Modeling filament supercoiling for nucleosome and viral spooling

FRANCESCA MAGGIONI[1] AND RENZO L. RICCA[2]

[1]Department of Mathematics Statistic, Computer Science and Applications , University of Bergamo ITALY,   francesca.maggioni@unibg.it
[2]Department of Mathematics and Applications, University of Milano-Bicocca ITALY

ABSTRACT

In this poster we study different time-dependent evolutions of filament coiling for modeling DNA proteic coding, viral spooling and chromosome packing. For this, we introduce the concept of hierarchical kinematics to describe the super-position of curve evolutions of increasing complexity, starting from a base (primary) curve and evolving towards secondary and tertiary structures, to capture higher-order coiling. Preliminary work [1] [2] has been gradually extended to model mechanisms of proteic coding and viral spooling [3], and here we extend these results further to investigate the role of geometric quantities such as writhing, curvature and torsion localization, and relative rates, in relation to elastic deformation energy, filament compaction and packing efficiency.

1 The filament model

The DNA filament $\mathcal{F}$ is modelled by a thin inexestensible rod of constant length $L = 2\pi$ and of uniform circular cross–section of area $A = \pi a^2$ ($a \ll L$).
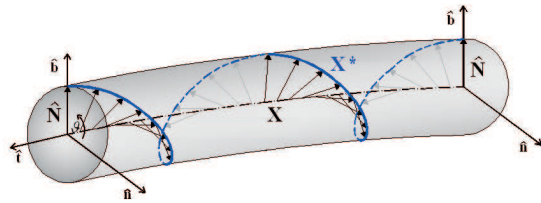
- The filament axis $\mathscr{C}$ is given by a simple, smooth space curve $\mathbf{X} = \mathbf{X}(\xi)$ where $\xi \in [0, 2\pi]$.

2 Global geometric and topological quantities

2.1 Measures of coiling ($\mathcal{K}$), folding (Wr) and twist (Tw)

Let $\mathscr{C}$ be a closed, smooth, simple curve in $\mathbb{R}^3$ given by $\mathbf{X}(\xi) : [0, L] \longrightarrow \mathbb{R}^3$, with curvature $c(\xi)$ and torsion $\tau(\xi)$ where ξ is a parameter along the curve and $\hat{\mathbf{t}}(\xi) \equiv \mathbf{X}'(\xi)/\|\mathbf{X}'(\xi)\|$ is the unit tangent to $\mathcal{C}$ at ξ.

We consider the following quantities:

- **normalized total curvature**

$$\mathcal{K}(\mathscr{C}) := \frac{1}{2\pi} \oint_{\mathscr{C}} c(\xi) \|\mathbf{X}'(\xi)\| \, d\xi ;\tag{1}$$

- **writhing number** (Fuller 1971)

$$Wr := \frac{1}{4\pi} \oint_{\mathscr{C}} \oint_{\mathscr{C}} \frac{\hat{\mathbf{t}}(\xi) \times \hat{\mathbf{t}}(\xi^*) \cdot [\mathbf{X}(\xi) - \mathbf{X}(\xi^*)]}{|\mathbf{X}(\xi) - \mathbf{X}(\xi^*)|^3} \|\mathbf{X}'(\xi)\| \|\mathbf{X}'(\xi^*)\| \, d\xi d\xi^* ;\tag{2}$$

- **total twist number**

$$Tw := \frac{1}{2\pi} \oint_{\mathscr{C}} \tau(\xi) \|\mathbf{X}'(\xi)\| \, d\xi + \frac{1}{2\pi}[\Theta]_{\mathcal{F}} = \mathcal{T} + \mathcal{N} ,\tag{3}$$

where $\mathcal{T}$ is the normalized total torsion and $\mathcal{N}$ the normalized intrinsic twist of the fibers of $\mathcal{F}$ around $\mathscr{C}$.

2.2 Călugăreanu–White formula

In the case of a closed filament $\mathcal{F}$ in isolation the sum of Wr and Tw is a topological invariant according to the well-known formula:

$$Lk = Wr + Tw ,\tag{4}$$

where Lk is the linking number of the filament $\mathcal{F}$.

