Modeling filament supercoiling for nucleosome and viral spooling

Francesca Maggioni$^{(*)}$
Mathematics Department, University of Bergamo ITALY

$^{(*)}$joint work with **Renzo L. Ricca**

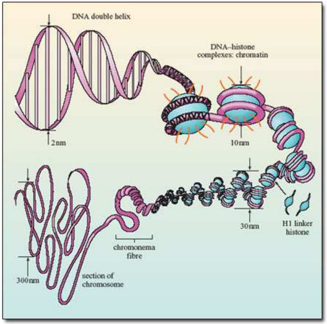
Conference on Knots and other Entanglements in Biopolymers: Topological and Geometrical Aspects of DNA, RNA and Protein Structures

Trieste, 14-19 September, 2008

DNA supercoiling for nucleosome and viral spooling

DNA supercoiling

- geometric and topological informations;
- energetic aspects;
- filament compaction;
- packing efficiency;



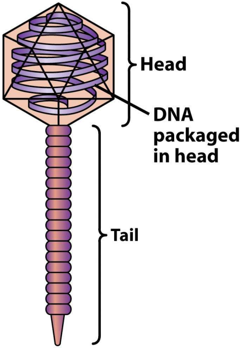
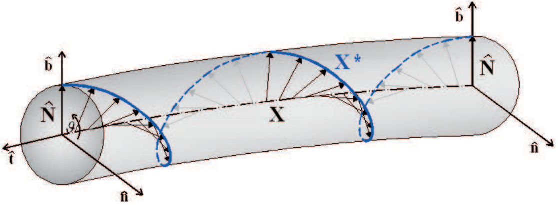


Figure 8-4b Principles of Genetics, 4/e

The filament model

- The DNA filament $\mathscr{F}$ is modelled by a thin inexestensible rod of constant length $L = 2\pi$ and uniform circular cross-section of area $A = \pi a^2$ with $a/L \ll 1$.



- The filament axis $\mathscr{C}$ is given by a simple, smooth space curve $\mathbf{X}(s)$.
- Each fiber $\mathscr{C}^*$ is given by

$$\mathbf{X}^*(s) = \mathbf{X}(s) + \epsilon\hat{\mathbf{N}}(s)$$

with $\hat{\mathbf{N}}(s) = \hat{\mathbf{n}}\cos\vartheta(s) + \hat{\mathbf{b}}\sin\vartheta(s)$.
- $\left(\mathbf{X}, \hat{\mathbf{N}}\right)$ defines a *ribbon* of edges $\mathbf{X}$ and $\mathbf{X}^*$.

Global geometric and topological quantities

Let $\mathscr{C}$ be a simple closed, smooth curve in $\mathbb{R}^3$: $\mathbf{X}(s) : [0, L] \longrightarrow \mathbb{R}^3$;

Definition

- The **writhing number** (Fuller 1971)

$$Wr(\mathscr{C}) \equiv \frac{1}{4\pi} \oint_{\mathscr{C}} \oint_{\mathscr{C}} \frac{\hat{\mathbf{t}}(s) \times \hat{\mathbf{t}}(s^*) \cdot [\mathbf{X}(s) - \mathbf{X}(s^*)]}{|\mathbf{X}(s) - \mathbf{X}(s^*)|^3} \,\mathrm{ds}\,\mathrm{ds}^* \;; \qquad (1)$$

- The **total twist number** Tw (Love 1944)

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

Theorem (Călugăreanu, 1959 and White, 1969)

Linking number $\quad Lk = Wr + Tw \;; \qquad (3)$

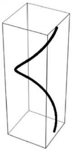
Hierarchical kinematics for folding mechanism

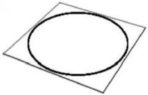
We explore the folding mechanism by a family of time-dependent curves $\mathbf{X} = \mathbf{X}(\xi, t)$ (where t is a kinematical time) given by

$$\mathbf{X}(\xi, t) = \mathbf{Y}(\xi, t) + \mathbf{Z}(\xi, t) + \ldots \text{(higher-order folding)} \ , \tag{4}$$

where

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





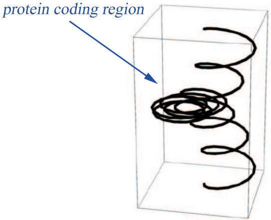
- $\mathbf{Z} = \mathbf{Z}(\xi, t)$ generates coiling and prescribes the evolution of the *primary folding*.

Modeling nucleosome spooling

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

$$\mathbf{X} = \mathbf{X}(\xi, t; n) \;:\; \begin{cases} x = [\cos\xi - t\cos(n\xi)]/l(t) \\ y = [\sin\xi - t\sin(n\xi)]/l(t) \\ z = [\xi + t\sin\xi]/l(t) \end{cases} , \qquad (5)$$

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



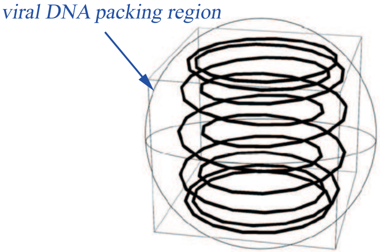
Example with n=10

Modeling viral spooling

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

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

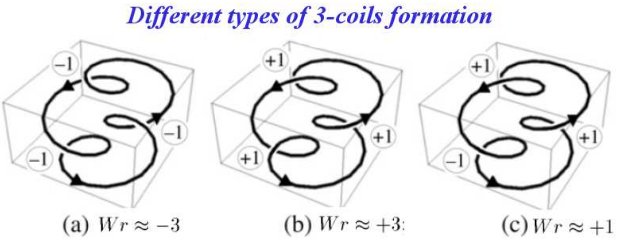
where $n > 0$ and $l(t)$ the length function.



