Retrospect

- Last lecture (Underlying principles behind life)
- We have learned the concept of thermal motion and others in lecture 2.
- We'll try to understand: *How does the thermal motion control the sub-cellular world?*
Lecture 3 Molecular dance: Brown motion & Random walks

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Main contents

- Probability
- Understanding the laws of ideal gas
- Brown motion & Random walks
- Friction and diffusion
- Configuration of polymers
- Biological applications of diffusion
§3.1 Probability
Suppose some variable $X$ can take only discrete values $x_1, x_2, ..., x_M$. Suppose we have measured $x$ on $N$ unrelated occasions, finding $X$ takes $x_1$ on $N_1$ occasions, takes $x_2$ on $N_2$ occasions, and so on.

**Definition:**

$$P(x_i) = \lim_{N \to \infty} \frac{N_i}{N} \quad 0 \leq P(x_i) \leq 1$$

**Normalized condition:**

$$\sum_{i=1}^{M} P(x_i) = \frac{(N_1 + N_2 + ... + N_M)}{N} = N/N = 1$$
Continuous distribution

Suppose variable \( X \) can take on any value in a continuous interval \( a \leq x \leq b \)

Definition of distribution function:

\[
p(x)dx = \lim_{N \to \infty} \left[ \frac{d \bar{N}(x)}{N} \right]
\]

Normalized condition:

\[
\int_{a}^{b} p(x) \, dx = 1
\]
• Probability of finding $X$ in interval $(x_1, x_2) \subset (a, b)$

$$P_{x_1}^{x_2} = \int_{x_1}^{x_2} p(x) \, dx \quad \implies \quad P_{x_1}^{x_2} \leq 1$$

• **Uniform** distribution in interval $(a, b)$

$$p(x) = \begin{cases} 
\frac{1}{b-a}, & x \in (a, b) \\
0, & x \notin (a, b) 
\end{cases}$$

• **Gaussian** distribution (bell curve, normal distribution)

$$p(x) = A e^{-\frac{(x-x_0)^2}{2 \sigma^2}}$$

$$\int_{-\infty}^{\infty} p(x) \, dx = 1 \Rightarrow A = \frac{1}{\sqrt{2 \pi \sigma^2}}$$
Mean and variance

• **Mean** (expectation value)

\[
\langle x \rangle = \begin{cases} 
\sum_i x_i P(x_i), & \text{discrete} \\
\int x p(x) \, dx, & \text{continuous}
\end{cases}
\]

If \( f \) is a function of \( x \)

\[
\langle f \rangle = \begin{cases} 
\sum_i f(x_i) P(x_i), & \text{discrete} \\
\int f(x) p(x) \, dx, & \text{continuous}
\end{cases}
\]

• **Variance** (方差)

\[
\text{variance}(x) = \langle (x - \langle x \rangle)^2 \rangle = \langle x^2 \rangle - \langle x \rangle^2
\]

Standard deviation (root-mean-square deviation or RMS deviation)

\[
s = \sqrt{\text{variance}(x)}
\]

Problem: If \( p(x) \) is a **gaussian** distribution, please prove that \( s = \sigma \).
Addition and multiplication rules

• Addition rule

For a discrete distribution, the probability that the next measured value of $X$ is either $x_i$ or $x_j \,(i \neq j)$ equals

$$P(x_i) + P(x_j).$$

For a continuous distribution, the probability that the next measured value of $x$ is either in $(a,b)$ or $(c,d)$ equals

$$\int_a^b p(x) \,dx + \int_c^d p(x) \,dx$$

provided the two intervals don't overlap.
Multiplication rule

Suppose we measure two independent quantities $X$ and $Y$. The probability that $X$ takes value $x_i$ and $Y$ takes value $y_j$, simultaneously, is

$$P_{\text{joint}}(x_i, y_j) = P_X(x_i)P_Y(y_j).$$

Note: For two connected events (for example, the chance of rain and wind) we don’t get such a simple relation.
• More complicated example

Wind gives random shifts to the \( X \) component of your arrows' arrival locations, and independent random shifts to the \( Y \) component.

Assume:

\[
\begin{align*}
p_X(x) &= \frac{1}{\sqrt{2\pi \sigma^2}} e^{-\frac{x^2}{2\sigma^2}} \\
p_Y(y) &= \frac{1}{\sqrt{2\pi \sigma^2}} e^{-\frac{y^2}{2\sigma^2}}
\end{align*}
\]

Problem: Find the probability, \( p(r)dr \), that an arrow lands a distance between \( r \) and \( r + dr \) from the center.

Multiplication rule

\[
p_{XY}(x, y) \, dx\,dy = p_X(x) \, dx \times p_Y(y) \, dy
\]

\[
\Rightarrow p_{XY}(x, y) = \frac{1}{2\pi \sigma^2} e^{-\frac{(x^2+y^2)}{2\sigma^2}} = \frac{1}{2\pi \sigma^2} e^{-\frac{r^2}{2\sigma^2}}
\]

Addition rule

\[
p(r) \, dr = \sum p_{XY}(x, y) \, dx\,dy
\]

\[
= \frac{1}{2\pi \sigma^2} e^{-\frac{r^2}{2\sigma^2}} \times 2\pi r \, dr
\]

\[
\Rightarrow p(r) = \frac{r}{\sigma^2} e^{-\frac{r^2}{2\sigma^2}}
\]
§3.2 The laws of ideal gas
Thermal equilibrium state

- A state of a system of a huge number of particles
- In this state
  - all past history is forgotten
  - all macroscopic quantities (such as $P$, $V$, $T$, ...) cease to change with time
  - probability distributions of microscopic physical quantities (such as $r$, $v$, ...) don’t change with time
Temperature reflects the average kinetic energy of thermal motion

- Law of ideal gas

\[ P = n k_B T \]

Note: here \( P \) is the pressure!

Problem: please check the dimension!

