Chapter 9

Cooperative transitions in macromolecules

Hooke gave in 1678 the famous law of proportionality of stress and strain which bears his name, in the words "Ut tensio sic vis." This law he discovered in 1660, but did not publish until 1676, and then only under the form of an anagram, "ceiiinossssttuv."
—A. Love, *A treatise on the mathematical theory of elasticity*, 1906

The preceding chapters may have shed some light on particular molecular forces and processes, but they also leave us with a deeper sense of dissonance. On one hand, we have seen that the activity of individual small molecules is chaotic, leading to phenomena like Brownian motion. We have come to expect predictable, effectively deterministic behavior only when dealing with vast numbers of molecules, for example, the diffusion of a drop of ink or the pressure of air in a bicycle tire. On the other hand, Chapter 2 showed a gallery of exquisitely structured *individual* macromolecules, each engineered to do specific jobs reliably. So which image is right—should we think of macromolecules as being like gas molecules, or like tables and chairs?

More precisely, we'd like to know how individual molecules, held together by weak interactions, nevertheless retain their structural integrity in the face of thermal motion and, indeed, perform specific functions. The key to this puzzle is the phenomenon of cooperativity.

Chapter 8 introduced cooperativity, showing that it makes the micelle transition sharper than we would otherwise expect it to be. This chapter will extend the analysis and also deepen our understanding of macromolecules as brokers at the interface between the worlds of mechanical and chemical forces. Section 9.1 begins by studying how an external force affects the conformation of a macromolecule, first in a very simplified model and then in a second model adding the cooperative tendency of each monomer to do what its nearest neighbors are doing. The ideas of Chapter 6 and the partition function method for calculating entropic forces (from Section 7.1) will be very useful here. Next, Section 9.5 will extend the discussion to transitions induced by changes in the *chemical* environment. The final sections argue briefly that the lessons learned from simple model systems can help us understand qualitatively the sharp state transitions observed in biologically important systems, the allosteric proteins.

The Focus Questions for this chapter are

Biological question: Why aren't proteins constantly disrupted by thermal fluctuations? The cartoons in cell biology books show proteins snapping crisply between definite conformations as they carry out their jobs. Can a floppy chain of residues really behave in this way?

Physical idea: Cooperativity sharpens the transitions of macromolecules and their assemblies.

9.1 Elasticity models of polymers

Roadmap   The following sections introduce several physical models for the elasticity of DNA. Section 9.1.2 begins by constructing and justifying a physical picture of DNA as an elastic rod. Although physically simple, the elastic rod model is complex to analyze mathematically. Thus we work up to it with a set of reduced models, starting with the "freely jointed chain" (Section 9.1.3). Section 9.2 introduces experimental data on the mechanical deformation (stretching) of single molecules and interprets it, using the freely jointed chain model. Section 9.4 argues that the main feature neglected by the freely jointed chain is cooperativity between neighboring segments of the polymer. To redress this shortcoming, Section 9.4.1 introduces a simple model, the "one-dimensional cooperative chain." Later sections apply the mathematics of cooperativity to structural transitions within polymers, for example, the helix–coil transition.

Figure 2.15 on page 45 shows a segment of DNA. It's an understatement to say that this molecule has an elaborate architecture! Atoms combine to form bases. Bases bind into basepairs by hydrogen bonding; they also bind chemically to two outer backbones of phosphate and sugar groups. Worse, the beautiful picture in the figure is in some ways a *lie:* It doesn't convey the fact that a macromolecule is dynamic, with each chemical bond constantly flexing and involved in promiscuous, fleeting interactions with other molecules not shown (the surrounding water molecules, with their network of H-bonds, and so on). It may seem hopeless to seek a simple account of the mechanical properties of this baroque structure.

Before giving up on a simple description of DNA mechanics, though, we should pause to examine the length scales of interest. DNA is roughly a cylindrical molecule of diameter $2\,\mathrm{nm}$. It consists of a stack of roughly flat plates (the basepairs), each about $0.34\,\mathrm{nm}$ thick. But the total *length* of a molecule of DNA (for example, in one of your chromosomes), can be $2\,\mathrm{cm}$, or ten million times the diameter! Even a tiny virus such as the **lambda phage** has a genome $16.5\,\mu\mathrm{m}$ long, still far bigger than the diameter. We may hope that the behavior of DNA on such long length scales may not depend very much on the details of its structure.

9.1.1 Why physics works (when it does work)

There is plenty of precedent for such a hope. After all, engineers do not need to account for the detailed atomic structure of steel (nor, indeed, for the fact that steel is made of atoms at all) when designing bridges. Instead, they model steel as a continuum with a certain resistance to deformation, characterized by just *two numbers* (called the bulk modulus and shear modulus; see Section 5.2.3 on page 148). Similarly, the discussion of fluid mechanics in Chapter 5 made no mention of the detailed structure of the water molecule, its network of hydrogen bonds, and so on. Instead, we again summarized the properties of water relevant for physics on scales bigger than a couple of nanometers by just *two numbers,* mass density ρ_{m} and viscosity η. Any other Newtonian fluid, even with a radically different molecular structure, will flow like water if it matches the values of

these two **phenomenological parameters**. What these two examples share is a deep theme running through all of physics:

> *When we study a system with a* **large number** *of* **locally interacting, identical** *constituents on a far* **bigger scale** *than the size of the constituents, then we reap a huge simplification: Just a* **few effective degrees of freedom** *describe the system's behavior, with just a* **few phenomenological parameters**.

(9.1)

Thus the fact that bridges and pipes are *much bigger* than iron atoms and water molecules underlies the success of continuum elasticity theory and fluid mechanics.

Much of physics amounts to the systematic exploitation of Idea 9.1. A few more examples will help explain the statement of this principle. Then we'll try using it to address the questions of interest to this chapter.

Another way to express Idea 9.1 is to say that Nature is hierarchically arranged by length scale into levels of structure and that each successive level of structure forgets nearly everything about the deeper levels. It is no exaggeration to say that this principle explains why physics is possible at all. Historically, our ideas of the structure of matter have gone from molecules, to atoms, to protons, neutrons, electrons, and beyond this to the quarks composing the protons and neutrons, and perhaps to even deeper levels of substructure. Had it been necessary to understand *every* deeper layer of structure before making any progress, then the whole enterprise could never have started! Conversely, even now that we do know that matter consists of atoms, we would never make any progress understanding bridges (or galaxies) if we were obliged to consider them as collections of atoms. The simple rules emerging as we pass to each new length scale are examples of the emergent properties mentioned in Sections 1.2.3 and 6.3.2.

Continuum elasticity   In elasticity theory, we pretend that a steel beam is a continuous object, ignoring the fact that it's made of atoms. To describe a deformation of the beam, we imagine dividing it into cells of, say, $1\,\mathrm{cm}^3$ (much smaller than the beam but much bigger than an atom). We label each cell by its position in the beam in its unstressed (straight) state. When we put a load on the beam, we can describe the resulting deformation by reporting the change in the position of each element relative to its neighbors, which is much less information than a full catalog of the positions of each atom. If the deformation is not too large, we can assume that its elastic energy cost per unit volume is proportional to the square of its magnitude (a Hooke-type relation; see Section 5.2.3 on page 148). The constants of proportionality in this relationship are examples of the phenomenological parameters mentioned in Idea 9.1. In this case, there are two of them, because a deformation can either stretch or shear the solid. We could try to predict their numerical values from the fundamental forces between atoms. But we can just as consistently take them to be experimentally measured quantities. As long as only one or a few phenomenological parameters characterize a material, we can get many falsifiable predictions after making only a few measurements to nail down the values of those parameters.