Example with n=10

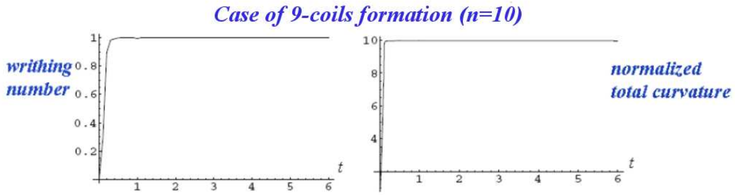
Bounded writhe and twist

- Interpretation of Wr in terms of the **average number of signed crossings**:



- **Bounded writhing number $Wr \in [0, 1]$** irrespectively of the number $N = n - 1$ of coils formed (case (c) in the Figure above).
- During coils formation the **topology is conserved**, then the **total twist number Tw is bounded** too.

Comparative analysis of writhing rates and 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 $\boldsymbol{\mathcal{K}} \in [\mathbf{0}, \boldsymbol{n}]$ i.e. it is limited by the number $N = n - 1$ of coils formed.

Bending, torsional and mean twist energy

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

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

$$E = E_b + E_t + \ldots (\text{higher order terms}) \tag{7}$$

where

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

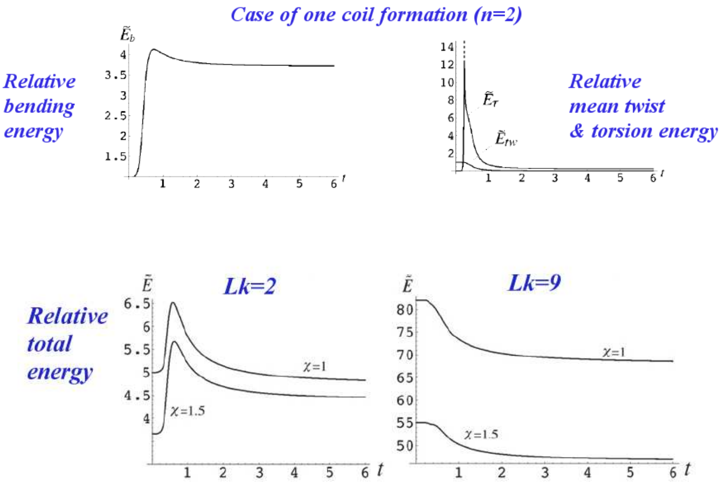
$$\tilde{E}_t(t) = \frac{E_t(t)}{E_0} = \frac{1}{2\pi}\oint_{\mathscr{C}} (\Omega(\xi))^2 |\mathbf{X}'(\xi)|^2 \mathrm{d}\xi \quad \textbf{norm. torsional energy}$$

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

$$\tilde{E}_{tw} = E_t|_{\Omega_0} = (Lk - Wr(t))^2 \quad \textbf{norm. mean twist energy} \;;$$

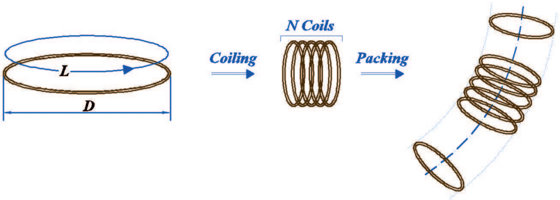
$$E_0 = \frac{K_b}{2}\oint_{\mathscr{C}} c_0^2\, \mathrm{d}s \quad \textbf{reference energy} = \pi K_{\mathrm{b}} \;.$$

Comparative behaviour of relative energy: 1 coil formation



Compactibility and packing rate

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



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 $N(t)$.

Future work and References

Future work

- Structural complexity and packing;
- Inflexional states and energy localization.

References

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

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

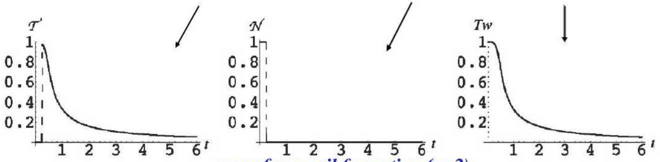
Maggioni, F. & Ricca, R.L., (2007)
DNA supercoiling modeling of nucleosome and viral spooling,
In *Proceedings of ICIAM07*, Zürich, **7**(1), 2120011-2120012.

Loop deformation and inflexional states

Generic behaviour (Moffatt & Ricca, 1992):

$$\tau(\xi,t) = \frac{\mathbf{X}' \times \mathbf{X}'' \cdot \mathbf{X}'''}{|\mathbf{X}' \times \mathbf{X}''|^2} \to \infty \text{ as } \{\xi,t\} \to \{\xi_i,t_i\}, \text{ but } [\mathcal{T}] = 1 \; .$$

$$\underbrace{\frac{1}{2\pi}\int_{\mathscr{C}} \tau(\xi)\left|\mathbf{X}'(\xi)\right| \mathrm{d}\xi}_{\mathcal{T}} + \underbrace{\frac{1}{2\pi}[\Theta]_{\mathscr{F}}}_{\mathcal{N}} = Tw$$



case of one coil formation (n=2)