- The origin of \( P \)

\[ \Delta t = \frac{2L}{v_x} \quad \text{(a round trip)} \]

\[ f_1 = \frac{2m v_x}{\Delta t} = m v_x^2 / L \]

\[ p_1 = f_1 / L^2 = m v_x^2 / L^3 \]

\[ P = \langle \sum p_1 \rangle = \sum \langle p_1 \rangle = \left( \frac{N}{L^3} \right) m \langle v_x^2 \rangle = n m \langle v_x^2 \rangle \]
• Interpretation of temperature

\[
P = n k_B T \\
\Rightarrow \frac{1}{2} m \langle v_x^2 \rangle = \frac{1}{2} k_B T = \frac{1}{2} m \langle v_y^2 \rangle = \frac{1}{2} m \langle v_z^2 \rangle
\]

The average energy per DOF is \( \frac{k_B T}{2} \).

\[\sqrt{\langle v^2 \rangle} \approx 500 \text{ m/s} \quad \text{for air molecules at room temperature}\]
Maxwell-Boltzmann distribution

- Distribution of molecular velocities

\[
\frac{dN(v_x, v_y, v_z)}{N} \equiv p(v_x, v_y, v_z) \, dv_x \, dv_y \, dv_z
\]

Distribution function

Maxwell distribution

\[
p(v_x, v_y, v_z) = A e^{-m v^2/2 k_B T}
\]

\[
v^2 = v_x^2 + v_y^2 + v_z^2
\]

Problem: find A?

\[
\int_{-\infty}^{\infty} dv_x \int_{-\infty}^{\infty} dv_y \int_{-\infty}^{\infty} dv_z \, p(v_x, v_y, v_z) = 1 \Rightarrow A = \left( \frac{m}{2 \pi k_B T} \right)^{3/2}
\]
The **proportionate number** of molecules with velocities between \( u \) and \( u + du \)

\[
\begin{align*}
    u &= |\mathbf{v}| = \sqrt{v_x^2 + v_y^2 + v_z^2} \\
    \frac{dN(u)}{N} &= p(u) \, du = \sum p(v_x, v_y, v_z) \, dv_x \, dv_y \, dv_z \\
    &= \left( \frac{m}{2 \pi k_B T} \right)^{3/2} e^{-m u^2 / 2 k_B T} \times 4 \pi u^2 \, du \\
    p(u) &= \left( \frac{2}{\pi} \right)^{1/2} \left( \frac{m}{k_B T} \right)^{3/2} u^2 e^{-m u^2 / 2 k_B T}
\end{align*}
\]

**Question:** what will happen when \( T \to 0 \)?

**Problem:** please prove

\[
p(E_K) \propto \sqrt{E_K} e^{-E_K / k_B T}
\]

\([(T/m)_1 < (T/m)_2 < (T/m)_3] \)
Stern distribution [Zeits. f. Physik 2 (1920) 49]

Question: What's the number of molecules that can escape from a slit in a given time $t_0$ with velocities between $u$ and $u+du$?

\[
\frac{dN_{\text{escape}}}{dN(u)} = \frac{A \times u dt}{\text{total Volume}}
\]

\[
\frac{dN(u)}{N} = \left(\frac{2}{\pi}\right)^{1/2} \left(\frac{m}{k_B T}\right)^{3/2} u^2 e^{-mu^2/2k_B T} du
\]

\[
dN_{\text{escape}} = Cu^3 e^{-mu^2/2k_B T} du
\]

$C$ is a constant

Related problem: the escaping of RNA from the nuclear pores.
Experiment [Miller & Kusch, Phys. Rev. 99(1955)1314]

\[ u = \frac{L}{T_0} = \frac{L}{(2 \pi / \omega)} = \omega L / 2 \pi \]

\[ d \, T_0 = (2 \pi - \delta)/\omega \]

Angle corresponds to slots

Problem: please prove \( du \propto u \)?

\[ dN_{\text{escape}} = C u^3 e^{-m u^2 / 2 k_B T} \, du \]

\[ dN_{\text{detect}} (u) = C_1 u^4 e^{-m u^2 / 2 k_B T} \]

\[ dN_{\text{detect}} (\bar{u}) = C_2 \bar{u}^4 e^{-2 \bar{u}^2} \]

\[ \bar{u} = u \sqrt{m / 4 k_B T} \]

Maxwell distribution is correct!
• **Boltzmann distribution**

\[
p(\text{state}) = e^{-\frac{E(\text{state})}{k_B T}}
\]

What's the **state** and the **\(E(\text{state})\)** for \(N\) particles?

\[
\{ r ; v \} = \{ x_1, y_1, z_1, \ldots, x_N, y_N, z_N ; v_{1x}, v_{1y}, v_{1z}, \ldots, v_{Nx}, v_{Ny}, v_{Nz} \}
\]

\[
= \{ r_1, \ldots, r_N ; v_1, \ldots, v_N \}
\]

\[
E(\{ r ; v \}) = U( r_1, \ldots, r_N ) + \sum_{i=1}^{N} \frac{1}{2} m_i v_i^2
\]

\[\text{Potential energy}\]

\[\text{Kinetic energy}\]

**Configuration space** (构形空间)

configuration \(\equiv\{ r_1, \ldots, r_N \}\)
Chemical reaction

- **Reaction coordinate & activation barrier**

  Reaction coordinate (反应坐标): the fast reaction path from reactant to resultant in the configuration space.

  \[ \Delta E_a \text{: activation energy} \]
• **Reaction rate in simple reaction**

Intuitively, the molecules of reactant with $E_K \geq \Delta E_a$ can escape from the barrier. Thus the reaction rate

\[
\dot{r} \propto \frac{dN(E_K \geq \Delta E_a)}{N}
\]
Problem: please prove

\[ \frac{dN \left( E_K \geq \Delta E_a \right)}{N} = e^{-\Delta E_a / k_B T} \]

\[ dN(E_K \geq \Delta E_a) = \text{number of molecules outside the ellipse} \]

\[ p(v_1, v_2) dv_1 dv_2 \propto e^{-(m_1 v_1^2 + m_2 v_2^2) / 2 k_B T} \]

\[ p(V_1, V_2) dV_1 dV_2 \propto e^{-m(V_1^2 + V_2^2) / 2 k_B T} \]

\[ p(V) dV \propto V e^{-mV^2 / 2 k_B T} \]

\[ \frac{dN \left( E_K \geq \Delta E_a \right)}{N} = \int_0^\infty p(V) dV = e^{-\Delta E_a / k_B T} \]

Hard Question: What is missed in our discussion?

\[ r \propto e^{-\Delta E_a / k_B T} \]

Arrhenius rate law
• How to increase the reaction rate?

$$r = r_0 e^{-\Delta E_a / k_B T}$$

Arrhenius rate law

Two ways to increase the reaction rate:
(1) increase temperature (heat);
(2) decrease the activation barrier (enzyme)
Relaxation to equilibrium

- Our experience: when a system is left to itself under constant external conditions for a long time, it usually arrives at a thermal equilibrium state. This process is called relaxation to equilibrium.

