Statistical Mechanics of Chain Molecules: An Overview

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1 Introduction

Before we can perform theoretical and computational studies on biomolecules, it would behoove us to have an idea of how other, similar molecules that are not associated with living organisms behave. The molecules of life – DNA, RNA and proteins – are chain molecules; however, their behavior is remarkably different than other chain molecules, such as might be found in household plastics. Here we will investigate the statistical physics of chain molecules using simple but well-studied models. We will start by defining some statistical measures of chain conformations, and then look at successively more complicated models. In the end we will see that simple models reveal a surprising amount of information about the statistical properties of chains, but that simple models are not sufficient for describing the general properties of proteins. Additional information on the topics covered here can be found in the texts of Flory [1], Dill [2], Phillips [3] and Hiemenz [4].

2 Statistical Measures of Chain Conformation

First we will establish some conventions for discussion. Consider a chain as an ordered set of N *beads*, or *particles*, $1 \ldots N$, connected by $N-1$ *links*. For convenience, it will be useful to define $n \equiv N-1$ as the number of links. Depending on our system of study, beads may be atoms, residues, monomers, etc., and links may be bonds (between atoms) or pseudobonds (e.g., between C_α atoms in a protein. The location of bead i is given by $\mathbf{r}_i = (x_i, y_i, z_i)^T$, and link i points from bead i to bead $i+1$: $\mathbf{l}_i = \mathbf{r}_{i+1} - \mathbf{r}_i$ and has length $l_i = \sqrt{(\mathbf{r}_{i+1} - \mathbf{r}_i)^2}$.

The link length l_i does not have to be the same for all i, but we will often assume that this is the case for simplicity. When considering proteins, for example, there are three distinct backbone bond lengths, corresponding to N-Cα, Cα-C and C-N bonds. If all backbone atoms are treated as beads, then there will be three different bond lengths. If instead only Cα atoms act as beads, then all links will have approximately equal length (3.8Å). The primary use of the link length (and other chain details) in these notes is to calculate statistical averages, so the average link length, $l = \frac{1}{n}\sum_{i=1}^{n}\sqrt{\mathbf{l}_i \cdot \mathbf{l}_i}$ is in general sufficient.

The position of the first bead on the chain, $\mathbf{r}_1$, is arbitrary. Given $\mathbf{r}_1$, we can use the definition of $\mathbf{l}_1$ to find the position of the second bead as $\mathbf{r}_2 = \mathbf{r}_1 + \mathbf{l}_1$. Continuing in this way, the position of

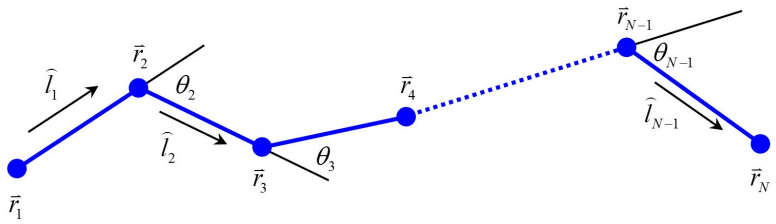


Figure 1: A simple model chain molecule.

bead i is

$$\mathbf{r}_i = \mathbf{r}_1 + \sum_{j=1}^{i-1} \mathbf{l}_j \ .$$

The *end-to-end vector* is defined as

$$\begin{aligned} \mathbf{h} &\equiv \mathbf{r}_N - \mathbf{r}_1 \\ &= \sum_{i}^{N-1} \mathbf{l}_i \ . \end{aligned} \tag{1}$$

For practical reasons, $\mathbf{h}$ is not a particularly informative measure of chain conformation. Real chain molecules move – not just internally, but externally. A rigid chain will tend to rotate and translate in space, even in the absence of internal motions of its beads relative to each other. This rotation is spatially isotropic, meaning that all orientations are equally likely. Thus, if we average $\mathbf{h}$ over all chain orientations, we will find that it becomes zero: $\langle \mathbf{h} \rangle = 0$.

2.1 End-to-end distance

A slightly better measure, and the one that will get us started on calculating statistical features of chains, is the end-to-end *distance*:

$$h \equiv \langle |\mathbf{h}|^2 \rangle^{1/2} \ . \tag{2}$$

The squared end-to-end distance will prove useful in many calculations and can be found:

$$\begin{aligned} h^2 &= \langle \left(\sum_{i=1}^{N-1} \mathbf{l}_i \right) \cdot \left(\sum_{j=1}^{N-1} \mathbf{l}_j \right) \rangle \\ &= \langle \sum_{i=1}^{N-1} \sum_{j=1}^{N-1} \mathbf{l}_i \cdot \mathbf{l}_j \rangle \\ &= \langle \sum_{i=1}^{N-1} \mathbf{l}_i \cdot \mathbf{l}_i + \sum_{i=1}^{N-1} \sum_{j \neq i} \mathbf{l}_i \cdot \mathbf{l}_j \rangle \\ &= \sum_{i=1}^{N-1} \langle \mathbf{l}_i \cdot \mathbf{l}_i \rangle + \sum_{i=1}^{N-1} \sum_{j \neq i} \langle \mathbf{l}_i \cdot \mathbf{l}_j \rangle \\ &= nl^2 + \sum_{i=1}^{N-1} \sum_{j \neq i} \langle \mathbf{l}_i \cdot \mathbf{l}_j \rangle \ , \end{aligned} \tag{3}$$

where we have made use of the average squared link length, l^2, in the last step. The first term in Eq. 3 captures a universal dependence of h on the number of links and their average length. The second term depends on the constraints of the chain and is model-dependent.

Fun as it is to calculate expressions like Eq. 3, they are often of little use in reality. The mean end-to-end distance is difficult to accurately measure in experiments, and it only provides information on two of the beads on the chain. The remainder of the chain, which is often of great interest, is ignored by h, leaving something to be desired. Nonetheless, the simple form of h^2 is useful because it relates to more descriptive measures of chain conformation.

