On the Topology of Chromatin Fibers

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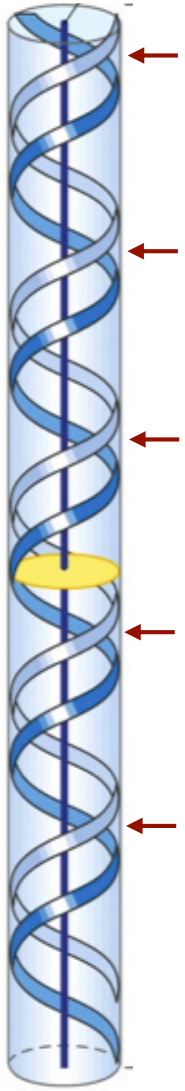
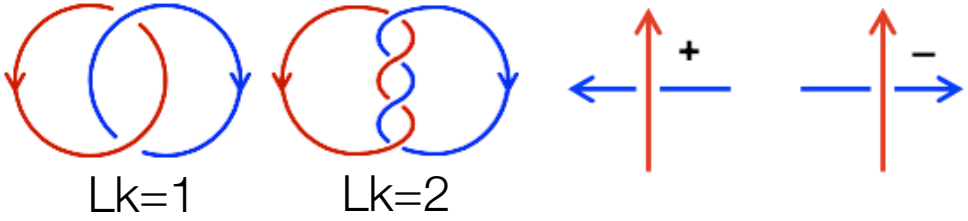
Topology of DNA

DNA
double helix

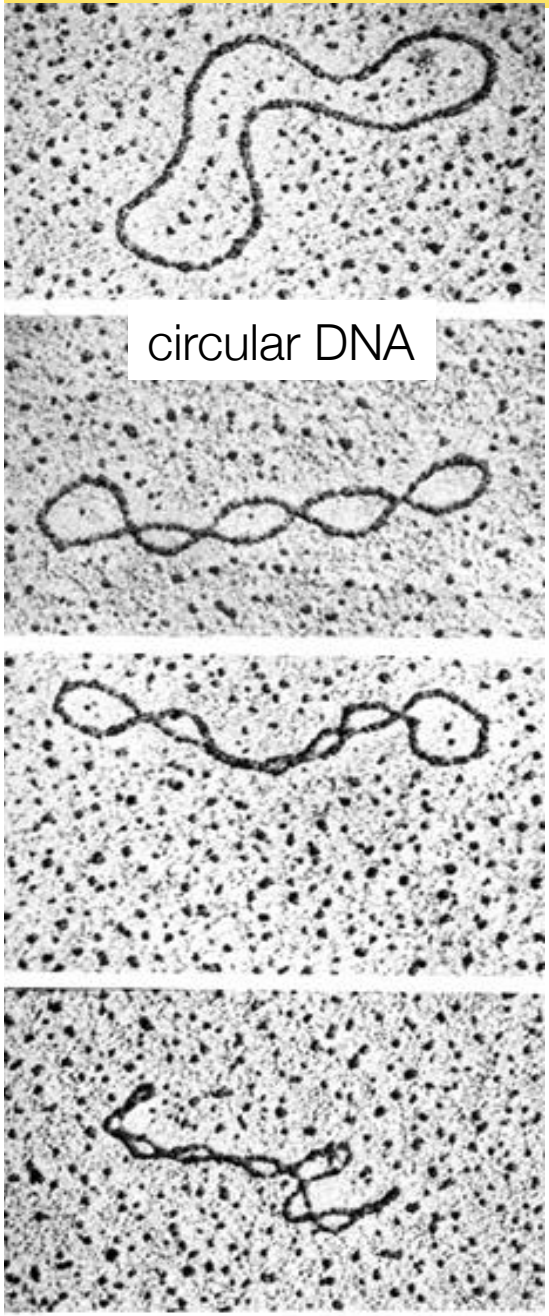


linking number Lk of two curves



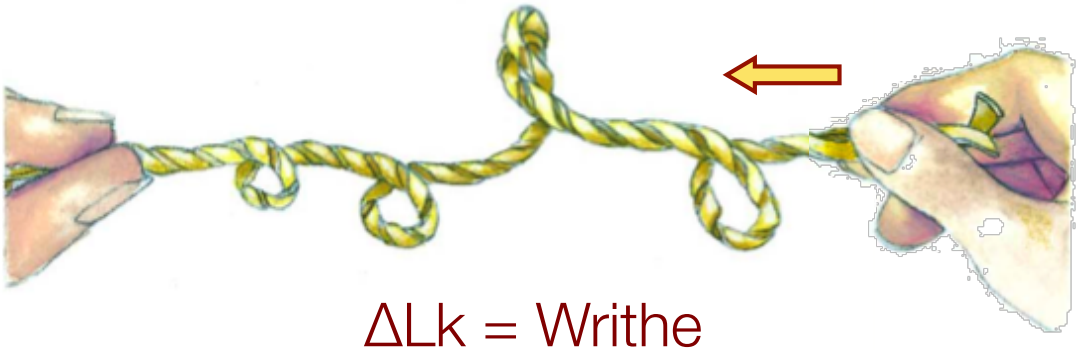
unconstrained B-DNA:
Lk_0 = +1/10.5 turns/basepairs (bps)
(right handed double helix)

Topology of DNA



White-Fuller theorem

ΔLk = Twist



ΔLk = Writhe

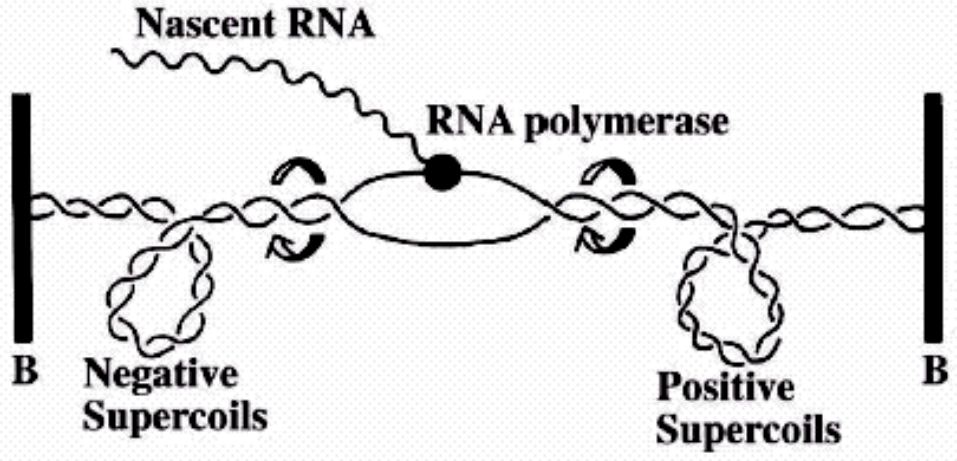
$\Delta Lk = Tw + Wr$

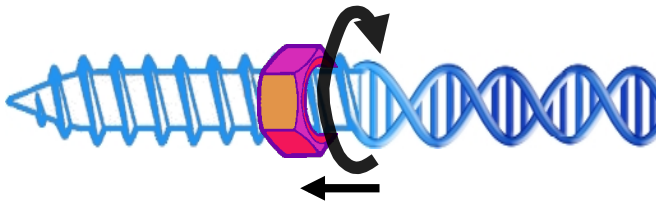
conserved quantity for
closed curves or fixed ends

SUPERCOILING *IN VIVO* AND *IN VITRO*

in vivo - transcription

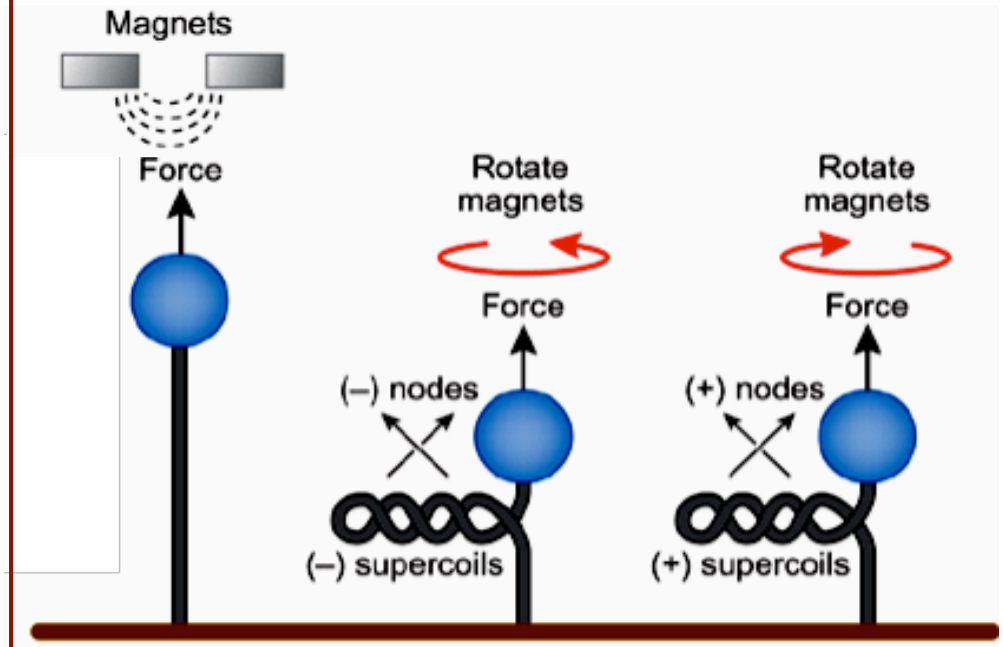
twin supercoiled domains
(Liu Wang 1987)

