ICFP M2 - Statistical physics 1 – TD n° 2
DNA elasticity: the "Freely-Jointed-Chain" and the "Worm-Like-Chain" models

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Experiments realized in the 90's allowed to measure the force-elongation curve of DNA molecules. In these experiments, single DNA molecules were chemically attached by one end to a glass surface and by their other end to a magnetic bead, on which an external force was applied. The results are reported on Fig. 3 for a molecule of length $L = 32.7\mu m$ (i.e. 97000 base pairs). The aim of this tutorial is to describe these experimental results by studying two different models of DNA elasticity: (i) the "freely-jointed-chain" and (ii) the "worm like chain" models.

1 The freely jointed chain model

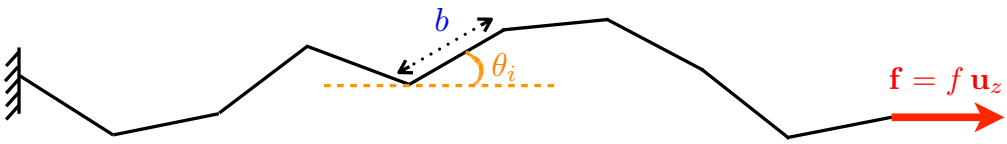

Figure 1: The freely jointed chain model with $N = 9$ monomers, each of length b, with one fixed end and subjected to an external force $\mathbf{f} = f\mathbf{u}_z$.

1. We consider a three-dimensional chain consisting of N rigid rods (monomers) of length $b = L/N$ (with one extremity being fixed at the origin). The orientation of rod "i" is indexed by the angle θ_i (see Fig. 1) and is independent of the orientations and positions the neighboring monomers. In this simple model, there are no interactions between the rods and the energy of the polymer is independent of its shape – all configurations being equally likely. In presence of an external force $\mathbf{f} = f\mathbf{u}_z$ applied at the free end (see Fig. 1), elongated configurations are favored such that the energy of a configuration is given by

$$E = -f\,z = -b\,f\sum_{i=1}^{N}\cos\theta_i\ . \tag{1}$$

   Assuming thermal equilibrium at temperature T, compute the corresponding partition function $\mathcal{Z}$ of the model corresponding to (1).

2. Compute the mean elongation $\langle z(f)\rangle$ and show that

$$\langle z(f)\rangle = L\left[\coth\left(\frac{f\,b}{k_B\,T}\right) - \left(\frac{k_B\,T}{f\,b}\right)\right]\ . \tag{2}$$

3. The curves shown in Fig. 3 (top) show several comparisons between this formula (2) and experimental data. Which conclusions can you draw from this comparison?

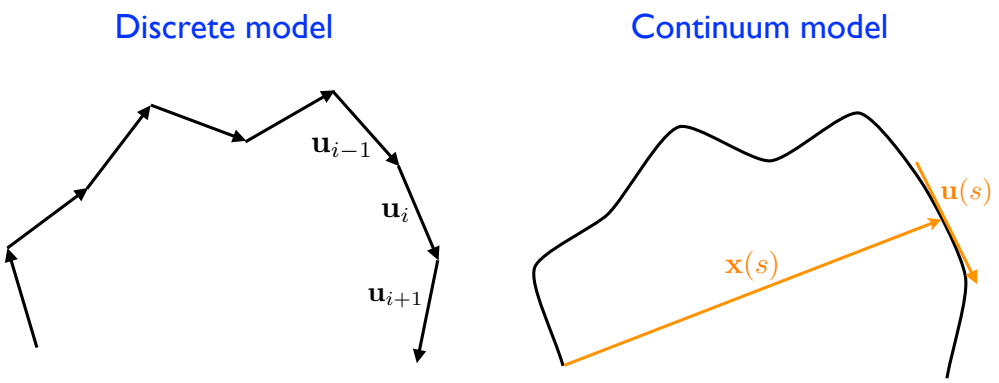

Figure 2: Illustration of the worm-like-chain model. Left: discrete model as in Eq. (3). Right: continuum limit as in Eq. (4) corresponding to the scaling limit where the size of monomers is small $b \to 0$ while their number is large $N \to \infty$ keeping the total length $L = N\,b$ fixed.

