Lecture 25: Polymers: Entropic Elasticity and DNA Packing

Problem Set 4, officially due today, Nov. 8, but will be accepted Wednesday, Nov. 10.
Reading for Lectures 22—24: PKT Chapter 8

One more conceptual topic before we go on to talk about biological applications:

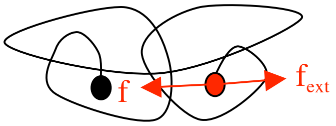
Random-coil polymers as entropic springs:

Fact: A random-coil polymer acts as a spring with a spring constant proportional to temperature.
This is true even for a freely-jointed (random-walk) chain where all configurations have the same energy, so there is ZERO energy involved in the stretching! It is entirely an entropic effect.

The end-to-end distribution $P_N(R) \sim e^{-\frac{3R^2}{2\langle R^2\rangle}}$ shows that the probable separation of the ends peaks at R=0.

Claim: If you fix the ends at distance R>0, there will be a force f=-k_{spring}R (like a spring) pulling the ends closer with $k_{spring} = \frac{dk_BT}{\langle R^2\rangle}$, where d is the dimension of space.

The black end is fixed; you (the external force) pull on the red end.



This is a subtle effect: There is zero *energetic* springiness in the polymer. At T=0, the freely-jointed chain is completely floppy. The red and black ends are connected by what is, in effect, a thread. Nevertheless, when T increases a force f is required to keep the red end in one place. That force increases with T. You can visualize this as jostling of the chain by thermal fluctuations.
If that force is allowed to do work, the energy comes from the thermal reservoir, not from any change of internal energy E of the polymer. $\bar{d}Q = dE + \bar{d}W$, i.e., dE=0, so energy $\bar{d}Q$ flows in from the reservoir in order that the polymer should do work $\bar{d}W$.
Conversely, if you do work on the polymer, then heat flows into the reservoir.

Notes:
Heating of stretched rubber band!
Close analogy with ideal-gas isothermal expansion!

I am now going to show you how to calculate the spring constant in two different ways:

A. Directly from the random-walk distribution (3D).

As we saw generally, the analog of energy in a system at fixed T is the Helmholtz free energy F=E-TS.
For the freely jointed polymer E=0, so F=-TS.
If I were looking at an energetic effect, then I would calculate $E(\vec{R})$ and find the force as $\vec{f}(\vec{R}) = -\nabla_{\vec{R}} E$.

For those of you not familiar with gradients, this is just the 3D version of $f = -\frac{dE(x)}{dx}$.

Thus, for example, suppose $E(x) = \frac{kx^2}{2}$, then $f = -\frac{dE}{dx} = -kx$ for the 1D spring.

Similarly, in 3D, if $E(\vec{R}) = \frac{k}{2}R^2$, then $\vec{f} = -\vec{\nabla}E = -k\vec{R}$.

Thus, what I need in order to do the same thing for system in contact with a thermal bath is the Helmholtz free energy $F(\vec{R})$, and then I can calculate the force as $\vec{f} = -\vec{\nabla}_{\vec{R}}F$. Thus, for the polymer $\vec{f} = +T\vec{\nabla}_{\vec{R}}S(\vec{R})$, where $S(\vec{R}) = k_B \ln W(\vec{R})$ is the entropy of the polymer when its ends are held at displacement $\vec{R}$.
We could go back now and calculate the number of microstates $W_N(\vec{R})$ when ends are held at $\vec{R}$.

But, we don't have to, because that's exactly what we did in calculating $P_N(\vec{R})$: **25.2**

$P_N(\vec{R}) = \dfrac{W_N(\vec{R})}{\text{normalisation}}$. It follows that

$S(\vec{R}) = k_B \ln P_N(\vec{R}) + \text{independent of } \vec{R} = -k_B \cdot \dfrac{3R^2}{2\langle R^2 \rangle} + \text{constant}$, so $\boxed{\vec{f} = T\vec{\nabla}_{\vec{R}} S(\vec{R}) = -\dfrac{3k_BT}{\langle R^2 \rangle}\vec{R},}$ from which we can identify the entropic spring constant, as claimed above.

Comment: This is only valid for displacements $|\vec{R}| \sim a$, since that is the range for which we derived the Gaussian distribution. Clearly, something else happens as $|\vec{R}| \to aN \equiv L$. Which brings me to:

B. Calculation of the Helmholtz free energy in a constant-force ensemble (1D)

I'll give you this as a homework problem, but let me set it up here:
I consider the polymer fixed at one end and with a constant external force f applied to the other. That force does work as the polymer changes length, so the energy of each microstate E_n is given by
$E_n = fX_n = fa\sum_{k=1}^{N}\sigma_k$ with the step variables $\sigma_k = \pm 1$, as in the coin-toss problem.

Comments:
1. The f as defined above is the (negatve) force that the polymer exerts on the external source of the fixed force. Thus, when X increases (f is nagative), E decreases, i.e., there is less energy stored in the external force source (e.g., a very long spring).
2. The strategy here is to calculate the mean extension $\langle X \rangle$ of the polymer as a function of the force f and then to invert this to get the force as a function of the extension.