3 Kinematic equations for folding mechanism

We explore the folding mechanism by a family of time-dependent curves $\mathbf{X} = \mathbf{X}(\xi, t)$ (where t is a kinematical time) given by

$$\mathbf{X} = \mathbf{Y} + \mathbf{Z} + \dots \text{(higher-order folding)} ,\tag{5}$$

where

- $\mathbf{Y} = \mathbf{Y}(\xi, t)$ is a base curve which stands for the *primary structure* of the macromolecule;

- $\mathbf{Z} = \mathbf{Z}(\xi, t)$ generates coiling and prescribes the evolution of the *primary folding*.
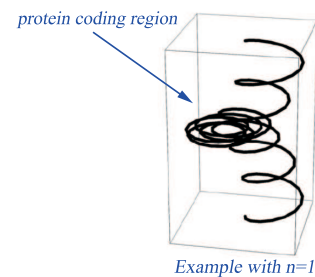
3.1 Modeling nucleosome spooling

A simplified model of nucleosome spooling is provided by the following example:

$$\mathbf{X} = \mathbf{X}(\xi, t; n) : \quad \begin{cases} x = [\cos\xi - t\cos(n\xi)]/l(t) \\ y = [\sin\xi - t\sin(n\xi)]/l(t) \\ z = [\xi + t\sin\xi]/l(t) \end{cases} ,\tag{6}$$

where

- the base curve is a standard helix $\mathbf{Y} = (\cos\xi, \sin\xi, \xi)$;

- multiple coils $N = n - 1$ are generated by the super-position of the secondary function $\mathbf{Z} = (t\cos(n\xi), t\sin(n\xi), t\sin\xi)$;

- in order to ensure the inexstensibility we have normalized by the *length function $l(t)$*.
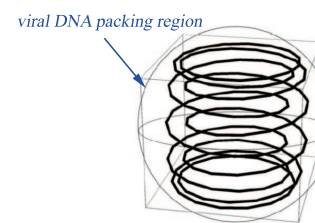

Example with n=10

3.2 Modeling viral spooling

A simplified model of viral spooling is provided by the following example:

$$\mathbf{X} = \mathbf{X}(\xi, t; n) : \quad \begin{cases} x = [\cos\xi - t\cos(n\xi)]/l(t) \\ y = [\sin\xi - t\sin(n\xi)]/l(t) \\ z = t\sin\xi/l(t) \end{cases} ,\tag{7}$$

where

- the base curve is a circle $\mathbf{Y} = (\cos\xi, \sin\xi, 0)$;

- toroidal folding ($N = n - 1$ coils) is produced by the super-position of the kinematics $\mathbf{Z} = (t\cos(n\xi), t\sin(n\xi), t\sin\xi)$.
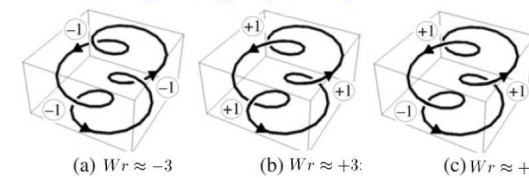

*Example with n=10*

4 Bounded writhe and twist

- The writhing number Wr admits a physical interpretation in terms of the *average number of signed crossings* made by the filament strands in space (Fuller, 1971).

Different types of 3-coils formation

(a) $Wr \approx -3$ (b) $Wr \approx +3$ (c) $Wr \approx +1$

- The model equations (7), irrespectively of the number $N = n - 1$ of coils formed, are characterized by **bounded writhing number $Wr \in [0, 1]$** (case (c) in the Figure above).

- Since the *linking number Lk is conserved*, then the **total twist number Tw is bounded** too (very important for energy considerations).

Case of 9-coils formation (n=10)

writhing number / normalized total curvature
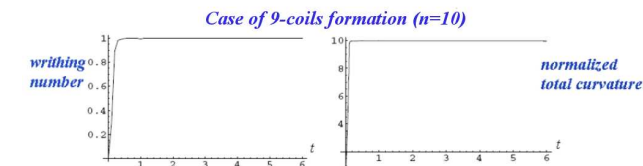
- *Similarity* in functional behavior between the *growths of the writhing number Wr* and *normalized total curvature $\mathcal{K}$*.

- The normalized total curvature $\mathcal{K} \in [0, n]$ i.e. it is limited by the number $N = n - 1$ of coils formed.

5 Energetics of folding

Let us consider the **linear elastic theory** for a uniformly homogeneous and isotropic filament ($\chi = K_b/K_t = 1$ with K_b bending rigidity and K_t torsional rigidity) .

