



The dependence of DNA supercoiling on solution electrostatics

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ABSTRACT

We develop an elastic–isotropic rod model for twisted DNA in the plectonemic regime. We account for DNA elasticity, electrostatic interactions and entropic effects due to thermal fluctuations. We apply our model to single-molecule experiments on a DNA molecule attached to a substrate at one end, while subjected to a tensile force and twisted by a given number of turns at the other end. The free energy of the DNA molecule is minimized subject to the imposed end rotations. We compute values of the torsional stress, radius, helical angle and key features of the rotation–extension curves. We also include in our model the end loop energetic contributions and obtain estimates for the jumps in the external torque and extension of the DNA molecule seen in experiments. We find that, while the general trends seen in experiments are captured simply by rod mechanics, the details can be accounted for only with the proper choice of electrostatic and entropic interactions. We perform calculations with different ionic concentrations and show that our model yields excellent fits to mechanical data from a large number of experiments. Our methods also allow us to consider scenarios where we have multiple plectonemes or a series of loops forming in the DNA instead of plectonemes. For a given choice of electrostatic and entropic interactions, we find there is a range of forces in which the two regimes can coexist due to thermal motion.

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1. Introduction

The mechanical and electrostatic properties of DNA directly affect various cellular processes, such as replication, transcription, compaction and protein–DNA binding. This is the motivation behind this study of DNA supercoils, which are also known as plectonemes. Plectonemes in DNA molecules are manipulated by several molecular machines during key processes, such as transcription and DNA repair [1]. In several scenarios, the action of these molecular machines or enzymes on DNA has been found to depend on the mechanical stress present in the molecules [2,3]. Consequently, DNA supercoiling remains a subject of study for theorists and experimentalists alike.

Experimentally, DNA supercoiling has been investigated using several biochemical and biophysical methods, including single-molecule experimental techniques, where individual DNA molecules can be stretched and twisted under physiologically relevant conditions [4–8]. In these experiments, it is possible to apply a force and/or moment parallel to the filament axis of a DNA molecule, and to measure the elastic response in terms of elongation and angle of twisting about the filament axis. In rotation–extension experiments, the vertical extension of the DNA filament and the external moment are recorded as a function of the number of turns.

It is a well-known feature of the experimental curves that there is a regime, corresponding to the formation of plectonemes, where there is almost a linear relationship between the DNA extension and the applied number of turns. Also, as shown in the recent experiments of Forth et al. [4], Lipfert et al. [5] and Mosconi et al. [6], the external moment is approximately constant in the plectonemic regime.

Plectonemes have been studied theoretically as elastic rods by many authors [9–14]. In order to interpret single-molecule experiments, Purohit [15,16] accounts for the effects of thermal fluctuations as well as electrostatics in plectonemes and straight portions of DNA, and shows that many features seen in the recent experiments of Forth et al. [4] can be qualitatively reproduced using an elastic rod model. Furthermore, as seen in Fig. 5 in Purohit [16], his theoretical results for the slope of the linear region in vertical extension of the DNA vs. number of turns of the bead are around twice the value of those found in experiments by Forth et al. [4]. One of the goals of this paper is to address this problem and get more quantitative agreement with single-molecule experiments. Our approach follows those of van der Heijden et al. [14] and Clauvelin et al. [17,18], who use a variational formulation to solve for the geometry of the plectoneme. The analysis in van der Heijden et al. [14] considers only the elastic energy of the filament, but Clauvelin et al. [17,18] and other authors [19] consider electrostatic interactions together with the elasticity, and are able to reproduce some of the features of the rotation–extension experiments. In agreement

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