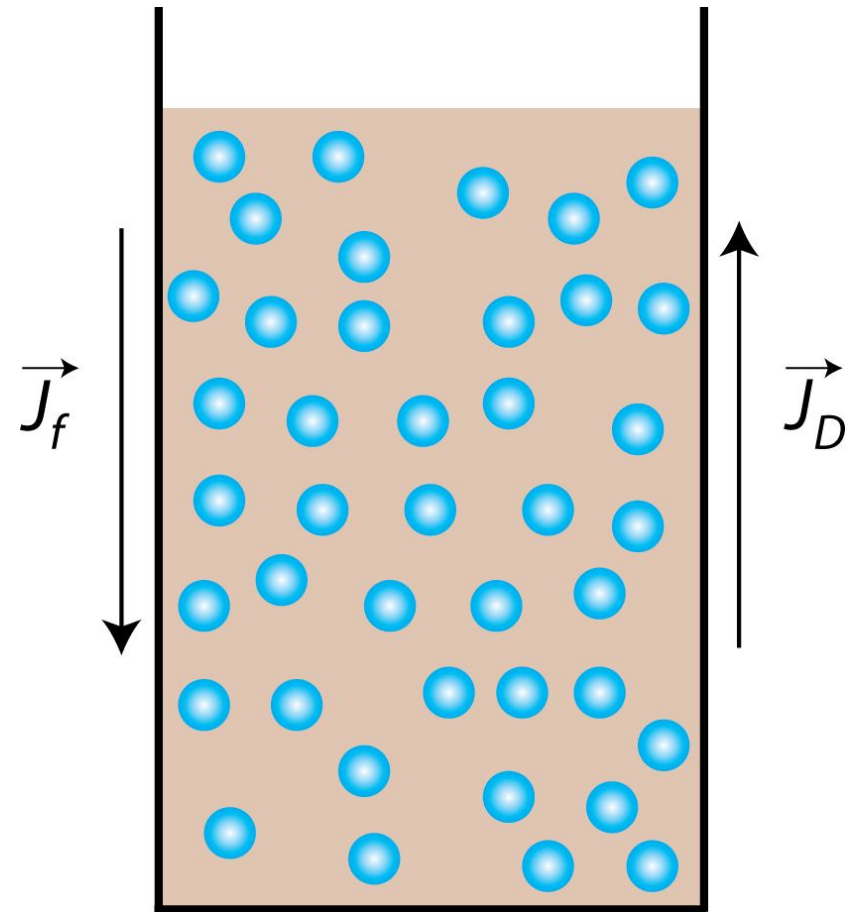
Now, flux due to diffusion

$$\vec{J_D} = -D\vec{\nabla}C = -D\frac{\partial C}{\partial x}\hat{\imath} = \frac{DCf}{k_B T}\hat{\imath}$$

In equilibrium $\quad \vec{J_f} + \vec{J_D} = 0$

$$\Rightarrow \qquad \frac{Cf}{6\pi\eta r}\hat{\imath} = \frac{DCf}{k_B T}\hat{\imath}$$

$$\Rightarrow \qquad 6\pi\eta r D = k_B T$$

$$\boxed{\gamma D = k_B T}$$

Einstein Relation: Significance

$$\gamma D = k_B T$$

Einstein relation published in 1905 paper

Gas Constant

$$D = \frac{R\,T}{N} \; \frac{1}{6\,\pi\,k\,P}$$

Viscosity   Size of Particle

$$D = \frac{k_B T}{6\pi\eta r} = \frac{RT}{N6\pi\eta r}$$

$$\therefore R = N k_B$$

Connects Diffusion to Damping

Fluctuations and Dissipation

ON THE MOVEMENT OF SMALL PARTICLES SUSPENDED IN STATIONARY
LIQUIDS REQUIRED BY THE MOLECULAR-KINETIC THEORY OF HEAT

by A. Einstein

[*Annalen der Physik* 17 (1905): 549-560]

It will be shown in this paper that, according to the molecular-kinetic theory of heat, bodies of microscopically visible size suspended in liquids must, as a result of thermal molecular motions, perform motions of such magnitude that these motions can easily be detected by a microscope. It is possible that the motions to be discussed here are identical with the so-called "Brownian molecular motion"; however, the data available to me on the latter are so imprecise that I could not form a definite opinion on this matter.

If it is really possible to observe the motion to be discussed here, along with the laws it is expected to obey, then classical thermodynamics can no longer be viewed as strictly valid even for microscopically distinguishable spaces, and an exact determination of the real size of atoms becomes possible. Conversely, if the prediction of this motion were to be proved wrong, this fact would provide a weighty argument against the molecular-kinetic conception of heat.