Fluid mechanics   The flow behavior of a fluid can also be characterized by just a few numerical quantities. An isotropic Newtonian fluid, such as water, has no memory of its original (undeformed) state. Nevertheless, we saw in Chapter 5 that a fluid resists certain motions. Again dividing the fluid into imagined macroscopic cells, the effective degrees of freedom are each cell's velocity. Neighboring cells pull on one another via the viscous force rule (Equation 5.4 on page 143). The constant η

appearing in that rule—the viscosity—relates the force to the deformation rate; it's one of the phenomenological parameters describing a Newtonian fluid.

Membranes Bilayer membranes have properties resembling both solids and fluids (see Section 8.6.1 on page 280). Unlike a steel beam or a thin sheet of aluminum foil, the membrane is a fluid: It maintains no memory of the arrangement of molecules within its plane, so it offers no resistance to a constant shear. But unlike sugar molecules dissolved in a drop of water, the membrane does remember that it prefers to lie in space as a continuous, flat sheet—its resistance to bending is an intrinsic phenomenological parameter (see Idea 8.37 on page 284). Once again, one constant, the bend stiffness κ, summarizes the complex intermolecular forces adequately, as long as the membrane adopts a shape whose radius of curvature is everywhere much bigger than the molecular scale.

Summary The preceding examples suggest that Idea 9.1 is a broadly applicable principle. But there are limits to its usefulness. For example, the individual monomers in a protein chain are *not* identical. As a result, the problem of finding the lowest-energy state of a protein is far more complex than the corresponding problem for, say, a jar filled with identical marbles. We need to use physical insights when they are helpful, while being careful not to apply them when inappropriate. Later sections of this chapter will find systems where simple models do apply and seem to shed at least qualitative light on complex problems.

$\boxed{T_2}$ *Section 9.1.1′ on page 334 discusses further the idea of phenomenological parameters and Idea 9.1.*

9.1.2 Four phenomenological parameters characterize the elasticity of a long, thin rod

Let's return to DNA and begin to think about what phenomenological parameters are needed to describe its behavior on length scales much longer than its diameter. Imagine holding a piece of garden hose by its ends. Suppose that the hose is naturally straight and of length L_{tot}. You can make it deviate from this geometry by applying forces and torques with your hands. Consider a little segment of the rod that is initially located a distance s from the end and of length ds. We can describe deformations of the segment by giving three quantities (Figure 9.1):

- The **stretch** $u(s)$ (or extensional deformation) measures the fractional change in length of the segment: $u = \Delta(ds)/ds$. The stretch is a dimensionless **scalar** (that is, a quantity with no spatial direction).

- The **bend** $\boldsymbol{\beta}(s)$ (or bend deformation) measures how the hose's unit tangent vector $\hat{\mathbf{t}}$ changes as we walk down its length: $\boldsymbol{\beta} = d\hat{\mathbf{t}}/ds$. Thus the bend is a vector with dimensions $\mathbb{L}^{-1}$.

- The **twist density** $\omega(s)$ (or torsional deformation) measures how each succeeding element has been rotated about the hose's axis relative to its neighbor. For example, if you keep the segment straight but twist its ends by a relative angle $d\phi$, then $\omega = d\phi/ds$. Thus the twist density is a scalar with dimensions $\mathbb{L}^{-1}$.

Your Turn 9A

Show that all three of these quantities are independent of the length ds of the small element chosen.
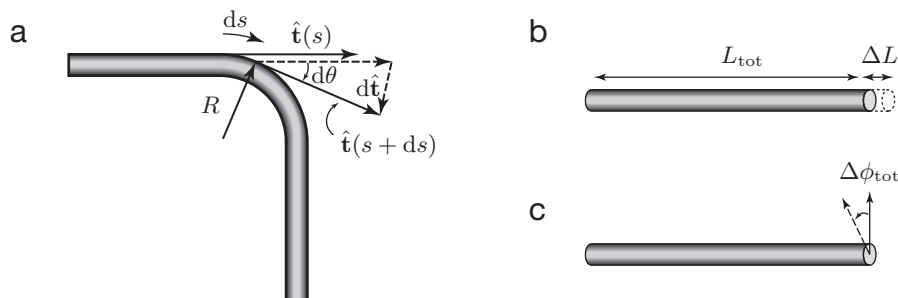

Figure 9.1: (Schematic.) Deformations of a thin elastic rod. (a) Definition of the bend vector, $\boldsymbol{\beta} = \mathrm{d}\hat{\mathbf{t}}/\mathrm{d}s$, illustrated for a circular segment of a thin rod. The parameter s is the contour length (also called arc length) along the rod. The tangent vector $\hat{\mathbf{t}}(s)$ at one point of the rod has been moved to a nearby point a distance $\mathrm{d}s$ away (*dashed arrow*), then compared with the tangent vector there, or $\hat{\mathbf{t}}(s+\mathrm{d}s)$. The difference of these vectors, $\mathrm{d}\hat{\mathbf{t}}$, points radially inward and has magnitude equal to $\mathrm{d}\theta$, or $\mathrm{d}s/R$. (b) Definition of stretch. For a uniformly stretched rod, $u = \Delta L/L_{\mathrm{tot}}$. (c) Definition of twist density. For a uniformly twisted rod, $\omega = \Delta\phi_{\mathrm{tot}}/L_{\mathrm{tot}}$.

The stretch, bend, and twist density are local (they describe deformations near a particular location, s), but they are related to the overall deformation of the hose. For example, the total **contour length** of the hose (the distance a bug would have to walk to get from one end to the other) equals $\int_0^{L_{\mathrm{tot}}} \mathrm{d}s\,(1+u(s))$. Note that the parameter s gives the contour length of the *unstretched* hose from one end to a given point, so it always runs from 0 to the total unstretched length, L_{tot}, of the rod.

In the context of DNA, we can think of the stretch as measuring how the contour length of a short tract of N basepairs differs from its natural (or "relaxed") value of $(0.34\,\mathrm{nm}) \times N$ (see Figure 2.15 on page 45). We can think of the bend as measuring how each basepair lies in a plane tilted slightly from the plane of its predecessor. To visualize twist density, we first note that the relaxed double helix of DNA in solution makes one complete helical turn about every 10.5 basepairs. Thus we can think of the twist density as measuring the rotation $\Delta\psi$ of one basepair relative to its predecessor, minus the relaxed value of this angle. More precisely,

$$\omega = \frac{\Delta\psi}{0.34\,\mathrm{nm}} - \omega_0, \quad \text{where} \quad \omega_0 = \frac{2\pi}{10.5\,\mathrm{bp}}\frac{1\,\mathrm{bp}}{0.34\,\mathrm{nm}} \approx 1.8\,\mathrm{nm}^{-1}.$$

Following Idea 9.1, we now write down the elastic energy cost E of deforming our cylindrical hose (or any long, thin elastic rod). Again divide the rod arbitrarily into short segments of length $\mathrm{d}s$. Then E should be the sum of terms $\mathrm{d}E(s)$ coming from the deformation of the segment at each position s. By analogy to the Hooke relation, we now argue that $\mathrm{d}E(s)$ should be a quadratic function of the deformations, if these are small. The most general expression we can write is

$$\mathrm{d}E = \frac{1}{2}k_{\mathrm{B}}T\left[A\boldsymbol{\beta}^2 + Bu^2 + C\omega^2 + 2Du\omega\right]\mathrm{d}s. \tag{9.2}$$

The phenomenological parameters A, B, and C have dimensions $\mathbb{L}$, $\mathbb{L}^{-1}$, $\mathbb{L}$, respectively; D is dimensionless. The quantities $Ak_{\mathrm{B}}T$ and $Ck_{\mathrm{B}}T$ are called the rod's bend stiffness and twist stiffness at temperature T, respectively. It's convenient to express these quantities in units of $k_{\mathrm{B}}T$, which is why we introduced the **bend persistence length** A and the **twist persistence length** C. The remaining constants $Bk_{\mathrm{B}}T$ and $Dk_{\mathrm{B}}T$ are called the stretch stiffness and twist–stretch coupling, respectively.

