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Analytical results for the plectonemic response of supercoiled DNA

Nicolas Clauvelin · Basile Audoly · Sébastien Neukirch

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Abstract The DNA molecule is modeled as an elastic rod with bending and twisting rigidities, subjected to external tension and twist applied at one end, the other end being clamped. We study the plectonemic equilibrium of such a rod, taking into account the impenetrability constraint. Numerical solutions of this boundary value problem have previously shown that purely elastic models can reproduce the supercoiling response of the DNA molecule. Using a variational approach, we derive analytical formulae for the elastic response of the filament, and extend former numerical results.

Keywords DNA supercoiling · Twist storing polymer · Elastic rods

1 Introduction

The mechanical properties of the DNA molecule play an important role in the biology of the cell, but at present we only have an imprecise view of the way DNA responds to various constraints. There is currently an upsurge of interest in this question as nanotechnologies make it possible to apply forces onto an isolated DNA filament [1]. This new kind of experiments, called single-molecule experiments, is a very helpful tool for exploring mechanical and other properties of DNA [2,3] or other filamentary macromolecules.

A typical loading that can be performed experimentally on a double-stranded DNA or a double-stranded RNA [4] is shown in Fig. 1: a DNA molecule is fixed at one end on a glass pane while the other end is attached to a magnetic bead [5]. Using a magnet, it is possible to pull on the bead while twisting it around a vertical axis [6]. For a fixed pulling force, the

N. Clauvelin (✉)
UMR 7190, Institut Jean le Rond d'Alembert, UPMC Univ Paris 06 and CNRS, 4, Place Jussieu, F-75005 Paris, France
e-mail: ncpub@lmm.jussieu.fr

B. Audoly · S. Neukirch
UMR 7190, Institut Jean le Rond d'Alembert, CNRS and UPMC Univ Paris 06, 4, Place Jussieu, F-75005 Paris, France

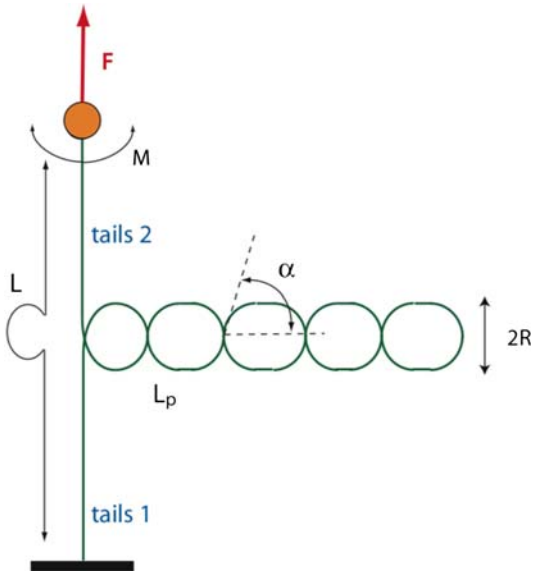

Fig. 1 Principle of the experiment

molecule wraps around itself in a helical way, when the rotation angle of the bead exceeds a threshold value: the resulting structure is called a plectonem.

These experiments can be performed for different pulling forces, molecule contour lengths or salt concentrations since the filament is in a salt aqueous solution. The salt concentration is in fact a very important parameter as it drives the electrostatic effects of the DNA molecule in solution [7]. More specifically, it imposes a theoretical barrier, the Debye length, below which a precise formulation of the electrostatic potential of the molecule in solution is not clearly established.

2 Elastic model for the plectonemic regime

We first investigate the equilibrium behavior of an elastic rod under the constraints described above. The rod, with bending rigidity K_0, and twisting rigidity K_3, is considered inextensible, with a circular cross section of constant radius a, and a total contour length L. We note s the arclength with $s = 0$ for the end fixed to the glass and $s = L$ for the other end. The external loads are the pulling force $F(L)$ and the torsional moment $M(L)$.

2.1 Plectonems geometry

To analyze the mechanical response of plectonems we make an *Ansatz* on the geometry of the twisted filament, relevant only for twist larger than the torsional buckling threshold. We assume that the plectonems can be assimilated with two identical and perfect helices (each of these helices is itself a double-stranded DNA), and we also suppose that curvature and twist are uniform in the plectonemic part. In the tails we further consider the twist to be uniform and the curvature to vanish, and we neglect both the end loop of the plectonems and the region connecting the tails and the plectonemic part.

