

BB 101

MODULE: *PHYSICAL BIOLOGY*

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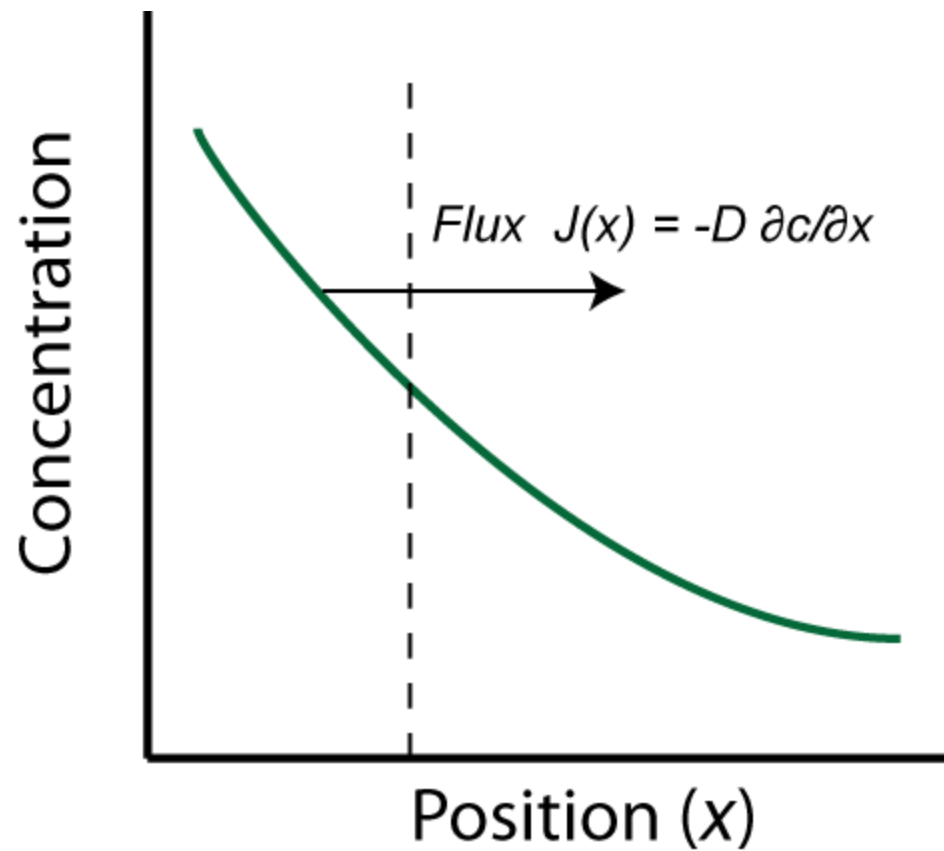
Review of Lecture 3

- Thermal Energy and its relative importance
- Boltzmann's law and its applications
- Diffusion Equation using Fick's law and Continuity Equation

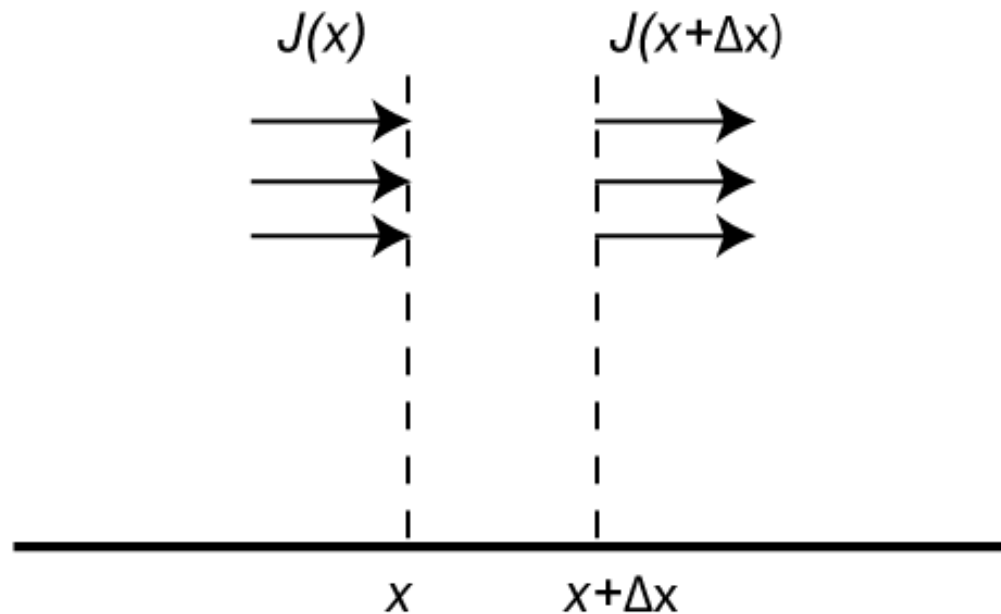
Diffusion Equation

- Links change of concentration in time to change of concentration in space
- Combining Fick's law and continuity equation