It may seem as though we have forgotten some possible quadratic terms in Equation 9.2, for example, a twist–bend cross-term. But the energy must be a scalar, whereas $\boldsymbol{\beta}\omega$ is a vector; terms

of this sort have the wrong geometrical status to appear in the energy.

In some cases, we can simplify Equation 9.2 still further. First, many polymers consist of monomers joined by single chemical bonds. The monomers can then rotate about these bonds, destroying any memory of the twist variable and eliminating twist elasticity: $C = D = 0$. In other cases (for example, the one to be studied in Section 9.2), the polymer is free to swivel at one of its attachment points, again leaving the twist variable uncontrolled; then ω again drops out of the analysis. A second simplification comes from the observation that the stretch stiffness $k_\mathrm{B}TB$ has the same dimensions as a *force*. If we pull on the polymer with an applied force much less than this value, the corresponding stretch u will be negligible, and we can forget about it, treating the molecule as an **inextensible rod**, that is, a rod having fixed total length. Making both these simplifications leads us to a *one-parameter* phenomenological model of a polymer, with elastic energy

$$E = \frac{1}{2}k_\mathrm{B}T \int_0^{L_\mathrm{tot}} \mathrm{d}s\, A\boldsymbol{\beta}^2. \qquad \text{simplified } \textbf{elastic rod model} \tag{9.3}$$

Equation 9.3 describes a thin, inextensible rod made of a continuous, elastic material. Other authors call it the Kratky–Porod or wormlike chain model (despite the fact that real worms are highly extensible). It is certainly a simple, ultrareductive approach to the complex molecule shown in Figure 2.15! Nevertheless, Section 9.2 will show that it leads to a quantitatively accurate model of the mechanical stretching of DNA.

$\boxed{T_2}$ *Section 9.1.2′ on page 335 mentions some finer points about elasticity models of DNA.*

9.1.3 Polymers resist stretching with an entropic force

The freely jointed chain Section 4.3.1 on page 107 suggested that a polymer could be viewed as a chain of N freely jointed links and that it assumes a random-walk conformation in certain solution conditions. We begin to see how to justify this image when we examine Equation 9.3. Suppose that we bend a segment of our rod into a quarter-circle of radius R (see Figure 9.1 and its caption). Each segment of length $\mathrm{d}s$ then bends through an angle $\mathrm{d}\theta = \mathrm{d}s/R$, so the bend vector $\boldsymbol{\beta}$ points inward, with magnitude $|\boldsymbol{\beta}| = \mathrm{d}\theta/\mathrm{d}s = R^{-1}$. According to Equation 9.3, the total elastic energy cost of this bend is then one half the bend stiffness, times the circumference of the quarter-circle, times $\boldsymbol{\beta}^2$, or

$$\text{elastic energy cost of a } 90° \text{ bend } = (\frac{1}{2}k_\mathrm{B}TA) \times (\frac{1}{4}2\pi R) \times R^{-2} = \frac{\pi A}{4R}k_\mathrm{B}T. \tag{9.4}$$

The key point about this expression is that it gets smaller with increasing R. That is, a 90° bend can cost as little as we like, provided its radius is big enough. In particular, when R is much bigger than A, then the elastic cost of a bend will be negligible relative to the thermal energy $k_\mathrm{B}T$! In other words,

> *Any elastic rod immersed in a fluid will be randomly bent by thermal motion*
> *if its contour length exceeds its bend persistence length A.* $\tag{9.5}$

Idea 9.5 tells us that two distant elements will point in random, uncorrelated directions as long as their separation is much greater than A. This observation justifies the name "bend persistence length" for A: Only over separations less than A will the molecule remember which way it was pointing.[1]

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[1] The situation is quite different for two-dimensional elastic objects, for example, membranes. We already found in Section 8.6.1 that the energy cost to bend a patch of membrane into, say, a hemisphere, is $4\pi\kappa$, a constant
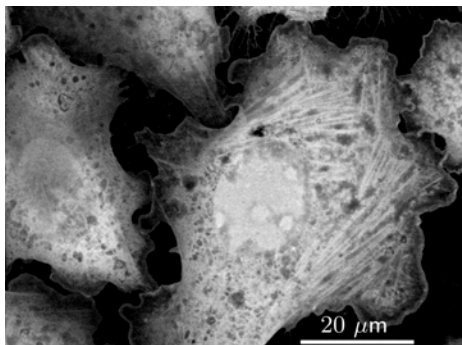
Figure 9.2: (Wet scanning electron micrograph.) Actin bundles in a stained CHO cell. Each bundle has a bend persistence length that is much larger than that of a single actin filament. The bundles are straight, not thermally bent, because their bend persistence length is longer than the cell's diameter. [Digital image kindly supplied by A. Nechushtan and E. Moses.]

A few structural elements in cells are extremely stiff, and so can resist thermal bending (Figure 9.2). But most biopolymers have persistence lengths much shorter than their total length. Because a polymer is rigid on the scale of a monomer, yet flexible on length scales much longer than A, it's reasonable to try the idealization that its conformation is a chain of *perfectly straight* segments, joined by *perfectly free* joints. We take the **effective segment length**, L_{seg}, to be a phenomenological parameter of the model. (Many authors refer to L_{seg} as the **Kuhn length**.) We expect L_{seg} to be roughly the same as A; because A is itself an unknown parameter, we lose no predictive power if we instead phrase the model in terms of L_{seg}.[2] We call the resulting model the **freely jointed chain** (or **FJC**). Section 9.2 will show that for DNA, $L_{seg} \approx 100\,\text{nm}$; conventional polymers like polyethylene have much shorter segment lengths, generally less than $1\,\text{nm}$. Because the value of L_{seg} reflects the bend stiffness of the molecule, DNA is often called a "stiff," or **semiflexible**, polymer.

The FJC model is a reduced form of the underlying elastic rod model (Equation 9.3). We will improve its realism later. But it at least incorporates the insight of Idea 9.5, and it will turn out to be mathematically simpler to solve than the full elastic rod model.

In short, we propose to study the conformation of a polymer as a random walk with step size L_{seg}. Before bringing any mathematics to bear on the model, let's first see if we find any qualitative support for it in our everyday experience.

The elasticity of rubber   At first sight, the freely jointed chain may not seem like a promising model for polymer elasticity. Imagine pulling on the ends of the chain until it's nearly fully stretched, then releasing it. If you try this with a chain made of paperclips, the chain stays straight after you let go. But a rubber band, which consists of many polymer chains, will *recoil* when stretched and released. What have we missed?

The key difference between a macroscopic chain of paperclips and a polymer is scale: The thermal energy $k_B T$ is negligible for macroscopic paperclips but significant for the nanometer-scale

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independent of the radius. Hence membranes do *not* rapidly lose their planar character on length scales larger than their thickness.

[2] $\boxed{T_2}$ Section 9.1.3′ on page 336 shows that the precise relation is $L_{seg} = 2A$.

monomers of a macromolecule. Suppose that we pull our paperclip chain out straight, then place it on a vibrating table, where it gets random kicks many times larger than $k_\mathrm{B}T$: Its ends *will* spontaneously come closer together as its shape gradually becomes random. Indeed, we would have to place the ends of the chain under constant, gentle tension to *prevent* this shortening, just as we must apply a constant force to keep a rubber band stretched.

