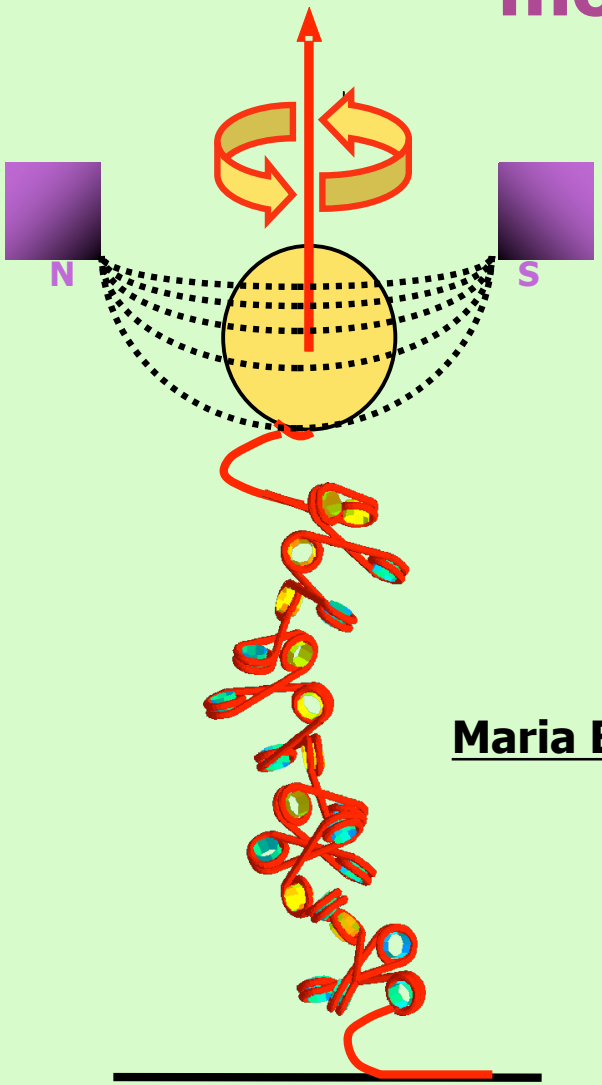


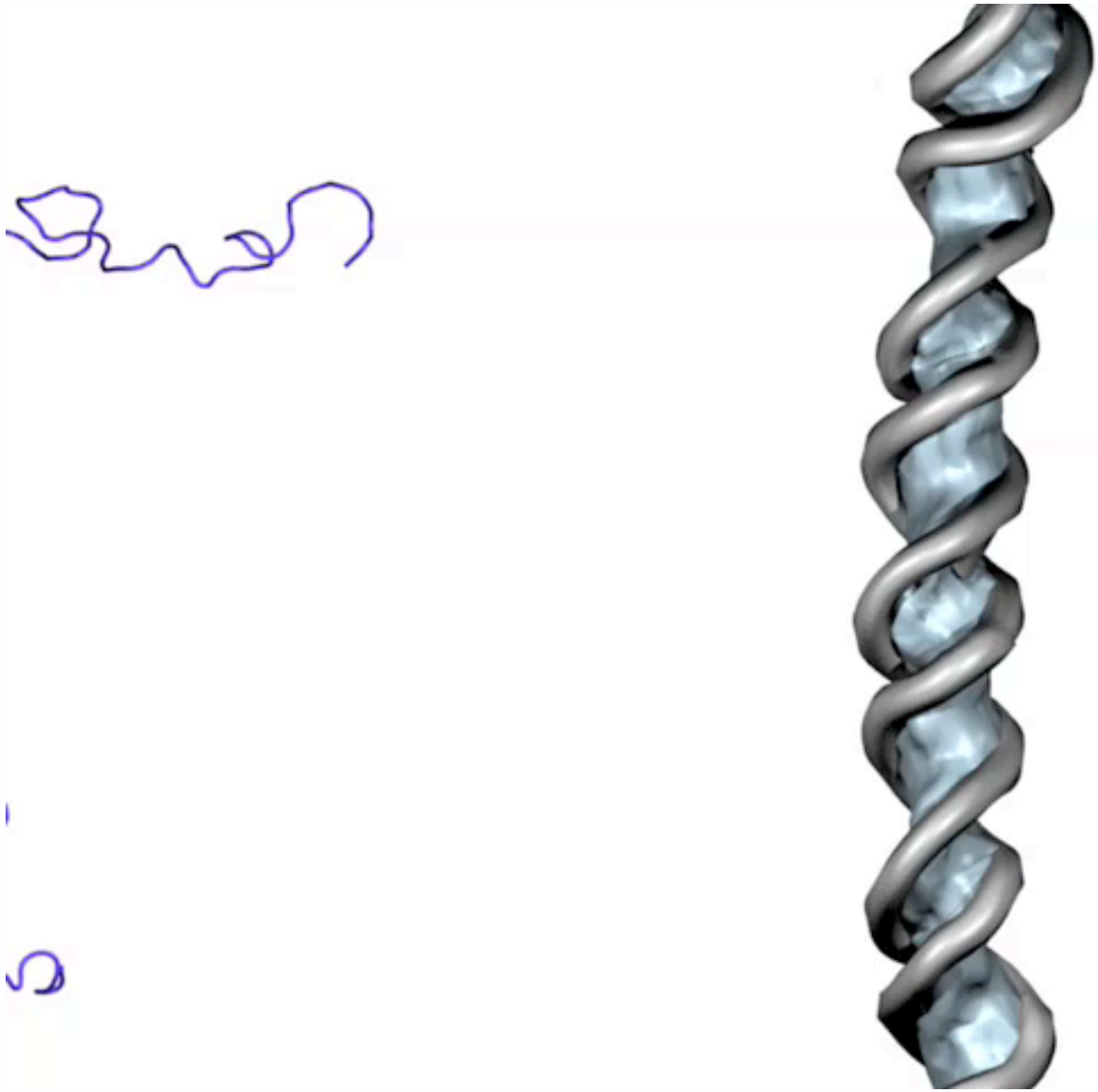
modeling the hysteretic behavior of chromatin fibers under magnetic tweezers:

why are nucleosomes left handed?

Maria Barbi, **Jean-Marc Victor, Julien Mozziconacci, Hua Wong**
Laboratoire de Physique Théorique
de la Matière Condensée,
Paris, France

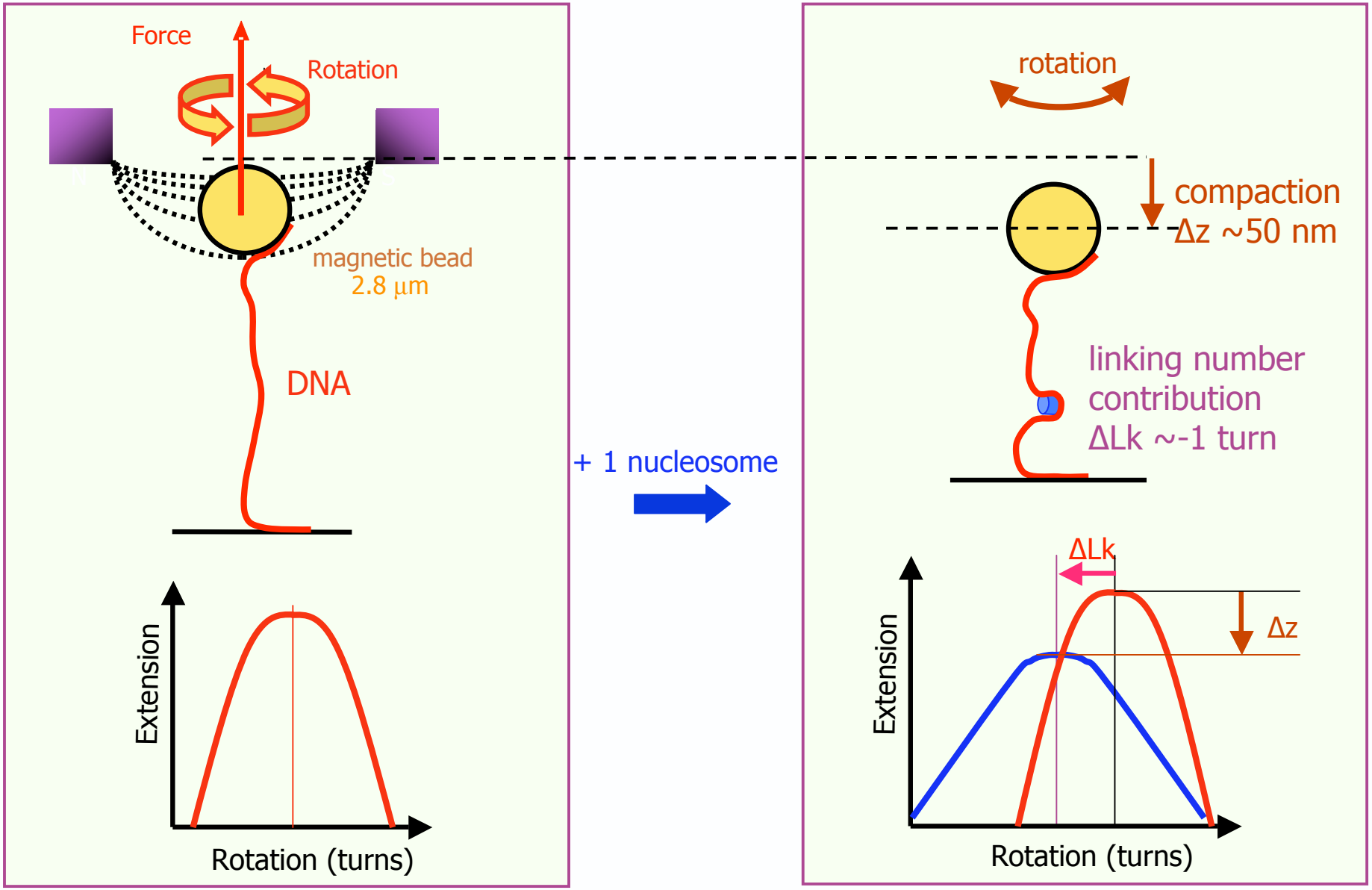
experimental group:
Jean-Louis Viovy, Institut Curie, Paris

