ICFP M1 - Phase Transitions – TD n° 8
DNA Elasticity and Polymers Models

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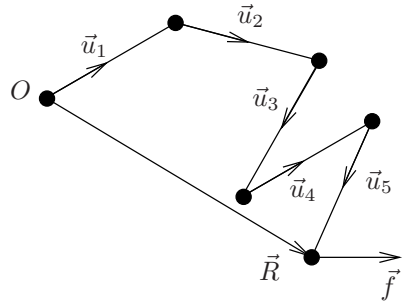
Experimental progresses in manipulation techniques allow now to realize experiments on single molecules, in particular crucial ones for the biology as DNA. By attaching the two extremities of a single DNA molecule, from one side on a plate and from the other side to a magnetic or dielectric bead, one can exert a controlled force on the molecule and measure its resulting elongation. The elasticity of the molecule is thus characterized by the function linking the force and the elongation. The results given on the figures have been obtained for a molecule of length $L = 32.7$ μm (97000 basepairs).

In this problem we shall study two simple modelizations of polymers and compare their predictions to the experimental results. In the two models one consider a polymer of total length L, made of N rigid segments of length $b = L/N$. One end of the polymer is fixed at the origin O, the position of the other end is denoted $\vec{R}$. The microscopic configuration of the system is given by the N unit vectors $\vec{u}_1, \ldots, \vec{u}_N$ colinear to each of the segments.



The polymer is at equilibrium with its environment at temperature T (one denotes $\beta = 1/(k_{\mathrm{B}}T)$), and submitted to a force $\vec{f}$ exerted on its free end. The density of probability of a microscopic configuration is then

$$p(\vec{u}_1, \ldots, \vec{u}_N) = \frac{1}{Z(T, \vec{f})} e^{-\beta[E(\vec{u}_1,\ldots,\vec{u}_N) - \vec{f}\cdot\vec{R}]} \,, \tag{1}$$

where $E(\vec{u}_1, \ldots, \vec{u}_N)$ is the energy arising from the internal interactions of the polymer, and the partition function $Z(T, \vec{f})$ ensures the normalization of this law.

1. Express the average position of the free end, $\langle \vec{R} \rangle$, in terms of $Z(T, \vec{f})$.
2. Express $\vec{R}$ as a function of $\vec{u}_1, \ldots, \vec{u}_N$.

1 The freely jointed chain model

3. In this first model one assumes that the energy $E(\vec{u}_1, \ldots, \vec{u}_N)$ is the same for all microscopic configurations. What kind of interactions are neglected ?
4. Compute the partition function $Z(T, \vec{f})$; the axis (Oz) will be taken parallel to the exerted force. Deduce from it the average position $\langle \vec{R} \rangle$ of the free end, and show in particular that the average elongation along the axis z is

$$z(f) = L\left[\coth\left(\frac{f\,b}{k_{\mathrm{B}}\,T}\right) - \left(\frac{k_{\mathrm{B}}\,T}{f\,b}\right) \right] . \tag{2}$$

Draw the shape of this curve. Study its behavior in the limits of small and large forces. You can use that $\coth(x) = \frac{1}{x} + \frac{x}{3} + O(x^3)$ for $x \to 0$.