2.2 Radius of Gyration

A more commonly used statistical descriptor of chain conformation is the *radius of gyration*, R_g, defined as the average distance of any bead from the chain's center of mass. Recall that the center of mass is given by

$$\mathbf{r}_{CM} = \frac{\sum_{i=1}^{N} m_i \mathbf{r}_i}{\sum_{i=1}^{N} m_i} \ ,$$

where m_i is the mass of bead i. Defining the position of bead i relative to the center of mass as $\mathbf{s}_i \equiv \mathbf{r}_i - \mathbf{r}_{CM}$, the radius of gyration is

$$R_g \equiv \langle s^2 \rangle^{1/2} \ . \tag{4}$$

Eq. 4 is valid not only for chains, but for any distribution of points in space. R_g is a measure of the spread of a distribution: Small R_g implies a compact distribution, whereas large R_g indicates an open or extended distribution. It can be shown that R_g is related to the average distance between particles. An expression that is equivalent to Eq. 4 is

$$R_g^2 = \frac{1}{N^2} \sum_{i=1}^{N} \sum_{j>i} \langle |r_{ij}|^2 \rangle \ . \tag{5}$$

Here r_{ij} simply means the distance between particles i and j. As with h, it is often easier to work with R_g^2. Not only can R_g apply to any distribution of discrete points, it can also be generalized to continua:

$$R_g^2 = \int \mathrm{d}V \rho(\mathbf{r})(\mathbf{r} - \mathbf{r}_{CM})^2 \ .$$

Applying the above expression to a uniform sphere of radius R, we can see that $R_g = \sqrt{\frac{3}{5}}R$.

It might be fun to think about the relationship between h and R_g. Consider a chain in a random conformation with some R_g. Without knowing anything else about the chain, we might assume that its beads are distributed uniformly in space, amounting to something like a sphere of radius $R = \sqrt{\frac{5}{3}}R_g$. The first bead of the chain has an equal probability of being anywhere in the sphere, as does the last bead. From Eq. 5, we know that the average distance between the ends of the chain is R_g. So we might expect $R_g^2 \sim h^2$, naively. This can be shown rigorously for various cases, but as a simple approximation, it shows that knowing h^2 tells us something about R_g^2. Thus, if you can't calculate R_g, it may suffice to calculate h^2. Our initial excursion into the end-to-end distance wasn't all for naught, after all.

2.3 Persistence length

A third measure of chain conformation that may come in handy is the *persistence length*,

$$\begin{aligned} \xi_p &= \frac{1}{l}\sum_{j=i}^{n}\langle \mathbf{l}_i \cdot \mathbf{l}_j \rangle \\ &= \frac{1}{l}\left[\langle \mathbf{l}_i \cdot \mathbf{l}_i \rangle + \langle \mathbf{l}_i \cdot \mathbf{l}_{i+1} \rangle + \ldots + \langle \mathbf{l}_i \cdot \mathbf{l}_n \rangle\right] \ . \end{aligned} \tag{6}$$

Flory [1] defines this as the "average sum of the projections of all bonds $j : j \geq i$ on an arbitrary bond i in an indefinitely long chain." Persistence length is a measure of the chain's tendency to remain straight, or the average distance that a chain travels before turning 90°.

Happily, ξ_p is also related to h^2. The arbitrary link that we have referenced is somewhere in the middle of the chain, far removed from either of the ends, so we could just as easily calculated ξ_p by summing from 1 to i instead of from i to n:

$$\xi_p = \langle \frac{\mathbf{l}_i}{l} \cdot \sum_{j=i}^{n} \mathbf{l}_j \rangle = \langle \frac{\mathbf{l}_i}{l} \cdot \sum_{j=1}^{i} \mathbf{l}_j \rangle \ .$$

Combining these two equivalent definitions for ξ_p,

$$2\xi_p = \frac{1}{l}\sum_{j=1}^{n}\langle \mathbf{l}_i \cdot \mathbf{l}_j \rangle + \frac{1}{l}\langle \mathbf{l}_i \cdot \mathbf{l}_i \rangle \ .$$

Understanding that for a homogeneous chain, ξ_p should be independent of the reference link, one

can average it over all links:

$$2\xi_p = \frac{1}{n}\sum_{i=1}^{n}\frac{1}{l}\sum_{j=1}^{n}\langle \mathbf{l}_i \cdot \mathbf{l}_j \rangle + l$$
$$\xi_p = \frac{h^2}{2nl} + \frac{l}{2} \; . \tag{7}$$

Once again, we can relate an informative quantity, ξ_p, to an easily calculable one, h^2.

3 Freely Jointed Chain

The simplest model of a chain is the Freely Jointed Chain, or Random Flight. This model assumes no restrictions on bond angles and amounts to a random walk in three dimensions. Even though the assumptions (no bond angle restrictions, no penalty for self-intersection, no solvent) may make this model appear to be comically simple, it makes a surprisingly accurate first attempt at exploring chain molecules.

3.1 FJC: End-to-end distance

From Eq. 3,

$$h^2 = nl^2 + \sum_{i=1}^{n}\sum_{j\neq i}\langle \mathbf{l}_i \cdot \mathbf{l}_j \rangle \; . \tag{8}$$

The second term on the right-hand side of Eq. 8 is zero. The chain is free to rotate about all bonds, so $\langle \mathbf{l}_i \cdot \mathbf{l}_j \rangle = l^2\delta_{ij} \; \forall \; i,j$. This can be shown easily by integrating over the conformations of the chain. Note that this result implies that $\xi_p = l$ for the freely jointed chain, indicating that the chain has no persistence past one link. The end-to-end distance,

$$h = \sqrt{n}l \; , \tag{9}$$

recovers the scaling that we find for a random walk.

3.2 FJC: Radius of gyration

That was easy enough, right? Now, what about the radius of gyration of the FJC? Let's start from Eq. 5:

$$\begin{aligned} R_g^2 &= \frac{1}{N^2}\sum_{i=1}^{N}\sum_{j>i}\langle|r_{ij}|^2\rangle \\ &= \frac{1}{N^2}\sum_{i=1}^{N}\sum_{j>i}|j-i|l^2 \\ &= \frac{l^2}{N^2}\sum_{k=1}^{N-1}k(N-k) \\ &= \frac{l^2}{N^2}\left[N\sum_{k=1}^{N-1}k-\sum_{k=1}^{N-1}k^2\right] . \end{aligned} \tag{10}$$

The two geometric series in Eq. 10 can be simplified algebraically. The first one is just the number of elements in the upper triangle of a square matrix, but the closed form of the second series is more involved (A simple derivation appears in the Appendix). Substituting:

$$\begin{aligned} R_g^2 &= \frac{l^2}{N^2}\left[\frac{N^2(N-1)}{2}-\frac{N(N-1)(2N-1)}{6}\right] \\ &= \frac{l^2}{6}\left[N-\frac{1}{N}\right] . \end{aligned} \tag{11}$$

For $N \gg 1$, the second term is negligible, leaving

$$\begin{aligned} R_g^2 &\approx \frac{Nl^2}{6} \\ &= \frac{h^2+l^2}{6} . \end{aligned}$$

So R_g^2 indeed goes like h^2 for FJC, agreeing with our earlier approximation. In the limit of small l, $R_g^2 \sim h^2/6$.