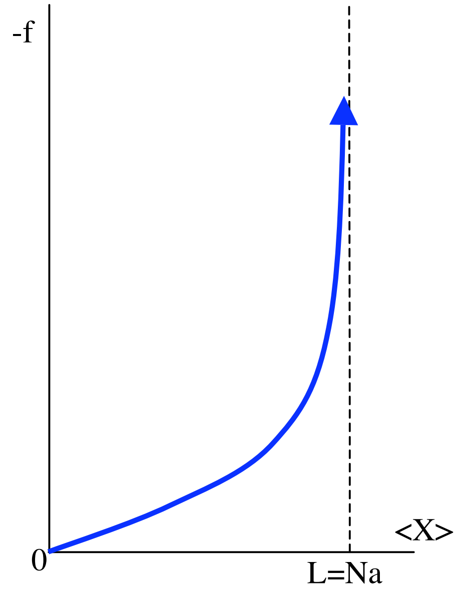
The Helmholtz free energy of this system is $F = -kT\ln Z$.
Your job will be to calculate $\langle X \rangle$ as a function of f. And, then, to invert to get f as a function of $\langle X \rangle$. The final result is:

$$f = -\frac{k_BT}{a}\tanh^{-1}\left(\frac{\langle X \rangle}{Na}\right) = -\frac{k_BT}{2a}\ln\left(\frac{Na + \langle X \rangle}{Na - \langle X \rangle}\right).$$

When x is small, then $\tanh^{-1} x \approx x + O(x^3)$, so

$f \approx -\dfrac{k_BT}{Na^2}\langle X \rangle = -\dfrac{k_BT}{\langle X^2 \rangle}\langle X \rangle$, showing the entropic-spring behavior for small displacement. But, now, we have the full behavior, including large displacements. Note that $f \to \infty$ as $\langle X \rangle \to Na \equiv L$, which makes sense.

Comment: For large N, fluctuations of X are small.



Applications: (Many!)

1. DNA packing:

DNA data:
1/3 nm/bp; radius~1 nm; volume/bp=1 nm^3
persistence length $\xi_{DNA} = 53$ nm or 150 bp. So, $\ell_K = 2\xi_p = 106\ nm \sim 300\ bp$ and

$N_K = \dfrac{4.6 \times 10^6}{300} = 1.5 \times 10^4$.

Thus, $\langle R^2 \rangle = 2\xi_p L = 2 \cdot 53 \cdot \dfrac{1}{3} \cdot N \Rightarrow \sqrt{\langle R^2 \rangle} \approx 6\sqrt{N}$ nm.

Comment: "Radius of Gyration":

A different and commonly used measure of polymer size is $\left\langle R_G^2 \right\rangle = \frac{\xi_p}{3} L = \frac{1}{6} \cdot 2\xi_p L$. It answers the question, " What is the mean-square distance of a typical monomer from the polymeric C of M?"

Consider, for example, the E. coli genome at 4.6x10^6, so $L = \frac{1}{3} \cdot 4.6 \times 10^6 = 1.5 \times 10^6$ nm $= 1.5$ mm, and $\sqrt{\left\langle R^2 \right\rangle} = 1.3 \times 10^4$ nm $= 13\ \mu m$.

Consider the other limit: volume=$v = 1 \cdot 4.6 \times 10^6\ nm^3 = \frac{4\pi}{3} r^3 \Rightarrow r = 103\ nm = 0.1\ \mu m$ if it were rolled up in a ball.

Message: E. coli genome does not fit inside cell in its random-coil state. PKT Fig. 8.6

Somehow, it is reduced in size:

Constrained by cell membrane (indeed, it is constrained inside "nucleoid")

Loop structure (E. coli genome is a single DNA loop) reduces size by $\sim \sqrt{2}$.

Supercoiling

Tethering to cell wall

Internal connections

All these strategies are used.

More generally, there is a trade-off which biology has had to optimize:

- pack the genome away in some (orderly?) manner
- make genes accessible for transcription
- handle all this for replication and cell division

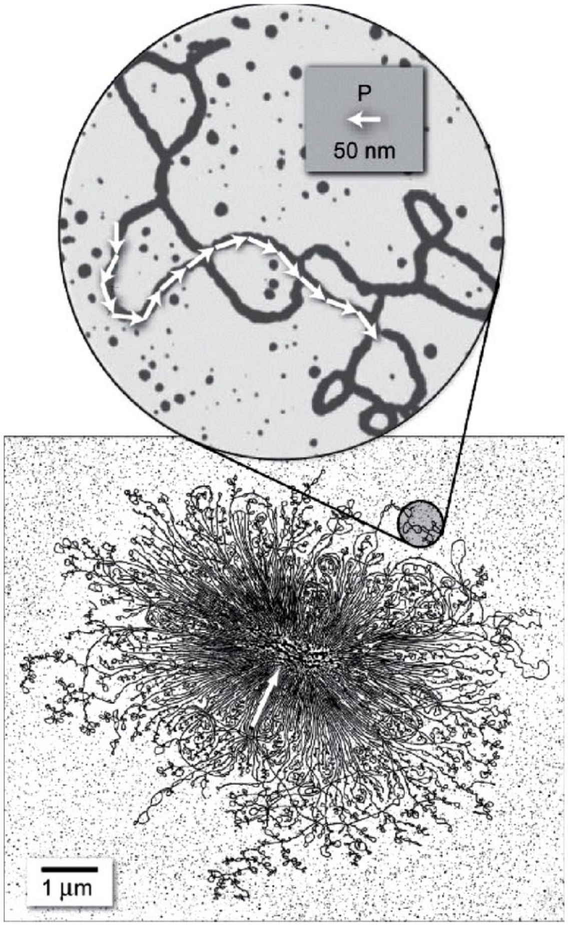


Figure 8.6 Physical Biology of the Cell (© Garland Science 2009)