On the Topology of Chromatin Fibers

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**Topology of DNA**

DNA double helix

Linking number $L_k$ of two curves

- $L_k = 1$
- $L_k = 2$

Unconstrained B-DNA:

$L_{k_0} = +1/10.5$ turns/basepairs (bps)

(right handed double helix)
Topoogy of DNA

White-Fuller theorem

\[ \Delta L_k = \text{Twist} \]

\[ \Delta L_k = \text{Writhe} \]

\[ \Delta L_k = \text{Tw} + \text{Wr} \]

conserved quantity for closed curves or fixed ends
Supercoiling *in vivo* and *in vitro*

*in vivo* - transcription

- twin supercoiled domains
  - (Liu Wang 1987)

*in vitro* - magnetic tweezers

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**Diagram:**
- Nascent RNA
- RNA polymerase
- Negative Supercoils
- Positive Supercoils

**Equations:**
- $V \sim 20 \text{ bps/sec}$
- $\omega_0 \sim 2 \text{ turns/sec}$
- torque $> +5 \text{ pN}\cdot\text{nm}$
- (Harada 2001)
DNA in the nucleus: chromatin, a multiscale functional structure.
Chromatin Fiber

a closer view

nucleosome
a left handed superhelix
(crystallographic structure)

fiber
key accordable structure in
regulating DNA accessibility

movie by Hua Wong
Chromatin Fiber Topology

how to calculate the DNA twist and writhe in the fiber?

“two angle model”: linker DNA between 2 nucleosomes are assumed to be straight

twist is additive, writhe is not!

but

regular fiber $\rightarrow$ Tw, Wr, Lk contribution *per nucleosome*
Fiber under Magnetic Tweezers

hysteresis (high positive torsion)

experiments by JL Viovy
Institut Curie, Paris
**Nucleosome Chiral Inversion**

A plastic nucleosome!

Left handed \(<\Delta L k> \sim -1\)

Nucleosome

Chiral transition

Right handed \(<\Delta L k> \sim +1\)

Reversome
Statistical Mechanics and the Fit

Gibbs potential $G = F - \Gamma \theta$

$nucleosome \leftrightarrow reversome$

$\Gamma = 0$

$a torque-induced transition$

$fit$
Reversome: a Topological Buffer

absorbing torsion constraint trough transition to reversome

coarse grained model simulations

what about transcription? (next episode...)

10/10
M3V group

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- Annick Lesne (CNRS)
- Jean-Marc Victor (CNRS)
- Julien Mozziconacci (UPMC)
- Hua Wong (doc 2005–2008)
- Fabien Paillusson (doc 2007–2010)
- Christophe Bécavin (doc 2007–2010)
- Pascal Carrivain (doc 2008–2011)
- Christophe Lavelle (postdoc 2003–2004)

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- A. Bancaud et al. Torsional manipulation of chromatin fibers reveals a highly flexible structure Mol Cell 2007
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back to \textit{in vivo}: transcription in a compact fiber

compact fiber \implies \text{steric hindrance prevents nucleosome transitions}

RNA-polymerase exerts a positive, large torque

the \textit{first} nucleosome pass to reversome, then the second…

\implies \text{creation of a “reversome front”}

\[ v_{\text{RNApol}} = 20 \text{ bps/s} \rightarrow 2 \text{ turns/s} \rightarrow 1 \text{ reversome/s} \rightarrow v_{\text{front}} = 200 \text{ bps/s} \]
**Signature of Nucleosomes**

- Extension
- Rotation (turns)
- Force
  - Rotation

**Diagram Details:**
- Magnetic bead: 2.8 µm
- Rotation: +1 nucleosome
- Linking number: \( Lk \sim -1 \) turn
- Compaction: \( \Delta z \sim 50 \) nm

Graphs:
- Extension vs. Rotation (turns)
- \( \Delta z \) vs. Rotation (turns)
Fiber under Magnetic Tweezers

1. Torsional resilience
   - DNA of same length
   - $\approx n \times 1.8$ turns

2. Hysteresis (higher torsion)
   - $\approx n \times 2$ turns

Experiments by LJ Viovy
Institut Curie, Paris
4 Nucleosome States

a plastic nucleosome!

negatively crossed open positively crossed reversome

<table>
<thead>
<tr>
<th>state</th>
<th>Neg.</th>
<th>Open</th>
<th>Pos.</th>
<th>barrier</th>
<th>Rev.</th>
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<tbody>
<tr>
<td>$\alpha$</td>
<td>54°</td>
<td>-30°</td>
<td>30°</td>
<td>/</td>
<td>30°</td>
</tr>
<tr>
<td>$\beta$</td>
<td>115°</td>
<td>90°</td>
<td>115°</td>
<td>/</td>
<td>80°</td>
</tr>
<tr>
<td>d (nm)</td>
<td>4.1</td>
<td>8.3</td>
<td>2.8</td>
<td>/</td>
<td>2.0</td>
</tr>
<tr>
<td>$\Delta Lk$ per nuc.</td>
<td>-1.4</td>
<td>-0.4</td>
<td>-0.2</td>
<td>-0.15</td>
<td>+0.9</td>
</tr>
<tr>
<td>E (kT)</td>
<td>0.7</td>
<td>0</td>
<td>2</td>
<td>28</td>
<td>10</td>
</tr>
</tbody>
</table>
Statistical Mechanics and the Fit

\[ \text{eq. eq. } k_1 \]
\[ \text{nég. ↔ ouv. ↔ pos. } \Rightarrow \text{4ème état } k_1 \]

a torque-induced transition

\[ \Gamma \theta \]

\[ \text{potentiel de Gibbs } G = F - \Gamma \theta \]

\[ \Gamma = 0 \]

\[ +\Gamma \]

\[ -\Gamma \]

rotation (turns)
1. normal modes analysis

2. nucleosome structuration

DNA proteins

3. Brownian dynamics at constant torque

result: chiral transition:

left → right!
**Reversome Front Speed**

linking number conservation:

\[ \frac{\omega_0 t}{2\pi} = \left[ \Lambda \Delta Lk + \frac{\tau}{2\pi} \right] \cdot x(t) \]

RNA pol rotation  
reversome fiber internal twist  
(\(\Delta Lk\) nucl to rev)  
reversome fiber torsion  
(<<)

Reversome front progression:

\[ x(t) = v t + c, \quad v = \frac{\omega_0}{2\pi \Lambda \Delta Lk + \tau_c} \approx \frac{\omega_0 / 2\pi}{\Lambda \Delta Lk} \]

\[ \Lambda \left( \frac{1}{\Delta Lk} \right) \text{ nucl./s} \]

Becavin et al, Bioph J 2009
**Petesh-Lis Experiment**

A wave of nucleosome disruption

**Interpretation:**
- **RNA pol at start**
  - 100 bps elongation → 10 turns, 5 rev., 1000 bps
  - 600 bps elongation → 60 turns, 30 rev., 6000 bps
  - 1200 bps elongation → 120 turns, 60 rev., 12000 bps
  - ...

(Zlatanova and Victor, HFSP J 2009)
**Topology of DNA**

- Single (closed) curve
- Linking number $L_k$