Any homework questions on 7.4, Problem J, or 7.7?

Macromolecule Structure

DNA and to a lesser degree proteins can be modeled as random walks.

Ways in which they are not random walks:

- proteins form α-helices and β-sheets
- more generally, amino acids interactions — hydrophobic, polar, or charged — affect the structure (PDB)
- DNA is typically confined to a smaller volume
- DNA is bound into chromosomes

Nevertheless, a random walk model is a very good starting point, particularly for DNA. Confinement and binding sites can be incorporated into a random walk model.

Also: provides a framework for thinking about entropic forces.

Freely-Jointed Chain Random Walk

Rigid segments of length a (Kuhn length), with random angles at the connection points.

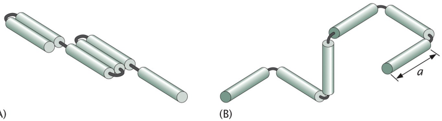


Figure 8.1 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

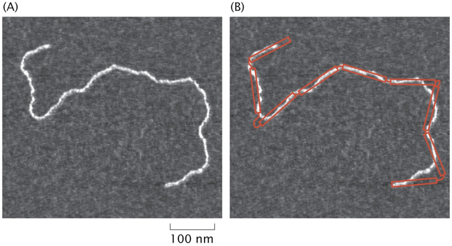


Figure 8.2 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Fig. 8.2: Illustration of how a DNA segment looks like a two-dimensional freely-jointed chain. $\leftarrow$

One Dimensional Random Walk

- N steps of length a, each with a probability $1/2$ of moving left or right.
- There are 2^N possible sequences (LRRRLR...) and we assume they are all equally probable.
- The end-to-end distance: $R = \sum_{i=1}^{N} x_i$, where $x_i = \pm a$
- Then $\langle R \rangle = \left\langle \sum_{i=1}^{N} x_i \right\rangle = \sum_{i=1}^{N} \langle x_i \rangle = 0$
- So the average position is zero. Note that the angle brackets are averages over all sequences.
- To get a sense of the size, need to measure $\langle R^2 \rangle$ ...

One Dimensional Random Walk, continued

$$\langle R^2 \rangle = \left\langle \left(\sum_{i=1}^{N} x_i \right) \left(\sum_{j=1}^{N} x_j \right) \right\rangle = \left\langle \sum_{i=1}^{N} \sum_{j=1}^{N} x_i x_j \right\rangle$$

This is just multiplication. Check for $N = 2$:

$$\underbrace{(x_1 + x_2)(x_1 + x_2)}_{\text{product of sums}} = \underbrace{x_1 x_1 + x_1 x_2 + x_2 x_1 + x_2 x_2}_{\text{sum of products}}$$

Now break up the sum:

$$\langle R^2 \rangle = \left\langle \sum_{i=1}^{N} x_i^2 \right\rangle + \left\langle \sum_{i \neq j = 1}^{N} x_i x_j \right\rangle = N a^2 + 0$$

So we have learned that the end-to-end distance goes like $R_{\text{rms}} = \sqrt{\langle R^2 \rangle} = a\sqrt{N}$.

Statistical Treatment of One Dimensional Random Walk

Given N steps, with n_r to the right, then $N - n_r$ are to the left. For a given N and n_r, the binomial coefficient tells us how many sequences are possible:

$$W(n_r, N) = \frac{N!}{n_r!(N - n_r)!}$$

Each has a probability $1/2^N$, so the probability of n_r right steps is

$$p(n_r, N) = W(n_r, N) = \frac{N!}{n_r!(N - n_r)!}\frac{1}{2^N}$$

Convert this into R: derive an expression for R in terms of N, n_r, and a ...

should get $R = (n_r - n_l)a = (2n_r - N)a$

Then we solve for n_r and $N - n_r$ and plug in above...

Statistical Treatment of One Dimensional Random Walk

- A lot of Stirling approximation math ensues, along with expansions of the logarithm: $\ln(1+x) \approx x - x^2/2 + \ldots$
- You will work through this in Problem 8.1 and get to the result that

$$p(R, N) = \frac{2}{\sqrt{2\pi N}} e^{-R^2/2Na^2}$$

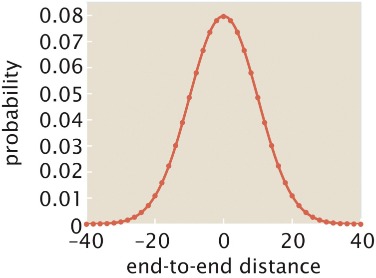


Figure 8.4 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Convert to a Probability Density $P(R,N)$

- $p(R,N)$ is the probability of the end being at exactly some R value that is a multiple of $2a$.
- $P(R,N)\,dR$ is the probability of the end being between R and $R+dR$
- Assume $dR \gg 2a$, and that $p(R,N)$ is essentially constant in range R to $R+dR$:

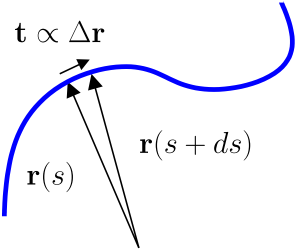
$$P(R,N)\,dR = \frac{dR}{2a} \times p(R,N) = \frac{1}{\sqrt{2\pi N a^2}} e^{-R^2/2Na^2}\,dR$$

- Generalize to three dimensions:

$$P(\mathbf{R},N)\,d^3R = \left(\frac{3}{2\pi N a^2}\right)^{1/2} e^{-3R^2/2Na^2}\,d^3R$$

Continuous Polymer Chain

Let s be a coordinate measured along the polymer, and $\mathbf{r}(s)$ describe the polymer structure.