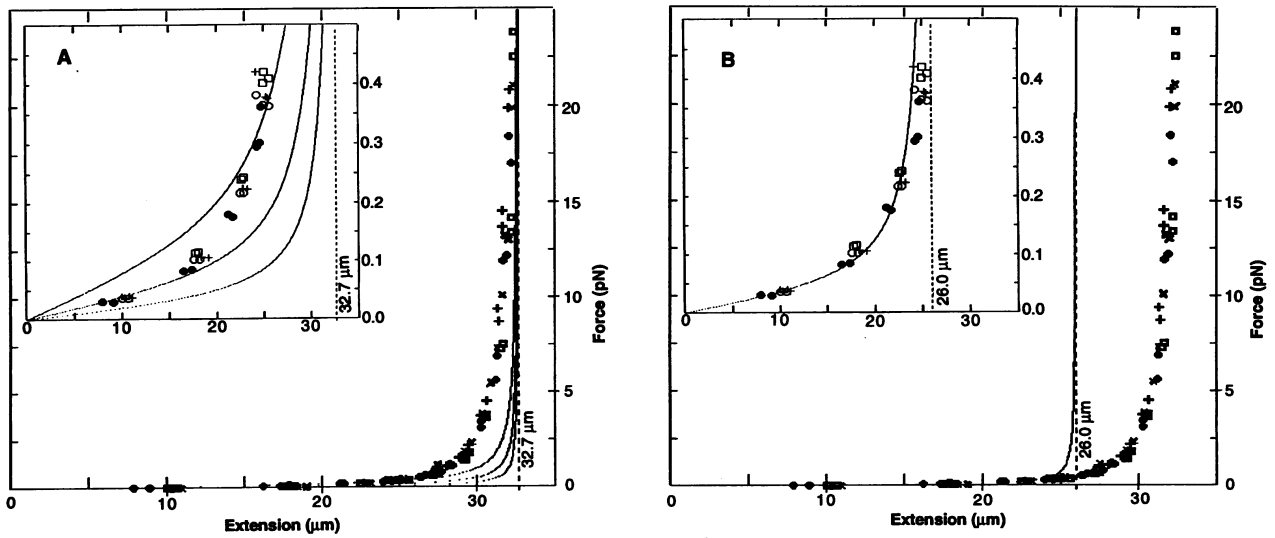


Fig. 3. (**A**) Force versus extension data for four different λ-dimer molecules (●, □, +, and ○) in 5 mM Na_2HPO_4 buffer (10 mM Na^+, pH 8.3). Inset: expanded vertical scale (0 to 0.5 pN). Continuous curves are from Eq. 2 assuming L = 32.7 μm and b = 500 Å (top), 1000 Å (middle), and 2000 Å (lower). 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 1 – From S. Smith, L. Finzi, C. Bustamante, *Direct Mechanical Measurements of the Elasticity of Single DNA Molecules by Using Magnetic Beads*, Science **258**, 1122 (1992).

5. Comment the results of figure 1, that shows several comparisons of this formula with the experimental data, for different values of b and L.

2 The worm-like chain model

6. In this second model one supposes instead that the molecule has some local rigidity : at each articulation between two successive segments one associates an energetic cost $(J/b)(\vec{u}_{i+1} - \vec{u}_i)^2$, where J has thus the dimension of an energy multiplied by a length. Write down the total energy $E(\vec{u}_1, \ldots, \vec{u}_N)$.
7. We shall consider a continuous limit, where $N \to \infty$ and $b \to 0$ with the total length of the polymer $L = Nb$ fixed. In this limit the microscopic configuration $(\vec{u}_1, \ldots, \vec{u}_N)$ becomes a function $\vec{u}(s)$, where $s \in [0, L]$ is the curvilinear abscissa along the molecule, and $\vec{u}(s)$ the unit tangent vector at this point. The correspondence between discrete and continuous description is $\vec{u}_i \leftrightarrow \vec{u}(s = Li/N = bi)$. Show that the energy $E(\vec{u}_1, \ldots, \vec{u}_N)$ becomes a functional,

$$E[\{\vec{u}(s)\}] = k_{\mathrm{B}}T \, \frac{A}{2} \int_0^L \mathrm{d}s \, \left(\frac{\mathrm{d}\vec{u}}{\mathrm{d}s} \right)^2 \, , \tag{3}$$

and express A in terms of the constants of the problem. What is the dimension of A ? Propose a physical interpretation for it. Express $\vec{R}$ in terms of $\vec{u}(s)$.

8. We shall first determine the behaviour of $z(f)$ in the large force limit.
   (a) Draw the shape of a typical configuration of the polymer in the limit $f \to \infty$.
   (b) Let us write $\vec{u}(s) = \vec{u}_\perp(s) + u_\parallel(s)\vec{e}_z$, where $\vec{u}_\perp$ is perpendicular to the axis of the exerted force. Expand the expression of $\vec{R}$ and of the energy (including the term proportional to the force) at the second order in $\vec{u}_\perp$.
   (c) Deduce from this that in this limit one can write $z(f) = L - \int_0^L \mathrm{d}s \, \langle v(s)^2 \rangle$, where the average is taken with the Gaussian weight

$$\exp\left[-\frac{1}{2} \int_0^L \mathrm{d}s \, \left(A \left(\frac{\mathrm{d}v}{\mathrm{d}s} \right)^2 + \beta f \, v(s)^2 \right) \right] \, . \tag{4}$$

(d) To compute the previous expression one performs a Fourier transform,

$$v(s) = \sum_{q\in\mathbb{Z}} \widehat{v}_q \, e^{2i\pi \frac{s}{L} q} \quad \leftrightarrow \quad \widehat{v}_q = \frac{1}{L} \int_0^L \mathrm{d}s \, v(s) \, e^{-2i\pi \frac{s}{L} q} \ . \tag{5}$$

Which constraint on $\widehat{v}_q$ arises from the reality of $v(s)$? Rewrite the expressions of the Gaussian weight (4) and of $z(f)$ in terms of the variables $\widehat{v}_q$.