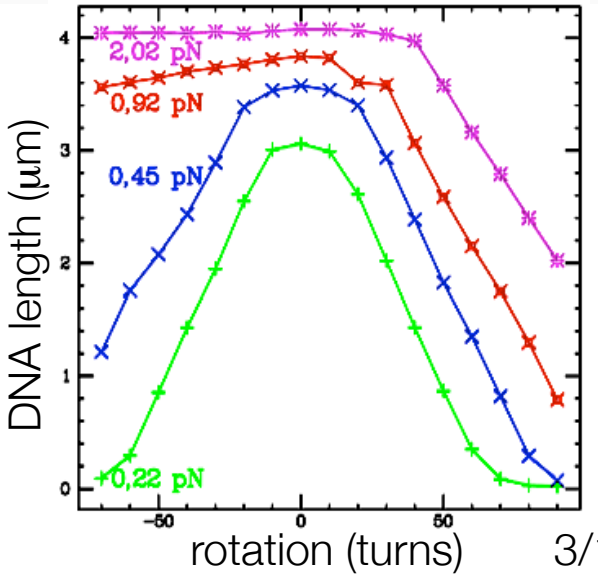




V ~ 20 bps/sec
ω_0 ~ 2 turns/sec
torque > +5 pN·nm
(Harada 2001)

in vitro - magnetic tweezers

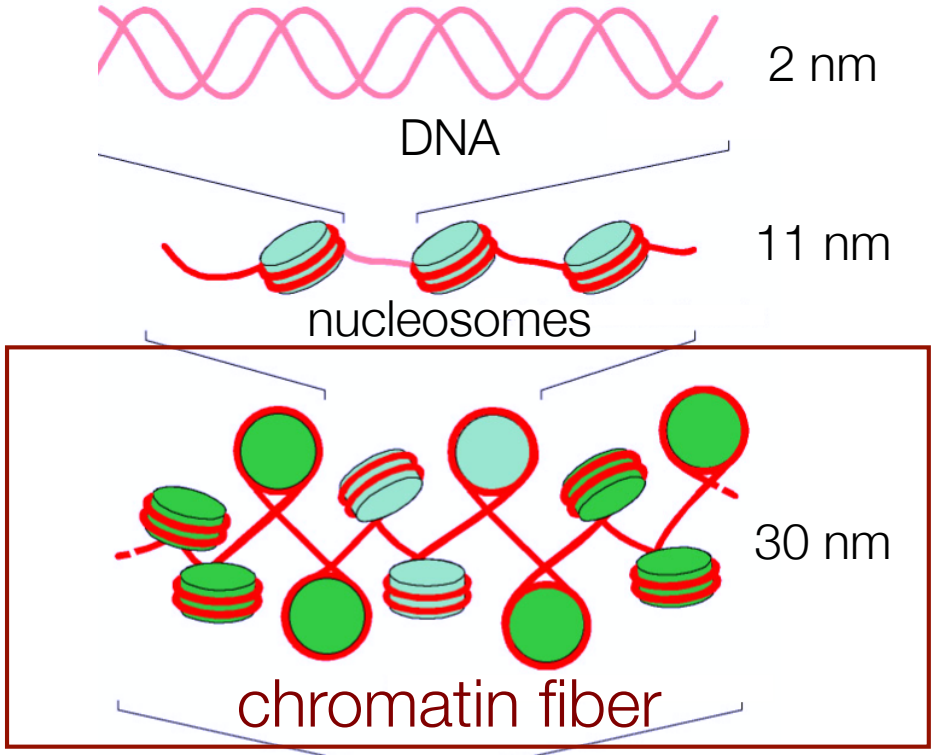


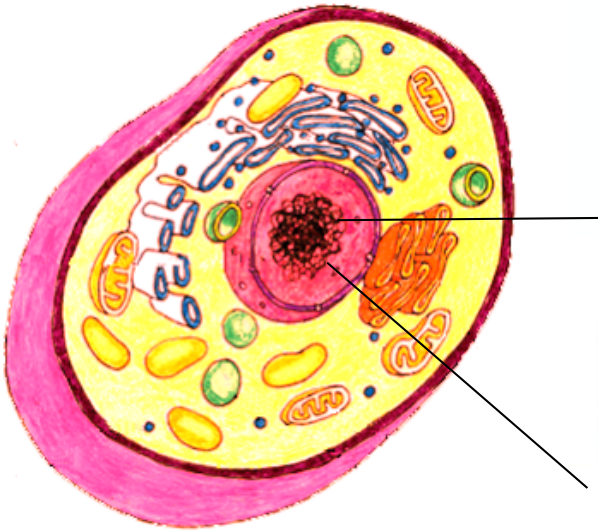


Chromatin Fiber

DNA in the nucleus: chromatin

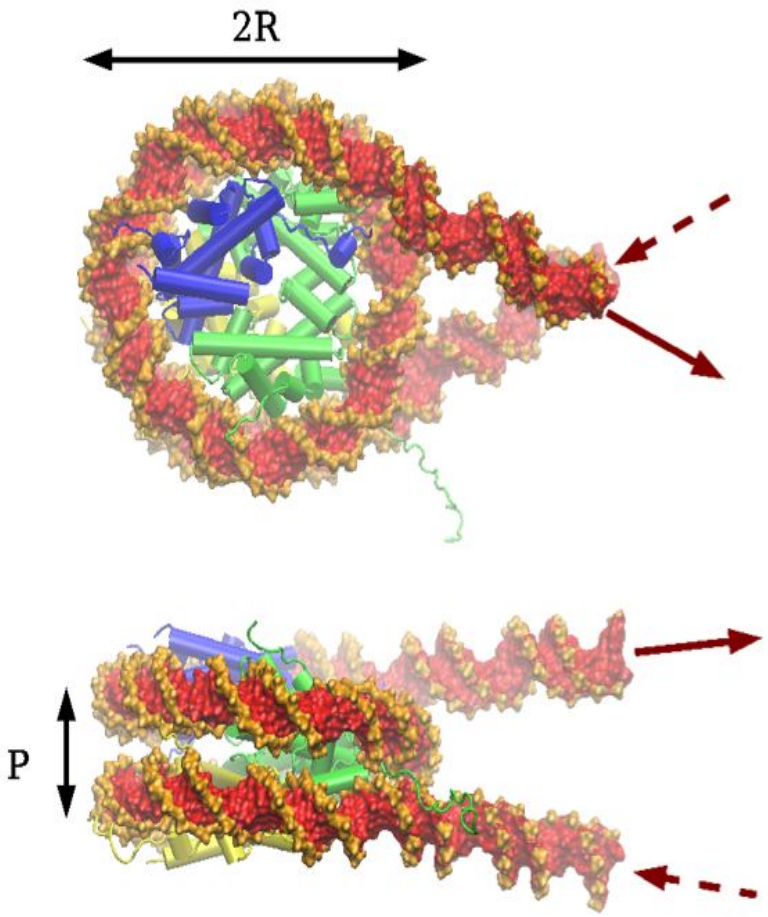
a multiscale functional structure





Chromatin Fiber

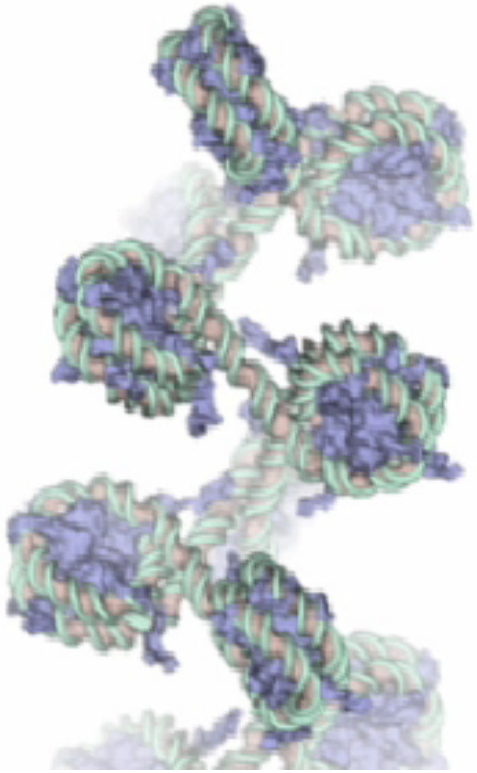
a closer view



nucleosome

a left handed superhelix

(crystallographic structure)