We can understand the retracting tendency of a stretched polymer by using ideas from Chapters 6 and 7. A long polymer chain of length L_tot can consist of hundreds (or millions) of monomers, with a huge number of possible conformations. If there's no external stretching, the vast majority of these conformations are spherelike blobs, with mean-square end-to-end length z much shorter than L_tot (see Section 4.3.1 on page 107). The polymer adopts these random-coil conformations because there's *only one way* to be straight but many ways to be coiled up. Thus, if we hold the ends a fixed distance z apart, the entropy decreases when z increases. According to Chapter 7, there must then be an entropic force opposing such stretching. That's why a stretched rubber band spontaneously retracts:

> *The retracting force supplied by a stretched rubber band is entropic in origin.*   (9.6)

Thus the retraction of a stretched polymer, which increases disorder, is like the *expansion* of an ideal gas, which also increases disorder and can perform real work (see the heat engine Example, page 186). In either case, what must go down is not the elastic energy E of the polymer but the *free* energy, $F = E - TS$. Even if E *increases* slightly upon bending, still we'll see that the increase in entropy will more than offset the energy increase, driving the system toward the random-coil state. The free energy drop in this process can then be harnessed to do mechanical work, for example, flinging a wad of paper across the room.

Where does the energy to do this work come from? We already encountered some analogous situations while studying thermal machines in Sections 1.2.2, and Problem 6.3. As in those cases, the mechanical work done by a stretched rubber band must be extracted from the *thermal* energy of the surrounding environment. Doesn't the Second Law forbid such a conversion from disordered to ordered energy? No, because the disorder of the polymer molecules themselves increases upon retraction: Rubber bands are free energy transducers. (You'll perform an experiment to confirm this prediction and support the entropic force model of polymer elasticity in Problem 9.4.)

Could we actually build a heat engine based on rubber bands? Absolutely. To implement this idea, first notice a surprising consequence of the entropic origin of polymer elasticity. If the free energy increase upon stretching comes from a decrease in entropy, then the formula $F = E - TS$ implies that the free energy cost of a given extension will depend on the temperature. The tension in a stretched rubber band will thus increase with increasing T. Equivalently, if the imposed tension on the rubber is fixed, then the rubber will *shrink* as we heat it up—its coefficient of thermal expansion is negative, unlike, say, a block of steel.

To make a heat engine exploiting this observation, we need a cyclic process, analogous to the one symbolized by Figure 6.6 on page 188. Figure 9.3 shows one simple strategy.

The remainder of this chapter will develop heavier tools to understand polymers. But this section has a simple point: The ideas of statistical physics, which we have developed mainly in the context of ideal gases, are really of far greater applicability. Even without writing any equations, these ideas have already yielded an immediate insight into a very different-seeming system, one with applications to living cells. Admittedly, your body is not powered by rubber-band heat engines, nor by any other sort of heat engine. Still, understanding the entropic origin of polymer elasticity
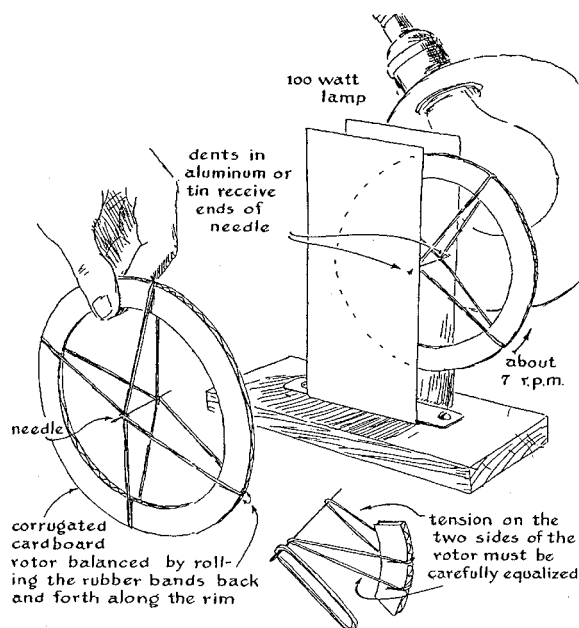
Figure 9.3: (Engineering sketch.) Rubber-band heat engine. The light bulb sequentially heats the rubber bands on one side of the disk, making them contract. The other side is shielded by the sheet metal screen; here the rubber bands cool. The resulting asymmetrical contraction unbalances the wheel, which turns. The turning wheel brings the warm rubber bands into the shaded region, where they cool; at the same time, cool rubber bands emerge into the warm region, making the wheel turn continuously. [From Stong, 1956.]

is important for our goal of understanding cellular mechanics.

$\boxed{T_2}$ *Section 9.1.3′ on page 336 gives a calculation showing that the bend stiffness sets the length scale beyond which a fluctuating rod's tangent vectors lose their correlation.*

9.2   Stretching single macromolecules

9.2.1   The force–extension curve can be measured for single DNA molecules

We'll need some mathematics to calculate the free energy $F(z)$ as a function of the end-to-end length z of a polymer chain. Before doing this, let's look at some of the available experimental data.

To get a clear picture, we'd like to pass from pulling on rubber bands, with zillions of entangled polymer chains, to pulling on *individual* polymer molecules with tiny, precisely known forces. S. Smith, L. Finzi, and C. Bustamante accomplished this feat in 1992; a series of later experiments improved both the quality of the data and the range of forces probed, leading to the picture shown in Figure 9.4. Such experiments typically start with a DNA molecule of known length (for example, lambda phage DNA). One end is anchored to a glass slide, the other to a micrometer-sized bead, and the bead is then pulled by optical or magnetic tweezers (see Section 6.7 on page 196).

Figure 9.4 shows five distinct regimes of qualitative behavior as the force on the molecule increases:
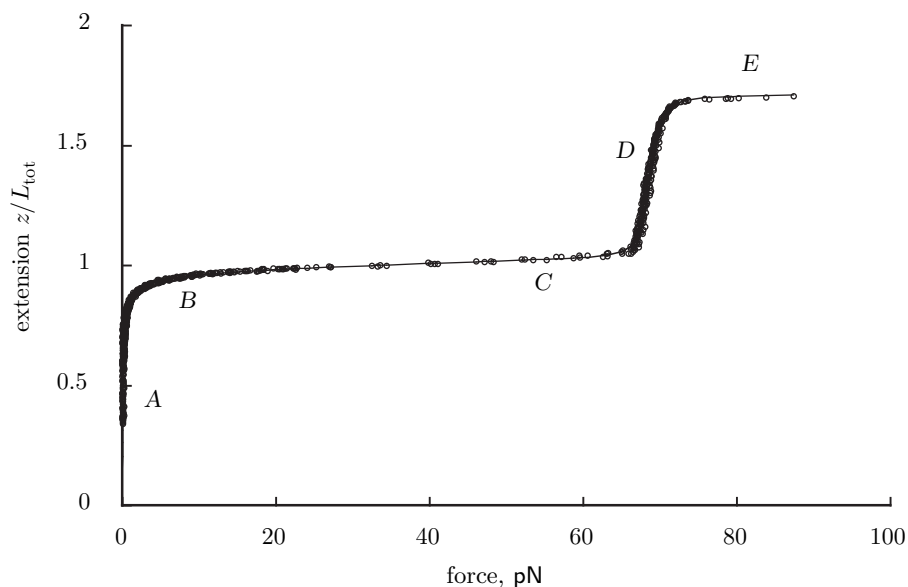
Figure 9.4: (Experimental data with fit.) Force f versus relative extension z/L_{tot} for a DNA molecule made of 10 416 basepairs, in high-salt solution. The regimes labeled A, B, C, D, and E are described in the text. The extension z was measured by video imaging of the positions of beads attached to each end; the force was measured by using the change of light momentum exiting a dual-beam optical tweezers apparatus (see Section 6.7 on page 196). L_{tot} is the DNA's total contour length in its relaxed state. The quantity z/L_{tot} becomes larger than 1 when the molecule begins to stretch, at around 20 pN. The *solid curve* shows a theoretical model obtained by a combination of the approaches in Sections 9.4.1′ and 9.5.1. [Experimental data kindly supplied by S. B. Smith; theoretical model and fit kindly supplied by C. Storm.]

