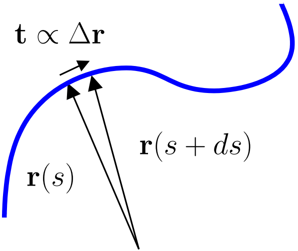
Any homework questions on 7.4, Problem J, 7.7, or 8.1?

I'll talk about 8.2 next . . .

For R_G use the Continuous Polymer Chain



$$\mathbf{t}(s) = \frac{d\mathbf{r}}{ds} \quad \Rightarrow \quad \mathbf{r}(s) = \int_0^s ds' \, \mathbf{t}(s')$$

$$R_G^2 = \left\langle \frac{1}{L} \int_0^L ds \, (\mathbf{r}(s) - \mathbf{r}_{\mathsf{CM}})^2 \right\rangle$$

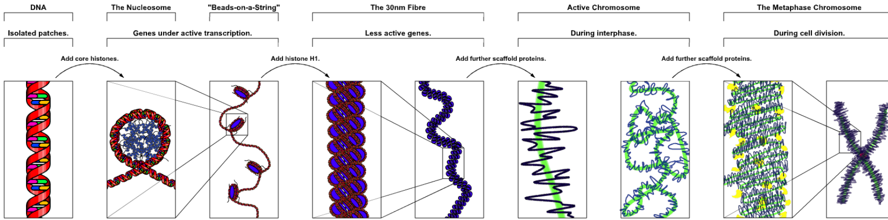
$$\text{where } \mathbf{r}_{\mathsf{CM}} = \frac{1}{L} \int_0^L \mathbf{r}(s) \, ds$$

Basic trick: For any $\mathbf{r}(s)$, sub in integral of the tangent vector. Then averages will take the form

$$\int_0^s ds' \int_0^u du' \langle \mathbf{t}(s') \cdot \mathbf{t}(u') \rangle = \int_0^s ds' \int_0^u du' \, e^{-|s'-u'|/\xi_p}$$

$$\simeq \min(u, s) 2\xi_p$$

Chromosomes — Packing of DNA in Eukaryotes



Chromatin

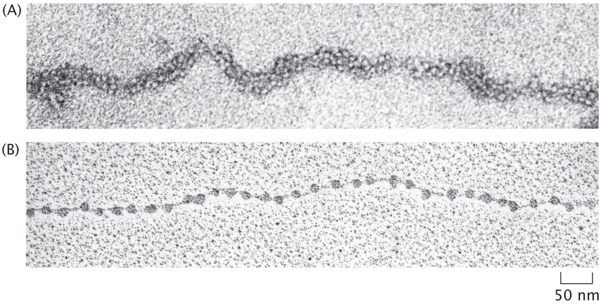


Figure 8.7 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

$\leftarrow$ 30 nm fiber

$\leftarrow$ 10 nm fiber

$$\text{Base pairs per length: } \nu \approx \begin{cases} 100 \text{ bp/nm} & \text{for 30 nm fiber} \\ 8 \text{ bp/nm} & \text{for 10 nm fiber} \\ 3 \text{ bp/nm} & \text{for pure DNA} \end{cases}$$

Length of strand $L = Na = N_{\text{bp}}/\nu$

Chromosome Tethering

- Book argues (p. 324) that yeast's 16 chromosomes each have a radius of gyration larger than the nucleus, so the chromosomes must be in an "entangled melt-like configuration".
- But this is inconsistent with observed segregation: each chromosome is confined to its own region.
- Conclusion: chromosomes are likely tethered to the nuclear wall. How would we test this experimentally?