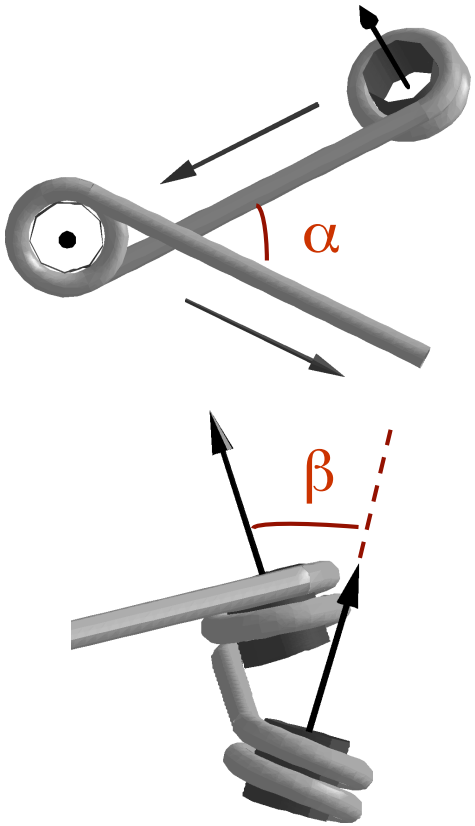
fiber

key accordable structure in regulating DNA accessibility

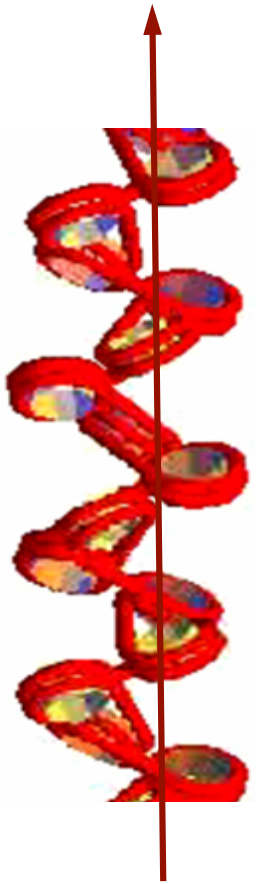
movie by Hua Wong

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

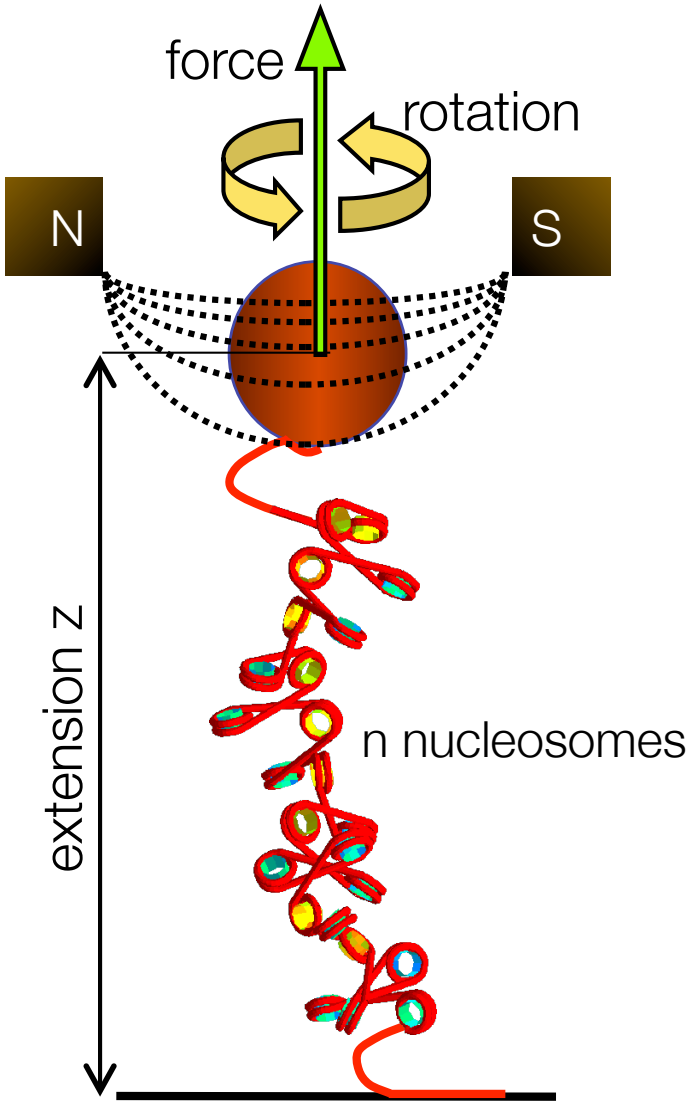


twist is additive, writhe is not!

but

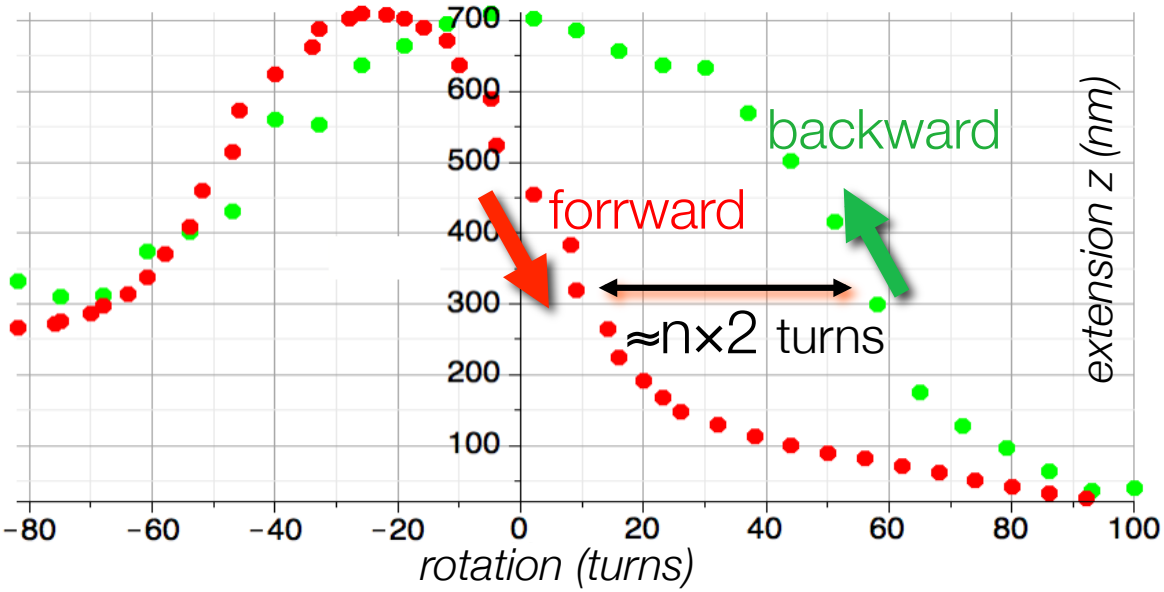
regular fiber → Tw, Wr, Lk contribution *per nucleosome*

Fiber under Magnetic Tweezers



experiments by JL Viovy
Institut Curie, Paris

hysteresis (high positive torsion)



Nucleosome Chiral Inversion

a plastic nucleosome!