3.3 Distribution of end-to-end vector for FJC

As its alternate name ("Random Flight") implies, the FJC is just diffusion in three dimensions. We know that, in one dimension, the probability for traveling a distance Δx after taking n steps of length l is

$$P(n,\Delta x) = \frac{1}{\sqrt{2\pi n l^2}}\exp\left\{-\frac{x^2}{2nl^2}\right\} .$$

We can conceptually extend this to a random flight in three dimensions by altering the step size or the number of steps. Consider a random walk on a 3D lattice. There is no difference between $x-$,

$y-$ and $z-$ directions, so we expect $P(n, \Delta x) = P(n, \Delta y) = P(n, \Delta z)$. If our walk has n total steps, then we expect $n/3$ steps to be taken in each direction. Alternatively, we might argue that a single step of length l in 3D can be decomposed into $x-$, $y-$ and $z-$ components: $l^2 = l_x^2 + l_y^2 + l_z^2$. Again invoking spatial isotropy, we find $l_x = l_y = l_z = l/\sqrt{3}$. Thus, if we perform a 3D random walk starting at the origin and using steps of length l, the probability of the walk having some $x-$component after n steps is

$$P'(n, x) = \sqrt{\frac{3}{2\pi n l^2}} \exp\left\{-\frac{3x^2}{2nl^2}\right\} ,$$

and similarly for the $y-$ and $z-$ components. As usual, this result can be shown more rigorously by those so inclined. The probability of finding a final displacement vector $\mathbf{h}$ after n steps of a random flight in 3D is then

$$\begin{aligned} P(n, \mathbf{h}) &= P'(n, h_x) P'(n, h_y) P'(n, h_z) \\ &= \left[\frac{3}{2\pi n l^2}\right]^{3/2} \exp\left\{-\frac{3h^2}{2nl^2}\right\} . \end{aligned} \tag{12}$$

Does this result make sense? It indicates that the probability of winding up at $\mathbf{h}$ depends on the magnitude, but not the direction, of $\mathbf{h}$, consistent with spatial isotropy. The width of the distribution is $\sigma = l\sqrt{n/3}$, just as we would expect for a random walk. It is also peaked at $\mathbf{h} = 0$, indicating that the chain returns to the origin. That might seem peculiar, and will be discussed more below; however, we can confirm this with another simple calculation. From the definition of the end-to-end vector (Eq. 1) we find

$$\begin{aligned} \langle \mathbf{h} \rangle &= \langle \mathbf{r}_N - \mathbf{r}_1 \rangle \\ &= \langle \sum_{i=1}^{N-1} \mathbf{l}_i \rangle \\ &= \sum_{i=1}^{n} \langle \mathbf{l}_i \rangle \\ &= 0 . \end{aligned}$$

Finally, there is a non-zero probability of finding a chain with length greater than nl. This is obviously unphysical and results from approximating a multinomial distribution with a Gaussian.

3.4 End-to-end distance revisited

So what about that FJC returning to the origin? Does this mean that we expect the distance between ends to be zero? Not at all. We might reason that the probability for finding a particular $\mathbf{h}$ vector will decrease with its magnitude. If we consider a sphere of radius h centered at $\mathbf{r}_1$ (which we will also take as the origin), then there is only one vector $\mathbf{h}$ that corresponds to zero distance between the chain ends. As h increases, the allowed area onto which the second chain end may fall increases, so the probability of a specific $\mathbf{h}$ vector for a given h decreases. More formally,

we can say that the probability $P(n,h)$ of finding an end-to-end *distance* h is just the sum of all probabilities of finding end-to-end *vectors* $\mathbf{h}$ with magnitude $|\mathbf{h}| = h$. This sum is the integral over the surface of the sphere with radius h:

$$\begin{aligned} P(n,h) &= \int_0^{2\pi} \mathrm{d}\phi \int_0^{\pi} \mathrm{d}\theta \; r^2 \sin\theta P(n, \mathbf{h} : |\mathbf{h}| = r) \\ &= 4\pi h^2 \left[\frac{3}{2\pi n l^2}\right]^{3/2} \exp\left\{-\frac{3h^2}{2nl^2}\right\} \; . \end{aligned} \tag{13}$$

Note that Eq. 13 is already normalized:

$$\int_0^{\infty} \mathrm{d}h \; P(n,h) = 1 \; .$$

Eq. 13 is the familiar Maxwell-Boltzmann distribution for particle speeds in a gas. Differentiation yields a maximum probability at $h = \sqrt{2nl^2/3}$.

So what is $\langle h^2 \rangle$? We find it by integrating, as usual:

$$\begin{aligned} \langle h^2 \rangle &= \int \mathrm{d}r \; r^2 P(n,r) \\ &= 4\pi h^2 \left[\frac{3}{2\pi n l^2}\right]^{3/2} \int_0^{\infty} \mathrm{d}r \; r^4 \exp\left\{-\frac{3r^2}{2nl^2}\right\} \\ &= nl^2 \; , \end{aligned} \tag{14}$$

where we have made use of the well-known result $\int_0^{\infty} \mathrm{d}x \; x^4 \mathrm{e}^{-\alpha x^2} = \frac{3}{8\alpha^2}\sqrt{\frac{\pi}{\alpha}}$. Eq. 14 is exactly the result that we expected: The distance of the walk increases with the square root of the number of steps, as we found in Eq. 9.