A. At very low stretching force, $f < 0.01$ pN, the molecule is still nearly a random coil. Its ends then have a mean-square separation $L_{seg}\sqrt{N}$ (see the formula above Idea 4.17 on page 108, and recall that the quantity L in that formula is the segment length divided by $\sqrt{3}$). For a molecule with 10 416 basepairs, Figure 9.4 shows that this separation is less than $0.3L_{tot}$. Thus $L_{seg}\sqrt{L_{tot}/L_{seg}} < 0.3L_{tot}$, or $L_{seg} < (0.3)^2L_{tot} = 319$ nm. (In fact, L_{seg} will prove to be much smaller than this upper bound—it's closer to 100 nm.)

B. At higher forces, the relative extension begins to level off as it approaches unity. At this point, the molecule has been stretched nearly straight. Sections 9.2.2–9.4.1 will discuss regimes A and B.

C. At forces beyond about 10 pN, the extension actually exceeds the total contour length of the relaxed molecule. Section 9.4.2 will discuss this "intrinsic stretching" phenomenon.

D. At around $f = 65$ pN, we find a remarkable jump, as the molecule suddenly extends to about 1.6 times its relaxed length. Section 9.5.5 briefly discusses this "overstretching transitionDNA!overstretching transition."

E. Still higher forces again give elastic behavior, until eventually the molecule breaks.

9.2.2 A two-state system qualitatively explains DNA stretching at low force

The freely jointed chain model can help us understand regime A of Figure 9.4. We wish to compute the entropic force f exerted by an elastic rod subjected to thermal motion. This may seem like a daunting prospect. The stretched rod is constantly buffeted by the Brownian motion of the surrounding water molecules, receiving kicks in the directions perpendicular to its axis. Somehow all these kicks pull the ends closer together, maintaining a constant tension if we hold the ends a fixed distance z apart. How could we calculate such a force?

Luckily, our experience with other entropic forces shows how to sidestep a detailed dynamical calculation of each random kick: When the system is in thermal equilibrium, Chapter 7 showed that it's much easier to use the partition function method to calculate entropic forces. To use the method developed in Section 7.1.2, we need to elaborate the deep parallel between the entropic force exerted by a freely jointed chain and that exerted by an ideal gas confined to a cylinder:

- The gas is in thermal contact with the external world, and so is the chain.

- The gas has an external force squeezing it; the chain has an external force pulling it.

- The internal potential energy U_{int} of the gas molecules is independent of the volume. The chain also has fixed internal potential energy—the links are assumed to be free to point in any direction, with no potential-energy cost. In both systems, the kinetic energy is fixed by the ambient temperature, so it too is independent of the constraint. But, in both systems, the potential energy U_{ext} of the mechanism supplying the external force *will* vary.

In the polymer stretching system, U_{ext} goes up as the chain shortens:

$$U_{\text{ext}} = \text{const} - fz, \tag{9.7}$$

where f is the applied external stretching force. The total potential $U_{\text{int}} + U_{\text{ext}}$ is what we need when computing the system's partition function.

The observations just made simplify our task greatly. Following the strategy leading to Equation 7.5 on page 215, we now calculate the average end-to-end distance of the chain at a given stretching force f directed along the $+\hat{\mathbf{z}}$ axis.

In this section, we will work in one dimension for simplicity. (Section 9.2.2$'$ on page 338 extends the analysis to three dimensions.) Thus each link has a two-state variable σ, which equals $+1$ if the link points forward (along the applied force) or -1 if it points backward (against the force). The total extension z is then the sum of these variables:

$$z = L_{\text{seg}}^{(1\text{d})} \sum_{i=1}^{N} \sigma_i. \tag{9.8}$$

(The superscript "1d" reminds us that this is the effective segment length in the *one-dimensional* FJC model.) The probability of a given conformation $\{\sigma_1, \ldots, \sigma_N\}$ is then given by a Boltzmann factor:

$$P(\sigma_1, \ldots, \sigma_N) = Z^{-1} e^{-\left(-f L_{\text{seg}}^{(1\text{d})} \sum_{i=1}^{N} \sigma_i\right)/k_{\text{B}} T}. \tag{9.9}$$

Here Z is the partition function (see Equation 6.33 on page 195). The desired average extension is thus the weighted average of Equation 9.8 over all conformations, or

$$\langle z \rangle = \sum_{\sigma_1 = \pm 1} \cdots \sum_{\sigma_N = \pm 1} P(\sigma_1, \ldots, \sigma_N) \times z$$

$$= Z^{-1} \sum_{\sigma_1 = \pm 1} \cdots \sum_{\sigma_N = \pm 1} e^{-\left(-fL_{\text{seg}}^{(1d)} \sum_{i=1}^N \sigma_i\right)/k_B T} \times \left(L_{\text{seg}}^{(1d)} \sum_{i=1}^N \sigma_i\right)$$

$$= k_B T \frac{d}{df} \ln \left[\sum_{\sigma_1 = \pm 1} \cdots \sum_{\sigma_N = \pm 1} e^{-\left(-fL_{\text{seg}}^{(1d)} \sum_{i=1}^N \sigma_i\right)/k_B T} \right].$$

This looks like a formidable formula, until we notice that the argument of the logarithm is just the product of N independent, identical factors:

$$\langle z \rangle = k_B T \frac{d}{df} \ln \left[\left(\sum_{\sigma_1 = \pm 1} e^{fL_{\text{seg}}^{(1d)} \sigma_1 / k_B T} \right) \times \cdots \times \left(\sum_{\sigma_N = \pm 1} e^{fL_{\text{seg}}^{(1d)} \sigma_N / k_B T} \right) \right]$$

$$= k_B T \frac{d}{df} \ln \left(e^{fL_{\text{seg}}^{(1d)}/k_B T} + e^{-fL_{\text{seg}}^{(1d)}/k_B T} \right)^N$$

$$= N L_{\text{seg}}^{(1d)} \frac{e^{fL_{\text{seg}}^{(1d)}/k_B T} - e^{-fL_{\text{seg}}^{(1d)}/k_B T}}{e^{fL_{\text{seg}}^{(1d)}/k_B T} + e^{-fL_{\text{seg}}^{(1d)}/k_B T}}.$$

Recalling that $NL_{\text{seg}}^{(1d)}$ is just the total length L_{tot}, we have shown that

$$\boxed{\langle z/L_{\text{tot}} \rangle = \tanh(fL_{\text{seg}}^{(1d)}/k_B T). \qquad \text{force versus extension for the 1d FJC}} \qquad (9.10)$$

_____Your Turn 9B_____
If you haven't yet worked Problem 6.5, do it now. Explain why this is mathematically the same problem as the one we just solved.
_____

Solving Equation 9.10 for f shows that *the force needed to maintain a given extension z is proportional to the absolute temperature.* This property is the hallmark of any purely entropic force, for example, ideal-gas pressure or osmotic pressure; we anticipated it in Section 9.1.3.

The function in Equation 9.10 interpolates between two important limiting behaviors:

- •At high force, $\langle z \rangle \to L_{\text{tot}}$. This behavior is what we expect from a flexible but inextensible rod: Once it's fully straight, it can't lengthen any more.
- •At low force, $\langle z \rangle \to f/k$, where $k = k_B T/(L_{\text{tot}} L_{\text{seg}}^{(1d)})$.

The second point means that

> *At low extension, a polymer behaves as a spring, that is, it obeys a Hooke relation, $f = k\langle z \rangle$. In the FJC model, the effective spring constant k is proportional to the temperature.* (9.11)

Figure 9.5 shows experimental data obtained by stretching DNA, together with the function in Equation 9.10 (top curve). The figure shows that taking $L_{\text{seg}}^{(1d)} = 35\,\text{nm}$ makes the curve pass through the first data point. Although the one-dimensional freely jointed chain correctly captures the qualitative features of the data, clearly it's not in good quantitative agreement throughout the range of forces shown. That's hardly surprising in the light of our rather crude mathematical treatment of the underlying physics of the elastic rod model. The following sections will improve the analysis, eventually showing that the simplified elastic rod model (Equation 9.3) gives a very good account of the data (see the black curve in Figure 9.5).

