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Foreword

Computational modeling of materials behavior by multiscale materials modeling (MMM) approaches is becoming a reliable tool to underpin scientific investigations and to complement traditional theoretical and experimental approaches of component assessment. At transitional (microstructural) scales continuum approaches begin to break down and atomistic methods reach inherent limitations in time and length scale. Transitional theoretical frameworks and modeling techniques are developed to bridge the gap between the different length scales.

Industrial success in high technology fields relies on the possibility to specifically engineer materials and products with improved performance. The success factor is the ability to make these material related developments timely at relatively low-costs. This demands not only the rapid development of new or improved processing techniques but also better understanding and control of material chemistry, processing, structure, performance, durability, and their relationships. This scenario usually involves multiple length and time scales and multiple processing and performance stages, which are usually only accessible via multi-scale / multi-stage modeling or simulation.

In high-payoff, high-risk technologies such as the design of large structures in the aerospace and nuclear industries, the effects of aging and environment on failure mechanisms cannot be left to conservative approaches. Increasing efforts are now focused on advancing MMM approaches to develop new material systems components and devices. Appropriate validation experiments are crucial to verify that the models predict the correct behavior at each length scale. Thus, one of the advantages of these MMM approaches is that, at each scale, physically meaningful parameters are predicted and used in models for subsequent scales, avoiding the use of empiricism and fitting parameters.

Recent interest in nanotechnology is challenging the scientific community to design nanometer to micrometer size devices for applications in new generations of computers, electronics, photonics or drug delivery systems. These new application areas of multiscale materials modeling require novel and sophisticated science-based approaches for design and performance evaluation. Theory and modeling are playing an increasing role to reduce development costs and manufacturing times. With the sustained progress in computational power and MMM methodologies, new materials and new functionalities are increasingly more likely discovered by MMM approaches than by traditional trial and error approach. This is part of a paradigm shift in modeling, away from reproducing known properties of known materials towards simulating the behavior of hypothetical composites as a forerunner to finding real materials with these novel properties.

The MMM 2006 conference provides an international forum for the scientific advances of multiscale modeling methodologies and their applications.

I would like to thank the members of the international advisory committee, the local program committee and particularly the organizing team, the symposium organizers and the session chairs and the University of Freiburg for their engagement and support. Without their hard work and their devotion of time and ressources, the Third International Conference Multiscale Materials Modeling would not have been possible.

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Symposium 5

Biomaterials

Analytical Results For The Plectonemic Response Of Supercoiled DNA

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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.

1. Introduction

It is widely known that mechanical properties of the DNA molecule play an important role in the biology of 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.
A typical loading that can be performed experimentally on a double strand of DNA 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 [1]. By using a magnet, it is possible to pull on the bead while twisting it around a vertical axis [2]. For a fixed pulling force, the 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 done for different pulling forces, molecule contour lengths or salt concentrations.

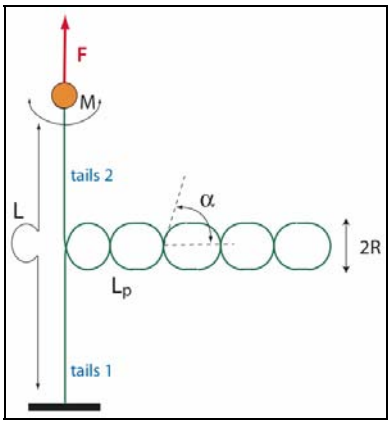

Figure 1. Simplified view of the experimental setup

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 constant circular cross section of 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 to large applied twist: we assume that the plectonems can be assimilated to two identical and perfect helices (each one of these helices is itself a double strand of 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 [3]. At the equilibrium the plectonems are described by five variables: the plectonemic radius *R*, the opening angle α, the value of the material twist ζ_p in the plectonems, the length L_p of the plectonemic region, and the material twist value ζ_t in the tails. We have for total curvature and twist the following expressions (where ε=+/- 1 stands for the chirality):

$$\kappa(s) = \begin{cases} 0 = \kappa_t & \text{if} \quad s \in \text{tails} \\ \frac{\sin^2 \alpha}{R} = \kappa_p & \text{if} \quad s \in \text{plecto} \end{cases}$$

$$\tau(s) = \begin{cases} \zeta_t = \tau_t & \text{if} \quad s \in \text{tails} \\ \zeta_p + \epsilon \frac{\sin \alpha \cos \alpha}{R} = \tau_p & \text{if} \quad s \in \text{plecto} \end{cases} \tag{1}$$

We model the self-contact of the filament by a hard-wall potential. Geometric impenetrability implies that the two helices contact along a straight line, as long as the opening angle is less than π/4. In this case the plectonemic radius equals to the circular cross section of the rod.