2 The worm-like-chain model

In fact, DNA is a stiff molecule, which means that successive monomers like to point in the same direction. Hence, we now assume that the DNA molecule possesses a local rigidity: the associated energy between two consecutive monomers along the chain, whose respective orientations are labeled by unit vectors $\mathbf{u}_i$ and $\mathbf{u}_{i-1}$ (see Fig. 2) is proportional to $(\mathbf{u}_i - \mathbf{u}_{i-1})^2$ such that the total energy of the chain is now given by

$$E_{WLC} = \frac{\kappa}{2\,b} \sum_{i=1}^{N} (\mathbf{u}_i - \mathbf{u}_{i-1})^2 \tag{3}$$

1. Show that in the continuum limit $b \to 0$, $N \to \infty$ keeping $L = N\,b$ fixed, the energy E_{WLC} in Eq. (3) can be written as

$$E_{WLC} \sim k_B T \frac{A}{2} \int_0^L ds\ (\partial_s \mathbf{u})^2 \tag{4}$$

where

$$\mathbf{u}(s) = \frac{d}{ds}\mathbf{x}(s) \tag{5}$$

is the unit tangent vector of the space curve along which the polymer runs. The parameter s is the arc length of the line elements, i.e., $ds = \sqrt{d\mathbf{x}^2}$. What is the unit of A in Eq. (4)? What is its physical meaning?

2. Compute the probability density $P(s, \mathbf{u})$ that the tangent vector in s is in the direction of $\mathbf{u}$ as the ratio of two path-integrals. Show that, in the absence of an external force, P satisfies the following evolution equation

$$\frac{\partial P}{\partial s} = \frac{1}{2\,A} \Delta_{\mathcal{S}} P\ , \tag{6}$$

where $\Delta_{\mathcal{S}}$ is the Laplacian on the unit sphere in three dimensions.

Hint: start from the discretized version as in Eq. (3) and then take the continuum limit to obtain (6).

3. We recall that the eigenvectors of $\Delta_{\mathcal{S}}$ are the spherical harmonics, $Y_{l,m}(\theta, \phi)$ with $l \in \mathbb{N}$ and $m = -l, -l+1, \cdots, l-1, l+1$, with corresponding eigenvalues $-l(l+1)$ (see Appendix). Suppose that one extremity (at $s = 0$) is along the z-direction. What is the probability that the tangent vector in s makes an angle θ with that z-axis? Explain why A is usually called the persistence length.

4. The molecule is now subjected to an external force $\mathbf{f} = f\,\mathbf{u}_z$. How does the equation satisfied by $P(s, \mathbf{u})$ (6) get modified in presence of this external force?

5. Show that in the limit $L/A \gg 1$, the average extension $\langle z(f) \rangle$ is dominated by the ground state of a Schrödinger-like operator associated to this statistical mechanics problem.

6. Compute $\langle z(f) \rangle$ (i) in the limit of small f and (ii) in the limit of large f – where the strand is almost straight.

7. In figure 3 (bottom) we show a comparison between the experimental data and the best fit (by such analytical formula) obtained for $A = 53.4nm$. What do you think about this result?

Appendix: spherical harmonics in three dimensions

In three dimensions, the Laplacian on the sphere $\Delta_{\mathcal{S}}$ reads explicitly, in spherical coordinates (θ, ϕ), with $\theta \in [0, \pi]$ and $\phi \in [0, 2\pi]$

$$\Delta_{\mathcal{S}} = \frac{1}{\sin\theta} \frac{\partial}{\partial\theta} \left(\sin\theta \frac{\partial}{\partial\theta} \right) + \frac{1}{\sin^2\theta} \frac{\partial^2}{\partial\phi^2} \, . \tag{7}$$

Note that $\Delta_{\mathcal{S}}$ is related to the angular momentum operator $\hat{\mathbf{L}}$ in quantum mechanics through the relation $\hat{\mathbf{L}}^2 = -\hbar^2 \Delta_{\mathcal{S}}$. The eigenvectors of $\Delta_{\mathcal{S}}$ are the well known spherical harmonics $Y_{l,m}(\theta, \phi)$ with $l \in \mathbb{N}$ and $m = -l, -l+1, \cdots, l-1, l+1$ with associated eigenvalues

$$\Delta_{\mathcal{S}} Y_{l,m}(\theta, \phi) = -l(l+1) Y_{l,m}(\theta, \phi) \, , \tag{8}$$

the degeneracy of each eigenvalue thus being $2l+1$. The spherical harmonics can be expressed explicitly in terms of the associated Legendre polynomials $P_l^m(z)$ as

$$Y_{l,m}(\theta, \phi) = (-1)^m \left(\frac{2l+1}{4\pi} \frac{(l-m)!}{(l+m)!} \right)^{1/2} P_l^m(\cos\theta) e^{im\phi} \, , \tag{9}$$

where

$$P_l^m(z) = \frac{(1-z^2)^{m/2}}{2^l l!} \frac{(l-m)!}{(l+m)!} \frac{d^{l+m}}{dz^{l+m}} (z^2-1)^l \, . \tag{10}$$