3.5 Elasticity in FJC

We can use our knowledge of distributions of the FJC to calculate its mechanical properties. Let us start by considering the free energy of the FJC. Recall

$$F = \langle E \rangle - TS$$

The $\langle E \rangle$ term is zero because there is neither a potential or motion in the FJC. Were we to assume that the chain can move, the lack of self-interaction would make the kinetic energy equal for all configurations, and $\langle E \rangle = 0$ still. We are left with

$$F = -TS \; .$$

The entropy for a chain of N beads with end-to-end vector $\mathbf{h}$ is

$$S(N, \mathbf{h}) = k_B \ln W(N, \mathbf{h})$$

where $W(N, \mathbf{h})$ is the number of conformations of chains of length N that have end-to-end vector $\mathbf{h}$. This is related to the probability of $\mathbf{h}$ (Eq. 12) by $W(N, \mathbf{h}) = P(N, \mathbf{h})W(N)$, where $W(N)$ is the total number of configurations of the freely jointed chain of N beads (i.e., considering all end-to-end vectors). We can then write the free energy as

$$\begin{aligned} F(N, \mathbf{h}) &= -k_B T \ln P(N, \mathbf{h}) - T \ln W(N) \\ &= \frac{3k_B T h^2}{2Nl^2} - \frac{3T}{2} \ln \left[\frac{3W(N)^{2/3}}{2\pi N l^2} \right] . \end{aligned} \tag{15}$$

Only the first term depends on the chain conformation; the second term is a constant of the system and can essentially be ignored. In fact, as we're dealing with free energies, it is really differences that we are interested in, so this constant term will explicitly drop out soon.

One thing that we see from Eq. 15 is that the minimum free energy occurs for $\mathbf{h} = 0$. We will use this as a reference point and ask how the free energy changes as we pull one end of the chain away from the other along some arbitrary vector $\mathbf{h}$. We have

$$\begin{aligned} \Delta F(N, \mathbf{h}) &\equiv F(N, \mathbf{h}) - F(N, 0) \\ &= -k_B T \ln \left[\frac{P(N, \mathbf{h})}{P(N, 0)} \right] \\ &= \frac{3k_B T h^2}{2nl^2} . \end{aligned} \tag{16}$$

Interestingly, the energy increases harmonically, just as if we were pulling a spring. More interesting still is that this effect arises solely from entropic considerations. Comparing Eq. 16 with Hooke's Law ($E = \frac{1}{2}k(\Delta x)^2$), we find that the effective force constant for the FJC is $k = 3k_B T/nl^2$. Thus, the restoring force that pulls the chain ends together increases with temperature but decreases with chain length.

3.6 How does FJC compare to proteins?

This model does not represent proteins well. We find that for globular proteins (see Fig. 2), $R_g \sim N^{0.380}$.

Among the many differences between proteins and the FJC are

- Proteins have restricted bond angles
- Proteins have side chains
- Proteins cannot self-intersect
- Proteins are solvated
- Protein residue-residue interactions have non-zero potential energies

We will look next at how fixed bond angles alter the properties of the model chain. The other issues are difficult to address and will have to wait.

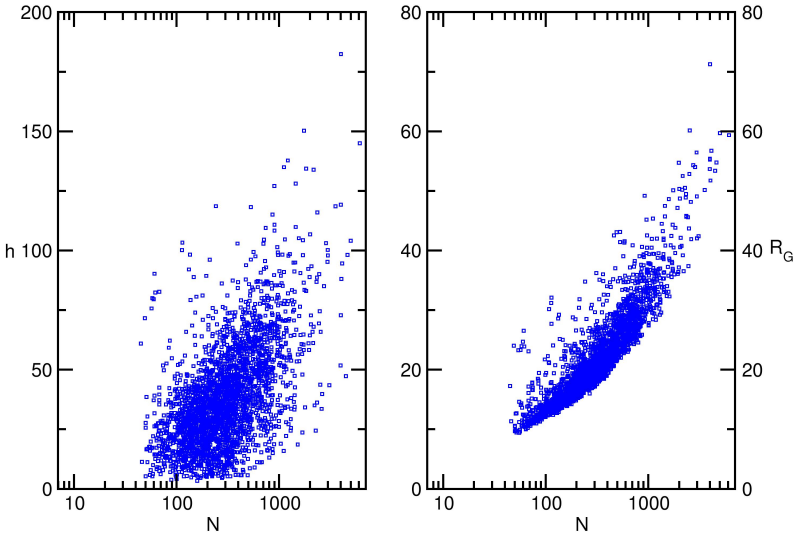


Figure 2: End-to-end distance and gyration radius for 2674 non-homologous globular proteins.

4 Freely Rotating Chain

The FJC is truly a minimalist representation of reality, but it's a start. Perhaps the simplest bit of complexity that we can tack on to it is a constraint on bond angles. Assume that we have a chain in which all bond angles have the fixed value θ. This is called the *Freely Rotating Chain*. The methods developed here can be generalized to more realistic systems, such a proteins, in which the bond angles are not all identical, but we will start with the simplest case. The convention that will

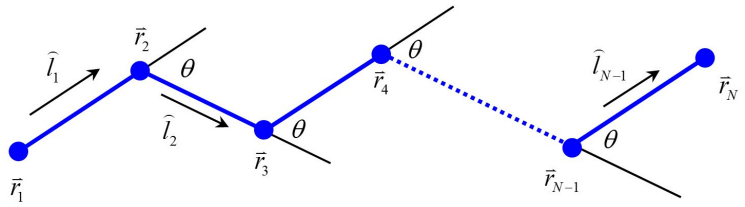


Figure 3: The freely jointed chain, wherein all bond angles are identical.

be used is that the bond angle at bead i satisfies (see Fig. 3)

$$\mathbf{l}_{i-1} \cdot \mathbf{l}_i = |\mathbf{l}_i||\mathbf{l}_{i+1}| \cos\theta_i \ .$$