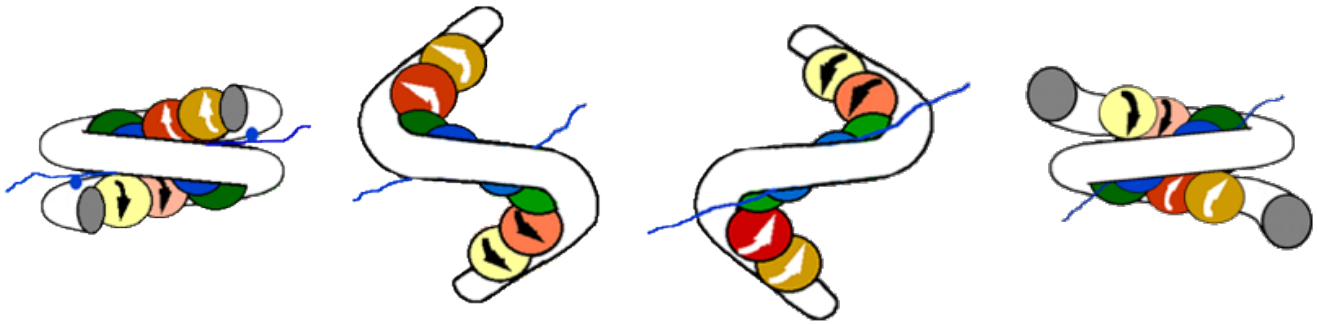
left handed <ΔLk> ~-1

nucleosome

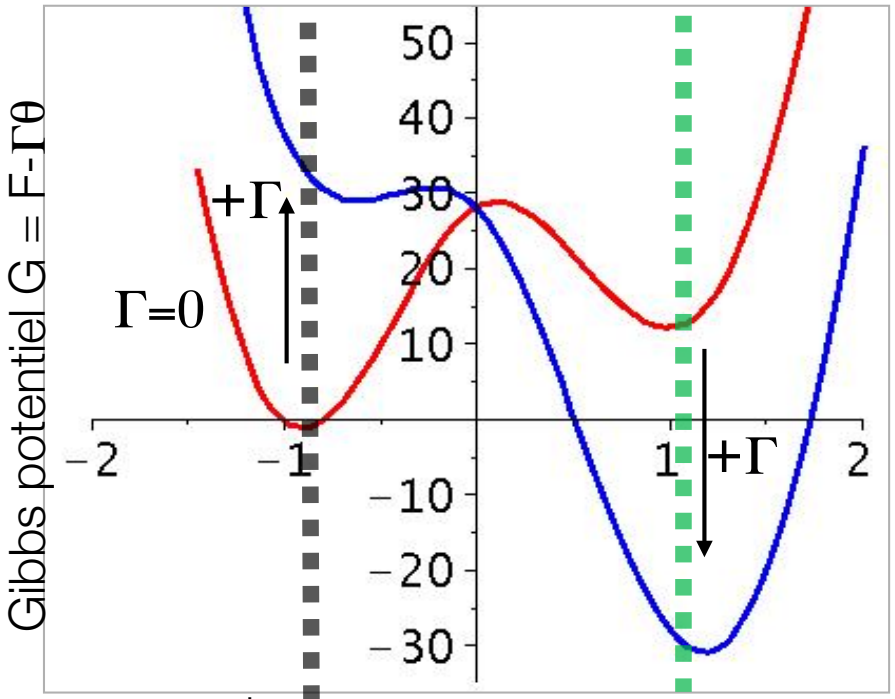
reversome

right handed <ΔLk> ~+1

chiral transition

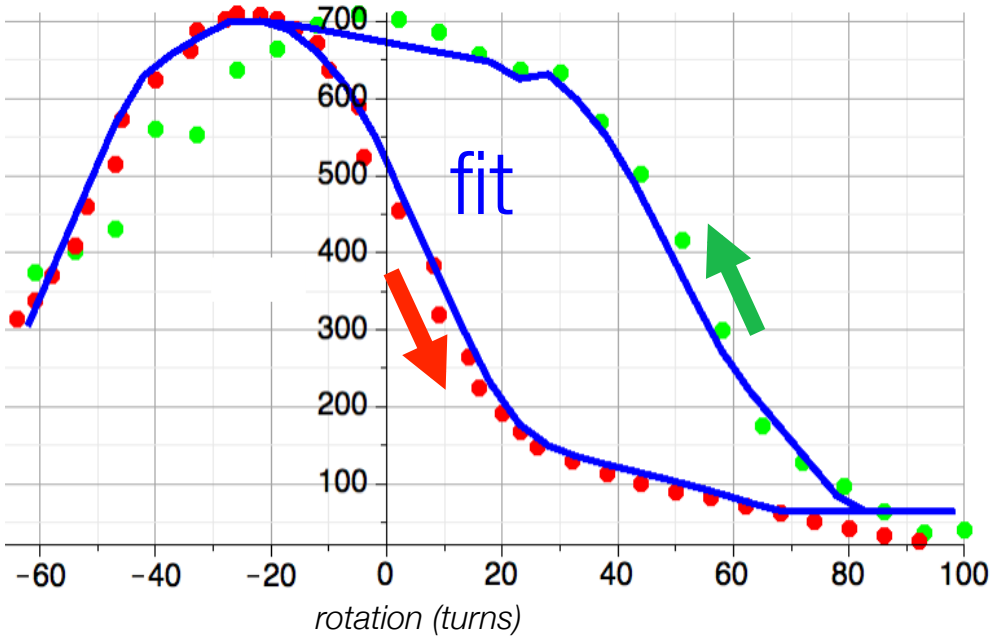


Statistical Mechanics and the Fit



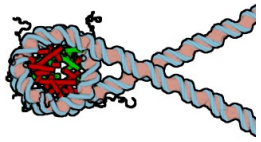
$$\text{nucleosome} \underset{k_{-1}}{\overset{k_1}{\leftrightarrows}} \text{reversome}$$

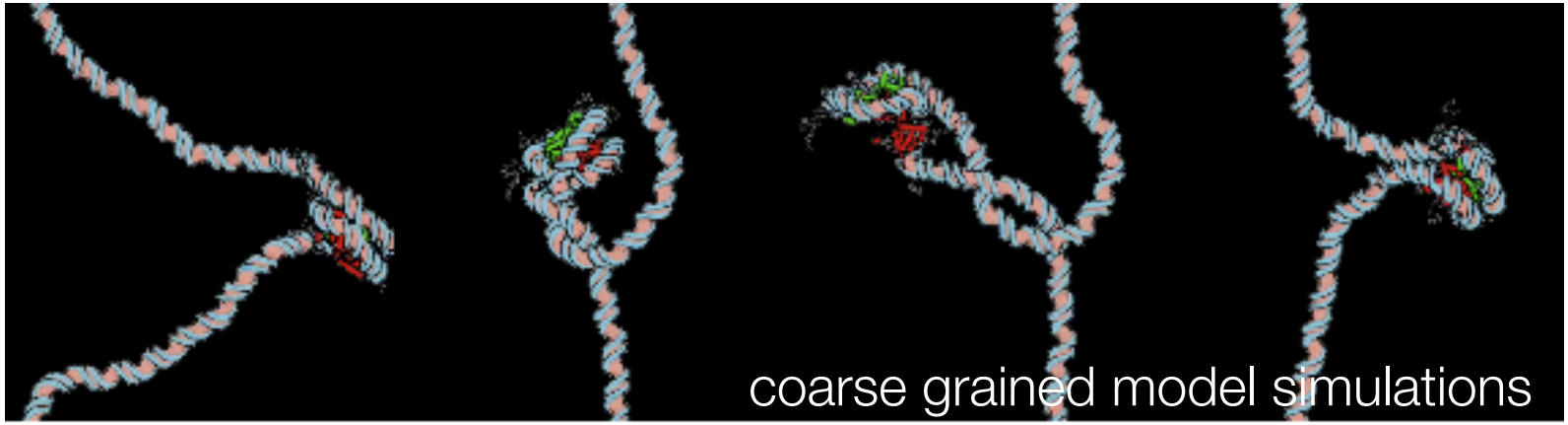
a torque-induced transition



Reversome: a Topological Buffer

absorbing torsion constraint trough transition to reversome





what about transcription? (next episode…)

M3V GROUP

- **Maria Barbi** (UPMC)
- **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)

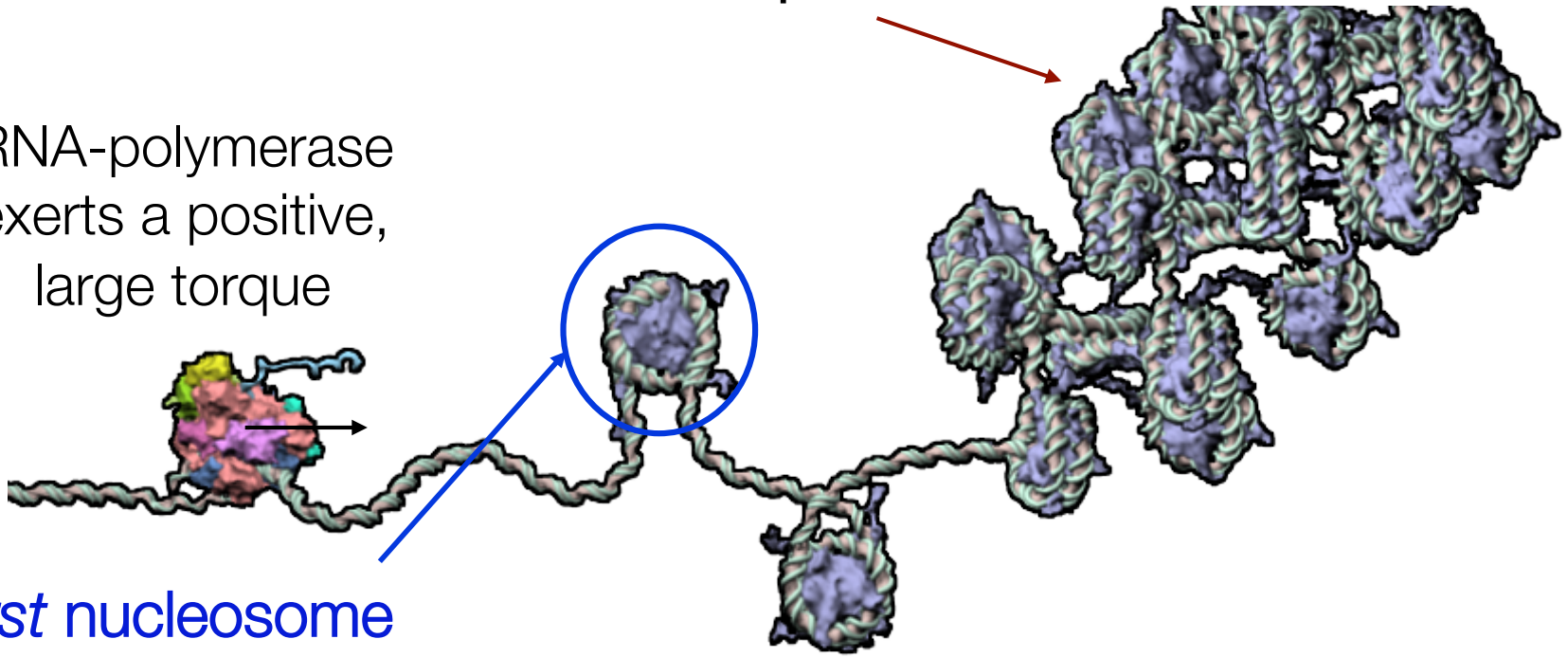
- M. Barbi et al. How the chromatin fiber deals with topological constraints Phys. Rev. E 2005
- J. Mozziconacci et al. A Physical Model for the Condensation … FEBS letters 2006
- A. Bancaud et al. Structural reorg. of chromatin fibers revealed by torsional nanomanipulation NSMB 2006
- A. Bancaud et al. Torsional manipulation of chromatin fibers reveals a highly flexible structure Mol Cell 2007
- C. Lavelle Transcription elongation through a chromatin template Biochimie 2007
- C. Lavelle Forces and torques in the nucleus: … Biochem. Cell Biol. 2009
- J. Zlatanova & JM. Victor How are nucleosomes disrupted during transcription elongation? HFSP J. 2009
- C. Bécavin et al. Transcription within Condensed Chromatin: … Biophys J. 2009
- P. Recouvreux et al. Linker histones incorporation mantains fiber plasticity Biophys. J. 2011