nucleosome structure

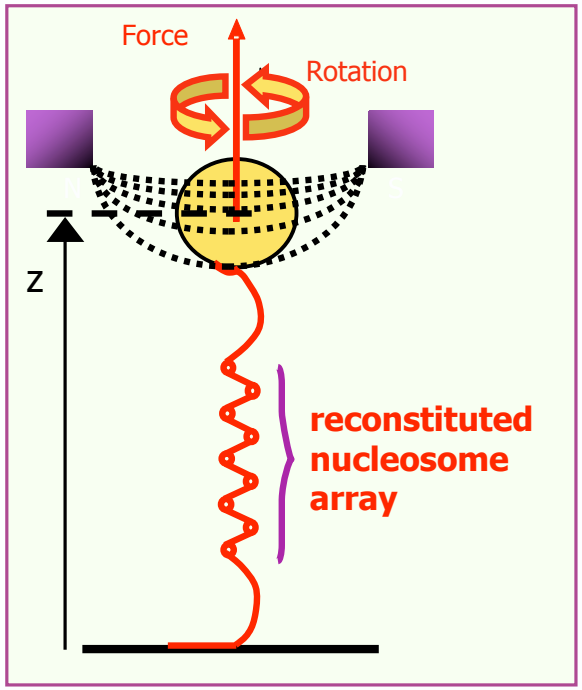


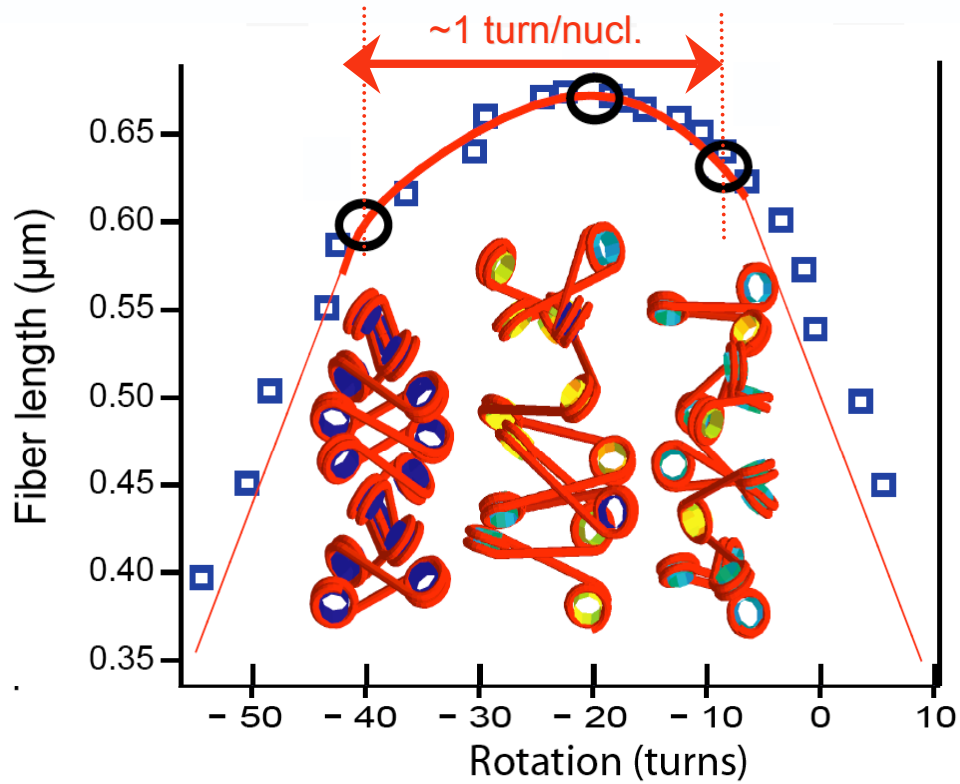
Animation by Hua Wong

probing structural features with magnetic tweezers: **nucleosome**



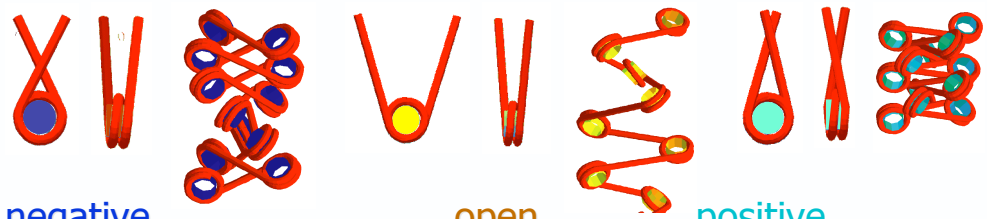
probing structural features with magnetic tweezers: **FIBER**





Model:

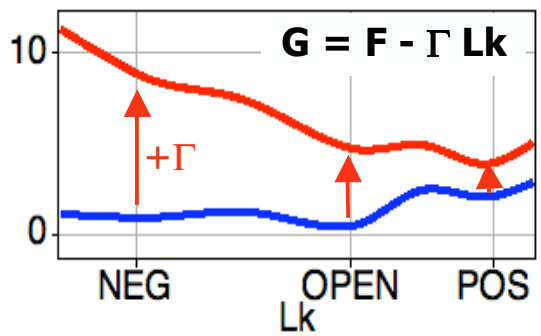
torque-dependent equilibrium between the 3 states of nucleosome



negative
ΔLk~-1.4

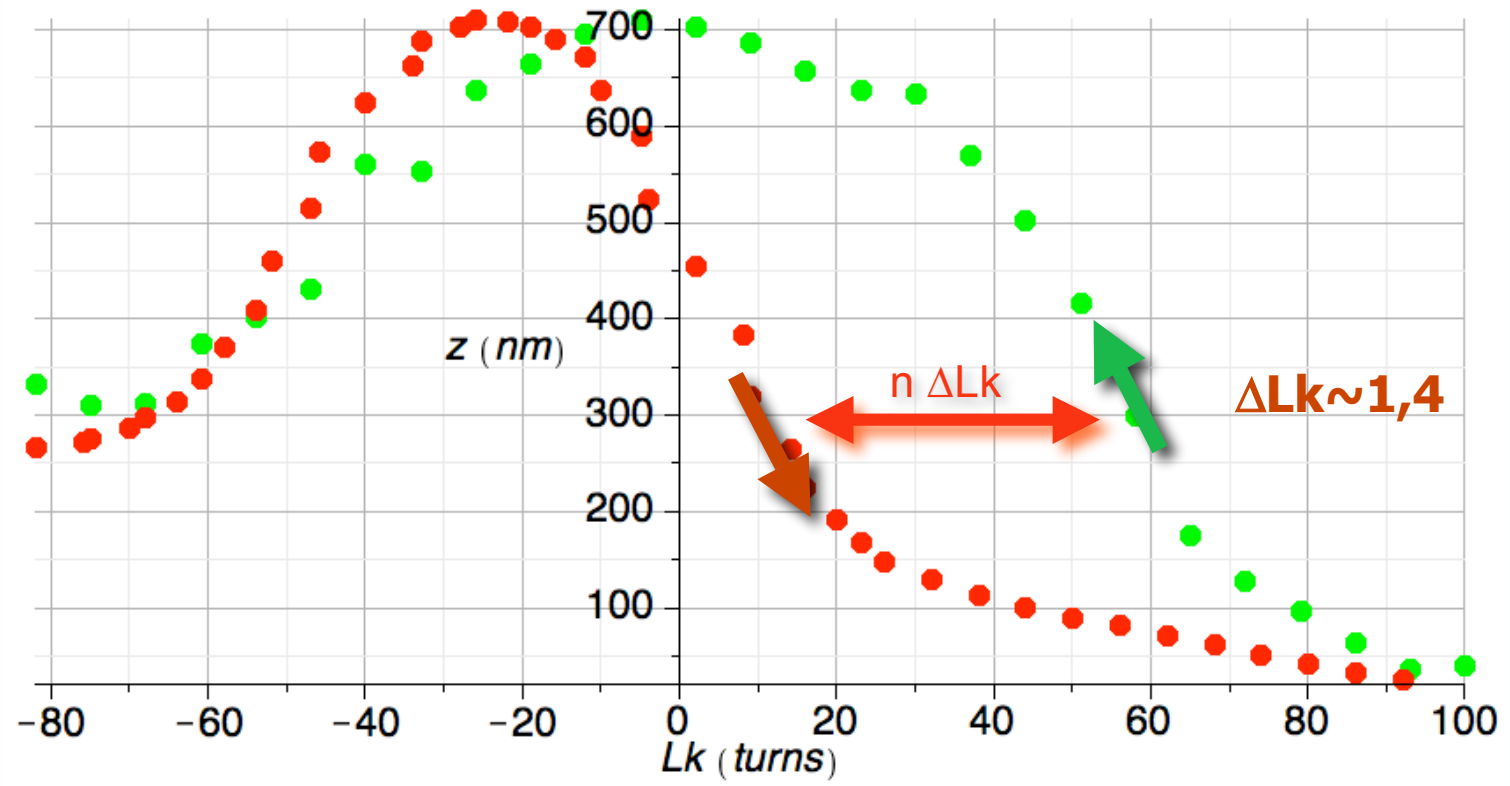
open
ΔLk~-0.7

positive
ΔLk~-0.4



Bancaud et al, NSMB 2006

hysteretic response under extensive torque

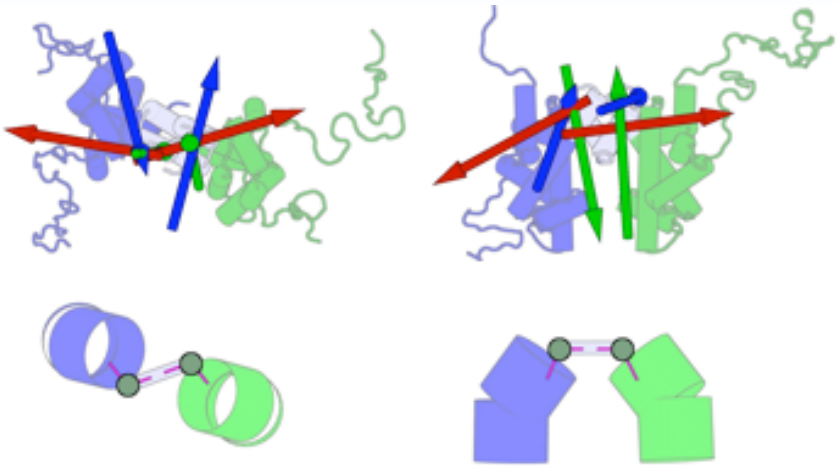


- not explained by nucleosome-nucleosome interactions
- compatible with a nucleosome internal rearrangement: **transition to a metastable altered state with** a larger (positive) ΔLk