$\boxed{T_2}$ *Section 9.2.2' on page 338 works out the three-dimensional freely jointed chain.*
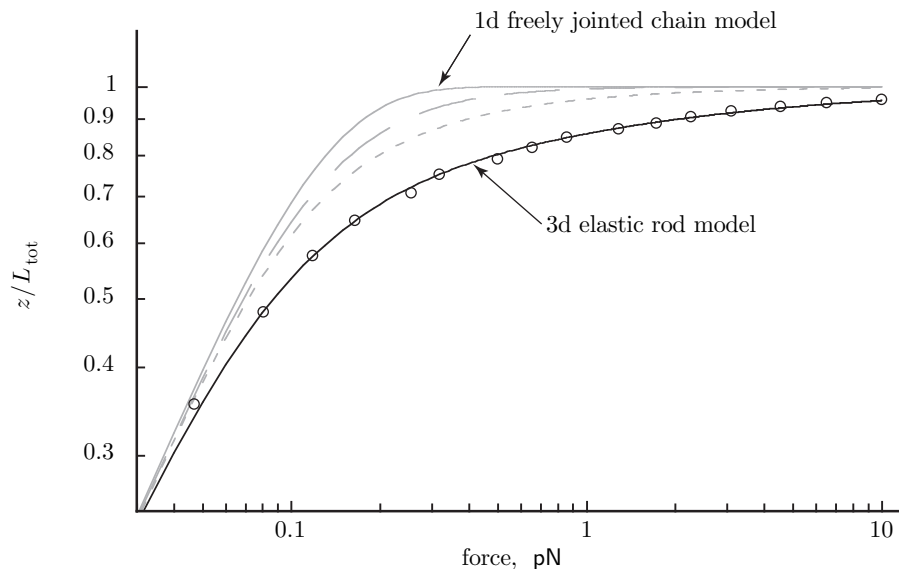
Figure 9.5: (Experimental data with fits.) Log-log plot of relative extension z/L_{tot} at low applied stretching force f for lambda phage DNA in 10 mM phosphate buffer. The points show experimental data corresponding to the regimes A–B in Figure 9.4. The curves show various theoretical models discussed in the text. For comparison, the value of L_{seg} has been adjusted in each model so that all the curves agree at low force. *Top curve:* One-dimensional freely jointed chain (Equation 9.10), with $L_{\text{seg}}^{(\text{1d})} = 35$ nm. *Long-dash curve:* One-dimensional cooperative chain (see Your Turn 9H (b)), with $L_{\text{seg}}^{(\text{1d})}$ held fixed at 35 nm and γ very large. *Short-dash curve:* Three-dimensional FJC (Your Turn 9O), with $L_{\text{seg}} = 104$ nm. *Black curve through data points:* Three-dimensional elastic rod model (Section 9.4.1′ on page 339), with $A = 51$ nm. [Data kindly supplied by V. Croquette; see also Bouchiat et al., 1999.]

9.3   Eigenvalues for the impatient

Section 9.4 will make use of some mathematical ideas not always covered in first-year calculus. Luckily, for our purposes only a few facts will be sufficient. Many more details are available in Shankar, 1995.

9.3.1   Matrices and eigenvalues

As always, it's best to approach this abstract subject through a familiar example. Look back at our force diagram for a thin rod being dragged through a viscous fluid (Figure 5.8 on page 153). Suppose, as shown in the figure, that the axis of the rod points in the direction $\hat{\mathbf{t}} = (\hat{\mathbf{x}} - \hat{\mathbf{z}})/\sqrt{2}$; let $\hat{\mathbf{n}} = (\hat{\mathbf{x}} + \hat{\mathbf{z}})/\sqrt{2}$ be the perpendicular unit vector. Section 5.3.1 stated that the drag force will be parallel to the velocity $\mathbf{v}$ if $\mathbf{v}$ is directed along either $\hat{\mathbf{t}}$ or $\hat{\mathbf{n}}$, but that the viscous friction coefficients in these two directions, $\zeta_\perp$ and $\zeta_\parallel$, are not equal: The parallel drag is typically $\frac{2}{3}$ as great as $\zeta_\perp$. For intermediate directions, we get a linear combination of a parallel force proportional to the parallel part of the velocity, plus a perpendicular force proportional to the perpendicular part of the velocity:

$$\mathbf{f} = \zeta_\parallel \hat{\mathbf{t}}(\hat{\mathbf{t}} \cdot \mathbf{v}) + \zeta_\perp \hat{\mathbf{n}}(\hat{\mathbf{n}} \cdot \mathbf{v}) = \zeta_\perp \left(\tfrac{2}{3}\hat{\mathbf{t}}(\hat{\mathbf{t}} \cdot \mathbf{v}) + \hat{\mathbf{n}}(\hat{\mathbf{n}} \cdot \mathbf{v}) \right). \tag{9.12}$$

This formula is indeed a linear function of v_x and v_z, the components of $\mathbf{v}$:

Your Turn 9C

Use the preceding expressions for $\hat{\mathbf{t}}$ and $\hat{\mathbf{n}}$ to show that

$$
\begin{bmatrix} f_x \\ f_z \end{bmatrix} = \zeta_\perp \begin{bmatrix} (\frac{1}{3} + \frac{1}{2})v_x + (-\frac{1}{3} + \frac{1}{2})v_z \\ (-\frac{1}{3} + \frac{1}{2})v_x + (\frac{1}{3} + \frac{1}{2})v_z \end{bmatrix}.
$$

Expressions of this form arise so frequently that we introduce an abbreviation:

$$
\begin{bmatrix} f_x \\ f_z \end{bmatrix} = \zeta_\perp \begin{bmatrix} (\frac{1}{3} + \frac{1}{2}) & (-\frac{1}{3} + \frac{1}{2}) \\ (-\frac{1}{3} + \frac{1}{2}) & (\frac{1}{3} + \frac{1}{2}) \end{bmatrix} \begin{bmatrix} v_x \\ v_z \end{bmatrix}. \tag{9.13}
$$

Even though Equation 9.13 is nothing but an abbreviation for the formula above it, let's pause to put it in a broader context. *Any* linear relation between two vectors can be written as $\mathbf{f} = \mathsf{M}\mathbf{v}$, where the symbol M denotes a **matrix**, or rectangular array of numbers. In our example we are interested in only two directions $\hat{\mathbf{x}}$ and $\hat{\mathbf{z}}$, so our matrix is two-by-two:

$$
\mathsf{M} \equiv \begin{bmatrix} M_{11} & M_{12} \\ M_{21} & M_{22} \end{bmatrix}.
$$

Thus the symbol M_{ij} denotes the entry in row i and column j of the matrix. Placing a matrix to the left of a vector, as in Equation 9.13, denotes an operation where we successively read across the rows of M, multiplying each entry we find by the corresponding entry of the vector $\mathbf{v}$ and adding to obtain the successive components of $\mathbf{f}$:

$$
\mathsf{M}\mathbf{v} \equiv \begin{bmatrix} M_{11}v_1 + M_{12}v_2 \\ M_{21}v_1 + M_{22}v_2 \end{bmatrix}. \tag{9.14}
$$

The key question is now: Given a matrix M, *what are the special directions of* $\mathbf{v}$ (if any) that get transformed to vectors parallel to themselves under the operation symbolized by M? We already know the answer for the example in Equation 9.13: We constructed this matrix to have the special axes $\hat{\mathbf{t}}$ and $\hat{\mathbf{n}}$, with corresponding viscous friction coefficients $\frac{2}{3}\zeta_\perp$ and $\zeta_\perp$, respectively. More generally, though, we may not be given the special directions in advance, and there may not even be any. The special directions of a matrix M, if any, are called its **eigenvectors**; the corresponding multipliers are called the **eigenvalues**.[3] Let's see how to work out the special directions, and their eigenvalues, for a general 2×2 matrix.