THE REVERSOME WAVE

back to *in vivo:* transcription in a compact fiber

compact fiber ⇒ steric hindrance prevents nucleosome transitions

RNA-polymerase exerts a positive, large torque

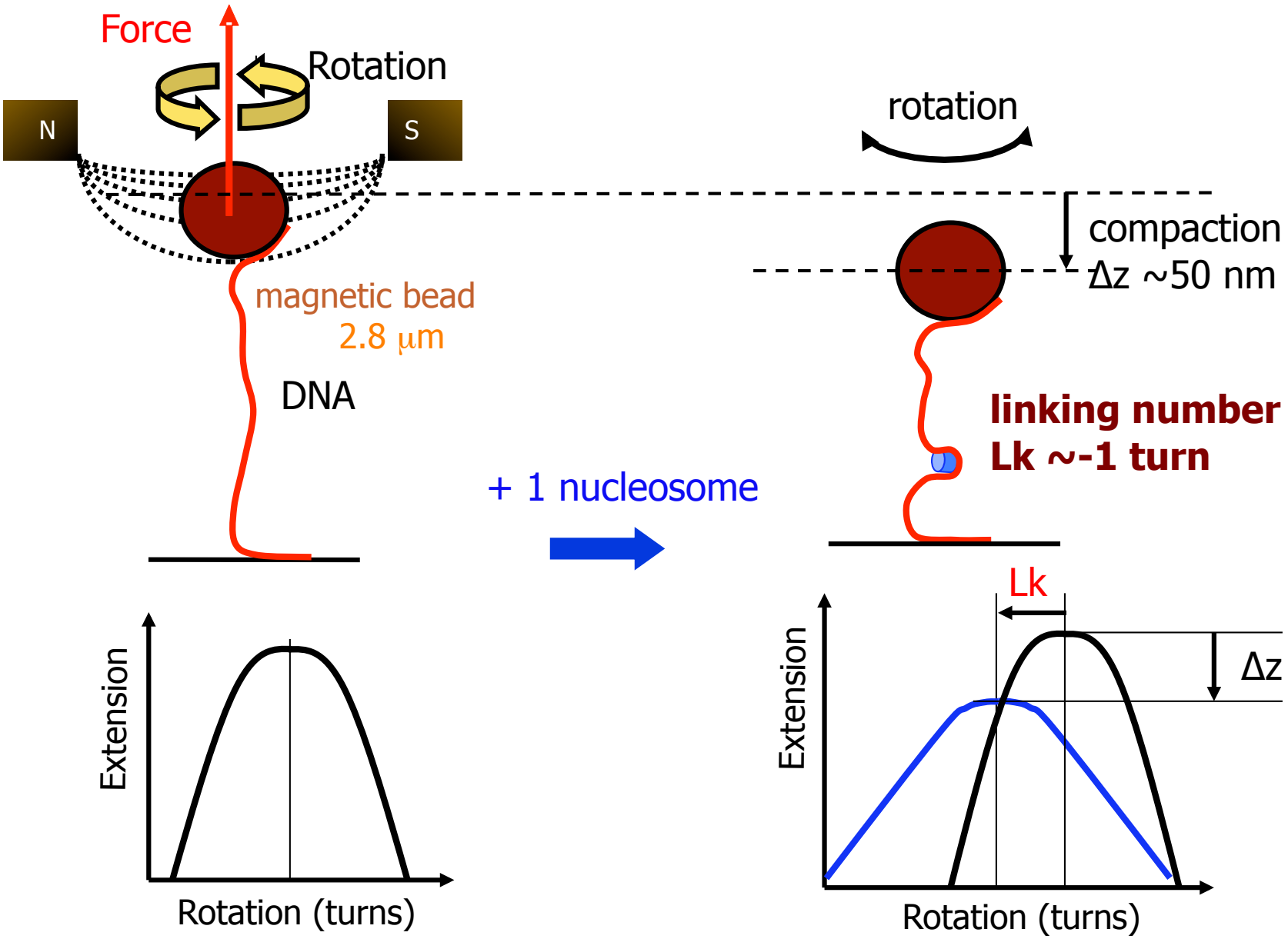


the *first* nucleosome pass to reversome, then the second…

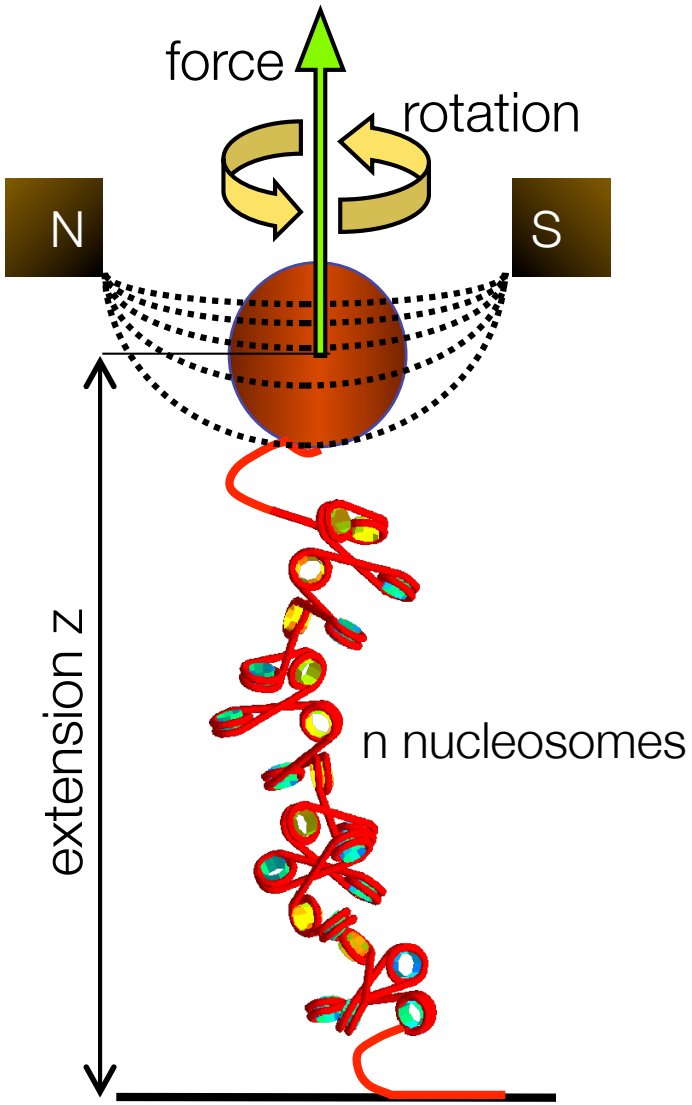
⇒ creation of a “reversome front”