Fick's Law



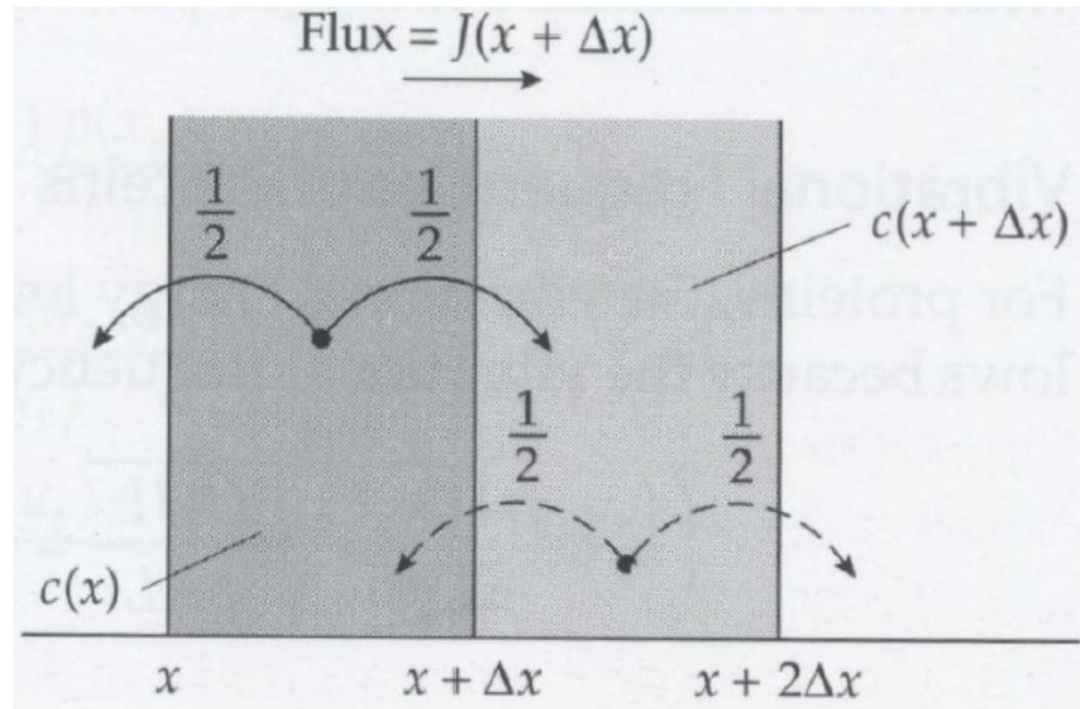
Continuity Equation



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

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

Fick's Law



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 $\rightarrow \frac{1}{2} c(x) \Delta x$

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

Fick's Law

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

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

Taking limit $\Delta x \rightarrow 0$

$$\text{Flux } J(x) = -D \frac{\partial c}{\partial x}$$

$$\text{where } D = \frac{1}{2} \frac{\Delta x^2}{\Delta t}$$

Relates diffusive flux to concentration gradient

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

$$\frac{\partial c(x, t)}{\partial t} = D \frac{\partial^2 c(x, t)}{\partial x^2}$$

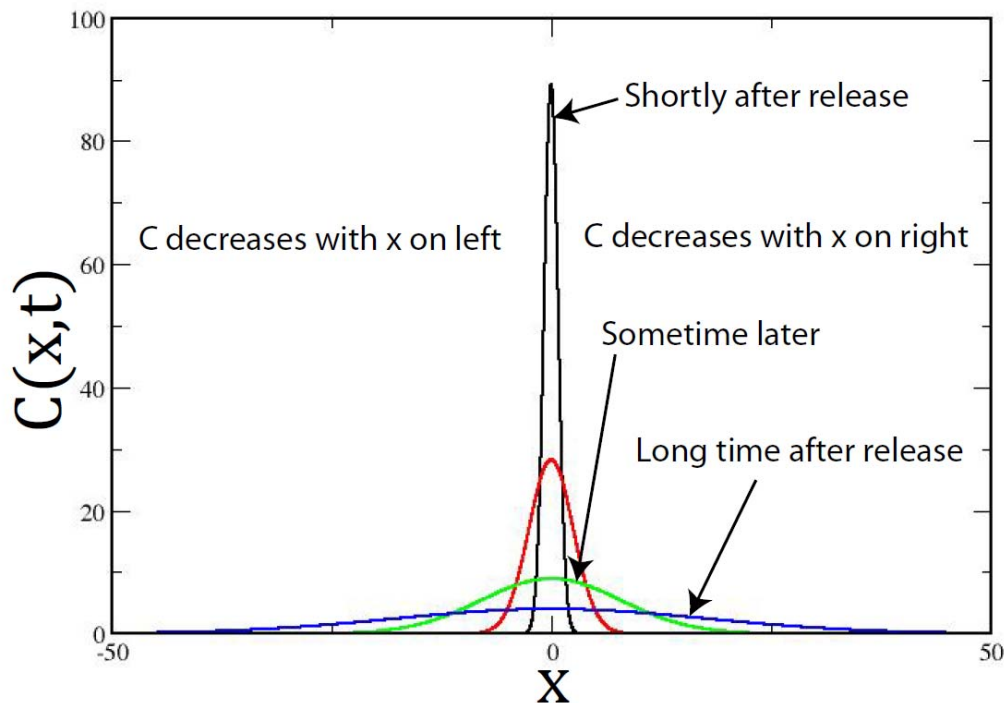
Solution of diffusion equation for given initial condition and boundary conditions is beyond the scope of this course