- Example 1: gas expansion

Thermal bath (constant $T$)

Disorder increases!
Example 2: high energy molecules injection

N particles is at an equilibrium state in an isolated box. A fast molecule is suddenly injected in the box.

Gas is not so idea, molecules have a size!

Problem: Prove that the fast one transfers a lot of its $E_K$ to the slow one when they collide elastically.

Now we have two medium-fast molecules; each is closer to the average than it was to begin with. the equilibrium distribution will be gradually approached with the more collisions.

The directed motion (mechanical energy) of the original molecule has degraded to the average random motion (thermal energy) of all molecules.

Friction: $E_K \rightarrow E_T$
§3.3 Brown motion & Random walks
Brief history of Brownian motion

- Brown (1828)
  - Pollen grains (1μm) suspended in water do a peculiar dance
  - The motion of the pollen never stopped
  - Totally lifeless particles do exactly the same thing

- Einstein (1905)
  - Quantitative explanation from thermal motion of water molecules
Random walks

- Drunkard's walk (醉汉走路)

Are there any rules on the position $R$ of the drunkard?

$\langle R \rangle = 0$

$\langle R^2 \rangle \geq 0$?

Note: $R$ is a vector
• **1D random walk**

![Diagram of 1D random walk]

- $L$ --- Length of each step
- $x_0 = 0$ --- start point
- $x_n$ --- position after the $n$-th step
- $k_n L$ --- displacement of the $n$-th step with $P(k_n = 1) = P(k_n = -1) = 1/2$

\[ x_n = x_{n-1} + k_n L \]

**Problem:** prove that $\langle x_n \rangle \geq 0$.

**Proof:**

\[ \langle k_n \rangle = 1 \times (1/2) + (-1) \times (1/2) = 0 \Rightarrow \]

\[ \langle x_n \rangle = \langle x_{n-1} + k_n L \rangle = \langle x_{n-1} \rangle + \langle k_n \rangle L = \langle x_{n-1} \rangle \Rightarrow \]

\[ = \langle x_{n-2} \rangle = \ldots = \langle x_1 \rangle = \langle x_0 \rangle = 0 \]
\[ \langle x^2_n \rangle = ? \]

\[ x^2_n = (x_{n-1} + k_n L)^2 = x^2_{n-1} + 2 L k_n x_{n-1} + k^2_n L^2 \]

\[ k^2_n = (\pm 1)^2 = 1 \]

\[ \langle k_n x_{n-1} \rangle = (+1) x_{n-1} P(+1) + (-1) x_{n-1} P(-1) = 0 \]

\[ \langle x^2 \rangle = \langle x^2_{n-1} + 2 L k_n x_{n-1} + k^2_n L^2 \rangle = \langle x^2_{n-1} \rangle + L^2 \]

\[ \Rightarrow \langle x^2_N \rangle = NL^2 \quad \iff \quad \langle x^2_N \rangle = 2Dt \]

\[ D = L^2 / 2 \Delta t \quad \text{diffusion constant} \]
• **2D** random walk

\[ \mathbf{r}_n = (x_n, y_n) = (x_{n-1}, y_{n-1}) + (k_{xn}, k_{yn})L \]

\[ \mathbf{r}_n^2 = x_n^2 + y_n^2 \]

**Problem:** prove that \( \langle \mathbf{r}_N^2 \rangle = 4Dt \)

\[
\begin{array}{cccc}
1 & 0 & 1/4 & 0 \\
0 & 1/4 & 0 & 1/4 \\
-1 & 0 & 1/4 & 0 \\
\end{array}
\]

• **3D** random walk

\[ \mathbf{r}_n = (x_n, y_n, z_n) = (x_{n-1}, y_{n-1}, z_{n-1}) + (k_{xn}, k_{yn}, k_{zn})L \]

\[ P(\pm 1,0,0) = P(0,\pm 1,0) = P(0,0,\pm 1) = 1/6; \text{ 0 for others.} \]

**Problem:** prove that \( \langle \mathbf{r}_N^2 \rangle = 6Dt \)
• Diffusion law

\[
\left\langle \left[ r\left(t\right) \right]^2 \right\rangle = 2 m D t
\]

Spacial dimension

\[
D = \frac{L^2}{2 \Delta t}
\]

Length of each step \quad Time of each step

Diffusion constant

Macroscopic measurable quantity

Microscopic parameters in brown motion
§3.4 Friction & diffusion
Einstein relation

- A ball in viscous fluid (macroscopic analysis)

\[ f_{\text{friction}} = \xi v \]

\[ a = \left( f_{\text{ext}} - f_{\text{friction}} \right) / m = \left( f_{\text{ext}} - \xi v \right) / m \]

(i): \( v < f_{\text{ext}} / \xi \Rightarrow a > 0 \Rightarrow v \uparrow \Rightarrow v \rightarrow f_{\text{ext}} / \xi \)

(ii): \( v > f_{\text{ext}} / \xi \Rightarrow a < 0 \Rightarrow v \downarrow \Rightarrow v \rightarrow f_{\text{ext}} / \xi \)

\[ v_{\text{drift}} \equiv f_{\text{ext}} / \xi \iff f_{\text{ext}} = f_{\text{friction}} \]
The process to reach the drift velocity in micrometer scale

\[
\frac{dv}{dt} = a = \left( f_{ext} - \xi v \right) / m = \xi (v_{drift} - v) / m \Rightarrow
\]

\[
v(t) = v_{drift} + \left[ v(0) - v_{drift} \right] e^{-\xi t / m}
\]

The larger \( \xi / m \), \( v \) reaches more quickly to \( v_{drift} \)

Stokes formula:

\[
\xi = 6 \pi \eta R
\]

\( \eta \)--viscosity

\( \eta_{water} \approx 10^{-3} \text{kg m}^{-1} \text{s}^{-1} \quad R_{pollen} \approx 1 \mu\text{m} \)

\[
\tau_c \equiv m / \xi \approx 10^{-7} \text{s}
\]