The $N-2$ bond angles for a chain of N beads have indices $2 \ldots (N-1)$. Let's start by considering h for the FRC, and let us assume that all links have the same length and all bonds have the same

angle. That is, $|\mathbf{l}_i| = l, \theta_i = \theta \; \forall \; i$. The second term in Eq. 3, $\sum_i \sum_j \langle \mathbf{l}_i \cdot \mathbf{l}_j \rangle$, does not vanish in this case; however, we can find it by recursion. By definition,

$$\mathbf{l}_i \cdot \mathbf{l}_{i+1} = l^2 \cos\theta \; .$$

Then,

$$\begin{aligned} \langle \mathbf{l}_i \cdot \mathbf{l}_{i+2} \rangle &= \mathbf{l}_i \cdot (\hat{\mathbf{l}}_{i+1} \cdot \mathbf{l}_{i+2}) \hat{\mathbf{l}}_{i+1} \\ &= l^2 \cos^2\theta \; , \end{aligned}$$

and in general

$$\langle \mathbf{l}_i \cdot \mathbf{l}_{i+k} \rangle = l^2 \cos^k \theta \; .$$

In the above, hats represent unit vectors. One can show that all terms orthogonal to the links average to zero owing to the freedom of the dihedral angles. We won't do that here. Going back to Eq. 3, we find

$$\begin{aligned} h^2 &= nl^2 + \sum_{i=1}^{n} \sum_{j \neq i} \langle \mathbf{l}_i \cdot \mathbf{l}_j \rangle \\ &= nl^2 + \sum_{i=1}^{n} \sum_{j \neq i} l^2 \cos^{|j-i|} \theta \\ &= nl^2 + 2 \sum_{i=1}^{n} \sum_{j > i} l^2 \cos^{|j-i|} \theta \end{aligned} \tag{17}$$

The second term is just l^2 times a sum of powers of $\cos\theta$. By restricting the sum to $j > i$, we are effectively looking at the upper triangle of the matrix of inner products of link vectors. The number of times that the k^{th} power of $\cos\theta$ appears is equal to the number of elements in the k^{th} diagonal above the main diagonal of the $n \times n$ matrix. Thus,

$$\begin{aligned} \sum_{i=1}^{n} \sum_{j \neq i} \langle \mathbf{l}_i \cdot \mathbf{l}_j \rangle &= 2 \sum_{k=1}^{n-1} (n-k) l^2 \cos^k \theta \\ &= 2nl^2 \sum_{k=1}^{n-1} \cos^k \theta - 2l^2 \sum_{k=1}^{n-1} k \cos^k \theta \\ &\approx 2l^2 \cos\theta \left[\frac{n}{1-\cos\theta} - \frac{1}{(1-\cos\theta)^2} \right] \; , \end{aligned} \tag{18}$$

where we have made use of the identities

$$\begin{aligned}\sum_{k=1}^{n} x^k &= \frac{x(1-x^n)}{1-x} \\ &\approx \frac{x}{1-x} \\ \sum_{k=1}^{n} kx^k &= \frac{x(1-x^{n+1})}{(1-x)^2} \\ &\approx \frac{x}{(1-x)^2}\end{aligned}$$

Then,

$$\begin{aligned}h^2 &= nl^2\left[\frac{1+\cos\theta}{1-\cos\theta} - \frac{2\cos\theta}{n(1-\cos\theta)^2}\right] \\ &\approx nl^2\left[\frac{1+\cos\theta}{1-\cos\theta}\right]\end{aligned}$$

Note that $\langle h^2\rangle \sim nl^2$, just like in the FJC; however, there is now an additional term of $(1+\cos\theta)/(1-\cos\theta)$, called the *stiffness*. For $\theta = \pi/2$, the result is exactly the same as the FJC. For $\theta < \pi/2$, $\langle h^2\rangle > Nl^2$, and the chain is more extended than the FJC. For $\theta > \pi/2$, $\langle h^2\rangle < nl^2$, and the chain is compact. At $\theta = 0$, the chain *should be* ballistic (i.e., $h^2 = n^2l^2$). Instead, we find that it has infinite length. This is a fault of the large n approximations that we have made. Returning to the last exact expression, Eq. 18, it can be seen that the chain is indeed ballistic for $\theta = 0$.

4.1 Characteristic Ratio

We have seen that for the FJC, $h^2 = nl^2$, whereas for the FRC, $h^2 = nl^2(1+\cos\theta)/(1-\cos\theta)$. Although we don't see this explicitly here, for a general chain molecule one might expect the *measured* square end-to-end distance, $\langle h^2\rangle_0$, (note the subscript) to scale as $\langle h^2\rangle_0 = C_n nl^2$. In the limit $n \to \infty$, we find for the FRC $C_\infty = (1+\cos\theta)/(1-\cos\theta)$. The constant C_∞ is called the *characteristic ratio*, and it can be experimentally determined for a variety of chain molecules. For carbon-based polymers, $4 \leq C_\infty \leq 12$, in general. By defining an *effective length* of $l_{eff} \equiv \sqrt{C_\infty}l$, we see that $h^2 = nl_{eff}^2$. That is, as far as the end-to-end distance is concerned, the FRC (and many other simple models) behave as a FJC with effective link length l_{eff}.

4.2 FRC: Persistence Length

Going back to Eq. 7, it can be seen that the persistence length of the FRC is

$$\begin{aligned}\xi_p &= \frac{l}{2}(C_\infty + 1) \\ &\approx \frac{C_\infty l}{2} \quad \text{for } l \to 0\end{aligned}$$

Or, starting from Eq. 6, it can be seen for the FRC:

$$\begin{aligned}
\xi_p &= \frac{1}{l}\sum_{j=i}^{n}\langle \mathbf{l}_i \cdot \mathbf{l}_j \rangle \\
&= \frac{1}{l}\sum_{j=1}^{n} l^2 \cos^{j-1}\theta \\
&= l\sum_{j=0}^{n-1}\cos^j\theta \\
&= l\left[\cos^0\theta + \sum_{j=1}^{n-1}\cos^j\theta\right] \\
&= l\left[1 + \frac{\cos\theta(1-\cos^{n-1}\theta)}{1-\cos\theta}\right] \\
&= l\left[\frac{1-\cos^n\theta}{1-\cos\theta}\right] \\
&\approx \frac{l}{1-\cos\theta}
\end{aligned}$$

where the final approximation is taken in the limit $n \to \infty$. We can see that when $\theta = 0$, ξ_p is infinite, which is in accord with what we would expect for a straight chain of infinitely many links. When $\theta = \pi/2$, $\xi_p = l$, once again agreeing with the FJC.