The tangent vector $\mathbf{t}$ can be defined as

$$\mathbf{t}(s) = \frac{\mathbf{r}(s + ds) - \mathbf{r}(s)}{ds} = \frac{d\mathbf{r}}{ds}$$

Persistence Length ξ_p

- generalization of the Kuhn length a in the freely-jointed chain
- Defined via the tangent correlation: $\langle \mathbf{t}(s) \cdot \mathbf{t}(u) \rangle = e^{-|s-u|/\xi_p}$.

Relation between Persistence Length and Chain Length

The end-to-end displacement $\mathbf{R}$ given by

$$\mathbf{R} = \mathbf{r}(L) - \mathbf{r}(0) = \int_0^L \frac{d\mathbf{r}}{ds}\, ds = \int_0^L \mathbf{t}(s)\, ds$$

Since $\langle \mathbf{R} \rangle = 0$, look at the square:

$$\langle R^2 \rangle = \left\langle \int_0^L \mathbf{t}(s)\, ds \cdot \int_0^L \mathbf{t}(u)\, du \right\rangle = \underbrace{\int_0^L ds}_{=L} \underbrace{\int_0^L du\, e^{-|s-u|/\xi_p}}_{=2\int_0^\infty e^{-x/\xi_p}\, dx}$$

$$= 2\xi_p L$$

Continuous polymer: $R_{\text{rms}} = \sqrt{2\xi_p L}$
Freely-jointed chain: $R_{\text{rms}} = a\sqrt{N} = \sqrt{aL}$

$$\Rightarrow \quad a = 2\xi_p$$

Radius of Gyration

End-to-end distance can fluctuate wildly. More robust measure of size:

$$\langle R_G^2 \rangle = \frac{1}{N} \sum_{i=1}^{N} (\mathbf{r}_i - \mathbf{r}_{\mathsf{CM}})^2$$

where $\mathbf{r}_{\mathsf{CM}} = (1/N) \sum_i \mathbf{r}_i$

HW Problem 8.2: show that $\sqrt{\langle R_G^2 \rangle} = \sqrt{L\xi_p/3}$.

Hints:

- work with freely jointed chain, and use $a = 2\xi_p$ at the end
- squaring sums: $(\sum_i x_i)^2 = (\sum_i x_i)(\sum_j x_j) = \sum_i \sum_j x_i x_j$

Typical sizes

For DNA, $\xi_p \simeq 50$ nm:

Bacteriophage T2 genome has 1.5×10^5 bp, so $L \sim 5 \times 10^4$ nm.

$$\sqrt{\langle R_G^2 \rangle} = \sqrt{L\xi_p/3}$$

$$= \sqrt{\frac{(5\times10^4)(50)}{3}} \simeq 900\,\text{nm}.$$

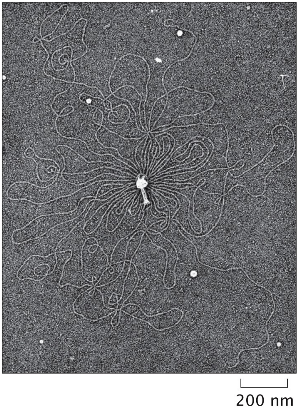


Figure 1.16 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Typical sizes

For DNA, $\xi_p \simeq 50$ nm:

Bacteria genome: $N_{\mathrm{bp}} \sim 4.6 \times 10^6$, so $L \sim 1.5 \times 10^3$ μm.

$$\sqrt{\langle R_G^2 \rangle} = \sqrt{L\xi_p/3}$$

$$= \sqrt{\frac{(1.5\times 10^3)(0.050)}{3}} \simeq 5\,\mu\text{m}.$$

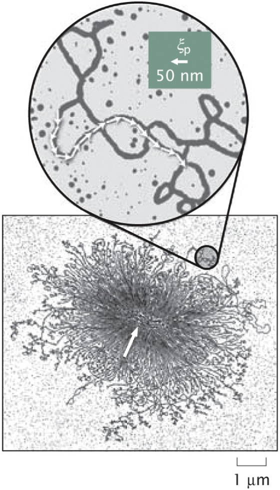


Figure 8.5 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

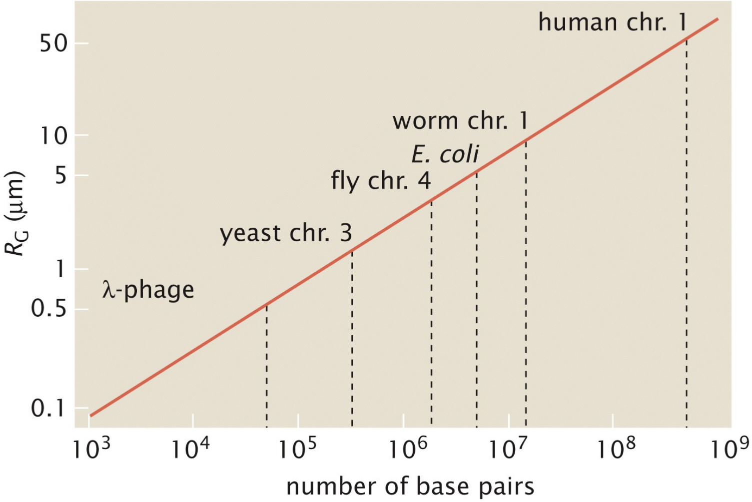


Figure 8.6 Physical Biology of the Cell, 2ed. (© Garland Science 2013)