v_{RNApol} = 20 bps/s → 2 turns/s → 1reversome/s → v_{front} = 200 bps/s

Signature of Nucleosomes

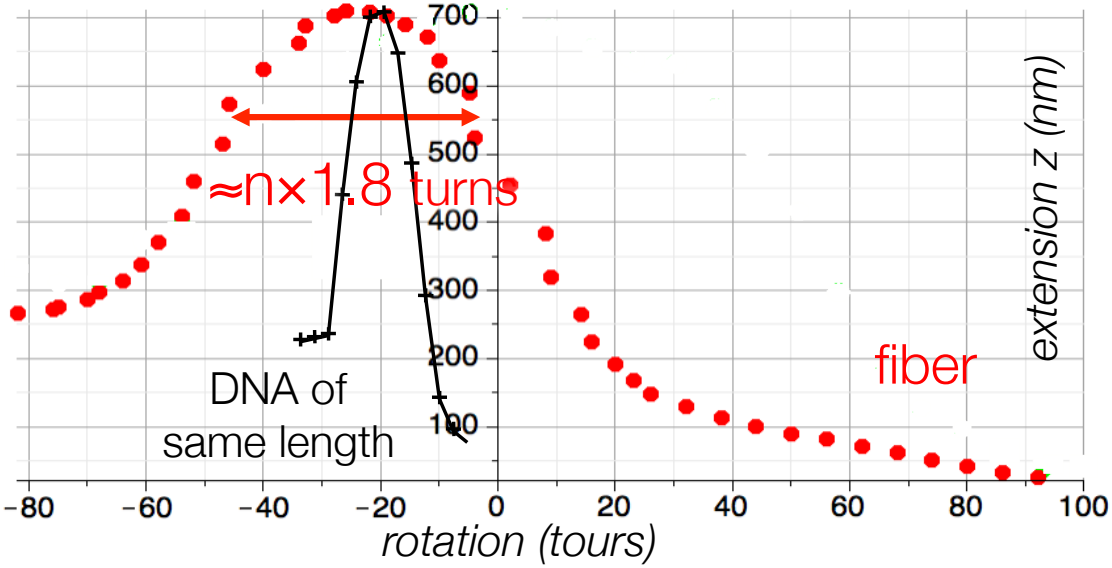


Fiber under Magnetic Tweezers

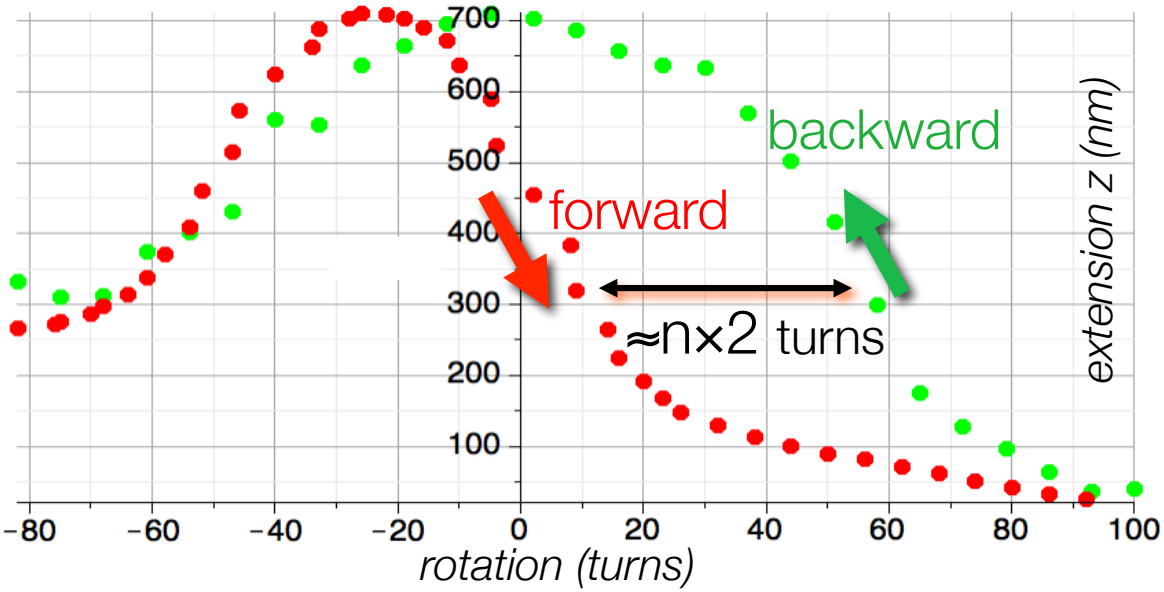


experiments by LJ Viovy
Institut Curie, Paris

1. torsional resilience

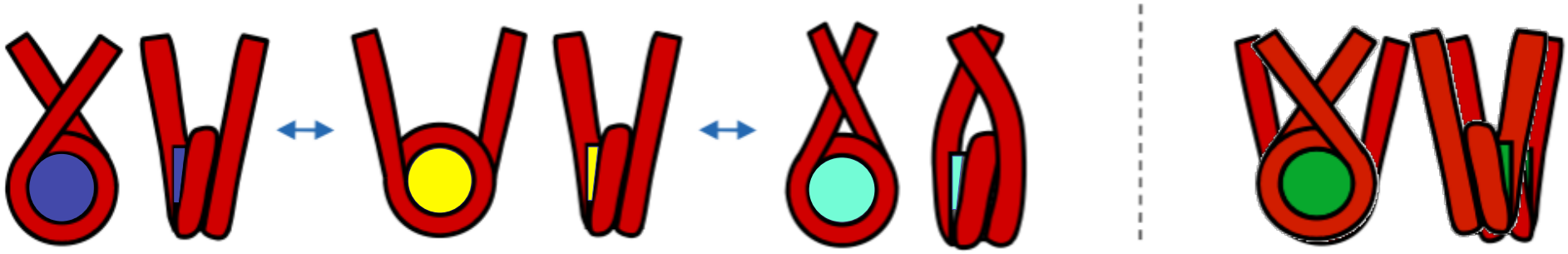


2. hysteresis (higher torsion)



4 Nucleosome States

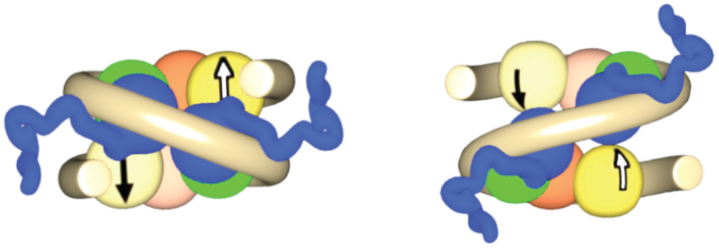
a plastic nucleosome!



negatively crossed | open | positively crossed | reversome

chiral transition

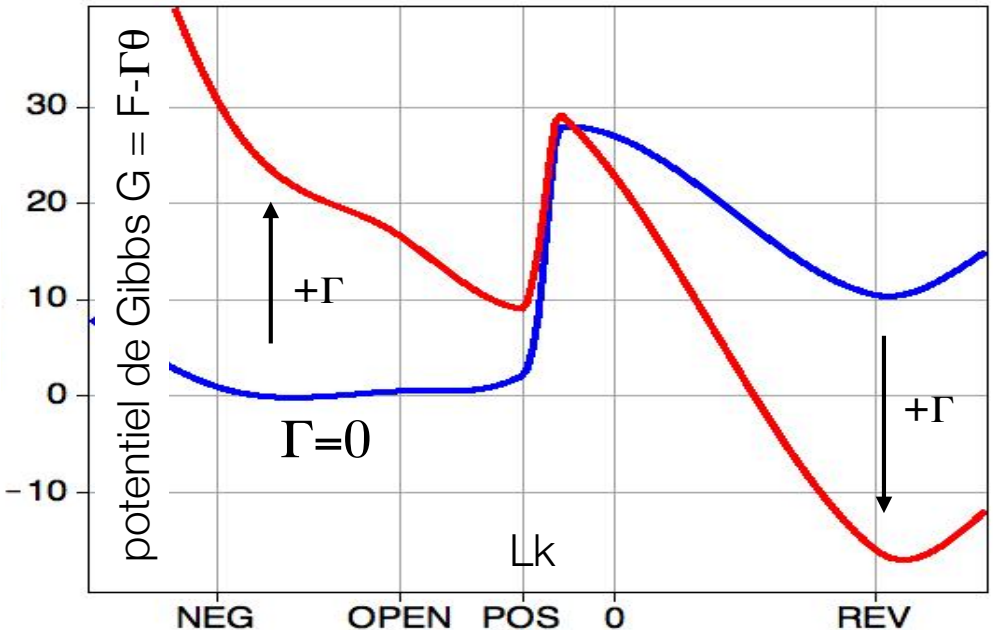
state	Neg.	Open	Pos.	barrier	Rev.
α	54°	-30°	30°	/	30°
β	115°	90°	115°	/	80°
d (nm)	4.1	8.3	2.8	/	2.0
ΔLk per nuc.	-1.4	-0.4	-0.2	-0.15	+0.9
E (kT)	0.7	0	2	28	10