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

Free diffusion from a point source

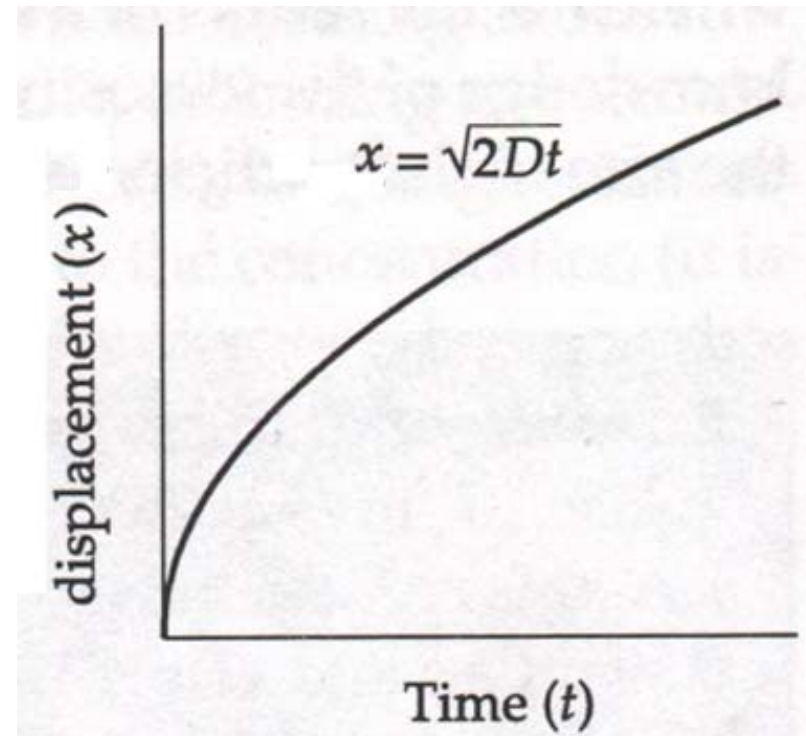
Free diffusion from a point source

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



1D Diffusion

$$\langle x^2 \rangle = 2Dt$$



3D Diffusion

$$\langle r^2 \rangle = 6Dt$$

Characteristics of diffusion

Need for Active Transport

Times for one-dimensional diffusion in aqueous solution

Object	Distance diffused			
	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)

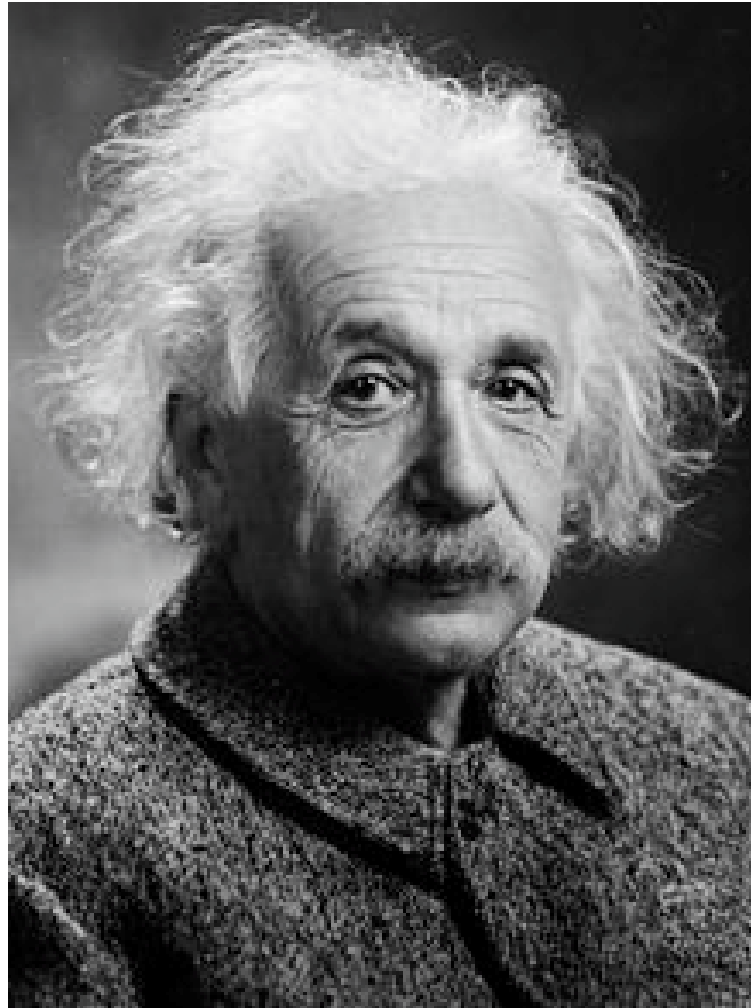
Note: K⁺: Radius ~0.1 nm, $T = 25^\circ\text{C}$, $D \cong 2000 \mu\text{m}^2/\text{s}$.
 Protein: Radius = 3 nm, viscosity = $0.6915 \text{ mPa}\cdot\text{s}^{-1}$, $T = 37^\circ\text{C}$, $D \cong 100 \mu\text{m}^2/\text{s}$.
 Organelle: Radius = 500 nm, viscosity = $0.8904 \text{ mPa}\cdot\text{s}^{-1}$, $T = 25^\circ\text{C}$, $D \cong 0.5 \mu\text{m}^2/\text{s}$.