\( v \rightarrow v_{drift} \) very quickly such that we can omit the process!
A ball in viscous fluid (microscopic analysis)

Assumption:
1. The collisions occur exactly once per $\Delta t$
2. In between kicks, the ball is free of random influences, so $a = f_{ext} / m$
3. $v_0$ is the starting value just after a kick
4. Each collision obliterates (抹去) all memory of the previous step

$$
(1)-(3) \Rightarrow \Delta x = v_{0x} \Delta t + \frac{1}{2} a \Delta t^2 = v_{0x} \Delta t + \frac{1}{2} (f_{ext} / m) \Delta t^2
$$

$$
(4) \Rightarrow \langle v_{0x} \rangle = 0
$$

$\nu_{drift} \equiv \frac{\langle \Delta x \rangle}{\Delta t} = \frac{f_{ext}}{\xi}$

$$
\xi = 2 \frac{m}{\Delta t}
$$
• **Einstein relation**

\[
D = \frac{L^2}{2 \Delta t} \\
\xi = \frac{2m}{\Delta t}
\]

\[\rightarrow \xi D = m \left( \frac{L}{\Delta t} \right)^2\]

In our discussion, we have confined \(L\) and \(\Delta t\) to be constant. In fact, they are also **stochastic quantities**. Strict derivation gives

\[
\xi D = m \left( \frac{L}{\Delta t} \right)^2 = m \langle v_x^2 \rangle \\
\frac{1}{2} m \langle v_x^2 \rangle = \frac{1}{2} k_B T
\]

**Hypothesis**

Heat is disordered molecular motion

**Testable prediction**

Einstein relation

\[\xi D = k_B T\]
More rigorous treatment

- Mean field thought

The collisions of water molecules are simplified as a white noise

$$\langle \Gamma(t) \rangle = 0, \quad \langle \Gamma(t) \Gamma(t') \rangle = g \delta(t-t')$$

Newton's law $\Rightarrow$ $m \frac{dv_x}{dt} = -\xi v_x + \Gamma(t)$ (Langevin equation)

Solution:

$$v_x = v_0 e^{-t/\tau_c} + \frac{1}{m} \int_0^t e^{-(t-s)/\tau_c} \Gamma(s) ds, \quad \tau_c \equiv m/\xi$$

$$x(t) = \int_0^t v_x dt = v_0 \tau_c \left[ 1 - e^{-t/\tau_c} \right] + \frac{1}{\xi} \int_0^t \left[ 1 - e^{-(t-s)/\tau_c} \right] \Gamma(s) ds$$
\[
v_x^2 = v_0^2 e^{-2t/\tau_c} + \frac{1}{m^2} \left[ \int_0^t e^{-(t-s)/\tau_c} \Gamma(s) \, ds \right]^2 + \frac{2v_0}{m} e^{-t/\tau_c} \int_0^t e^{-(t-s)/\tau_c} \Gamma(s) \, ds
\]

Assume that \( v_0 \) is independent of \( \Gamma(s) \):
\[
\langle v_0 \Gamma(s) \rangle = \langle v_0 \rangle \langle \Gamma(s) \rangle = 0
\]

\[
\langle v_x^2 \rangle = \langle v_0^2 \rangle e^{-2t/\tau_c} + \frac{1}{m^2} \left[ \int_0^t e^{-(t-s)/\tau_c} \Gamma(s) \, ds \right]^2
\]

\[
= \frac{g}{2m\xi} + \left( \langle v_0^2 \rangle - \frac{g}{2m\xi} \right) e^{-2t/\tau_c}
\]

The observed time scale \( t \gg \tau_c \)

\[
\langle v_x^2 \rangle = \frac{g}{2m\xi}
\]

\[
\frac{1}{2} m \langle v_x^2 \rangle = \frac{1}{2} k_B T
\]

\[
g / 2 \xi = k_B T
\]
\[
x^2(t) = v_0^2 \tau_c^2 \left[ 1 - e^{-t/\tau_c} \right]^2 + \frac{1}{\xi^2} \left\{ \int_0^t \left[ 1 - e^{-(t-s)/\tau_c} \right] \Gamma(s) \, ds \right\}^2
\]
\[
+ 2 \frac{v_0 \tau_c}{\xi} \left[ 1 - e^{-t/\tau_c} \right] \int_0^t \left[ 1 - e^{-(t-s)/\tau_c} \right] \Gamma(s) \, ds
\]
\[
\langle x^2(t) \rangle = \langle v_0^2 \rangle \tau_c^2 \left[ 1 - e^{-t/\tau_c} \right]^2 + \frac{1}{\xi^2} \left\{ \left\{ \int_0^t \left[ 1 - e^{-(t-s)/\tau_c} \right] \Gamma(s) \, ds \right\}^2 \right\}
\]
\[
= \left( \langle v_0^2 \rangle - \frac{g}{2 m \xi} \right) \tau_c^2 \left[ 1 - e^{-t/\tau_c} \right]^2 + \frac{g}{\xi^2} \left[ t + \tau_c \left( 1 - e^{-t/\tau_c} \right) \right]
\]

The observed time scale \( t \gg \tau_c \)

\[
\langle x^2(t) \rangle = \left( \frac{g}{\xi^2} \right) t \equiv 2Dt \Rightarrow
\]

\[
\Rightarrow D = \frac{g}{2 \xi^2}
\]

\[
g/2\xi = k_B T
\]

\[
\xi D = k_B T
\]
Diffusion equation

- What's meaning of the average?

e.g. \( \langle r^2(t) \rangle = 4Dt \) (2-dimensional random walk)

\[
\langle r^2(t) \rangle = \lim_{M \to \infty} \sum_{i=1}^{M} r_i^2(t) = 4Dt
\]

Equivalent to release simultaneously \( M \) particles at origin and then let them do independently random walk (diffuse to other places).
• **Fick's law**

Assumption--
- Large number particles
- Uniform in \( y, z \) direction
- Nonuniform in \( x \) direction
- Jump distance \( L \) per time \( \Delta t \)
- Same jump probability to left and right

\( N(x,t) \): the number of particles in the box between \( x-L/2 \) and \( x+L/2 \) at time \( t \).