(e) Discuss the statistical properties of the random variables $\widehat{v}_q$ under the weight (4), taking care of the constraint on $\widehat{v}_q$ due to the reality of $v(s)$, and complete the computation of $z(f)$ using the identity

$$\sum_{q\in\mathbb{Z}} \frac{1}{x + y\, q^2} = \frac{\pi}{\sqrt{xy}} \coth\left(\pi \sqrt{\frac{x}{y}}\right) \ . \tag{6}$$

Deduce that in the large force limit, $L - z(f) \sim \frac{L}{2}\sqrt{\frac{k_\mathrm{B}T}{Af}}$. Compare this behaviour to the result of the freely jointed chain model.

(f) Comment the comparison between the experimental results and the two models presented in Fig. 2.

(g) What are the average fluctuations $\langle X^2 \rangle$ of the position of a quantum harmonic oscillator of mass m and pulsation ω, in contact with a thermostat of temperature β_osc ? Check that the substitutions $\hbar \to 1$, $\beta_\mathrm{osc} \to L$, $m \to A$ and $\omega \to \sqrt{\frac{\beta f}{A}}$ gives back the value of $\langle v(s)^2 \rangle$ computed previously.

It is actually possible to compute the characteristic $z(f)$ of the worm-like chain model, without any hypothesis on f, by exploiting this analogy with quantum mechanics. In the following we shall sketch this method.

9. In the continuum limit, the partition function of the model for a polymer length L, with the constraints $\vec{u}(s=0) = \vec{u}_i$ and $\vec{u}(s=L) = \vec{u}_f$ on the orientations of its extremities, reads

$$\int_{\substack{\vec{u}(0)=\vec{u}_i \\ \vec{u}(L)=\vec{u}_f}} D\{\vec{u}(s)\} \, \exp\left[- \int_0^L \mathrm{d}s \, \left[\frac{1}{2} A \left(\frac{\mathrm{d}\vec{u}}{\mathrm{d}s} \right)^2 - \beta \vec{f} \cdot \vec{u}(s) \right] \right] = \langle \vec{u}_f | e^{-L\widehat{H}(f)} | \vec{u}_i \rangle \ , \tag{7}$$

where $\widehat{H}(f)$ is a quantum mechanical Hamiltonian. Give its expression, and precise the space on which it acts.

10. Deduce, in the limit of large polymer length L, an expression of the partition function in terms of $\varepsilon_0(f)$, the groundstate energy of $\widehat{H}(f)$.

11. Express then the average elongation $z(f)$ in terms of $|\psi_0(f)\rangle$, the normalized eigenstate of $\widehat{H}(f)$ associated to $\varepsilon_0(f)$.

12. Recall the basis of eigenstates of $\widehat{H}(f=0)$. What are the non-zero matrix elements of $\widehat{H}(f)$ in this basis ?

Fig. 1. Squares are experimental force versus extension data for 97 kb λ-DNA dimers from figure 3 of (*2*); solid line is a fit of the entropic force required to extend a worm-like polymer. The fit parameters are the DNA length (L = 32.80 ± 0.10 μm) and the persistence length (A = 53.4 ± 2.3 nm). Shown for comparison (dashed curve) is the freely jointed chain model (*2*) with L = 32.7 μm and a segment length b = 100 nm chosen to fit the small-x data.

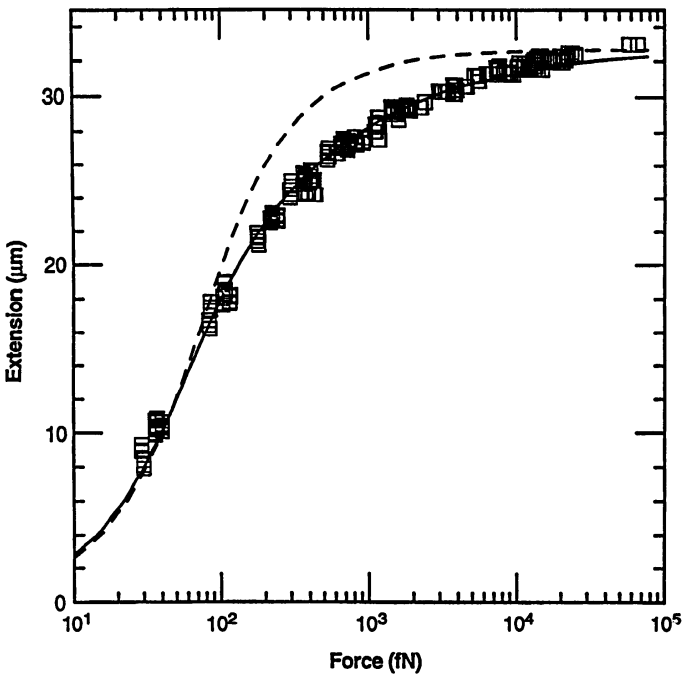


FIGURE 2 – From C. Bustamante, J. Marko, E. Siggia, S. Smith, *Entropic Elasticity of λ-Phage DNA*, Science **265**, 1599 (1994).