5 Local Coordinates

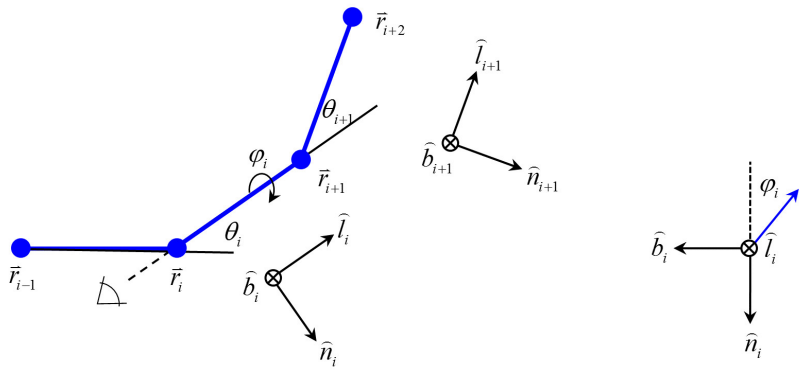
In general, chain molecules are not as simple as the FJC or FRC. Usually bond lengths and angles can vary in some range, as can dihedral angles. Frequently these values are correlated, as is the case for the ϕ and ψ backbone dihedrals in proteins. We can address the general case using matrices.

Suppose that we have a chain of N beads $[1 \ldots N]$. There are $n = (N-1)$ links $[1, \ldots, (N-1)]$, $N-2$ bond angles $[2, \ldots, (N-1)]$, and $N-3$ dihedral angles $[2, \ldots, (N-2)]$. With the exception of the dihedral angles, all of these have been previously defined. The dihedral ϕ_i is the clockwise rotation about link i from the *cis* conformation, and will be defined mathematically below.

For each internal bead i, define a local orthogonal coordinate basis $\hat{\mathbf{l}}_i, \hat{\mathbf{b}}_i, \hat{\mathbf{n}}_i$ as follows:

$$\begin{aligned}
\hat{\mathbf{l}}_i &\equiv \frac{\mathbf{r}_{i+1} - \mathbf{r}_i}{|\mathbf{r}_{i+1} - \mathbf{r}_i|} \\
\hat{\mathbf{b}}_i &\equiv \frac{\hat{\mathbf{l}}_i \times \hat{\mathbf{l}}_{i-1}}{\sin\theta_i} \\
\hat{\mathbf{n}}_i &\equiv \hat{\mathbf{b}}_i \times \hat{\mathbf{l}}_i
\end{aligned}$$

The selection of coordinates is not unique; there are other possibilities that are equally valid, such as that discussed by Flory [1]. The coordinates here have the following interpretation: $\hat{\mathbf{l}}_i$ is the



(a) Local coordinate systems (b) View along $\hat{l}_i$.

Figure 4: Local coordinates defined using backbone conformation.

unit link vector that we have been using all along; $\hat{\mathbf{b}}_i$ is a *binormal* vector that defines the plane containing beads $i-1$, i and $i+1$; $\hat{\mathbf{n}}_i$ is normal to the curve and perpendicular to both $\hat{\mathbf{l}}_i$ and $\hat{\mathbf{b}}_i$. The three form a right-handed coordinate system at bead i: $\hat{\mathbf{l}}_i \times \hat{\mathbf{n}}_i = \hat{\mathbf{b}}_i$. Nicely, we can construct a recursion relation to form coordinate systems from earlier systems:

$$
\begin{aligned}
\hat{\mathbf{l}}_{i+1} &= \cos\theta_{i+1}\hat{\mathbf{l}}_i + \sin\theta_{i+1}[-\cos\phi_i\hat{\mathbf{n}}_i - \sin\phi_i\hat{\mathbf{b}}_i] \\
\hat{\mathbf{b}}_{i+1} &= \frac{\hat{\mathbf{l}}_i \times \hat{\mathbf{l}}_{i-1}}{\sin\theta_i} \\
&= \frac{1}{\sin\theta_{i+1}} \begin{vmatrix} \hat{\mathbf{l}}_i & \hat{\mathbf{n}}_i & \hat{\mathbf{b}}_i \\ \cos\theta_{i+1} & -\sin\theta_{i+1}\cos\phi_i & -\sin\theta_{i+1}\sin\phi_i \\ 1 & 0 & 0 \end{vmatrix} \\
&= -\sin\phi_i\hat{\mathbf{n}}_i + \cos\phi_i\hat{\mathbf{b}}_i \\
\hat{\mathbf{n}}_{i+1} &= \hat{\mathbf{b}}_i \times \hat{\mathbf{l}}_i \\
&= \begin{vmatrix} \hat{\mathbf{l}}_i & \hat{\mathbf{n}}_i & \hat{\mathbf{b}}_i \\ 0 & -\sin\phi_i & \cos\phi_i \\ \cos\theta_{i+1} & -\sin\theta_{i+1}\cos\phi_i & -\sin\theta_{i+1}\sin\phi_i \end{vmatrix} \\
&= \sin\theta_{i+1}\hat{\mathbf{l}}_i + \cos\theta_{i+1}\cos\phi_i\hat{\mathbf{n}}_i + \cos\theta_{i+1}\sin\phi_i\hat{\mathbf{b}}_i
\end{aligned}
$$

Or,

$$
\begin{pmatrix} \hat{\mathbf{l}}_{i+1} \\ \hat{\mathbf{n}}_{i+1} \\ \hat{\mathbf{b}}_{i+1} \end{pmatrix} = \begin{pmatrix} \cos\theta_{i+1} & -\sin\theta_{i+1}\cos\phi_i & \sin\theta_{i+1}\sin\phi_i \\ \sin\theta_{i+1} & \cos\theta_{i+1}\cos\phi_i & \cos\theta_{i+1}\sin\phi_i \\ 0 & -\sin\phi_i & \cos\phi_i \end{pmatrix} \begin{pmatrix} \hat{\mathbf{l}}_i \\ \hat{\mathbf{n}}_i \\ \hat{\mathbf{b}}_i \end{pmatrix} \tag{19}
$$