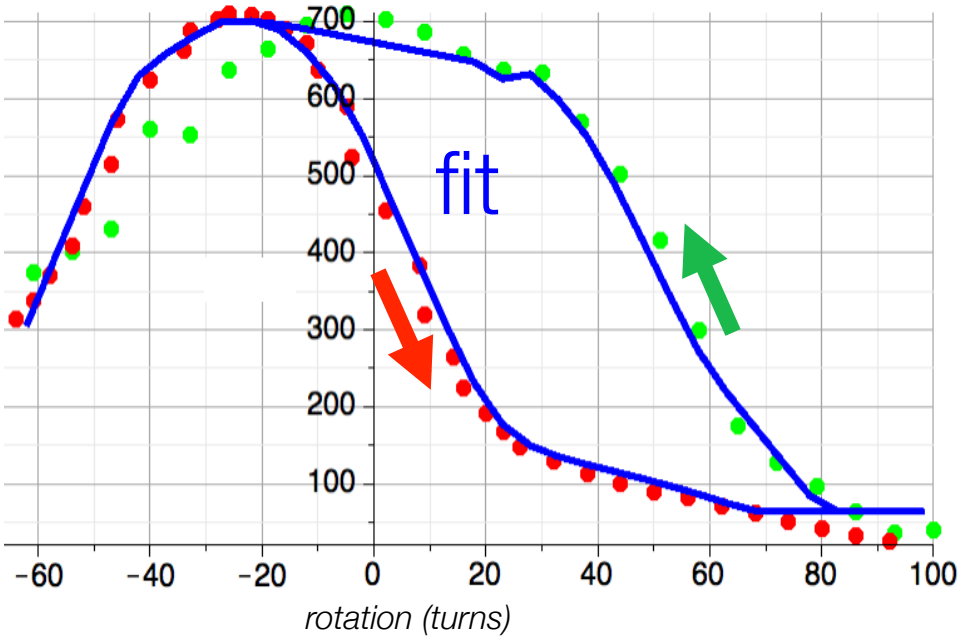


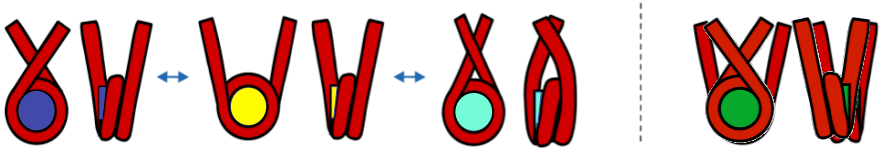
Statistical Mechanics and the Fit

eq. eq. k_1
nég. ↔ ouv. ↔ pos. ⇆ 4ème état
k_{-1}

a torque-induced transition

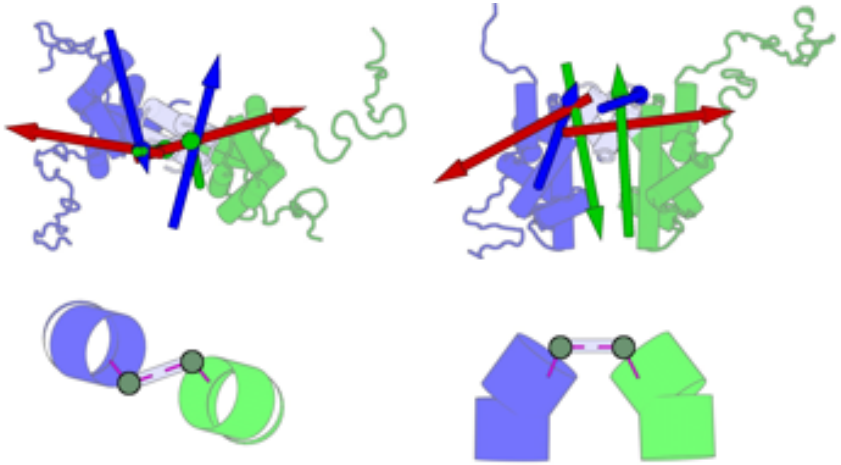




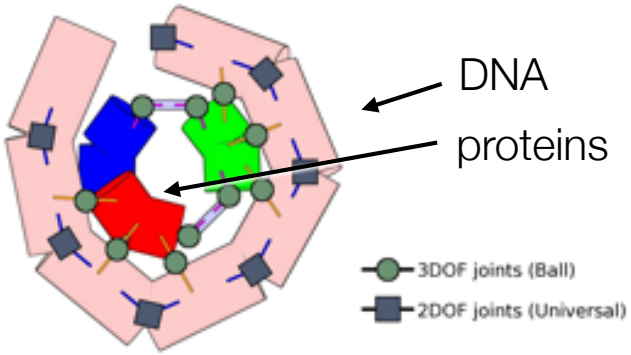


Rigid Body Dynamics + Skeletal Animation

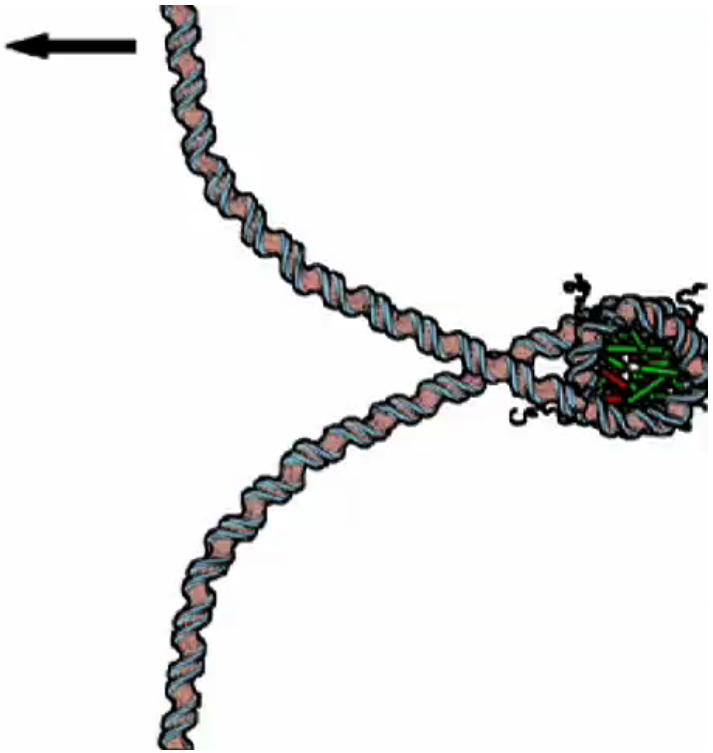
1. normal modes analysis



2. nucleosome structuration

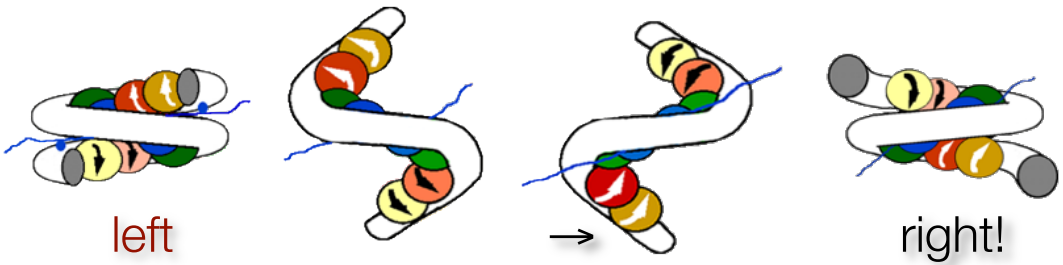


3. Brownian dynamics at constant torque

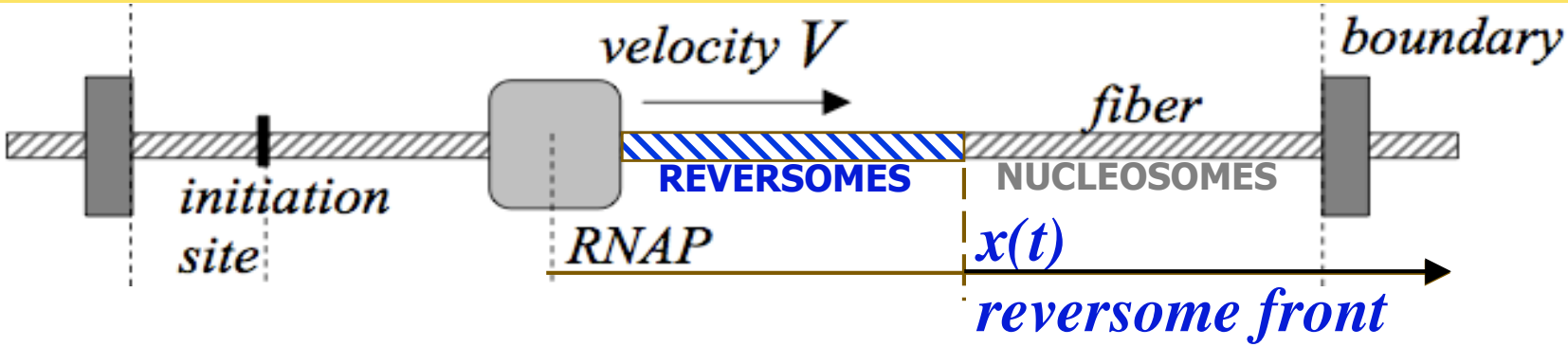


Animation by Hua Wong

result: chiral transition:



Reversome Front Speed



Becavin et al, Bioph J 2009

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 (ΔLk nucl to rev)

reversome fiber torsion (<<)

Λ *linear density*

Γ *applied torque*

L_P *twist pers. length*

$\tau = \dfrac{\Gamma}{L_P k_B T}$ *fiber torsion*

τ_c *critical torsion*

reversome front progression:

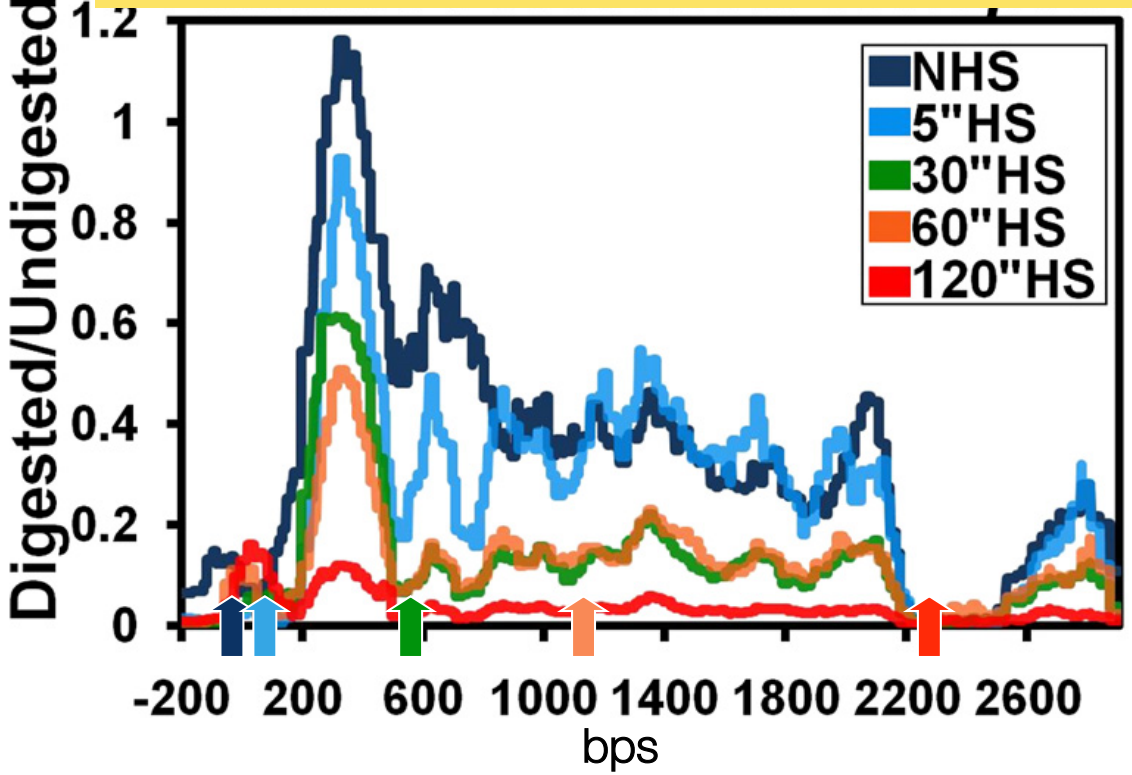
$$x(t) = v\,t + c, \quad v = \frac{\omega_0}{2\pi\ \Lambda\ \Delta Lk + \tau_c} \simeq \frac{\omega_0 / 2\pi}{\Lambda\ \Delta Lk}$$

→ V = 1 nucl./s

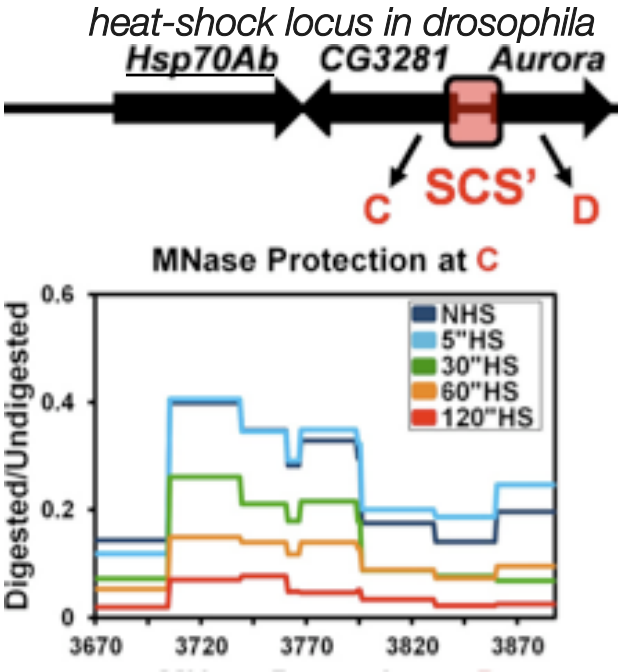
= 200 bps/s

Petesh-Lis Experiment

a wave of nucleosome disruption



(Petesh and Lis, Cell 2008)



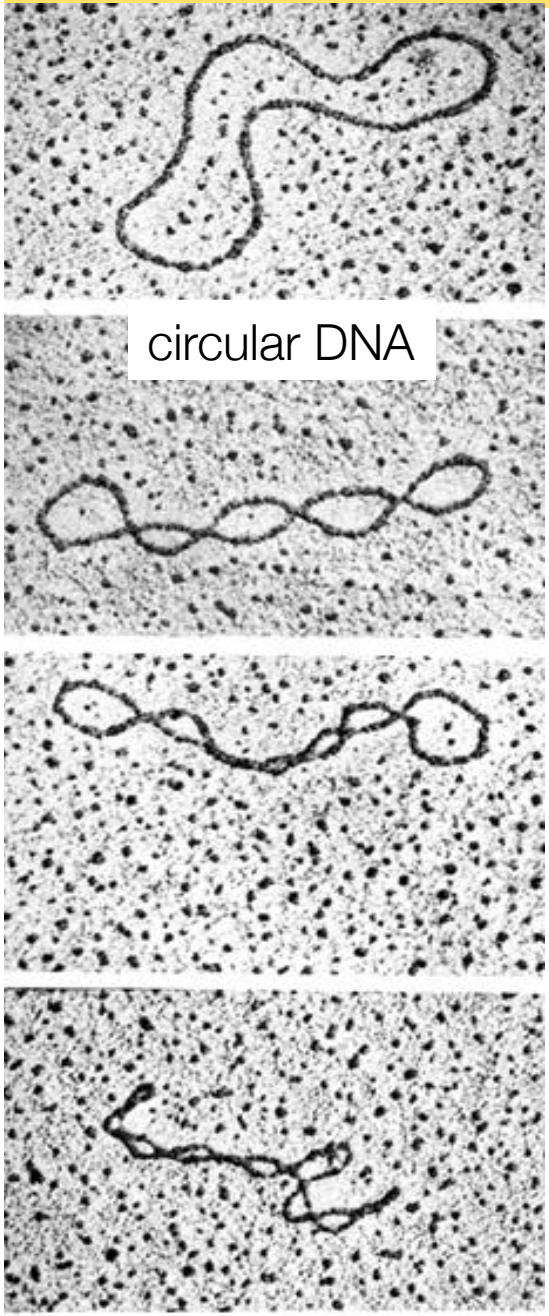
30" : all the loop and only the loop

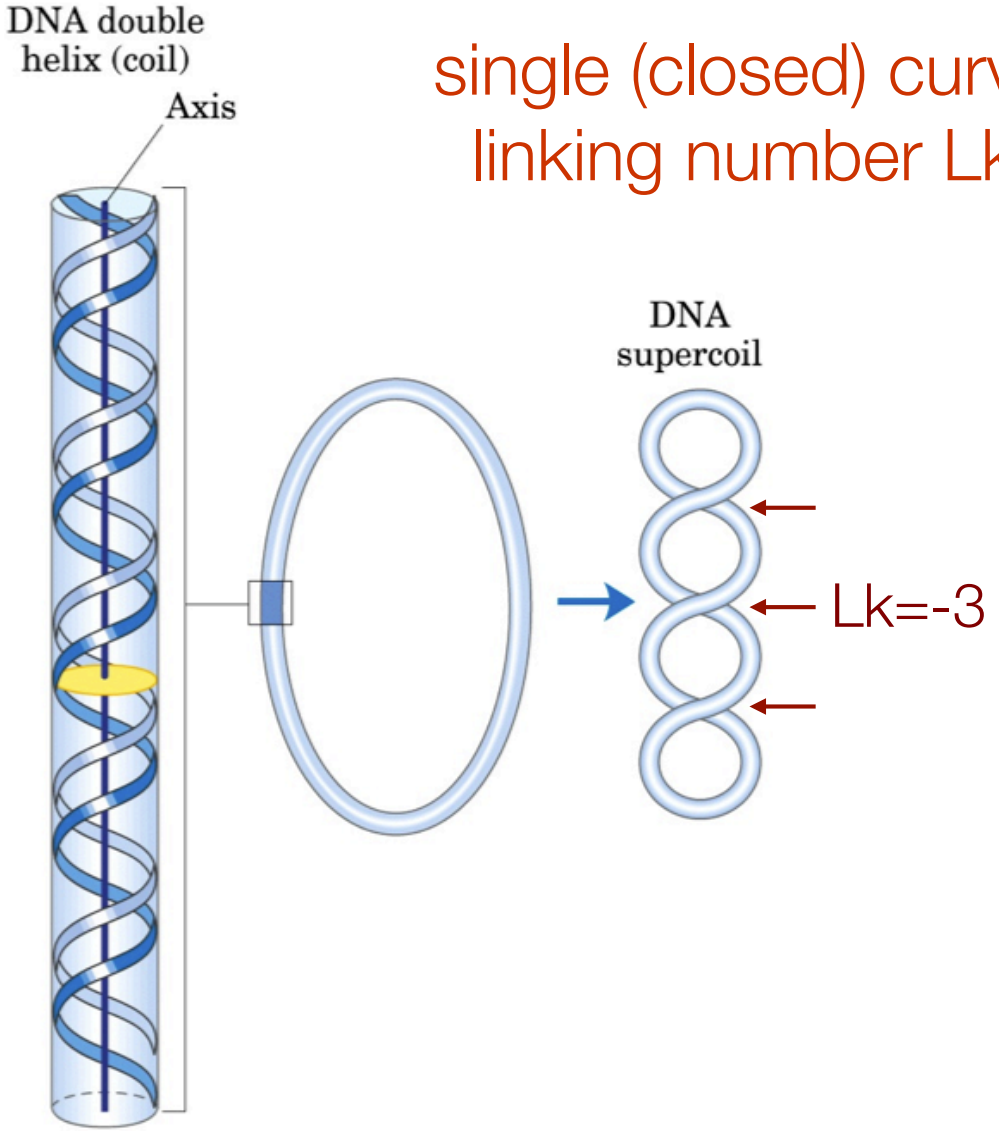
reversome-wave interpretation:

- 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 pbs
- …

(Zlatanova and Victor, HFSP J 2009)

Topology of DNA





single (closed) curve
linking number Lk