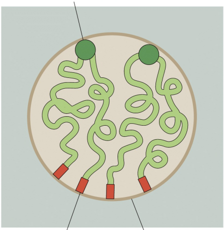


Figure 8.9a Physical Biology of the Cell, 2ed. (© Garland Science 2013)

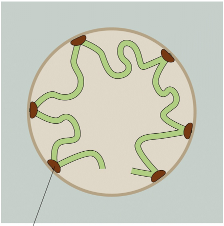


Figure 8.9b Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Measuring Chromosome Tethering

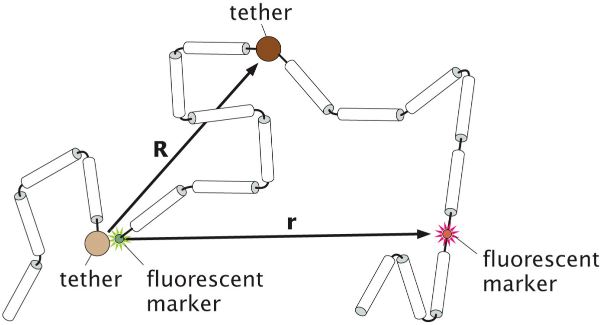


Figure 8.10 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Untethered: $P(\mathbf{r}) = \left(\frac{3}{2\pi N a^2}\right)^{3/2} e^{-3r^2/2Na^2}$

Tethered at **R**: $P(\mathbf{r}) = \left(\frac{3}{2\pi N' a^2}\right)^{3/2} e^{-3(\mathbf{r}-\mathbf{R})^2/2N'a^2}$

Problem 8.7

Turn these $P(\mathbf{r}) = P(r, \theta, \phi)$ into $P(r)$. Some hints:

- $P(r)\,dr$ is the probability of finding the tagged spot at a distance between r and $r + dr$ away:

$$P(r)\,dr = \underbrace{\int_r^{r+dr} r^2 dr}_{=r^2\,dr} \int_0^{\pi} \sin\theta\,d\theta \int_0^{2\pi} d\phi\,P(r, \theta, \phi)$$

- Untethered case pretty straightforward, since there is no θ, ϕ dependence.

- Tethered case: this is more work. We are free to choose the coordinate directions, so let's take $\mathbf{R} = R\hat{\mathbf{k}}$. Then

$$(\mathbf{r} - \mathbf{R})^2 = r^2 - 2\mathbf{r} \cdot \mathbf{R} + R^2 = r^2 - 2rR\cos\theta + R^2$$

  Now you've got some θ dependence to evaluate in the integral.

Measuring Chromosome Tethering

Untethered: $P(r) = \left(\frac{3}{2\pi N a^2}\right)^{3/2} 4\pi r^2\, e^{-3r^2/2Na^2}$

Tethered at **R**:

$$P(r) = \left(\frac{3}{2\pi N' a^2}\right)^{3/2} \frac{r}{R}\left(e^{-3(r-R)^2/2N'a^2} - e^{-3(r+R)^2/2N'a^2}\right)$$

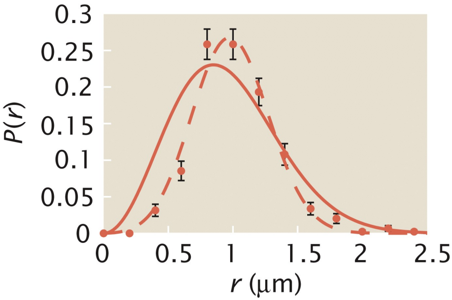


Figure 8.12 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Measuring Chromosome Density

Two points along the DNA that are a known genomic distance N_{bp} apart can be marked.

- From contour length:

$$Na = N_{\text{bp}}/\nu$$

- End-to-end distance

$$\langle R^2 \rangle = Na^2 = N_{\text{bp}} a/\nu$$

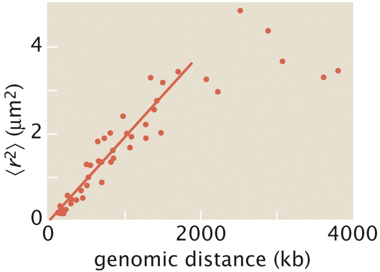


Figure 8.11 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

- a/ν is slope of $\langle R^2 \rangle$ versus N_{bp}.

Random Walk with a Boundary

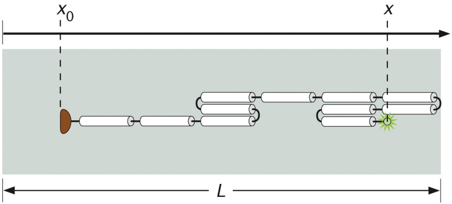


Figure 8.15 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Confined random walk probability density $P(x, N)$ no longer a gaussian.