\( (1/2)N(x,t) \) particles will pass through \( x-L/2 \) to the left in \( \Delta t \).

Simultaneously, \( (1/2)N(x-L,t) \) particles pass through \( x-L/2 \) to the right.

**Density of number**

\[
c(x,t) = \frac{N(x,t)}{A \times L}
\]

**Flux**

\[
j = \frac{1}{2} \left[ N(x-L,t) - N(x,t) \right]
\]

\[
\frac{1}{2 \Delta t \times A} = -D \frac{\partial c}{\partial x}
\]

\[
D = \frac{L^2}{2 \Delta t}
\]
Question: why is there a flux since each particle has the same jump probability to left and right? 

Reason for net flow: there are more particles in one slot than in the neighboring one.

- **Continuity equation**

\[
\Delta N(x, t) = \left[ j(x - \frac{L}{2}) - j(x + \frac{L}{2}) \right] A \Delta t
\]

\[
= - \frac{\partial j}{\partial x} L \times A \times \Delta t \quad \Rightarrow
\]

\[
\frac{\partial c}{\partial t} = - \frac{\partial j}{\partial x}
\]
• Diffusion equation and its solution

\[ j = -D \frac{\partial c}{\partial x} \]
\[ \frac{\partial c}{\partial t} = -\frac{\partial j}{\partial x} \]

\[ \frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} \]  
(Diffusion equation)

Pulse solution

\[ \frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} \]  
(Diffusion equation)

\[ c(x, 0) = \delta(x) \]  
(initial condition)

\[ c(x, t) = \frac{1}{\sqrt{4 \pi Dt}} e^{-x^2/4Dt} \]

Problem: Does the solution satisfy the diffusion equation and initial condition?
Fluctuation

Molecular thermal motion (random) $\Rightarrow$ Diffusion equation

Question: Why is diffusion equation deterministic?

Answer: Average on ensemble (collection of large number repeated systems). Available to describe a system of large number particles.

Finite particle system: its behavior deviated from the prediction of diffusion equation. This deviation is called statistical fluctuation.

Few particle system: Statistical fluctuations will be significant, and the system's evolution really will appear random, not deterministic.

Nanoworld of single molecules: need to take fluctuations seriously
§3.5 Configurations of polymers
Simple polymer

• Example

PE: polyethylene (聚乙烯)

Long-chain molecule

<table>
<thead>
<tr>
<th>Bond length</th>
<th>$x_0=1.44\text{Å}$</th>
<th>$k_1(x-x_0)^2/2$</th>
<th>$\sqrt{\langle(x-x_0)^2\rangle} \sim 10^{-2} \text{Å}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_1 \sim 57\text{eV}/\text{Å}^2$</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bond angle</th>
<th>$\alpha_0=120^\circ$</th>
<th>$k_2(\alpha-\alpha_0)^2/2$</th>
<th>$\sqrt{\langle(\alpha-\alpha_0)^2\rangle} \sim 10^{-2}\text{rad}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_2 \sim 84\text{eV}$</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Thermal motion does **NOT** excite the DOFs of bond length and angle!
Rotational DOF

$l_0, \theta$ fixed!
• Flexibility (柔性)

Locally static flexibility (局部静态柔性)

\[
\frac{P(gauche)}{P(trans)} = e^{-\Delta \epsilon / k_B T} \approx 1 \quad \text{for} \quad \Delta \epsilon < k_B T
\]

Gauche/trans conformations will be found in similar frequency in the local part of a polymer. Thus the local part of a polymer appears as a random coil.

\[
\frac{P(gauche)}{P(trans)} = e^{-\Delta \epsilon / k_B T} \approx 0 \quad \text{for} \quad \Delta \epsilon \gg k_B T
\]

Gauche conformations is seldom found in local part of a polymer. Only trans conformations. Locally like a rigid rod.
Persistence length (驻留长度) and Globally static flexibility

\[ l_p = l_0 e^{\frac{\Delta \epsilon}{k_B T}} \]

**Question:** what's physical meaning of \( l_p \)?

\[ e^{-\frac{\Delta \epsilon}{k_B T}} \]
Probability of gauche conformation between near neighbor bonds.

How many bonds will occur 1 gauche conformation?

\[ \frac{1}{e^{-\frac{\Delta \epsilon}{k_B T}}} = e^{\frac{\Delta \epsilon}{k_B T}} = l_p / l_0 \]

1 gauche conformation can occur in persistence length

(1) if total length < \( l_p \), the polymer seems a rigid rod.

(2) if total length >> \( l_p \), many gauche conformations occur in the polymer. The whole chain is random coil. Locally rigid while Globally flexible.
Persistence time (驻留时间) & Dynamic flexibility (动态柔性)

\[ \tau_p = \tau_0 e^{\frac{\Delta E}{k_B T}} \]

\[ \tau_0 \sim 10 \text{ ps} \]

Transition time from trans to gauche

(1) \( t_{\text{observe}} < \tau_p \), polymer is frozen in one configuration. Dynamically rigid.

(2) \( t_{\text{observe}} \gg \tau_p \), polymer transits in different configurations. Dynamically flexible.

Now, we only consider the case length \( l \gg l_p \) and \( t_{\text{observe}} \gg \tau_p \).
• End-to-end distance (首末端距)

Thus, \( R_N \) is a stochastic variable!

\[
\langle R_N \rangle = ?; \quad \langle R_N^2 \rangle = ?; \quad p(R_N) = ?
\]
Typical models for polymers

- **Freely jointed chain**

  \[ R_N = r_1 + r_2 + \cdots + r_N \]

  \( L \): segment length

  \( r_i \): vector for the \( i \)-th segment, random distribution vector with constant length

  \[ \langle R_N \rangle = 0 \quad \langle R_N^2 \rangle = NL^2 \]

  **Problem**: prove that

  **Discuss**: equivalent to random walk

  **Question**: valid condition for polymer? \( (L > l_p) \)
Problem: find the distribution function of $R_N$

We have known that
\[
p(r_n) = \frac{\delta(|r_n| - L)}{4\pi L^2}; \quad p(r_1, \ldots, r_N) = \prod p(r_n)
\]

\[
R_N = \sum r_n
\]

\[
p(R_N) = \int d^3 r_1 \cdots \int d^3 r_N \delta(R_N - \sum r_n) p(r_1, \ldots, r_N)
\]