You have seen (will see) one example of random walk in tutorial 2.
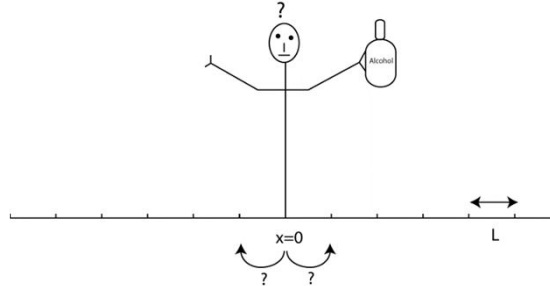
If a random walker takes steps of L in time Δt, either to left or right with equal probability, then his position x_N after taking N such random steps is given by $< (x_N)^2 > = NL^2 = \left(\frac{L^2}{\Delta t}\right) t$ $\square$ $< (x_N)^2 > \propto t$

We can predict average shape of the polymer using ideas of random walk

Regard polymer as a string of N units, where each unit is joint to the next by a perfectly flexible joint.

In the thermal equilibrium, joints will be at random angles

Conformation of polymers

An instantaneous snapshot of the polymer will be different at each time instant

There will be some resemblance in each of such snapshots: Each snapshot will look like a random walk
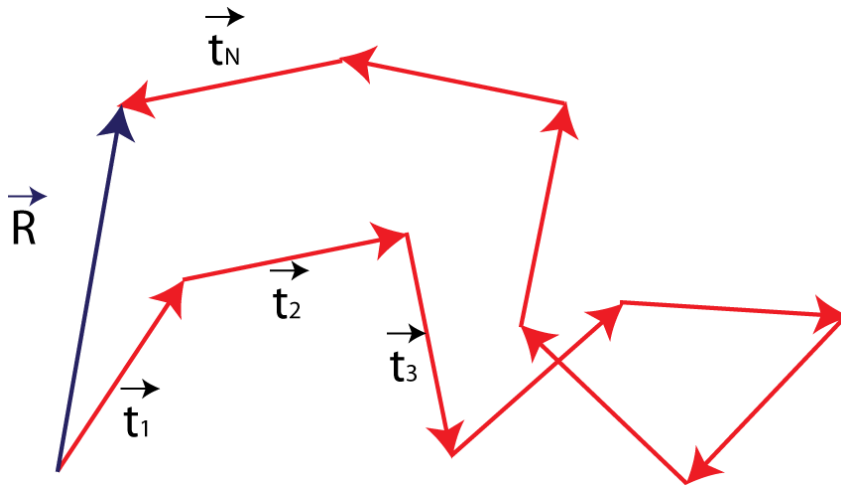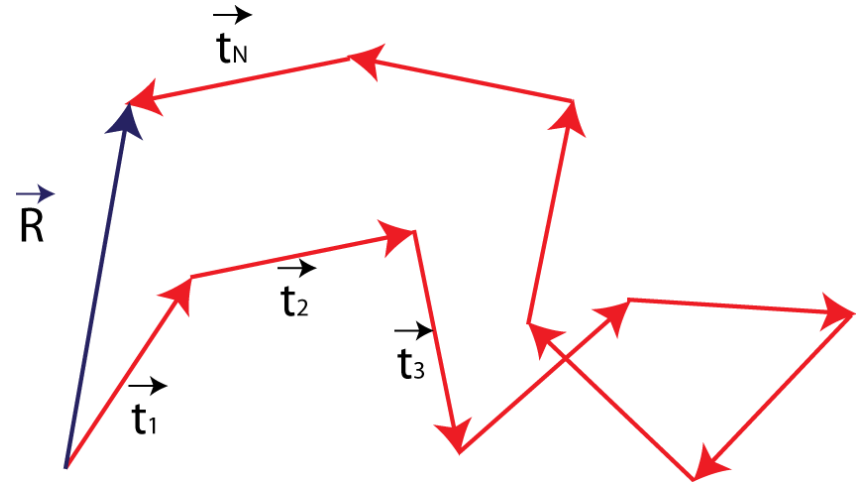

$$\left|\vec{t_1}\right| = \left|\vec{t_2}\right| = \cdots = \left|\vec{t_N}\right| = L$$

What is the values of end-to-end vector $\vec{R}$?

$\langle\vec{R}\rangle$=0   Since all directions are equally probable

Conformation of polymers

$$\langle R^2 \rangle = \langle \vec{R} \cdot \vec{R} \rangle = ?$$

$$\langle R^2 \rangle = \left\langle \left(\sum_{i=1}^{N} \vec{t_i} \right) \cdot \left(\sum_{j=1}^{N} \vec{t_j} \right) \right\rangle = \left\langle \left(\vec{t_1} + \vec{t_2} + \cdots + \vec{t_N} \right) \cdot \left(\vec{t_1} + \vec{t_2} + \cdots + \vec{t_N} \right) \right\rangle$$

$$= \left\langle \left(\sum_{i=1}^{N} \vec{t_i^2} \right) \right\rangle + \sum_{i=1}^{N} \sum_{j=1, j \neq i}^{N} \langle \vec{t_i} \cdot \vec{t_j} \rangle$$

$$\sum_{i=1}^{N} \sum_{j=1, j \neq i}^{N} \langle \vec{t_i} \cdot \vec{t_j} \rangle = 0 \Rightarrow \quad \langle R^2 \rangle = NL^2$$

Summary

- Fick's law, Continuity Equation and Diffusion Equation

- Free diffusion from a point source

- Need for active transport

- Einstein Relation and its significance

- Another random walk-conformation of polymers