Consider the matrix $\mathsf{M} = \begin{bmatrix} a & b \\ c & d \end{bmatrix}$. We want to know whether there is any vector $\mathbf{v}_*$ that turns into a multiple of itself after transformation by M:

$$
\mathsf{M}\mathbf{v}_* = \lambda\mathbf{v}_*. \qquad \text{eigenvalue equation} \tag{9.15}
$$

The notation on the right-hand side means that we multiply each entry of the vector $\mathbf{v}_*$ by the same constant λ. Equation 9.15 is actually *two* equations, because each side is a vector with two components (see Equation 9.14).

How can we solve Equation 9.15 without knowing in advance the value of λ? To answer this question, first note that there's always *one* solution, no matter what value we take for λ, namely,

---

[3]Like "liverwurst," this word is a combination of the German *eigen* ("proper") and an English word. The term expresses the fact that the eigenvalues are intrinsic to the linear transformation represented by M. In contrast, the entries M_{ij} themselves *change* when we express the transformation in some other coordinate system.

$\mathbf{v}_* = \begin{bmatrix} 0 \\ 0 \end{bmatrix}$. This is a boring solution. Regarding Equation 9.15 as two equations in the two unknowns v_1 and v_2, in general, we expect just one solution; in other words, *the eigenvalue equation, Equation 9.15, will in general have only the boring (zero) solution.* But for certain special values of λ, we may find a second, interesting solution after all. This requirement is what determines λ.

We are looking for solutions to the eigenvalue equation (Equation 9.15 with $\mathsf{M} = \begin{bmatrix} a & b \\ c & d \end{bmatrix}$) in which v_1 and v_2 are not both zero. Suppose that $v_1 \neq 0$. Then we can divide both sides of the eigenvalue equation by v_1 and seek a solution of the form $\begin{bmatrix} 1 \\ \omega \end{bmatrix}$. The first of the two equations represented by Equation 9.15 then says that $a + \omega b = \lambda$, or $b\omega = \lambda - a$. The second equation says that $c + d\omega = \lambda\omega$. Multiplying by b and substituting the first equation lets us eliminate ω altogether, finding

$$bc = (\lambda - a)(\lambda - d). \qquad \text{(condition for } \lambda \text{ to be an eigenvalue)} \qquad (9.16)$$

Thus only for certain special values of λ—the eigenvalues—will we find any nonzero solution to Equation 9.15. The solutions are the desired eigenvectors.

Your Turn 9D

a. Apply Equation 9.16 to the matrix appearing in the frictional drag problem (Equation 9.13). Find the eigenvalues, and the corresponding eigenvectors, and confirm that they're what you expect for this case.

b. For some problems, it's possible that v_1 may be zero; in this case, we can't divide through by it. Repeat the preceding argument, this time assuming that $v_2 \neq 0$, and recover the same condition as Equation 9.16.

c. It's possible that Equation 9.16 will have no real solutions. Show that it will always have two real solutions if $bc \geq 0$.

d. Show that, furthermore, the two eigenvalues will be different (not equal to each other) if $bc > 0$.

Your Turn 9E

Continuing the previous problem, consider a *symmetric* 2×2 matrix, that is, one with $M_{12} = M_{21}$. Show that

a. It always has two real eigenvalues.

b. The corresponding eigenvectors are perpendicular to each other, if the two eigenvalues are not equal.

9.3.2   Matrix multiplication

Here is another concrete example. Consider the operation that takes a vector $\mathbf{v}$, rotates it through an angle α, and stretches or shrinks its length by a factor g. You can show that this operation is linear, that its matrix representation is $\mathsf{R}(\alpha, g) = \begin{bmatrix} g\cos\alpha & g\sin\alpha \\ -g\sin\alpha & g\cos\alpha \end{bmatrix}$, and that it has *no* real eigenvectors (why not?).

Suppose we apply the operation R to a vector *twice*.

Your Turn 9F

a. Evaluate $\mathsf{M}(\mathsf{N}\mathbf{v})$ for two arbitrary 2×2 matrices M and N. (That is, apply Equation 9.14 twice.) Show that your answer can be rewritten as $\mathsf{Q}\mathbf{v}$, where Q is a new matrix called the **product** N and M, or simply MN. Find Q.

b. Evaluate the matrix product $\mathsf{R}(\alpha, g)\mathsf{R}(\beta, h)$, and show that it too can be written as a certain

combination of rotation and scaling. That is, express it as $\mathsf{R}(\gamma, c)$ for some γ and c. Find γ and c and explain why your answers make sense.

T_2 Section 9.3.2' on page 339 sketches the generalizations of some of the preceding results to higher-dimensional spaces.

9.4 Cooperativity

9.4.1 The transfer matrix technique allows a more accurate treatment of bend cooperativity

Section 9.2.2 gave a provisional analysis of DNA stretching. To begin improving it, let's recall some of the simplifications made so far:

- We treated a continuous elastic rod as a chain of perfectly stiff segments, joined by perfectly free joints.

- We treated the freely jointed chain as being one-dimensional (Section 9.2.2' on page 338 discusses the three-dimensional case).

- We ignored the fact that a real rod cannot pass through itself.

This section will consider the first of these oversimplifications.[4] Besides yielding a slight improvement in our fit to the experimental data, the ideas of this section have broader ramifications and go to the heart of this chapter's Focus Question.

Clearly, it would be better to model the chain, not as N segments with free joints, but as, say, $2N$ shorter segments with some "peer pressure," a preference for neighboring units to point in the same direction. We'll refer to such a effect as a cooperative coupling (or simply as **cooperativity**). In the context of DNA stretching, cooperativity is a surrogate for the physics of bending elasticity, but later we'll extend the concept to include other phenomena as well. To keep the mathematics simple, let's begin by constructing and solving a one-dimensional version of this idea, which we'll call the **1d cooperative chain model**. Section 9.5.1 will show that the mathematics of the one-dimensional cooperative chain is also applicable to another class of problems, the helix–coil transitions in polypeptides and DNA.

Just as in Section 9.2.2, we introduce N two-state variables σ_i, describing links of length ℓ. Unlike the FJC, however, the chain itself has an internal elastic potential energy U_{int}: When two neighboring links point in opposite directions ($\sigma_i = -\sigma_{i+1}$), we suppose that they contribute an extra $2\gamma k_{\text{B}}T$ to this energy, relative to when they point in parallel. We can implement this idea by introducing the term $-\gamma k_{\text{B}}T\sigma_i\sigma_{i+1}$ into the energy function; this term equals $\pm\gamma k_{\text{B}}T$, depending on whether the neighboring links agree or disagree. Adding contributions from all the pairs of neighboring links gives

$$U_{\text{int}}/k_{\text{B}}T = -\gamma \sum_{i=1}^{N-1} \sigma_i\sigma_{i+1}, \tag{9.17}$$

---

[4] *T_2 Section 9.4.1' on page 339 will tackle the first two together. Problem 7.9 discussed the effects of self-avoidance; it's a minor effect for a stiff polymer (like DNA) under tension. The discussion in this section will introduce yet another simplification, taking the rod to be infinitely long. Section 9.5.2 will illustrate how to introduce finite-length effects.

where γ is a new, dimensionless phenomenological parameter (the **cooperativity parameter**). We are assuming that only next-door neighbor links interact with each other. The effective link length ℓ need not equal the FJC effective link length $L_{\text{seg}}^{(1d)}$; again we will find the appropriate ℓ by fitting the model to data.