We parametrize the rod with Euler angles, and take into account material twist as well as geometrical torsion, which add up to give the total twist [8]. At equilibrium our model is described by five variables: the plectonemic radius R, the opening angle α, the value of the

material twist ξ_p in the plectonems, the length L_p of the plectonemic region, and the material twist value ξ_t in the tails. Using these notations we can express total curvature, $\kappa(s)$, and twist, $\tau(s)$, as piecewise functions:

$$\kappa(s) = \begin{cases} \kappa_t = 0 & \text{if } s \in \text{tails}, \\ \kappa_p = \frac{\sin^2\alpha}{R} & \text{if } s \in \text{plectonems}. \end{cases} \tag{1}$$

$$\tau(s) = \begin{cases} \tau_t = \xi_t & \text{if } s \in \text{tails} \\ \tau_p = \xi_p + \epsilon\frac{\sin\alpha\cos\alpha}{R} & \text{if } s \in \text{plectonems}. \end{cases} \tag{2}$$

Geometric impenetrability implies that the two helices contact along a straight line for opening angles less than $\pi/4$ [9]. In this case and as long as we treat the self-contact in the filament through a hard-wall potential the plectonemic radius is equal to the circular cross section radius: $R = a$. It means that we must take this condition into account in our variational process.

2.2 Potential energy of the rod

We are now able to write the potential energy of the elastic rod as the sum of three terms: the strain elastic energy, the work done by external loads, and the contact condition imposed by the hard-wall potential.

The previous considerations on the plectonems geometry yield the following expression for the strain elastic energy. Owing to the fact that we take the straight rod as the reference configuration, we write:

$$E_{el}(\alpha,\ R,\ L_p,\ \xi_t,\ \xi_p) = \frac{K_0\ L_p}{2}\kappa_p^2 + \frac{K_3\ L_p}{2}\tau_p^2 + \frac{K_3\ \left(L - L_p\right)}{2}\tau_t^2. \tag{3}$$

The work of external loads can be written as:

$$E_{ext}(L_p,\ \xi_t,\ \xi_p) = -F(L)\left(L - L_p\right) - M(L)\left((L - L_p)\xi_t + L_p\xi_p\right), \tag{4}$$

where the coefficient of $F(L)$ is the vertical extension of the filament, and the coefficient of $M(L)$ is the total rotation at the end of the filament, which is the number n of turns applied to the bead.

For the contact condition we introduce a Lagrange multiplier λ:

$$E_{hw}(R) = \lambda\,(R - a). \tag{5}$$

Finally the total potential energy of the rod reads:

$$V(\alpha,\ R,\ L_p,\ \xi_t,\ \xi_p) = E_{el} + E_{ext} + E_{hw}. \tag{6}$$

2.3 Results

We can now seek extrema of Eq. (6) with respect to the five variables $(\alpha,\ R,\ L_p,\ \xi_t,\ \xi_p)$ in order to obtain the equilibrium relations of the elastic rod.

Euler-Lagrange minimization with respect to the twist variables ξ_p and ξ_t yields the expressions:

$$M(L) = \begin{cases} K_3\xi_t & \text{if } s \in \text{tails}, \\ K_3\left[\xi_p + \epsilon\frac{\sin 2\alpha}{2R}\right] & \text{if } s \in \text{plectonems} \end{cases}$$

which show that the internal moment $M(s) = K_3\tau(s)$ is constant along the filament, as happens for a continuous rod with a circular cross section, and takes the value $M(L)$ imposed by the loading, both in the tails and in the plectonemic part.

Minimization with respect to the opening angle α gives the value of this internal moment:

$$M(L) = -2\epsilon \frac{K_0}{R} \frac{\cos\alpha \sin^3\alpha}{\cos 2\alpha}. \tag{7}$$

For the variable R we obtain the expression of the contact pressure in the rod:

$$p = \frac{K_0}{R^3} \frac{\sin^4\alpha}{\cos 2\alpha} \left(= -\frac{\lambda}{L_p}\right). \tag{8}$$

Finally for the variable L_p we find the relation between the pulling force and the plectonemic variables:

$$F(L) = \frac{K_0}{R^2} \sin^4\alpha \left(\frac{1}{2} + \frac{1}{\cos 2\alpha}\right). \tag{9}$$

We remark that this set of equations extends the numerical results of [10]. In all these relations the value of R is fixed by the condition of hard-wall contact $R = a$, and the values of $F(L)$ and $M(L)$ are also known since they are external parameters.

