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DNA supercoiling modeling of nucleosome and viral spooling

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New kinematic equations are used to model DNA supercoiling. These equations govern the simultaneous production of multiple folding and coiling of a filament in space by diffeomorphism of a reference curve. Here we show how to use these equations to model regions of highly localized filament coiling, where mechanisms of proteic coding or viral spooling are important.

1 Kinematic equations for DNA supercoiling

In many key biological processes DNA folding and coiling are essential for optimizing functions and packing information efficiently. New kinematic equations have been introduced (see Maggioni & Ricca, 2006) to model multiple coiling of a filament in space by continuous deformation of a reference curve. These equations have been used to investigate several geometric features of the reference curve, such as writhing, inflexional configuration, torsion and twist localization, in relation to properties of physical interest, such as elastic deformation energy and filament compaction. Writhing rates and packing efficiency have been also computed in relation to possible applications to DNA modeling (Ricca & Maggioni, in press). In this context, specific biological mechanisms such as proteic coding, site specific recombinations and transcriptional processes dictate conformational prescriptions that involve highly localized coiling (Baker, 2000). Here we show how to use these equations to capture some of these conformational features conveniently. For this purpose we refer to an inextensible, closed curve $\mathcal{C}$ in space, thought of as the central axis of a closed, double-stranded DNA filament. Each point on $\mathcal{C}$ is labeled by the position vector $\mathbf{X} = \mathbf{X}(\xi)$, where $\xi \in [0, 2\pi]$, that is

$$\mathcal{C} = \mathrm{Im}(\mathbf{X}) \,, \qquad \mathbf{X} \,:\, [0, L] \to \mathbb{R}^3 \,, \tag{1}$$

where L denotes total length of $\mathcal{C}$, with $\mathbf{X}(0) = \mathbf{X}(L)$. A useful time-dependent prescription is given by taking $\mathbf{X} = \mathbf{X}(\xi, t; n) = \mathbf{Y}(\xi) + \mathbf{Z}(n\xi, t)$, where $\mathbf{Y} = \mathbf{Y}(\xi)$ denotes a stationary base curve, representing the secondary structure of the macromolecule, and $\mathbf{Z} = \mathbf{Z}(n\xi, t)$ the equation that governs the coiling process of the tertiary structure. Coil production is controlled by a time function that, in general, comes from dynamics, while the number $(n-1)$ of coils produced may depend on several, functional factors.

2 Modeling nucleosome and viral spooling

Nucleosome spooling. The assembly of DNA into chromosomes reaches a condensation of almost 10^4-fold in length from the naked DNA molecule to the metaphase chromosome. As current research evidences (Snustad & Simmons, 2006), a large proportion of this condensation is due to DNA packaging into protein spool regions (nucleosome cores) of highly localized coiling. These regions are connected one another by helical strings of DNA (linker DNAs), forming a hierarchical, solenoid structure (chromatin fiber). A simplified model of the nucleosome spooling attached to helical linkers is provided by taking

$$\mathbf{X} = \mathbf{X}(\xi, t; n) \;:\; \begin{cases} x = [\cos\xi - t\cos(n\xi)]/l(t) \\ y = [\sin\xi) - t\sin(n\xi)]/l(t) \\ z = (\xi + t\sin\xi)/l(t) \end{cases} , \tag{2}$$

where we ensure inextensibility by normalizing each $\mathbf{X}$-component by the length function

$$l(t) = \frac{1}{2\pi}\int_0^{2\pi} \left[\left(\frac{\partial x}{\partial \xi}\right)^2 + \left(\frac{\partial y}{\partial \xi}\right)^2 + \left(\frac{\partial z}{\partial \xi}\right)^2\right]^{1/2} \mathrm{d}\xi \,. \tag{3}$$

Here re-scaling is chosen to ensure that total length is kept fixed at $L = L(0) = 2\pi$. As shown in Figure 1a, the base curve is identified with a stationary helix, while multiple coiling is generated by the super-position of the time-evolution of

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the secondary function. By adjusting conformational parameters, such as helical pitch and spatial characteristics of coiling, according to physical and biological information we can evaluate deformation energy and estimate electro-chemical potentials. These, in turn, may help to determine the role of packaging and regulatory functions.

(a) (b)

Fig. 1 Production of 9 coils ($n = 10$) by model equations: (a) localization of filament spooling on helical base curve plotted at time $t = 1$, according to eqs. (2); (b) toroidal folding generated by multiple coiling superimposed on a circular base curve plotted at time $t = 6$, according to eqs. (4).

Viral spooling. Chromosome packing in all icosahedral bacteriophages with double-stranded DNA genomes seems to obey similar conformational mechanisms and chiral organization (Arsuaga *et al.*, 2005). Modeling DNA filament compaction inside phage capsids has led to the formulation of several competing hypotheses, such as coaxial spooling, spiral or toroidal folding, etc., all of which require a certain degree of geometric organization to allow, on one hand high packing inside the capsid, on the other efficient spooling of the filament from capsid to tail. Evidence of toroidal folding and writhe bias suggest the following equations:

$$\mathbf{X} = \mathbf{X}(\xi, t; n) \; : \quad \begin{cases} x = [\cos\xi - t\cos(n\xi)]/l(t) \\ y = [\sin\xi - t\sin(n\xi)]/l(t) \\ z = t\sin\xi/l(t) \end{cases} , \tag{4}$$

where now the base curve is a circle, and toroidal folding is produced by the superimposed kinematics. Figure 4b shows filament arrangement at time $t = 6$. Comparative analysis on writhing and curvature production shows (Ricca & Maggioni, in press) that the two quantities can be matched by appropriate weighting, hence relating chirality with bending energy. Note that detailed analysis of coiling formation shows (Ricca & Maggioni, in press) that these kinematics pose an upper bound on the writhing number (hence, by conservation of linking number, on the total twist number) independently of the total number of coils produced.

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