Problem 8.5: show $P(x, N)$ satisfies diffusion equation:

$$\frac{\partial P(x, N)}{\partial N} = \frac{a^2}{2} \frac{\partial^2 P}{\partial x^2}$$

Hint:

$$P(x, N+1) = \frac{1}{2}[P(x+a, N) + P(x-a, N)]$$

Taylor expand l.h.s. about N, r.h.s. about x.

Diffusion Equation

- Use $G(x, N) = (\text{const.}) P(x, N)$ to avoid worrying about normalization until the end.
- Boundary conditions $G(0, N) = 0$ and $G(L, N) = 0$.
- Fourier series: $G(x, N) = \sum_{n=1}^{\infty} A_n(N) \sin\left(\frac{n\pi}{L} x\right)$
- "Initial" conditions ($N = 0$) give us $A_n(0)$. For example, take $G(x, 0) = \delta(x - x_0)$, gives

$$A_n(0) = \frac{2}{L} \sin\left(\frac{n\pi}{L} x_0\right)$$

- Now plug $G(x, N)$ expansion into the differential equation:

Fourier Expansion in Diffusion Equation

On the left hand side:

$$\frac{\partial G(x,N)}{\partial N} = \sum_{n=1}^{\infty} \frac{dA_n(N)}{dN} \sin\left(\frac{n\pi}{L}x\right)$$

On the right hand side:

$$\frac{\partial^2 G(x,N)}{\partial x^2} = -\sum_{n=1}^{\infty} A_n(N)\left(\frac{n\pi}{L}\right)^2 \sin\left(\frac{n\pi}{L}x\right)$$

Orthogonality says each individual Fourier mode must satisfy diffusion equation:

$$\frac{dA_n(N)}{dN} = -\frac{a^2}{2}\left(\frac{n\pi}{L}\right)^2 A_n(N)$$

Solution to Diffusion Equation

$$\frac{dA_n(N)}{dN} = -\frac{a^2}{2}\left(\frac{n\pi}{L}\right)^2 A_n(N)$$

This is just $df/dN = -\alpha f$ which has solution $f = f(0)e^{-\alpha N}$, so our coefficients are

$$A_n(N) = A_n(0)\exp\left[-\left(\frac{n\pi}{L}\right)^2 \frac{a^2}{2} N\right]$$

Plug back into expansion for $G(x, N)$, normalize to get $P(x, N)$ and you're done!

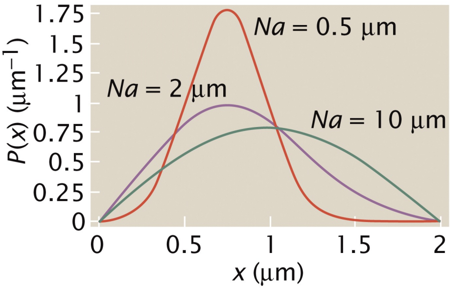


Figure 8.16a Physical Biology of the Cell, 2ed. (© Garland Science 2013)

DNA Looping and Return Probabilities

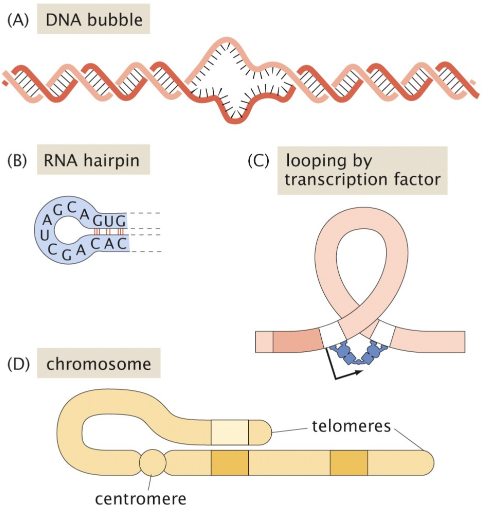


Figure 8.18 Physical Biology of the Cell, 2ed. (© Garland Science 2013)