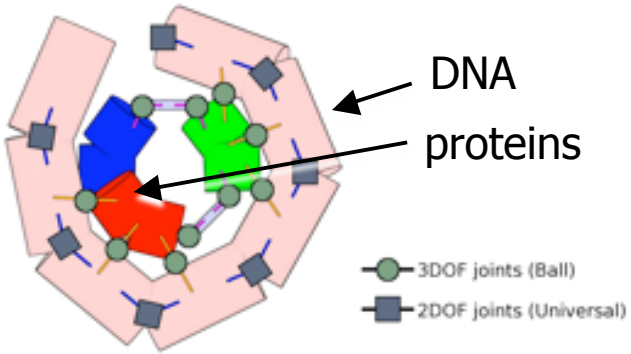
Bancaud et al, Mol Cell 2007

Rigid Body Dynamics with Skeletal Animation

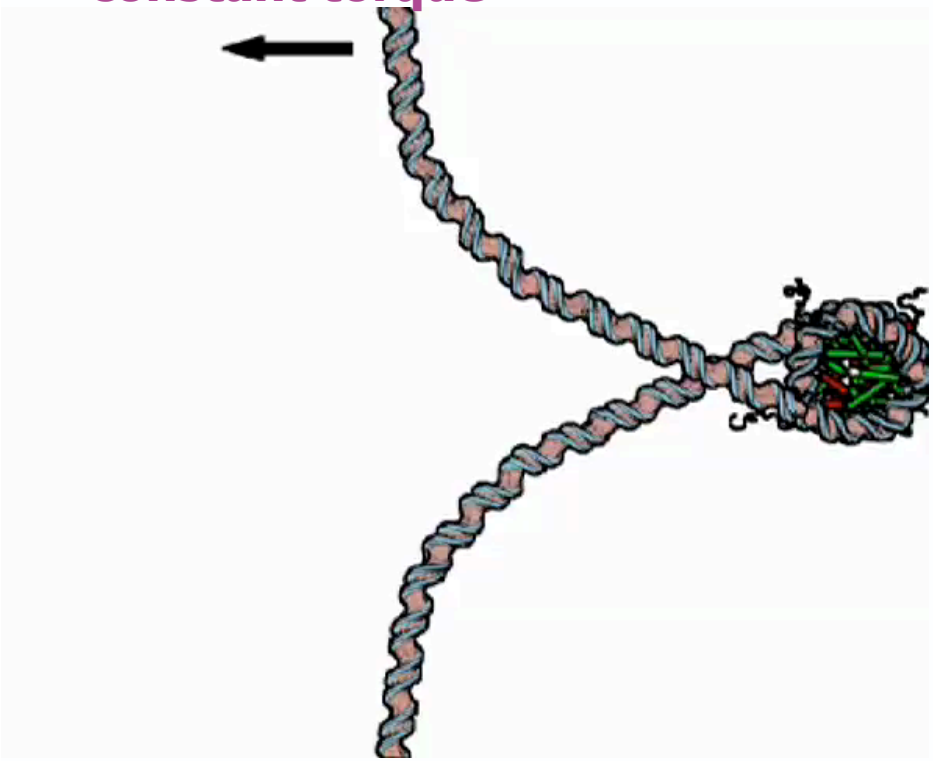
1. normal modes analysis



2. nucleosome structuration

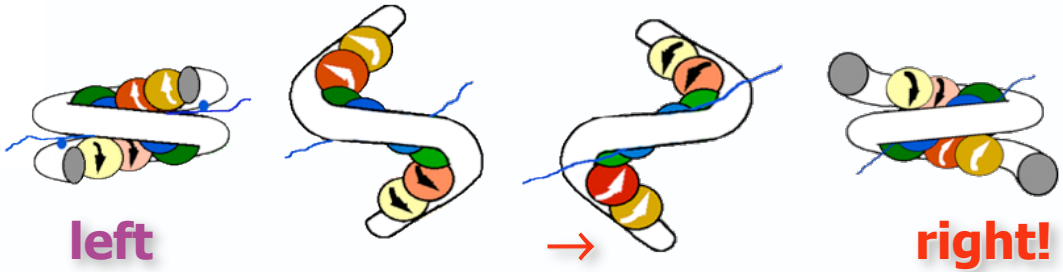


3. Brownian dynamics under constant torque



Animation by Hua Wong

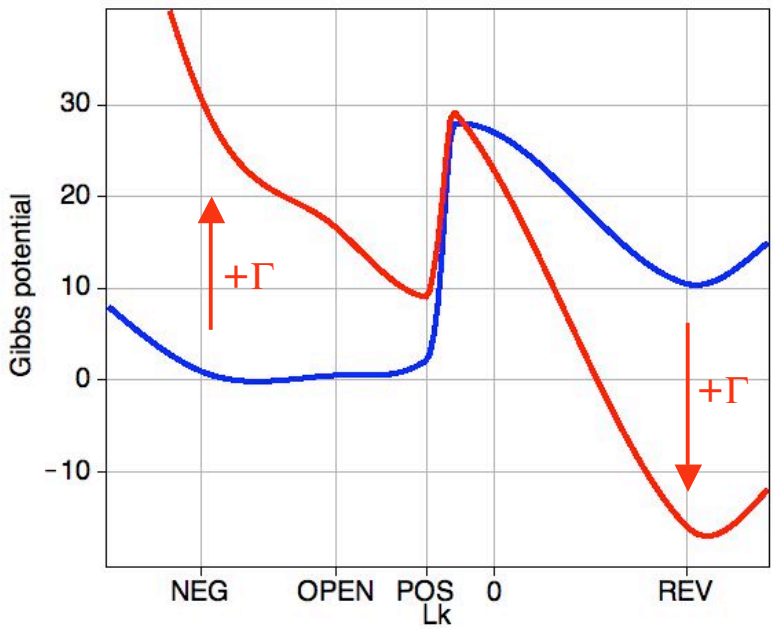
result: chiral transition:

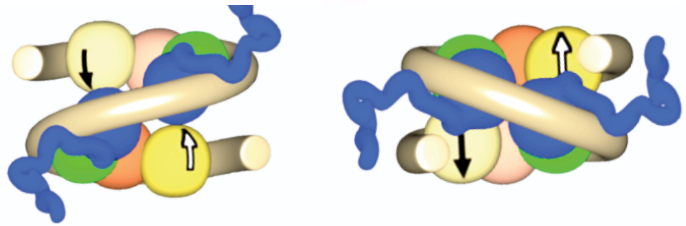


Reversome : a **right handed** metastable state…

stabilized by the applied torque

data fit: statistical equilibrium **between the 3 states**
+ kinetic equations for the passage to reversome:

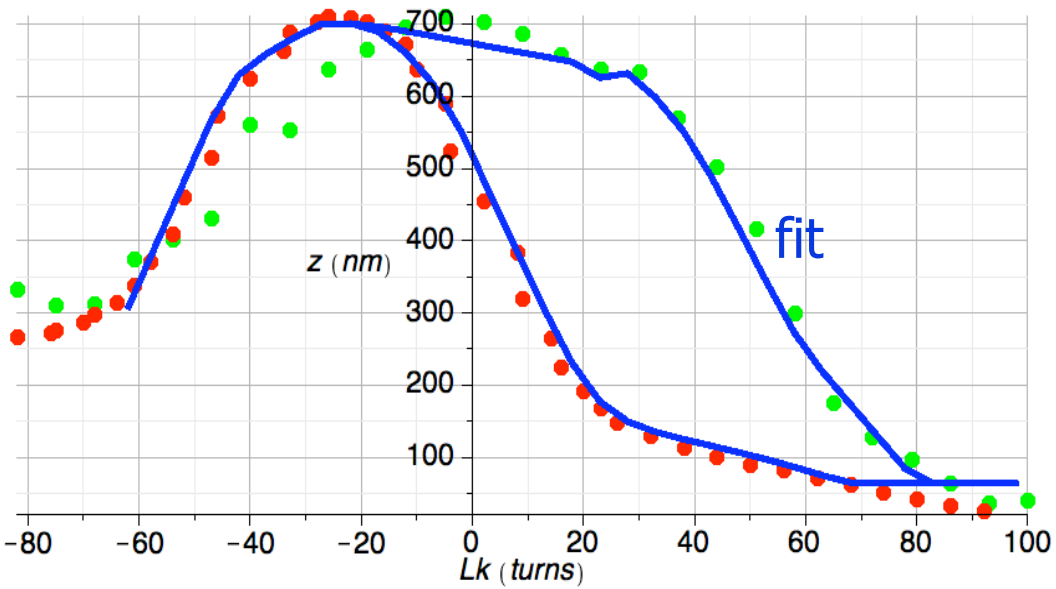




left $\xrightarrow{+\Gamma}$ **right**

ΔLk~-0.4 ΔLk>~+1

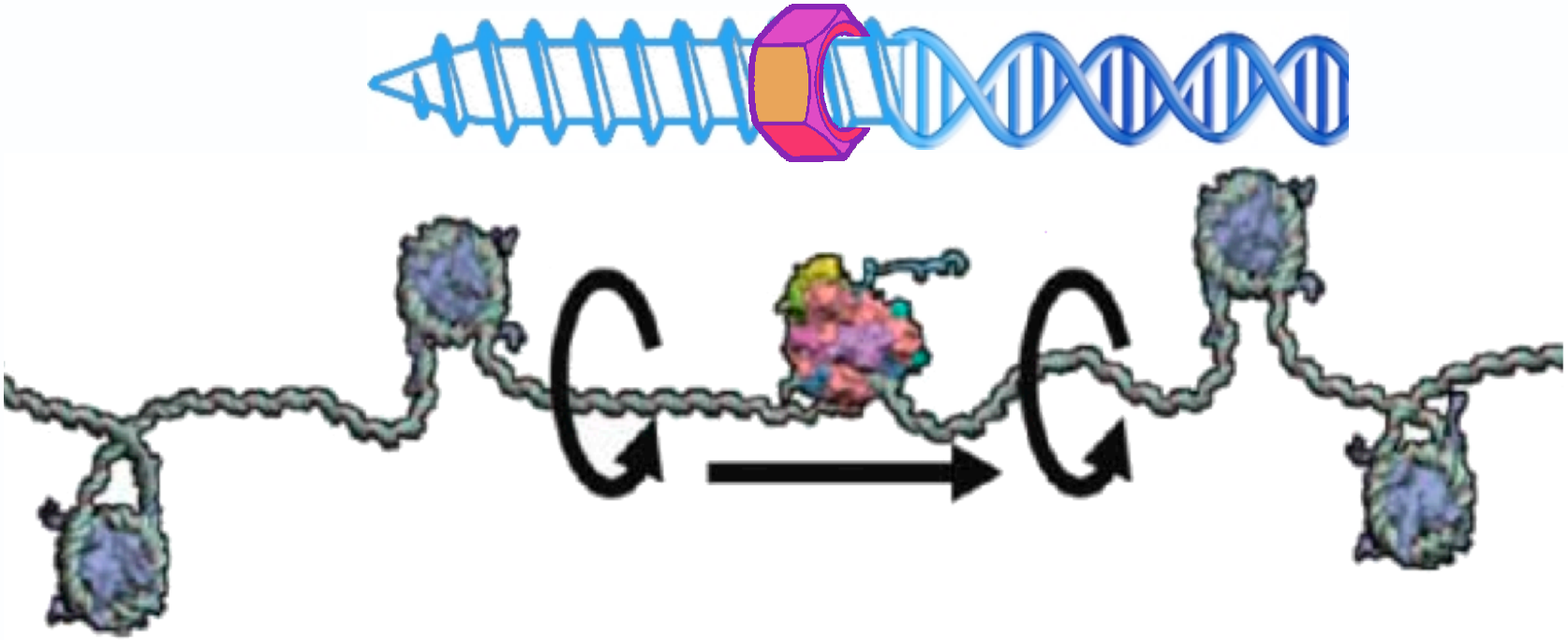
$$\text{neg.} \overset{\text{eq.}}{\leftrightarrow} \text{open} \overset{\text{eq.}}{\leftrightarrow} \text{pos.