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>

Einstein and Einstein Relation



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)

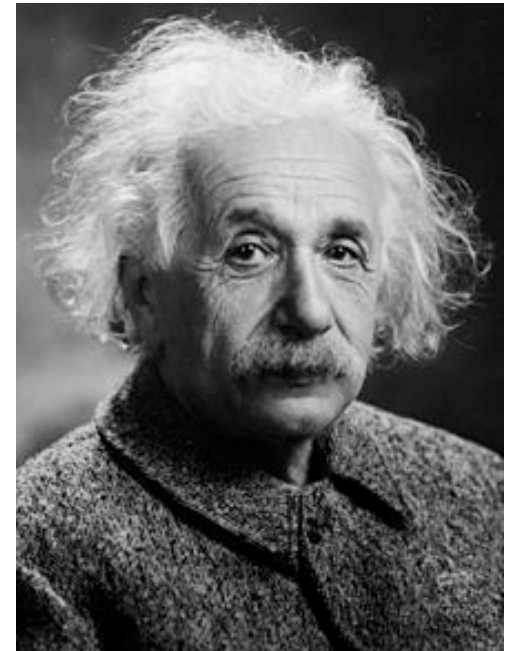
Title: "On the Movement of Small Particles Suspended in Stationary Liquids Required by the Molecular-Kinetic Theory of Heat" ("Über die von der molekularkinetischen Theorie der Wärme geforderte Bewegung von in ruhenden Flüssigkeiten suspendierten Teilchen")
(*Annalen der Physik* 17:549-560)

3. Special Relativity (June 1905)

Title: "On the Electrodynamics of Moving Bodies" ("Zur Elektrodynamik bewegter Körper") (*Annalen der Physik* 17:891-921)