(a classic math formula)

\[
= \frac{1}{(2\pi)^3} \int d^3 k \int d^3 r_1 \cdots \int d^3 r_N e^{i k \cdot (R_N - \sum r_n)} p(r_1, \ldots, r_N)
\]

\[
\int d^3 r_n e^{-i k \cdot r_n} p(r_n) = \frac{\sin kL}{kL} \Rightarrow p(R_N) = \frac{1}{(2\pi)^3} \int d^3 k e^{i k \cdot R_N} \left(\frac{\sin kL}{kL}\right)^N
\]

For $N \gg 1$, only $kL \approx 0$ is important!

\[
\frac{\sin x}{x} = 1, (x = 0)
\]

\[
\left| \frac{\sin x}{x} \right| < 1, (x > 0)
\]

\[
\frac{\sin x}{x} = 1 - \frac{x^2}{6} + O(x^4)
\]

\[
\frac{\sin kL}{kL} \approx 1 - \frac{k^2 L^2}{6} \approx e^{-k^2 L^2/6}
\]

\[
p(R_N) = \left(\frac{3}{2\pi NL^2}\right)^{3/2} e^{-3R_N^2/2 NL^2}
\]
• Freely rotating chain

\[ \Delta E = \Delta \epsilon = 0 \Rightarrow \text{freely rotating} \]

\[ |r_n| = l_0 \ (\text{bond length}) \]

\[
p(r_n) = p(r_n|r_{n-1})p(r_{n-1})
\]

\[
p(r_n|r_{n-1}) = \frac{\delta(\theta_n - \theta)\delta(|r_n| - l_0)}{2\pi l_0^2 \sin \theta}
\]

Problem: prove that

\[
\int d^3 r_n p(r_n|r_{n-1}) = 1
\]

\[
\langle r_n \rangle = \langle r_{n-1} \rangle \cos \theta
\]

\[
R_N = r_1 + r_2 + \cdots + r_N
\]

Problem: prove that

\[
\langle R_n \rangle = \frac{1 - \cos^N \theta}{1 - \cos \theta} \langle r_1 \rangle = 0 \text{ for random } r_1
\]
Problem: Prove that

\[ \langle r_n \cdot r_m < n \rangle = \langle r_{n-1} \cdot r_m < n \rangle \cos \theta = l_0^2 (\cos \theta)^{n-m} \]

Problem: Prove that for \( \theta \neq 0 \),

\[ \langle R_N^2 \rangle = \sum_{n=1}^{N} \langle r_n^2 \rangle + 2 \sum_{n=1}^{N} \sum_{m=1}^{n-1} \langle r_n \cdot r_m \rangle = Nl_0^2 + 2l_0^2 \sum_{n=1}^{N} \frac{\cos \theta - \cos^n \theta}{1 - \cos \theta} \]

\[ \rightarrow \langle R_N^2 \rangle = Nl_0^2 \frac{1 + \cos \theta}{1 - \cos \theta} \quad \text{when} \quad N \gg 1 \]

Question: what will happen if \( \theta = 0 \)?

\[ \langle R_N^2 \rangle = N^2 l_0^2 \]

Discuss: relationship between this model and random walk

(1) \( \theta = \pi/2 \), random walk \textbf{without} memory

(2) \( 0 < \theta < \pi/2 \), random walk \textbf{with} memory of last step's direction
Problem: find the distribution function of $R_N$

The exact result has not yet obtained for finite $N!$

$N >> 1$, divide: $N = N_1 + \nu + N_2$

$N_1 \approx N_2 \gg \nu$ \(\nu\) bonds is a point in macroscopic scale.

\(\nu\) large enough, such that

$$\left\langle r_{N_1 + \nu} \cdot r_{N_1} \right\rangle = l_0^2 (\cos \theta)^\nu \rightarrow 0$$

$$p(R_N) = \int d^3 R_{N_1} p_1(R_{N_1}) p_2(R_N - R_{N_1})$$

$$G(N, k) = \int d^3 R_N e^{ik \cdot R_N} p(R_N) = G(N_1, k) G(N - N_1, k)$$

$$G(N_1 + N_2, k) = G(N_1, k) G(N_2, k)$$

$$G(N, k) = e^{-f(k)N}$$

$N \gg 1$ requires $f(k) \rightarrow 0_+ \Rightarrow f(k) = a k^2 + O(k^4)$

$$p(R_N) = \frac{1}{(2\pi)^3} \int d^3 k e^{-ik \cdot R_N} G(N, k) = \frac{1}{(2\pi)^3} \int d^3 k e^{-i k \cdot R_N} e^{-ak^2 N}$$

$$= \left( \frac{\sqrt{1/4\pi aN}}{\pi} \right)^3 e^{-R_N^2/4aN}$$
Problem: find the positive number $a$

$$p(R_N) = \left(\sqrt{\frac{1}{4\pi aN}}\right)^3 e^{-\frac{R_N^2}{4aN}} \Rightarrow \langle R_N^2 \rangle = \int d_R R_N^2 p(R_N) = 6aN$$

$$\langle R_N^2 \rangle = NL_0^2 \frac{1 + \cos \theta}{1 - \cos \theta}$$

$$a = \frac{l_0^2}{6} \frac{1 + \cos \theta}{1 - \cos \theta}$$

$$p(R_N) = \left[\frac{3(1 - \cos \theta)}{2 \pi NL_0^2 (1 + \cos \theta)}\right]^{3/2} e^{-\frac{3(1 - \cos \theta)R_N^2}{2 NL_0^2 (1 + \cos \theta)}}$$

(Freely rotating chain, $N \gg 1$)

$$p(R_N) = \left(\frac{3}{2 \pi NL^2}\right)^{3/2} e^{-\frac{3R_N^2}{2NL^2}}$$

(Freely jointed chain, $N \gg 1$)

Thus, the **Gaussian form is universal** for the long chain polymer!
• **Ideal chain (Gaussian)**

**Definition:** a chain of finite length whose distribution of end-to-end vector satisfies

\[
p(R_N) = \left( \frac{3}{2 \pi N b^2} \right)^{3/2} e^{-\frac{3}{2} \frac{R_N^2}{N b^2}} \quad (b: \text{characteristic length})
\]