The matrix in Eq. 19 is a transformation matrix between the local coordinate system at i and that

at $i+1$. It is an orthogonal matrix, so its transpose,

$$\mathbf{T}_{i+1} = \begin{pmatrix} \cos\theta_{i+1} & \sin\theta_{i+1} & 0 \\ -\sin\theta_{i+1}\cos\phi_i & \cos\theta_{i+1}\cos\phi_i & -\sin\phi_i \\ \sin\theta_{i+1}\sin\phi_i & \cos\theta_{i+1}\sin\phi_i & \cos\phi_i \end{pmatrix}$$

is also its inverse. Multiplying both sides of Eq. 19 by $\mathbf{T}_{i+1}$ gives the coordinates of $\hat{\mathbf{l}}_{i+1}, \hat{\mathbf{b}}_{i+1}, \hat{\mathbf{n}}_{i+1}$ in the basis of $\hat{\mathbf{l}}_i, \hat{\mathbf{b}}_i, \hat{\mathbf{n}}_i$:

$$\begin{pmatrix} \hat{\mathbf{l}}_i \\ \hat{\mathbf{n}}_i \\ \hat{\mathbf{b}}_i \end{pmatrix} = \mathbf{T}_{i+1} \begin{pmatrix} \hat{\mathbf{l}}_{i+1} \\ \hat{\mathbf{n}}_{i+1} \\ \hat{\mathbf{b}}_{i+1} \end{pmatrix}$$

Or, in general,

$$\begin{pmatrix} \hat{\mathbf{l}}_i \\ \hat{\mathbf{n}}_i \\ \hat{\mathbf{b}}_i \end{pmatrix} = \left(\prod_{j=1}^{k} \mathbf{T}_{i+j} \right) \begin{pmatrix} \hat{\mathbf{l}}_{i+k} \\ \hat{\mathbf{n}}_{i+k} \\ \hat{\mathbf{b}}_{i+k} \end{pmatrix}$$

Note that $\left(\prod_{j=1}^{k} \mathbf{T}_{i+j} \right)$ is itself a matrix of inner products:

$$\left(\prod_{j=1}^{k} \mathbf{T}_{i+j} \right) = \begin{pmatrix} \hat{\mathbf{l}}_i \cdot \hat{\mathbf{l}}_k & \hat{\mathbf{l}}_i \cdot \hat{\mathbf{n}}_k & \hat{\mathbf{l}}_i \cdot \hat{\mathbf{b}}_k \\ \hat{\mathbf{n}}_i \cdot \hat{\mathbf{l}}_k & \hat{\mathbf{n}}_i \cdot \hat{\mathbf{n}}_k & \hat{\mathbf{n}}_i \cdot \hat{\mathbf{b}}_k \\ \hat{\mathbf{b}}_i \cdot \hat{\mathbf{l}}_k & \hat{\mathbf{b}}_i \cdot \hat{\mathbf{n}}_k & \hat{\mathbf{b}}_i \cdot \hat{\mathbf{b}}_k \end{pmatrix}$$

All of the above analysis is applicable only to chains with fixed conformations. Usually we will be interested in models in which the chain is free to move within some constraints, as in the FJC and FRC. In such cases, the matrices $\mathbf{T}_i$ must be replaced by their ensemble averages, $\langle \mathbf{T}_i \rangle$.

Now consider as an example the FRC with the special case that $\theta_i = \theta \; \forall \; i$. All internal beads are under identical conditions, and $\mathbf{T}_i$ is the same for all i. Further, $\langle \mathbf{T}_i \rangle$ is the same for all i, so the transformation matrix between i and j is just $\langle \mathbf{T} \rangle^{j-i}$.

To calculate $\langle \mathbf{T} \rangle$ for the FRC, we let ϕ vary freely:

$$\langle \mathbf{T} \rangle = \frac{\int_0^{2\pi} \mathrm{d}\phi \mathbf{T}}{\int_0^{2\pi} \mathrm{d}\phi}$$

yielding

$$\langle \mathbf{T} \rangle = \begin{pmatrix} \cos\theta & \sin\theta & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

and

$$\langle \mathbf{T}^k \rangle = \begin{pmatrix} \cos^k\theta & \cos^{k-1}\theta\sin\theta & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

6 Wormlike Chain

In many cases, when $n \gg l$, it becomes nonsensical to sum over n elements. Porod and Kratky [5] introduced the idea of taking the continuum limit of a discrete chain by letting $n \to \infty$ and $l \to 0$. The chain length, $L = nl$, remains constant, and the chain essentially becomes a smooth curve in space. The model of Kratky and Porod is often called the "Wormlike Chain", although it has been pointed out that unlike a worm, the chain is not extensible.

Consider a FRC. We find that the persistence length is

$$\xi_p = \frac{l}{\cos\theta}$$

so

$$\cos\theta = 1 - l/\xi_p \ .$$

Let's look at h^2, starting from Eqs. 17 and 18:

$$\begin{aligned} h^2 &= nl^2 + 2nl^2 \sum_{k=1}^{n-1} \cos^k\theta - 2l^2 \sum_{k=1}^{n-1} k\cos^k\theta \\ &= nl^2 + 2nl^2\left(\frac{\cos\theta}{1-\cos\theta}\right) - 2l^2\left(\frac{1-\cos^n\theta}{(1-\cos\theta)^2}\right) \\ &= nl^2\left(\frac{2-l/\xi_p}{l/\xi_p}\right) - 2l^2(1-l/\xi_p)\left(\frac{1-(1-l/\xi_p)^n}{(l/\xi_p)^2}\right) \\ &= nl\xi_p(2-l/\xi_p) - 2\xi_p^2(1-l/\xi_p)(1-\exp\{-nl/\xi_p\}) \ , \end{aligned}$$

where we have used the approximation $\mathrm{e}^{-nl/\xi_p} \approx 1 - nl/\xi_p$ in the last line. This holds as long as $nl \gg \xi_p$, which is the case if our chain is long and thin. Defining $L \equiv nl$ and taking the small l limit,

$$\lim_{n\to 0} h^2 = 2L\xi_p - 2\xi_p^2(1-\mathrm{e}^{-L/\xi_p}) \ . \tag{20}$$

This final result demonstrates that the end-to-end distance can be found without knowledge of microscopic details of the chain (n,l,θ): Only ξ_p and the total length are needed. This is an early hint at universality, or scale invariance, in chains. By defining an overall scaling factor $a \equiv L/\xi_p$,

$$\begin{aligned} h^2 &= 2a\xi_p^2 - 2\xi_p^2(1-\mathrm{e}^{-a}) \\ &= 2\xi_p^2(a-1-\mathrm{e}^{-a}) \end{aligned}$$

Even though the end-to-end distance scales with length, it is qualitatively the same for different chains with the same $L : \xi_p$ ratio.