4. Special Relativity: $E=mc^2$ (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)



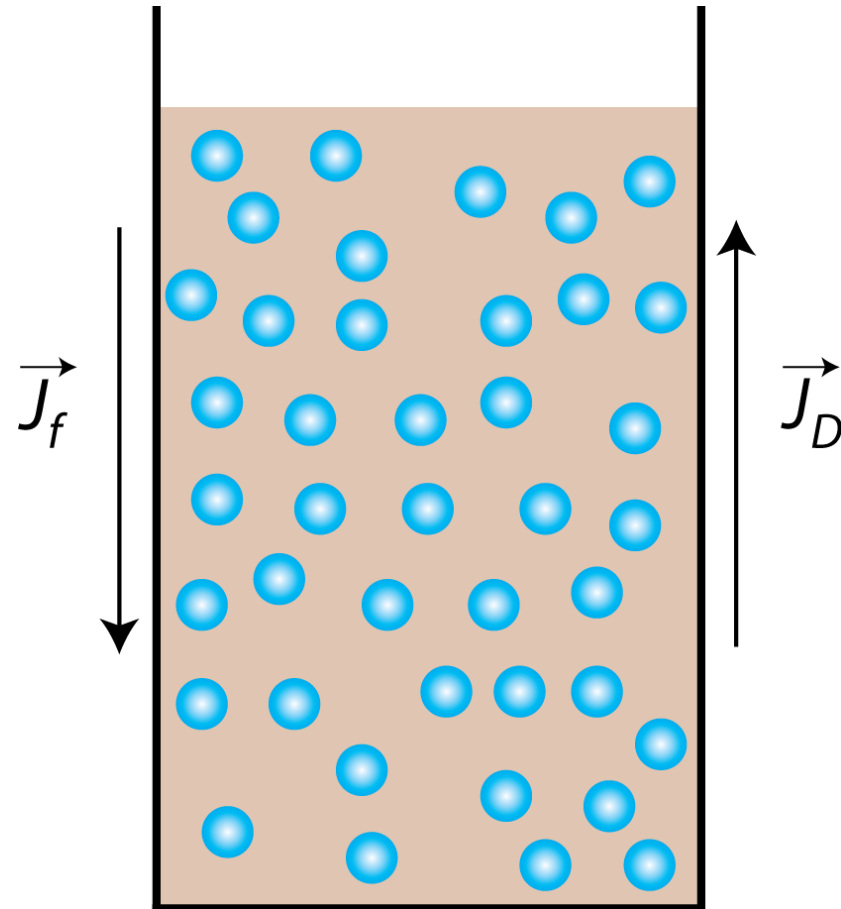
Einstein Relation

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

$$\vec{J}_D = -D \vec{\nabla} C = -D \frac{\partial C}{\partial x} \hat{i} = \frac{DCf}{k_B T} \hat{i}$$

In equilibrium $\vec{J}_f + \vec{J}_D = 0$

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

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

$$\gamma D = k_B T$$

Einstein Relation: Significance

$$\gamma D = k_B T$$

Einstein relation published in 1905 paper

$$D = \frac{RT}{N} \frac{1}{6\pi\eta r}$$

Gas Constant

Viscosity Size of Particle

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

$$\because R = N k_B$$

Connects Diffusion to Damping

Fluctuations and Dissipation

THE
LONDON, EDINBURGH, AND DUBLIN
PHILOSOPHICAL MAGAZINE
AND
JOURNAL OF SCIENCE.

[SIXTH SERIES.]

MARCH 1904.

XXIV. *On the Structure of the Atom: an Investigation of the Stability and Periods of Oscillation of a number of Corpuscles arranged at equal intervals around the Circumference of a Circle; with Application of the results to the Theory of Atomic Structure.* By J. J. THOMSON, F.R.S., Cavendish Professor of Experimental Physics, Cambridge.*

THE view that the atoms of the elements consist of a number of negatively electrified corpuscles enclosed in a sphere of uniform positive electrification, suggests, among other interesting mathematical problems, the one discussed in this paper, that of the motion of a ring of n negatively electrified particles placed inside a uniformly electrified sphere. Suppose when in equilibrium the n corpuscles are arranged at equal angular intervals round the circumference of a circle of radius a , each corpuscle carrying a charge e of negative electricity. Let the charge of positive electricity contained within the sphere be ve , then if b is the radius of this sphere, the radial attraction on a corpuscle due to the positive electrification is equal to ve^2a/b^3 ; if the corpuscles are at rest this attraction must be balanced by the repulsion exerted by the other corpuscles. Now the repulsion along OA, O being the centre of the sphere, exerted on a corpuscle at A by one at B, is equal to $\frac{e^2}{AB^2} \cos OAB$, and, if $OA=OB$,

this is equal to $\frac{e^2}{4OA^2 \sin \frac{1}{2}AOB}$: hence, if we have n corpuscles arranged at equal angular intervals $2\pi/n$ round the circumference of a circle, the radial repulsion on one corpuscle

* Communicated by the Author.

Phil. Mag. S. 6. Vol. 7. No. 39. March 1904.

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LXXIX. *The Scattering of α and β Particles by Matter and the Structure of the Atom.* By Professor E. RUTHERFORD, F.R.S., University of Manchester*.

§ 1. IT is well known that the α and β particles suffer deflexions from their rectilinear paths by encounters with atoms of matter. This scattering is far more marked for the β than for the α particle on account of the much smaller momentum and energy of the former particle. There seems to be no doubt that such swiftly moving particles pass through the atoms in their path, and that the deflexions observed are due to the strong electric field traversed within the atomic system. It has generally been supposed that the scattering of a pencil of α or β rays in passing through a thin plate of matter is the result of a multitude of small scatterings by the atoms of matter traversed. The observations, however, of Geiger and Marsden † on the scattering of α rays indicate that some of the α particles must suffer a deflexion of more than a right angle at a single encounter. They found, for example, that a small fraction of the incident α particles, about 1 in 20,000, were turned through an average angle of 90° in passing through a layer of gold-foil about 0.0004 cm. thick, which was equivalent in stopping-power of the α particle to 1.6 millimetres of air. Geiger ‡ showed later that the most probable angle of deflexion for a pencil of α particles traversing a gold-foil of this thickness was about $0^\circ.87$. A simple calculation based on the theory of probability shows that the chance of an α particle being deflected through 90° is vanishingly small. In addition, it will be seen later that the distribution of the α particles for various angles of large deflexion does not follow the probability law to be expected if such large deflexions are made up of a large number of small deviations. It seems reasonable to suppose that the deflexion through a large angle is due to a single atomic encounter, for the chance of a second encounter of a kind to produce a large deflexion must in most cases be exceedingly small. A simple calculation shows that the atom must be a seat of an intense electric field in order to produce such a large deflexion at a single encounter.