**Equivalent model:** \((N+1)\) beads connected by \(N\) spring with force constant \(3k_B T/b^2\)

\[
R_0 = 0
\]

\[
U(R_1, \ldots, R_N) = \frac{3 k_B T}{2 b^2} \sum_{n=1}^{N} (R_n - R_{n-1})^2
\]

Boltzmann distribution

\[
p(R_1, \ldots, R_N) \propto e^{-U/k_B T} = e^{-\frac{3}{2 b^2} \sum_{n=1}^{N} (R_n - R_{n-1})^2}
\]
Problem: find the distribution function of end-to-end vector

\[ p(R_N) = \int d^3 R_1 \cdots \int d^3 R_{N-1} p(R_1, \ldots, R_N) \]

\[ = C \int d^3 R_1 \cdots \int d^3 R_{N-1} e^{-\frac{3}{2b^2} \sum_{n=1}^{N} (R_n - R_{n-1})^2} = \int D[R_n] e^{-\beta (3/2b^2) \int \sum_{n=1}^{N} (d R_n / dn)^2} \]

Quantum Mechanics (free particle)  
Polymer

<table>
<thead>
<tr>
<th>time ( t )</th>
<th>the number of segments ( N )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( i/\hbar )</td>
<td>( -\beta = -1/k_B T )</td>
</tr>
</tbody>
</table>

Lagrangian \( \hat{L} = (m/2)(d\mathbf{r}/d\tau)^2 \)  
Potential energy \( U = (\eta/2)(d\mathbf{R}_n/dn)^2 \)

mass \( m \)  
\( \eta = 3/(\beta b^2) \)

propagator \( \hat{K} = \int D[\mathbf{r}(\tau)] \exp[(i/\hbar) \int_0^t \hat{L} d\tau] \)  
distribution function \( p = \int D[\mathbf{R}_n] \exp[-\beta \int_0^N U dn] \)

Hamiltonian \( \hat{H} = -\frac{\hbar^2}{2m} \nabla^2 \)  
\( \hat{G} = \frac{1}{2\eta\beta^2} \nabla^2 \)

\( i\hbar \partial \hat{K} / \partial t = \hat{H} \hat{K}, (t > 0) \)  
(\( 1/\beta \)) \( \partial p / \partial N = \hat{G} p \)

\( \Rightarrow \partial p / \partial N = (3/2b^2) \nabla^2 p \)
Initial condition \( p(R_0) = \delta(N) \)

\( \Rightarrow p(R_N) = \left( \frac{3}{2 \pi Nb^2} \right)^{3/2} e^{-\frac{3}{2Nb^2} \sum_{n=1}^{N} (R_n)^2} \)
Problem: please derive \( p(R_N) \) directly from

\[
p(R_N) = C \int d^3 R_1 \cdots \int d^3 R_{N-1} \, e^{-\frac{3}{2} b^2 \sum_{n=1}^{N} (R_n - R_{n-1})^2}
\]

Hints:

\[
\int d^3 R_{n+1} \, e^{-\alpha \left[ (R_{n+2} - R_{n+1})^2 + (R_{n+1} - R_n)^2 \right]} \propto e^{-\frac{\alpha (R_{n+2} - R_n)^2}{2}}
\]

\[
\int d^3 R_1 \cdots \int d^3 R_{N-1} \, e^{-\alpha \sum_{n=1}^{N} (R_n - R_{n-1})^2} \propto e^{-\frac{\alpha (R_N - R_0)^2}{N}} = e^{-\frac{\alpha R_N^2}{N}}
\]

\[
p(R_N) = C \, e^{-\frac{3 R_N^2}{2N b^2}}
\]

\[
\int d^3 R_N \, p(R_N) = 1
\]

\[
p(R_N) = \left( \frac{3}{2 \pi N b^2} \right)^{3/2} e^{-\frac{3 R_N^2}{2N b^2}}
\]
- **Worm-like chain**

\[ U = \frac{\epsilon}{2} \int_0^s \left[ \left( \frac{d t(s')}{ds'} \right)^2 \right] ds' \]

Correspondence principle=>

\[ \frac{\partial p(t(s))}{\partial s} = \lambda \nabla^2_t p(t(s)) \]

\[ \lambda \equiv k_B T / 2 \epsilon \quad \quad |t(s)| = 1 \Rightarrow \nabla^2_t \text{ is 2D Laplace operator} \]

\[ p(t(s)) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} \sqrt{(2l+1) \pi} e^{-l(l+1)\lambda s} Y_{lm}(\theta, \phi) \]  

[王竹溪, 特殊函数论]

\[ \langle t(s_1) t(s_2) \rangle = e^{-2\lambda |s_2 - s_1|} \]

\[ \langle R^2 \rangle = \int_0^{NL} ds_1 \int_0^{NL} ds_2 \langle t(s_1) t(s_2) \rangle = \frac{NL}{\lambda} - \frac{(1 - e^{-2\lambda NL})}{2 \lambda^2} \]

\[ p(R) = \left( \frac{3 \lambda}{2 \pi NL} \right)^{3/2} e^{-3 \lambda R^2 / 2 NL} ; \quad (N \gg 1) \]  

[Daniels (1952)]
Entropic elasticity

- Elasticity of crystals (change of internal energy)

\[ \Delta F_{\text{cryst}} = \Delta U - T \Delta S \]

The crystal still have good order, the entropy is almost unchanged.

\[ \Rightarrow \Delta F = \Delta U \]

Change of internal energy resists the deformation induced by external force!
Elasticity of polymers (entropy)

When a force is applied on the end of a polymer, both bond length and angle keep almost constant. Thus internal energy is unchanged.

The number of configurations (i.e. entropy) changes.

\[ \Rightarrow \Delta F = -T \Delta S \]

Change of entropy resists the deformation induced by external force!