6.1 Bending of WLC

To go from a discrete chain model to a continuous chain, consider a chain of equal length links bent at an angle θ_i at bead i. If the chain has the tendency to remain straight, we might impose upon it a harmonic potential that penalizes deflections from $\theta_i = 0$, such as

$$U_i = \frac{k}{2}\theta_i^2 \ .$$

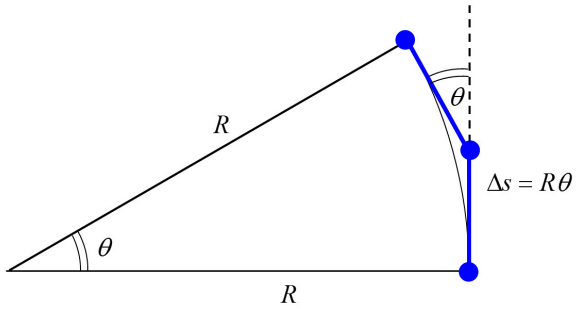


Figure 5: Bending a discrete chain with equally spaced beads. Bending the chain by an angle θ is equivalent to bending the chain around a radius $R \approx 2l/\theta$.

This is related to a harmonic spring restoring a linear displacement if we think of the displacement $\Delta s_i = R_i\theta_i$ as the length of the arc that connects bead $i-1$ to bead $i+1$ when bending the chain by θ_i about bead i produces an arc with radius R_i. It's safe to say that $\Delta s_i \approx 2l$, but here we are trying to avoid using l and θ_i in favor of the continuous variables R and s. Let us define s as a continuous variable representing the position along the chain. For the whole chain, the energy of bending is

$$\begin{aligned} U &= \frac{k}{2}\sum_{i=1}^{n-1}\theta_i^2 \\ &= \frac{k}{2}\sum_{i=1}^{n-1}\left(\frac{\Delta s}{R_i}\right)^2 \\ &= \frac{k\Delta s}{2}\sum_{i=1}^{n-1}\Delta s\left(\frac{1}{R_i}\right)^2 \\ &= \frac{K}{2}\int_0^L \mathrm{d}s\left(\frac{1}{R(s)}\right)^2 \\ &= \frac{K}{2}\int_0^L \mathrm{d}s\left|\frac{\mathrm{d}\mathbf{t}}{\mathrm{d}s}\right|^2, \end{aligned}$$

where $R(s)$ is the local curvature at s, $\mathbf{t}(s)$ is the tangent vector to the curve at s and K is the *bending modulus*. This is engineering here. Materials science stuff. The bending modulus has units of energy times distance.

7 Self-Avoiding Walk

Another ingredient that has been missing from our models is self-avoidance. To get a sense of the conformational ensemble adopted by self-avoiding chains, we can follow Flory [1] and construct some simple arguments based on scaling. We will minimize free energy with respect to the chain's size.

Start by introducing a potential that imposes a penalty for any contacting pairs:

$$U = \sum_{i=1}^{N} \sum_{j \neq i} H(R_c - |\mathbf{r}_j - \mathbf{r}_i|) U_{ij} \ , \tag{21}$$

where $H(x)$ is the Heavyside function, equal to 1 if its argument is positive and 1 otherwise. The potential of Eq. 21 contains one non-zero term for each contacting pair of beads. Assume that the density of contacts is more or less uniform throughout the volume occupied by the chain (i.e., $\rho =$ # of contacts/volume is constant). The number of contacts scales with the square of the number of beads, and the volume scales as a power of the chain radius, depending on dimension. In two dimensions, the chain volume is approximated by the area of a circle: $V_2 = 2\pi R^2$. In three dimensions, it is approximated by the volume of a sphere: $V_3 = 4/3\pi R^3$. In d dimensions,

$$\rho \sim N^2/R^d \ .$$

The free energy is given by

$$F = U - TS \ ,$$

where $S = k_B \ln W$. We have seen from previous models that the chain parameters tend to follow Gaussian distributions. Here we will continue this approximation

$$\begin{aligned} S &= k_B \ln W \\ &= k_B \ln P(h^2) + \text{const.} \\ &\approx k_B \ln(\exp\{-h^2/N\}) \end{aligned}$$

Yielding

$$F = c_1 N^2/R^d - c_2 R^2/N$$

Minimizing with respect to R,

$$\begin{aligned} 0 &= \partial F/\partial R \\ &= -c_1 d N^2 R^{-d-1} - 2c_2 R N^{-1} \\ R &\sim N^{\frac{3}{d+2}} \ . \end{aligned} \tag{22}$$

Eq. 22 indicates that the end-to-end distance (or R_g) will scale with the chain dimension. In one dimension, we see that $R \sim N$, and the chain is ballistic. In two dimensions, $R \sim N^{3/4}$. This is an exact result. In three dimensions, $R \sim N^{3/5}$. Computational results indicate that the scaling in three dimensions is more accurately $R \sim N^{0.588}$, which is remarkably close to the value arrived at through this simple exercise. The scaling of $R \sim N^{1/2}$ for a four-dimensional chain is again exact. Beyond four dimensions, the self-avoidance causes attraction ($R < N^{1/2}$), indicating that this simple scaling is not valid in higher dimensions.

Appendix

Where did Eq. 11 come from? It is just the simplification of a geometric series that can be derived easily as follows: We write the series for a higher power, expand it, rearrange terms, cancel, and viola!

$$\begin{aligned}
\sum_{k=0}^{n} k^3 &= \sum_{k=0}^{n} (k+1)^3 - (n+1)^3 \\
&= \sum_{k=0}^{n} k^3 + 3\sum_{k=0}^{n} k^2 + 3\sum_{k=0}^{n} k + \sum_{k=0}^{n} 1 - (n+1)^3 \\
3\sum_{k=0}^{n} k^2 &= (n+1)^3 - 3\sum_{k=0}^{n} k - \sum_{k=0}^{n} 1 \\
&= n^3 + 3n^2 + 3n + 1 - \frac{3n(n+1)}{2} - n - 1 \\
&= n^3 + \frac{3n^2}{2} + \frac{n}{2} \\
\sum_{k=0}^{n} k^2 &= \frac{n}{6}(n+1)(2n+1) \\
\sum_{k=1}^{n-1} k^2 &= \frac{n}{6}(n-1)(2n-1)
\end{aligned}$$

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