Recently Sir J. J. Thomson § has put forward a theory to

* Communicated by the Author. A brief account of this paper was communicated to the Manchester Literary and Philosophical Society in February, 1911.

† *Proc. Roy. Soc.* lxxii. p. 495 (1909).

‡ *Proc. Roy. Soc.* lxxiii. p. 492 (1910).

§ *Camb. Lit. & Phil. Soc.* xv. pt. 5 (1910).

Einstein thoughts on his results

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

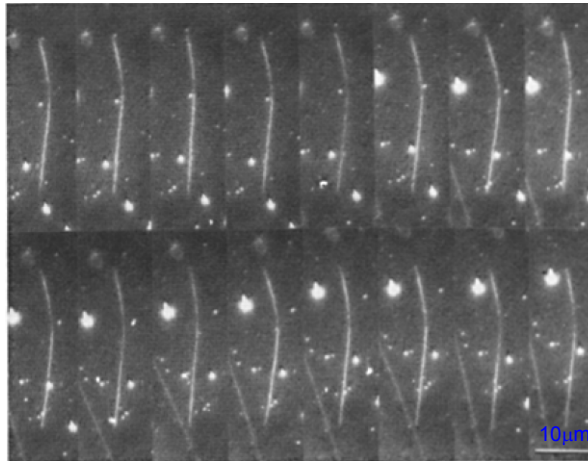
by A. Einstein

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

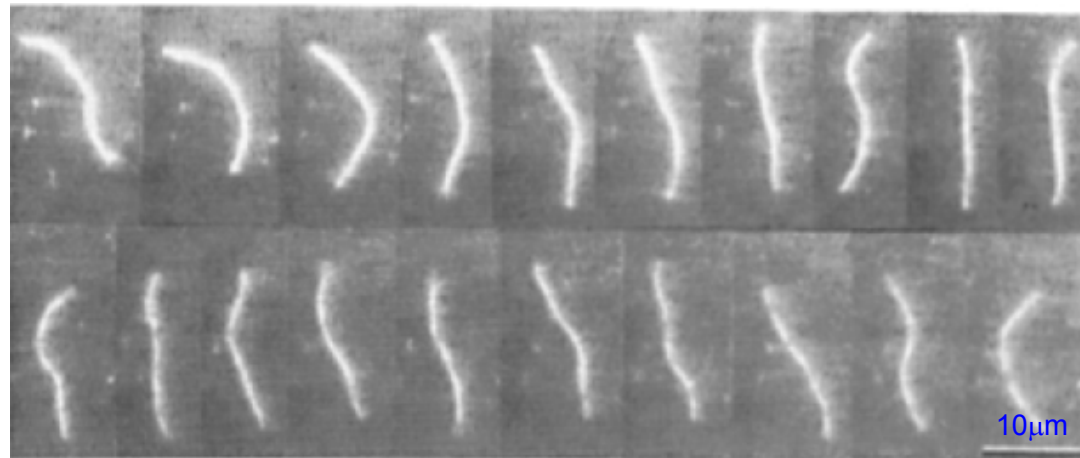
It will be shown in this paper that, according to the molecular-kinetic theory of heat, bodies of microscopically visible size suspended in liquids must, as a result of thermal molecular motions, perform motions of such magnitude that these motions can easily be detected by a microscope. It is possible 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.