- The **deformation energy** is given (to first order) by

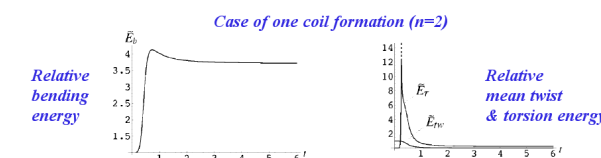$$E = E_b + E_t + \dots \text{(higher-order terms)}\tag{8}$$

where

$$\tilde{E}_b(t) = \frac{E_b(t)}{E_0} = \frac{1}{2\pi}\oint_{\mathscr{C}}(c(\xi, t))^2 \|\mathbf{X}'(\xi)\| \, d\xi \quad \text{norm. bending energy}$$

$$\tilde{E}_t(t) = \frac{E_t(t)}{E_0} = \frac{1}{2\pi}\oint_{\mathscr{C}}(\Omega(\xi))^2 \|\mathbf{X}'(\xi)\|^2 d\xi \quad \text{norm. torsional energy}$$

$$\tilde{E}_\tau(t) = \frac{E_\tau(t)}{E_0} = \frac{1}{2\pi}\oint_{\mathscr{C}}(\tau(\xi, t))^2 \|\mathbf{X}'(\xi)\| \, d\xi \quad \text{norm. torsion energy}$$

$$\tilde{E}_{tw} = E_t|_{\Omega_0} = (Lk - Wr(t))^2 \quad \text{norm. mean twist energy}$$
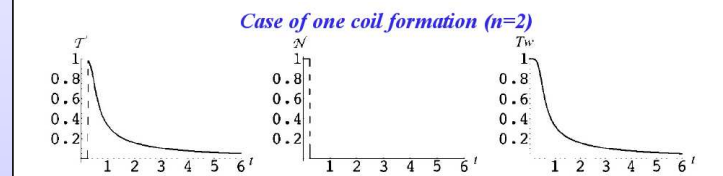
$$E_0 = \frac{K_b}{2}\oint_{\mathscr{C}} c_0^2 \, ds \quad \text{reference energy} = \pi K_b .$$

Case of one coil formation (n=2)

Relative bending energy / Relative mean twist & torsion energy

6 Loop deformation and inflexional states

Generic behaviour (Moffatt & Ricca, 1992): at the point of inflexion the *torsion is singular* but the *singularity is integrable*.
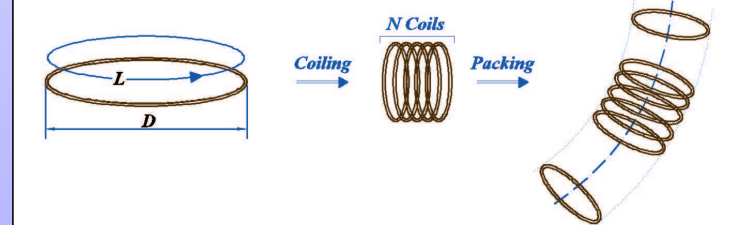
$$\tau(\xi, t) = \frac{\mathbf{X}' \times \mathbf{X}'' \cdot \mathbf{X}'''}{\|\mathbf{X}' \times \mathbf{X}''\|^2} \to \infty \text{ as } \{\xi, t\} \to \{\xi_i, t_i\} , \text{ but } [\mathcal{T}] = 1 .$$

Case of one coil formation (n=2)

- The jump $[\mathcal{T}] = 1$ is compensated by an equal and opposite jump in $\mathcal{N}$;

- Tw remains a smooth function of ξ and t.

7 Compactibility and packing rate

Typical *DNA compaction*: $D/L = O(10^{-5})$.

N Coils / Coiling / Packing

If ρ is the *average radius of curvature* of the coiled state, then we have

$$L = 2\pi = (N + 1) \, 2\pi\rho ;$$

if $N = N(t)$ then the *packing rate* is given by $\rho(t) = [N(t) + 1]^{-1}$.
In general, for the $k - th$ *order coiling*, starting from a fundamental structure of length l_0 to the final structure of length L we have

$$L = O(N^k l_0) \quad \text{where} \quad N = \prod_k N_k \quad \Longrightarrow \rho(t) = O(1/N(t)^k) ,$$

which clearly shows a *nonlinear dependence* on $N(t)$.

8 Conclusions

- Simple *models of supecoiling for nucleosome and viral spooling* are proposed;

- *geometric and energetic aspects* associated with the kinematics proposed are analized;

- by an alternating folding mechanism, the model considered can produce *high degree of coiling by keeping the writhing number bounded*.

References

[1] Maggioni, F. & Ricca, R.L. (2006) Writhing and coiling of closed filaments. *Proc. Roy. Soc. A*, **462**, 3151–3166.

[2] Ricca, R.L. & Maggioni, F. (2008) Multiple folding and packing in DNA modeling. *Comp. & Math. with Appl*, **55**, 1044–1053.

[3] Maggioni, F. & Ricca, R.L., DNA supercoiling modeling of nucleosome and viral spooling, In *Proceedings of ICIAM07*, Zürich, in press.