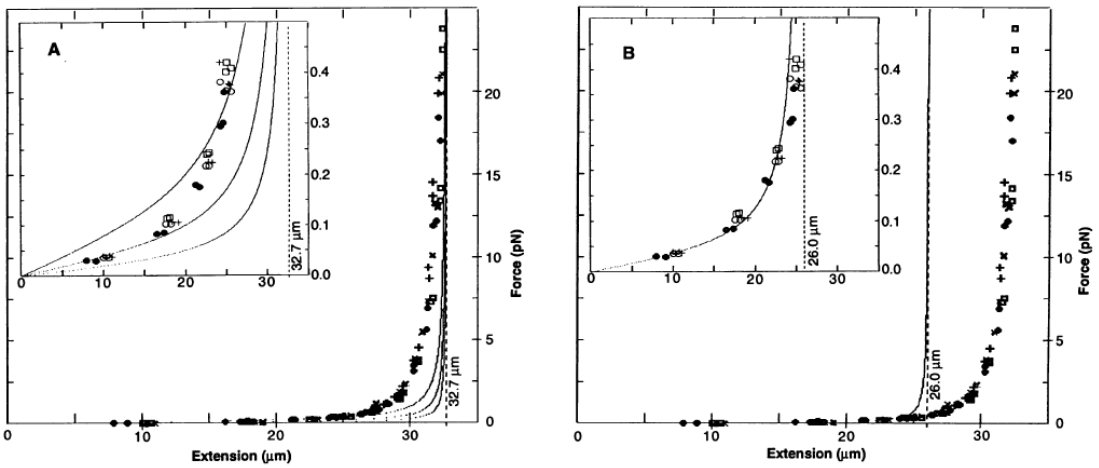

Fig. 3. (**A**) Force versus extension data for four different λ-dimer molecules (●, □, +, and ○) in 5 mM Na_2HPO_4 buffer (10 mM Na^+, pH 8.3). Inset: expanded vertical scale (0 to 0.5 pN). Continuous curves are from Eq. 2 assuming L = 32.7 μm and b = 500 Å (top), 1000 Å (middle), and 2000 Å (lower). L = 32.7 μm was chosen to agree with the accepted value of 3.37 Å rise per base pair (*30*), not to fit the data. (**B**) The same data compared with a Langevin curve L = 26 μm and b = 1400 Å. These values were chosen to match the low-force slope.

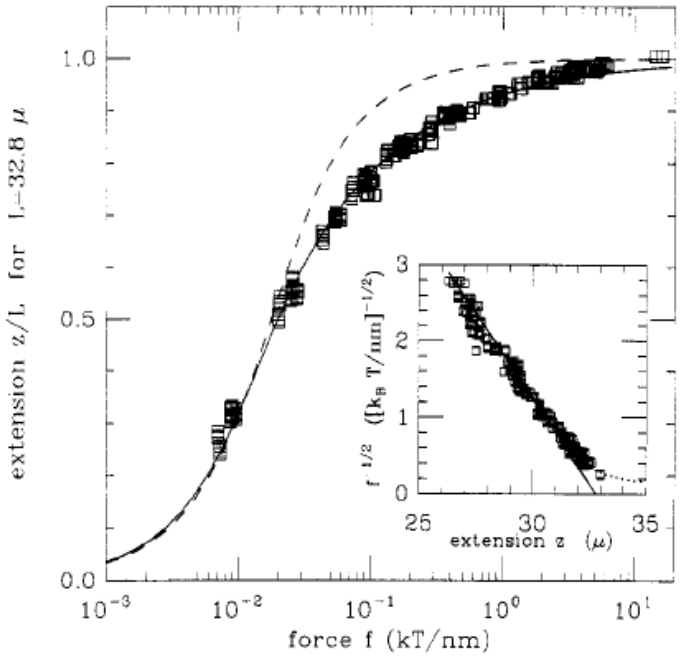

Figure 2. Fit of numerical exact solution of WLC force–extension curve to experimental data of Smith et al.[1] (97004 bp DNA, 10 mM Na^+). The best parameters for a global least-squares fit are $L = 32.8$ μm and $A = 53$ nm. The FJC result for $b = 2A = 100$ nm (dashed curve) approximates the data well in the linear low-f regime but scales incorrectly at large f and provides a qualitatively poorer fit. Inset: $f^{-1/2}$ vs z for the highest forces; the exact WLC result (solid line) is in this plot a straight line extrapolating to $L = 32.8$ μm from which the experimental points begin to diverge above $z \approx 31$ μm; including intrinsic elasticity (eq 19 with $\gamma = 500$ k_BT/nm, dotted curve) improves the fit.

Figure 3: **Top:** Force-elongation curve and comparison with the freely jointed chain from *S. B. Smith, L. Finzi, C. Bustamante, Science* **258**, *1122 (1992).* **Bottom** Force-elongation curve and comparison with the worm like chain from *J. Marko, E. Siggia, Macromolecules* **28**, *8760 (1995).*