} \underset{k_{-1}}{\overset{k_1}{\leftrightarrows}} \text{reversome}$$



So, why *standard* nucleosome is left handed ?

***In vivo* prediction:**

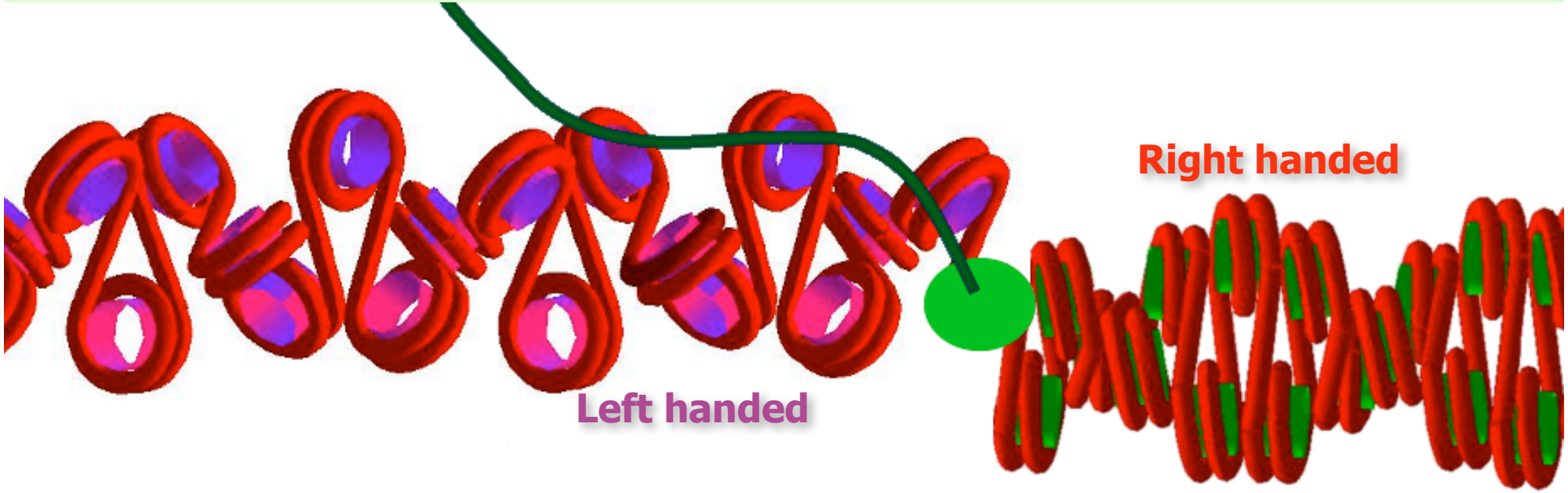
- **RNA-polymerase fixed in the transcription complex**
- **right handed DNA screws through the polymerase**