Problem: The entropy of the polymer decreases when an extension is applied. Is the 2nd law violated? (discussion!)
§3.6 Biological applications of diffusion
Limit on bacterial metabolism

- Idealized model

\[ c(\infty) = c_0 \]

\[ c(R) = 0 \]

O_2 is dissolved in the water, with a concentration \( c_0 \):

Bacterium immediately gobbles up (吞噬) O_2 at its surface:

Problem: Find the concentration profile \( c(r) \) and the maximum consumed number of O_2 per time
• Solution

$I(r)$: the number of $O_2$ per time passing through the fictitious (假想的) spherical shell

Assume: quasi-steady state, oxygen does not pile up (累积) anywhere:

$$I(r) = I \quad \text{(independent of } r)$$

Flux of $O_2$: $j(r) = I / 4\pi r^2$

Fick's law: $j(r) = -D dc/dr$

BCs: $c(R) = 0$ & $c(\infty) = c_0$

$I = 4\pi D c_0 R$

maximum consumed number of $O_2$ per time
• Limit on the size of the bacterium

The number of O_2 per time that a living body needs

\[ \dot{Q} \propto M^{2/3} \propto R^2 \]  

Metabolic rate (ref. Lecture 2)

The maximum consumed number of O_2 per time

\[ I = 4\pi Dc_0 R \]

\[ \dot{Q} \leq I \]

\[ R \leq R_{\text{max}} \]

There is an upper limit to the size of a bacterium!
Permeability of membranes

- Ion channel for passive transport

Fick's law

\[
j = -D \frac{dc}{dx} = -D \frac{c_L - c_0}{L} \equiv -\left( \frac{D}{L} \right) \Delta c
\]

permeation constant

渗透系数

1. A polar substance is more concentrated on the outside than the inside of the cell.
2. Binding of a stimulus molecule causes the pore to open...
3. ...and the polar substance can diffuse across the membrane.
• Idealized model: permeation of cell membrane

Assumptions:

1. $c_{out}$ is almost constant because the environment is infinite

2. $j_{out \rightarrow in} = -P_s \Delta c = -P_s (c_{in} - c_{out})$

$c_{in} = N_{in} / V$, $c_{out} > c_{in}$

$$d(N_{in}) / dt = j_{out \rightarrow in} A = -P_s A \Delta c$$

$$d(N_{in}) / dt = (1 / V) dN_{in} / dt$$

$$d(N_{in}) / dt = j_{out \rightarrow in} A = -P_s A \Delta c$$

$$d(\Delta c) / dt = -\left( P_s A / V \right) \Delta c$$ (relaxation of a concentration jump)

$$\Rightarrow \Delta c = \Delta c_0 e^{-t/\tau}$$

$\tau \equiv V / P_s A$ (decay constant)

**Problem:** analysis that $V / P_s A$ has the dimension of time.
Membrane potentials

- Drift and diffusion: ionic solution under E-field

\[ E = -\frac{\Delta V}{l} \]

\[ f_{\text{drift}} = qE = -q \frac{\Delta V}{l} \]

\[ \nu_{\text{drift}} = \frac{f_{\text{drift}}}{\xi} = -\frac{q \Delta V}{l} \frac{1}{\xi} \]

\[ \xi D = k_B T \]

\[ v_{\text{drift}} = -\frac{Dq \Delta V}{lk_B T} \]

\[ j_{\text{drift}} = c \nu_{\text{drift}} = - \left( \frac{Dq \Delta V}{lk_B T} \right) c \]

\[ j_{\text{diffusion}} = -D \frac{\partial c}{\partial x} \]

\[ j = j_{\text{drift}} + j_{\text{diffusion}} \]

\[ j = -D \left[ \frac{\partial c}{\partial x} + \left( \frac{q \Delta V}{lk_B T} \right) c \right] \]

(Nernst-Planck formula)
• Equilibrium state $j = 0$ at $\Delta V = \Delta V_{eq}$

$$j = -D \left[ \frac{\partial c}{\partial x} + \left( \frac{q \Delta V_{eq}}{l k_B T} \right) c \right] = 0 \Rightarrow \frac{d c}{d x} = -\left( \frac{q \Delta V_{eq}}{l k_B T} \right) c$$

$$\Rightarrow \frac{d \ln c}{d x} = -\frac{q \Delta V_{eq}}{l k_B T} \Rightarrow \frac{\Delta (\ln c)}{l} = -\frac{q \Delta V_{eq}}{l k_B T}$$

$$\Delta (\ln c) = -\frac{q \Delta V_{eq}}{k_B T} \quad \text{(Nernst relation)}$$

Membrane potentials maintains a concentration jump in equilibrium!

Discuss: Nernst relation and Boltzmann distribution.
Electrical conductivity of solutions

\[
j = -D \left[ \frac{\partial c}{\partial x} + \left( \frac{q \Delta V}{l k_B T} \right) c \right]
\]

(Nernst-Planck formula)

\[
j_q = -D \left( \frac{q \Delta V}{l k_B T} \right) c
\]

for constant \( c \)

\[
I_q = -j_q q A = \left( \frac{D q^2 c}{k_B T} \frac{A}{l} \right) \Delta V
\]

\[
I = I_e + I^e = \left( \frac{2 D e^2 c}{k_B T} \frac{A}{l} \right) \Delta V \quad \text{(Ohm's law)}
\]

Electrical conductivity \( \kappa \) \( \propto c \), \( \propto 1/T \)
§. Summary & further reading
Summary

- Probability
  - Discrete and continuous distributions
  - Mean and variance
  - Addition and multiplication rules

- Understanding the laws of ideal gas
  - Relation between temperature and $<E_K>$
  - Maxwell-Boltzmann distribution
  - Relaxation to equilibrium
• Brown motion & Random walks

\[ \langle [r(t)]^2 \rangle = 2 m D t \]

- Spacial dimension

• Friction and diffusion

- Einstein relation \[ \xi D = k_B T \]
- Fick's law \[ j = -D \frac{\partial c}{\partial x} \]
- Diffusion equation \[ \frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} \]
• Configuration of polymers
  − **Flexibility**: Persistence length, Persistence time
  − **End-to-end distance**
  − **Typical models**
    • Freely jointed chain, Freely rotating chain
    • Ideal chain (Gaussian)
    • Worm-like chain
  − **Entropic elasticity**

• Biological applications of diffusion
  − Bacterial **metabolism**
  − **Permeability** of membranes, membrane **potentials**
  − Electrical **conductivity** of solutions
Further reading

- L. E. Reichl, *A Modern Course in Statistical Physics*
- P. G. de Gennes, *Scaling concepts in polymer physics*
- M. Doi & S. F. Edwards, *The theory of polymer dynamics*