Thermal bending of bio-polymers: MT and Actin



Microtubule



Actin Filaments

Thermal bending of bio-polymers: Bacterial DNA

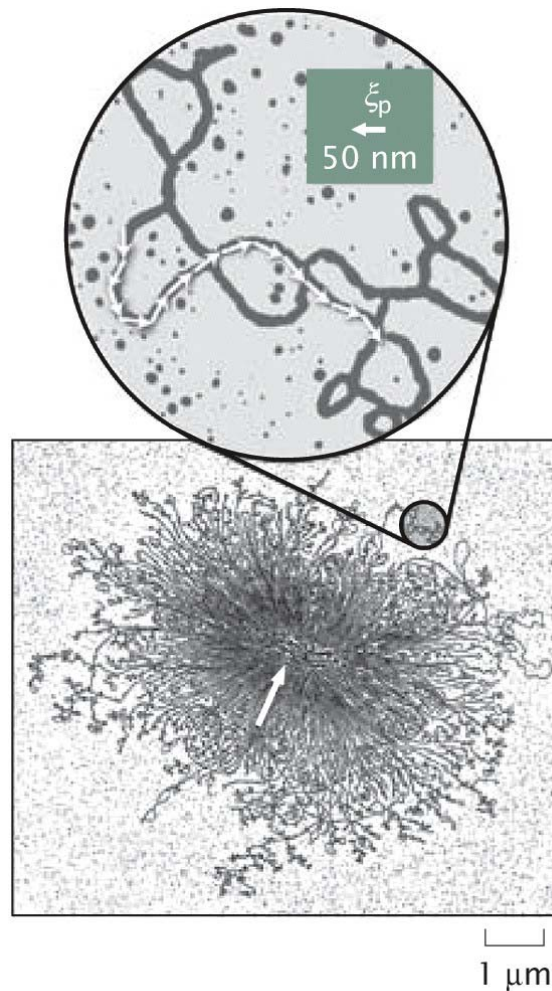
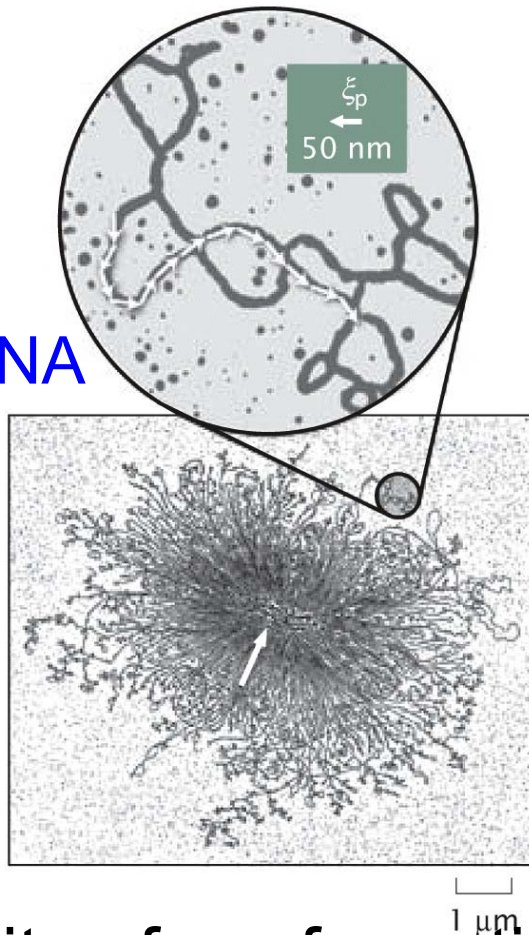


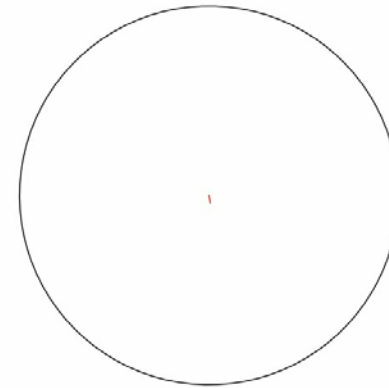
Figure 8.5 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Thermal bending of bio-polymers and Random Walk

Bacterial DNA



Random Walk!

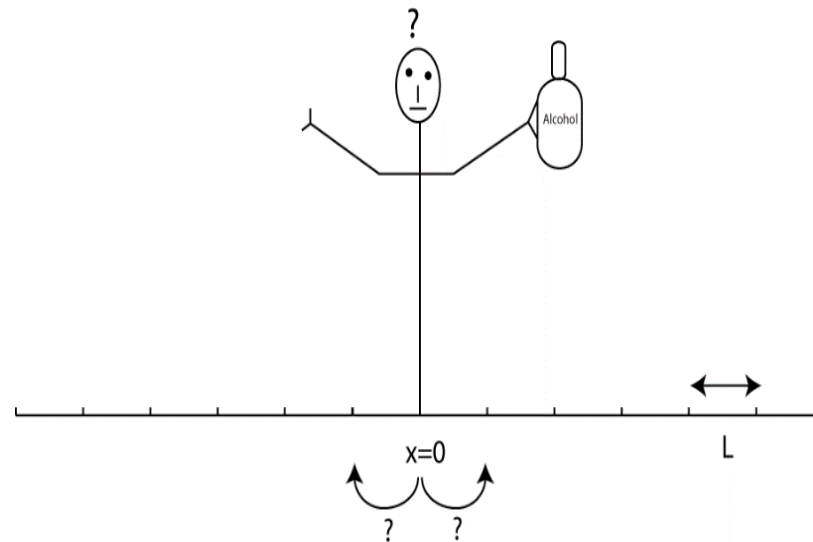


- Similarity of conformation of polymers with random walk.
- One can think of polymer as a chain consisting of many linear segments which are jointed freely.

