lec7.tex

Henrik Linder

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1 Repetition

Probability of binding in a certain volume is

$$P_b = \frac{1}{1+e^{\beta \Delta G}} = \frac{1}{1+\frac{1}{V}e^{-\beta\epsilon}} \tag{1}$$

depending on how you define your energy.

ΔG = free energy = energy + entropy

Huge entropy cost of folding DNA.

Non-specific binding means that $P_b = 1/2$

Corporate binding : counteract the entropy term in the binding prob by having two binding sites next to eachother.

$$\Delta G = \epsilon + \epsilon' - k_b T \ln(\Omega) + \epsilon_{R-R'} \tag{2}$$

where $k_b T \ln(\Omega)$ is the entropy. Ω is the # of boxes = V/a^3.

2 Stochastic dynamics in living systems

- Diffusion
- Target search

Examples:
- Protein diffusion: Molecule moving around in a cell.
If you want to move in a straight line, you will have to spend energy.
Random thermanl motion cossts nothing.
- Target search :
- Transcription initiation:

2.1 Diffusion

Incredibly low Reynolds numbers in cells.

Check out "Life at low Reaynolds numbers" again.

3D position of the particle:

$$\vec{r} = (x, y, z) \tag{3}$$

Equation of motion: patricle in a viscuous fluid.

N2:

$$m\frac{\mathrm{d}^2x}{\mathrm{d}t^2} = \text{drag force + noise (+ external force)} \tag{4}$$

Drag force $\propto$ velocity at low vel.s.

$$m\frac{\mathrm{d}^2x}{\mathrm{d}t^2} = \xi\frac{\mathrm{d}x}{\mathrm{d}t} = \eta(t) \tag{5}$$

where ξ is the hydrodynamic friction: $\xi =$(6πviscosity/radius)

in the high-friction limit:

$$\frac{\mathrm{d}^2x}{\mathrm{d}t^2} = 0 \tag{6}$$

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \frac{1}{\xi}\eta(t) \tag{7}$$

which is the Lengevin eq. (Brownian motion)

This is an unbiased random walk. (also used in stock market analysis (geometric brownian motion))

What is $\eta(t)$? White noise. Random noise with

1) mean = 0.

many types of averages. Ensemble average: "n statistical mechanics, the ensemble average is defined as the mean of a quantity that is a function of the microstate of a system, according to the distribution of the system on its micro-states in this ensemble."

$$< \eta(t) >= 0 \tag{8}$$

2) variance over time is constant.

3) uncorrelated

if you correlate two different regions, the correlation should be 0. Corr. between T_1 and $T_1 = 1$, but between T_1 and $T_n = 0$ for $n \neq 1$

White noise is the least biased noise you can add.

$$< \eta(t)\eta(t') >\leftarrow (t - t') \tag{9}$$

calculate displacement:

Integrate Langevin eq. ($\int_0^t \mathrm{d}u$)

$$x(t) - x(0) = \Delta x = \frac{1}{\xi}\int_0^t \eta(u)\mathrm{d}u \tag{10}$$

$$< \Delta x >=< \frac{1}{\xi} \int_0^t < \eta(u) > \mathrm{d}u = 0 \tag{11}$$

-Calc mean-squared displacement (MSD):

$$\begin{aligned} < \Delta x(t)^2 >=< \Delta x(t) \Delta x(t) > & \\ &=< \frac{1}{\xi} \int_0^t \eta(u) \mathrm{d}u \cdot \int_0^t \eta(v) \mathrm{d}v \\ &= \frac{1}{\xi^2} \int_0^t \int_0^t \mathrm{const} \cdot \delta(u-v) \mathrm{d}u \mathrm{d}v \\ &= \frac{C}{\xi^2} \int_0^t \mathrm{d}u \\ &= \frac{Ct}{\xi^2} \end{aligned} \tag{12}$$

which is $\equiv 2Dt$ where D is the diffusion constant.

special for diffusion: square of distance traveled is prop- to time, dist $\propto \sqrt{t}$, much slower than ballistic motion.

All directions are independent:

$$< \Delta x^2 >=< \Delta y^2 >=< \Delta z^2 > \tag{13}$$

gives that

$$< \Delta R^2 >=< \Delta \vec{R} \cdot \Delta \vec{R} >=< \Delta x^2 = \Delta y^2 + \Delta z^2 >= 3 < \Delta x^2 >= 6 \Delta t \tag{14}$$

How fast wiill RNAp diffuse across E.Coli?

Diameter 1 μm

$D = 5(\mu m^2)/s$

$< \Delta R^2 = 6Dt >$

$$t = \frac{< \Delta R^2 >}{6D} = 0.03 \tag{15}$$

seconds.

Pretty fast.

What about human cells?

Diameter 10 μm

$D = 5(\mu m^2)/s$

$< \Delta R^2 = 6Dt >$

$$t = 3 \tag{16}$$

seconds.

How long to diffuse along E.Coli's DNA?

1D diffusion.

$l_{DNA} = 1550 \mu m$ (calc from # BPs and size.)

$D = \frac{5(\mu m)^2}{s}$

$$t = \frac{l_{DNA}^2}{2D} = \frac{2.4e6(\mu m)^2}{2 \cdot 5\frac{(\mu m)^2}{s}} \approx 67hrs \approx 3\text{days} \tag{17}$$

2.2 What is the distribution of x?

P(x,t)

x is the sum of random numbers, so it will conform to a gaussion for large numbers.

Will tend to a gaussian curve with mean $M = 0$, $\sigma^2 = 2Dt$

$$\implies P(x,t) = \frac{e^{-(x-x_0)^2/4Dt}}{\sqrt{4\pi Dt}} \tag{18}$$

$P(x,t)$ satisfieas

$$\frac{\partial D}{\partial t} = D\frac{\partial^2 P}{\partial x^2} \tag{19}$$

independent directions, so

$$\begin{aligned} P(\vec{r},t) = p(x,y,z,t) &= p(x,t)p(y,t)p(z,t) \\ &= \frac{e^{-x^2/4Dt}}{\sqrt{4\pi Dt}} \cdot \frac{e^{-y^2/4Dt}}{\sqrt{4\pi Dt}} \cdot \frac{e^{-z^2/4Dt}}{\sqrt{4\pi Dt}} \\ &= \frac{e^{-(x^2+y^2+z^2)}}{(4\pi Dt)^{3/2}} \end{aligned} \tag{20}$$

2.3 Target search

Find the search time t from volume, D, a.

$$t \approx \frac{V}{aD} \tag{21}$$

$$t = \frac{V}{4\pi aD} \tag{22}$$