2.2 Potential energy of the rod

We now derive the potential energy of the elastic rod, which is the sum of three terms: the elastic energy, the work done by external loads, and the contact condition:

$$\begin{aligned} V(\alpha, R, L_p, \zeta_t, \zeta_p) = \frac{K_0 L_p}{2}\kappa_p^2 + \frac{K_3(L-L_p)}{2}\tau_t^2 + \frac{K_3 L_p}{2}\tau_p^2 \\ -F(L)(L-L_p) - M(L)\big((L-L_p)\zeta_t + L_p\zeta_p\big) \\ +\lambda(R-a) \end{aligned} \tag{2}$$

where the strain elastic energy is the sum of the square of the curvature and the square of the twist, and the external force works again extension and the external moment works again rotation. Finally the contact constraint is represented with a Lagrange multiplier, λ.

2.3 Results

We seek extrema of Eqn (2) with regard to the five variables. Euler-Lagrange minimization with respect to the twist variables ζ_p and ζ_t yields $K_3\zeta_t = M(L)$ and $K_3[\zeta_p + \epsilon \sin 2\alpha/(2R)] = M(L)$, which show that the internal moment *M(s)* is constant along the filament, 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 gives the value of this internal moment:

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

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

$$p = \frac{K_0}{R^3} \frac{\sin^4\alpha}{\cos 2\alpha} \tag{4}$$

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

$$F(L) = \frac{K_0}{R^2} \sin^4\alpha \left(\frac{1}{2} + \frac{1}{\cos 2\alpha}\right) \tag{5}$$

Notice that the value of *R* is fixed by the condition of hard-wall contact *R*=*a*. With the help of Eqn (5) we obtain the value of α since the value of *F(L)* is fixed, and we have checked that this set of equations accurately describes the numerical results of [4].

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 of 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 expression. For example [5] investigates the potential created by a charged cylinder, and [6] consider helical geometry but within the linear approximation.
We choose to avoid 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 for acting as a non-charged rod-like polymer. In fact it boils down to determinate the radius of the circular cross section introduced in the elastic model with hard-wall contact. We give in Fig 2 the effective radius as a function of the pulling force. These results are extracted from experimental data, as explained in [4], provided by G. Charvin and V. Croquette (LPS – ENS, Paris), on a dsDNA molecule of 11kbp.

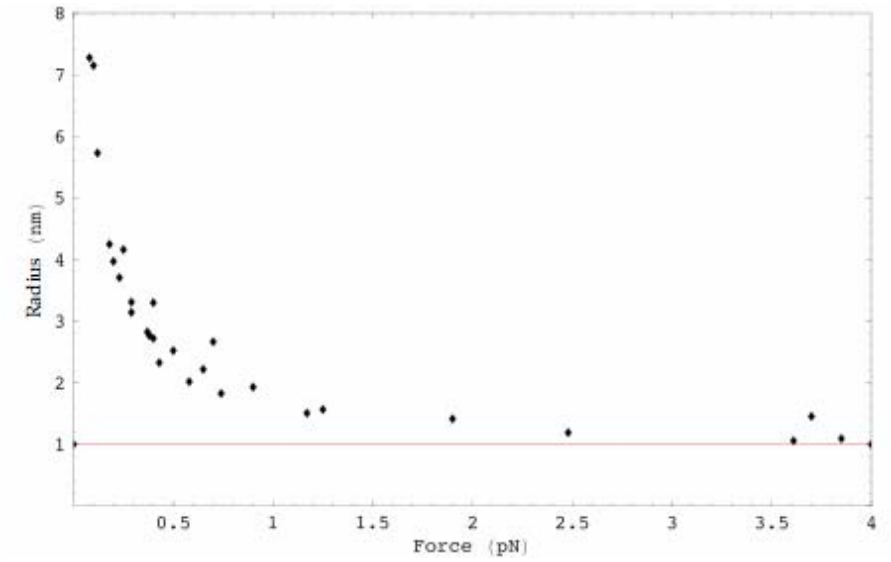

Figure 2. Effective radius versus pulling force

Fig 2 shows that at low 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 0.9nm to 1.2nm). The increase of the effective radius can be interpreted in term of the Manning condensation process [7], although it is probably not the only effect to take into account. Experimental studies on plasmids at zero force [8] shows that the salt concentration influences the effective radius of the DNA molecule in a manner still not understood.

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