Random Walk leads to diffusive behavior

1D Diffusion

$$\langle x^2 \rangle = 2Dt$$



$$\langle (x_N)^2 \rangle = NL^2$$

Conformation of the polymer can be treated as random walk and one can predict average shape of the polymer

Conformation of polymers as random walk

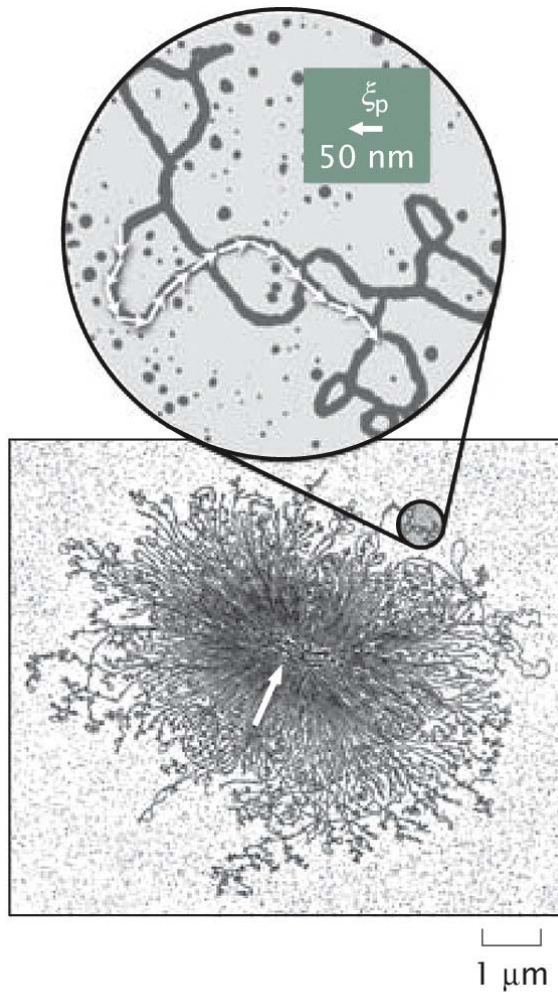


Figure 8.5 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

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.

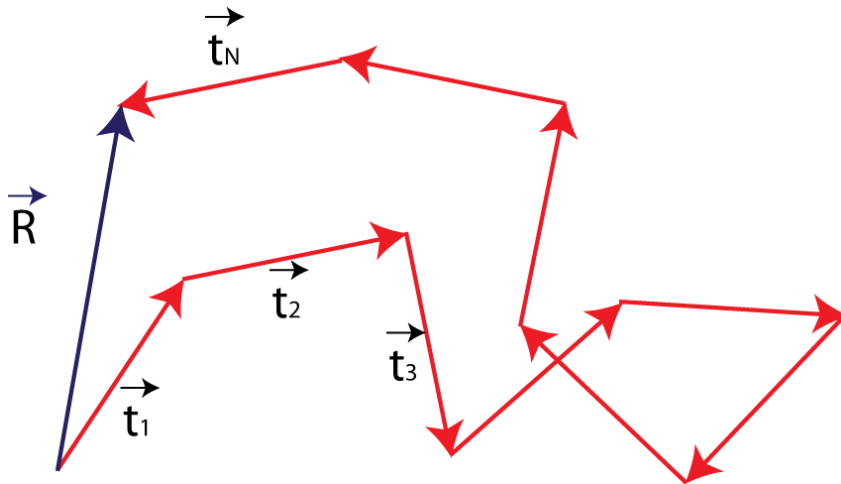
In the thermal equilibrium, joints will be at random angles

Bacterial DNA

Conformation of polymers: Freely Jointed Chain (FJC)

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



$$|\vec{t}_1| = |\vec{t}_2| = \dots = |\vec{t}_N| = L$$

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: Freely Jointed Chain (FJC)

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

$$\begin{aligned} \langle R^2 \rangle &= \left\langle \left(\sum_{i=1}^N \vec{t}_i \right) \cdot \left(\sum_{j=1}^N \vec{t}_j \right) \right\rangle = \left\langle \left(\vec{t}_1 + \vec{t}_2 + \cdots + \vec{t}_N \right) \cdot \left(\vec{t}_1 + \vec{t}_2 + \cdots + \vec{t}_N \right) \right\rangle \\ &= \left\langle \left(\sum_{i=1}^N \vec{t}_i^2 \right) \right\rangle + \sum_{i=1}^N \sum_{j=1, j \neq i}^N \langle \vec{t}_i \cdot \vec{t}_j \rangle \end{aligned}$$

$$\sum_{i=1}^N \sum_{j=1, j \neq i}^N \langle \vec{t}_i \cdot \vec{t}_j \rangle = 0 \Rightarrow \langle R^2 \rangle = \mathbf{N}L^2$$

Summary

- Fick's law, Continuity Equation and Diffusion Equation. Free diffusion from a point source
- Need for active transport
- Einstein Relation and its significance
- Thermal bending of biofilaments
- Freely Jointed Chain (FJC) model for biopolymers