We can again evaluate the extension $\langle z \rangle$ as the derivative of the free energy, computed by the partition function method (Equation 7.6 on page 215). Let $\alpha \equiv f\ell/k_BT$, a dimensionless measure of the energy term biasing each segment to point forward. With this abbreviation, the partition function is

$$Z(\alpha) = \sum_{\sigma_1 = \pm 1} \cdots \sum_{\sigma_N = \pm 1} \left[e^{\alpha \sum_{i=1}^{N} \sigma_i + \gamma \sum_{i=1}^{N-1} \sigma_i \sigma_{i+1}} \right]. \tag{9.18}$$

The first term in the exponential corresponds to the contribution U_{ext} to the total energy from the external stretching. We need to compute $\langle z \rangle = k_BT \frac{d}{df} \ln Z(f) = \ell \frac{d}{d\alpha} \ln Z(\alpha)$.

To make further progress, we must evaluate the summations in Equation 9.18. Sadly, the trick we used for the FJC doesn't help us this time: The coupling between neighboring links spoils the factorization of Z into N identical, simple factors. Nor can we have recourse to a mean-field approximation like the one that saved us in Section 7.4.3 on page 229. Happily, though, the physicists H. Kramers and G. Wannier found a beautiful end run around this problem in 1941. Kramers and Wannier were studying *magnetism*, not polymers. They imagined a chain of atoms, each a small permanent magnet that could point its north pole either parallel or perpendicular to an applied magnetic field. Each atom feels not only the applied field (analogous to the α term of Equation 9.18) but also the field of its nearest neighbors (the γ term). In a magnetic material like steel, the coupling tends to align neighboring atoms ($\gamma > 0$), just as in a stiff polymer the bending elasticity has the same effect. The fact that the solution to the magnet problem also solves interesting problems involving polymers is a beautiful example of the broad applicability of simple physical ideas.[5]

Suppose that there were just two links. Then the partition function Z_2 consists of just four terms; it's a sum over the two possible values for each of σ_1 and σ_2.

Your Turn 9G

a. Show that this sum can be written compactly as the matrix product $Z_2 = \mathbf{V} \cdot (\mathsf{T}\mathbf{W})$, where $\mathbf{V}$ is the vector $\left[\begin{smallmatrix} e^{\alpha} \\ e^{-\alpha} \end{smallmatrix} \right]$, $\mathbf{W}$ is the vector $\left[\begin{smallmatrix} 1 \\ 1 \end{smallmatrix} \right]$, and T is the 2×2 matrix with entries

$$\mathsf{T} = \left[\begin{array}{cc} e^{\alpha+\gamma} & e^{-\alpha-\gamma} \\ e^{\alpha-\gamma} & e^{-\alpha+\gamma} \end{array} \right]. \tag{9.19}$$

b. Show that for N links, the partition function equals $Z_N = \mathbf{V} \cdot (\mathsf{T}^{N-1}\mathbf{W})$.

c. $\boxed{T_2}$ Show that for N links the average value of the middle link variable is $\langle \sigma_{N/2} \rangle = \left(\mathbf{V} \cdot \mathsf{T}^{(N-2)/2} \left(\begin{smallmatrix} 1 & 0 \\ 0 & -1 \end{smallmatrix} \right) \mathsf{T}^{N/2}\mathbf{W} \right) / Z_N$.

Just as in Equation 9.14, the notation in Your Turn 9G (a) is a shorthand way to write

$$Z_2 = \sum_{i=1}^{2} \sum_{j=1}^{2} V_i T_{ij} W_j,$$

where T_{ij} is the element in row i and column j of Equation 9.19. The matrix T is called the **transfer matrix** of our statistical problem.

---
[5]Actually, an ordinary magnet is a *three*-dimensional array of coupled spins, not a one-dimensional chain. The exact mathematical solution of the corresponding statistical physics problem remains unknown to this day.

Your Turn 9G (b) gives us an almost magical resolution to our difficult mathematical problem. To see this, we first notice that T has two eigenvectors, because its off-diagonal elements are both positive (see Your Turn 9D (c)). Let's call these eigenvectors $\mathbf{e}_\pm$ and their corresponding eigenvalues $\lambda_\pm$. Thus $\mathsf{T}\mathbf{e}_\pm = \lambda_\pm \mathbf{e}_\pm$.

Any other vector can be expanded as a combination of $\mathbf{e}_+$ and $\mathbf{e}_-$; for example, $\mathbf{W} = w_+ \mathbf{e}_+ + w_- \mathbf{e}_-$. We then find that

$$Z_N = p(\lambda_+)^{N-1} + q(\lambda_-)^{N-1}, \tag{9.20}$$

where $p = w_+ \mathbf{V} \cdot \mathbf{e}_+$ and $q = w_- \mathbf{V} \cdot \mathbf{e}_-$. This is a big simplification. It gets better when we realize that for very large N, we can forget about the second term of Equation 9.20, because one eigenvalue will be bigger than the other (Your Turn 9D (d)), and when raised to a large power, the bigger one will be *much* bigger. Moreover, we don't even need the numerical value of p: You are about to show that we need $N^{-1} \ln Z_N$, which equals $\ln \lambda_+ + N^{-1} \ln(p/\lambda_+)$. The second term is small when N is large.

Now finish the derivation:

Your Turn 9H

a. Show that the eigenvalues are $\lambda_\pm = \mathrm{e}^\gamma \left[\cosh \alpha \pm \sqrt{\sinh^2 \alpha + \mathrm{e}^{-4\gamma}} \right]$.

b. Adapt the steps leading to Equation 9.10 on page 307 to find $\langle z/L_{\mathrm{tot}} \rangle$ as a function of f in the limit of large N.

c. Check your answer by setting $\gamma \to 0$, $\ell \to L_{\mathrm{seg}}^{(1\mathrm{d})}$, and showing that you recover the result of the FJC, Equation 9.10.

As always, it's interesting to check the behavior of your solution at very low force ($\alpha \to 0$). We again find that $\langle z \rangle \to f/k$, where now the spring constant is

$$k = k_{\mathrm{B}} T / (\mathrm{e}^{2\gamma} \ell L_{\mathrm{tot}}). \tag{9.21}$$

So at least we have not spoiled the partial success we had with the FJC: The low-force limit of the extension, where the FJC was successful, has the same form in the cooperative chain model, as long as we choose ℓ and γ to satisfy $\ell \mathrm{e}^{2\gamma} = L_{\mathrm{seg}}^{(1\mathrm{d})}$. We now ask whether the cooperative chain model can do a better job than the FJC of fitting the data at the *high*-force end.

The dashed curve in Figure 9.5 shows the function you found in Your Turn 9H. The cooperativity γ has been taken very large, while holding fixed $L_{\mathrm{seg}}^{(1\mathrm{d})}$. The graph shows that the cooperative one-dimensional chain indeed does a somewhat better job of representing the data than the FJC.

Our 1d cooperative chain model is still not very realistic. The lowest curve on the graph shows that the three-dimensional cooperative chain (that is, the elastic rod model, Equation 9.3 on page 301) gives a very good fit to the data. This result is a remarkable vindication of the highly reductionist model of DNA as a uniform elastic rod. Adjusting just one phenomenological parameter (the bend persistence length A) gives a quantitative account of the relative extension of DNA, a very complex object (see Figure 2.15 on page 45). This success makes sense in the light of the discussion in Section 9.1.1: It is a consequence of the large difference in length scales between the typical thermal bending radius ($\approx 100\,\mathrm{nm}$) and the diameter of DNA ($2\,\mathrm{nm}$).

$\boxed{T_2}$ *Section 9.4.1′ on page 339 works out the force–extension relation for the full, three-dimensional elastic rod model.*