As shown in [10] the vertical extension of the rod can be written as a linear function of n the number of turns imposed on the bead:

$$\frac{z}{L} = \left(1 + \frac{2\,K_0}{K_3} \frac{\sin^2\alpha}{\cos 2\alpha}\right) + \epsilon\, n \frac{4\,\pi\, R}{L \sin 2\alpha} = z_0 + B\, n. \tag{10}$$

As illustrated on Fig. 2, the typical shape of the experimental diagrams showing the extension versus the number of turns, exhibits a linear region. The expression Eq. (10) reproduce this linear part of these experimental diagrams.

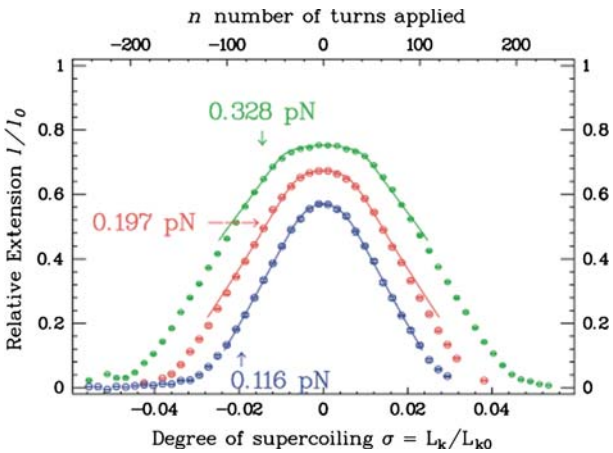

Fig. 2 Extension versus number of turns taken from [11]

3 Application to the DNA molecule

In order to apply our model to DNA molecules we must consider the electrostatic effects due to the bare charge of DNA and to the counter-ions present in the solution. Since the inter-strand distance is of the order of the Debye screening length, the Debye-Hückel approximation, leading to the linear Poisson-Boltzmann equation, is not valid in the case we consider. The study of the non-linear case is, according to our knowledge, only possible numerically, and therefore does not yield any analytical expressions. For example [12] investigates the potential created by a charged cylinder, and [13] consider helical geometry but within the linear geometry. Note that other approaches using the DLVO theory [14] are not more helpful in our case.

We work around these difficulties by calculating an *effective radius* of the DNA molecule in the plectonemic regime. By *effective radius* we mean the radius that the molecule must have in order to act as a non-charged rod-like polymer. We give in Fig. 3 the effective radius as a function of the pulling force $F(L)$. These results are extracted from experimental data, provided by G. Charvin and V. Croquette (LPS–ENS, Paris), on a dsDNA molecule of 11kbp. The experimental data listed the slope B as a function of the force. We plot Fig. 3 by solving Eq. (9) and Eq. (10) for α and R (with $K_0 = 50\,\mathrm{nm}\,k_B\,T$).

Fig. 3 shows that at high forces the effective radius of the molecule is about 1nm, which is in good agreement with ordinary values of the core radius of dsDNA (from 0.9 nm to 1.2 nm). The increase of the effective radius can be interpreted in term of the Manning condensation process [7], which is illustrated on Fig. 4, although it is probably not the only effect at play. Experimental studies on plasmids [15] shows that the salt concentration influences the effective radius of the DNA molecule in a manner still not understood.

4 Conclusion

It is surprising that the DNA molecule can be modeled as an uncharged elastic rod, omitting all the chemical details, and yet reproduce the plectonemic regime of supercoiled DNA. Even though the electrostatic properties of the DNA molecule in solution are very complex to describe, it is nevertheless possible to understand single-molecule experiments. Indeed the main results of these experiments can be explained with the use of rod-like models. In order to predict the detailed mechanical behavior of the DNA molecule one needs to take

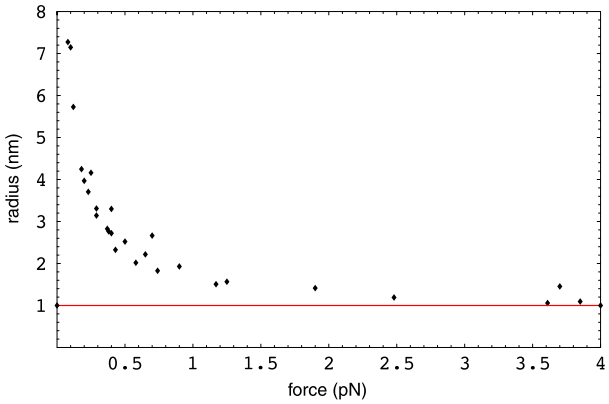

Fig. 3 Effective radius versus pulling force

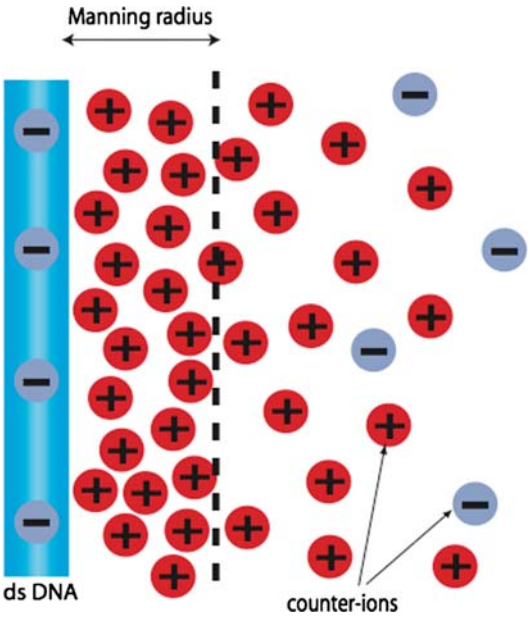

Fig. 4 Symbolic representation of the Manning condensation process

into account electrostatic and thermal effects. This ambitious goal is a step toward the full understanding of how DNA mechanical properties influence biological process in the cell.

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References

1. Ritort, F.: Single-molecule experiments in biological physics. J. Phys-Condens. Matt. **18**(8), R531–R583 (2006)
2. Charvin, G., Allemand, J.-F., Strick, T., Bensimon, V., Croquette, V.: Twisting DNA: single molecule studies. Contemp Phys. **45**(5), 383–406 (2004)
3. Bustamante, C., Mascosko, J.C., Wuite, G.J.L.: Grabbing the cat by the tails: manipulating molecules one by one. Nat. Rev. Mol. Cell Biol. **1**(2), 130–136 (2000)
4. Abels, J.A., Moreno-Herrero, F., van der Heijden, T., Dekker, C., Dekker, N.H.: Single-molecule measurements of the persistence length of double-stranded RNA. Biophys. J. **88**, 2737–2744 (2005)
5. Smith, S.B., Finzi, L., Bustamante, C.: Direct mechanical measurements of the elasticity of single DNA molecules by using magnetic beads. Science **258**(5085), 1122–1126 (1992)
6. Strick, T.R., Allemand, J.F., Bensimon, D., Bensimon, A., Croquette, V.: The elasticity of a single supercoiled DNA molecule. Science **271**(5257), 1835–1837 (1996)
7. Manning, G.S.: Limiting laws and counterion condensation in polyelectrolyte solutions-I: colligative properties. J. Chem. Phys. **51**(3), 924–933 (1969)
8. van der Heijden, G.H.M., Thompson, J.M.T.: Helical and localised buckling in twisted rods: a unified analysis of the symmetric case. Nonlinear Dynam. **21**, 71–99 (2000)
9. Neukirch, S., van der Heijden, G.H.M.: Geometry and mechanics of uniform n-plies: from engineering ropes to biological filaments. J. Elasticity. **69**(1), 41–72 (2002)
10. Neukirch, S.: Extracting DNA twist rigidity from experimental supercoiling data. Phys. Rev. Lett. **93**(19), 198107 (2004)
11. Strick, T., Dessinges, M.N., Charvin, G., Dekker, N.H., Allemand, J.F., Bensimon, D., Croquette, V.: Stretching of macromolecules and proteins. Rep. Prog. Phys. **66**(1), 1–45 (2003)

12. Stigter, D.: The charged colloidal cylinder with a gouy double layer. J. Colloid Interf. Sci. **53**(2), 296–306 (1975)
13. Ubbink, J., Odjik, T.: Electrostatic-undalotory theory of plectonemically supercoiled DNA. Biophys. J. **76**(5), 2502–2519 (1999)
14. Chapot, D., Bocquet, L., Trizac, E.: Interaction between charged anisotropic macromolecules: application to rod-like polyelectrolytes. J. Chem. Phys. **120**(8), 3969–3982 (2004)
15. Rybenkov, V.V., Vologodskii, A.V., Cozzarelli, N.R.: The effect of ionic conditions on DNA helical repeat, effective diameter and free energy of supercoiling. Nucleic Acids Res. **25**(7), 1412–1418 (1997)