⇒ **RNA polymerase exerts a pulling force and a positive torque on DNA**

So, why *standard* nucleosome is left handed ?

Conclusion: a possible functional role for nucleosome:

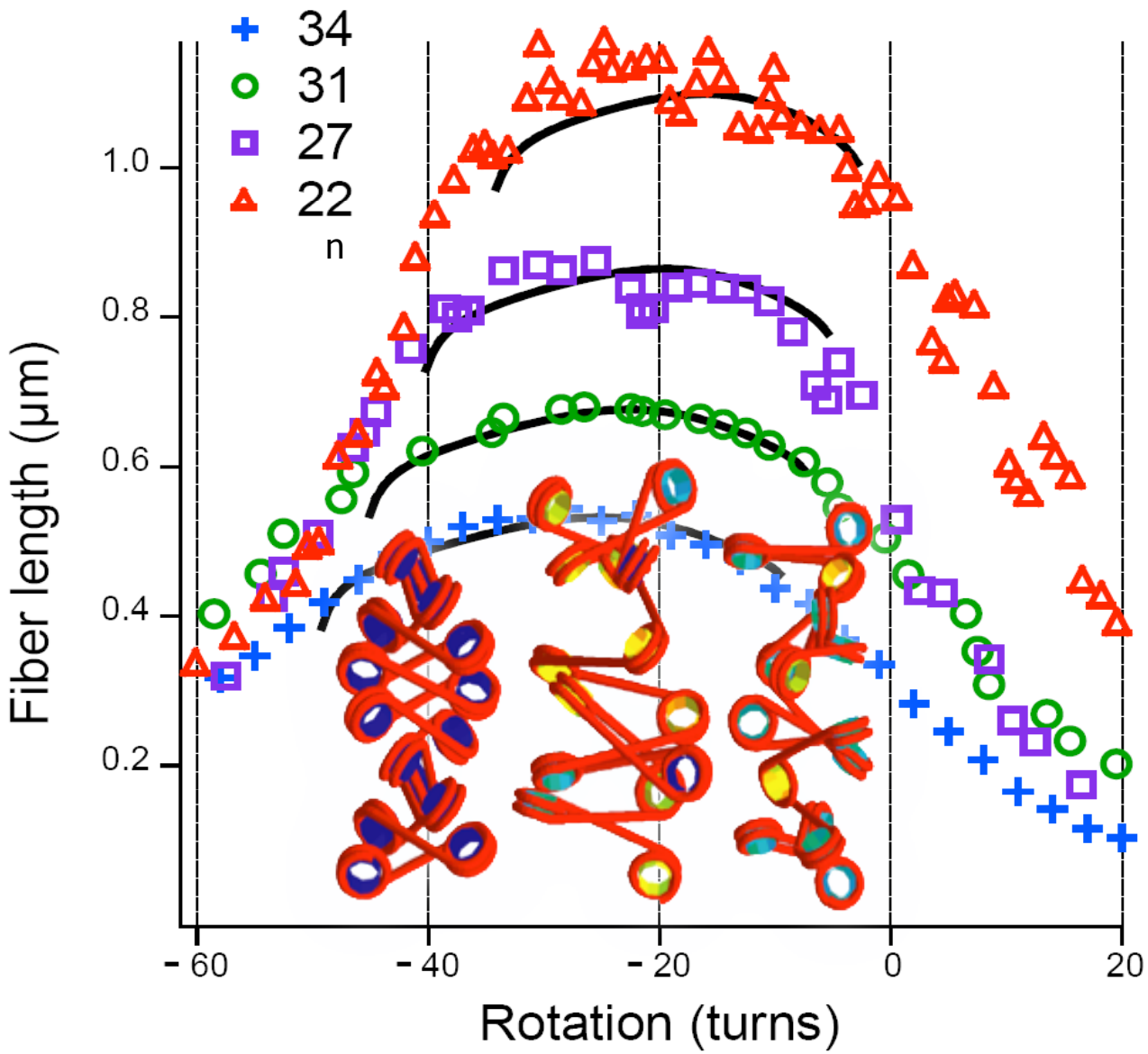


- **nucleosome → reversome transition absorbs turns and thus releases supercoiling constraint**
- **reversome is a destabilized state favoring the passage of the RNA-polymerase**

M3V Group

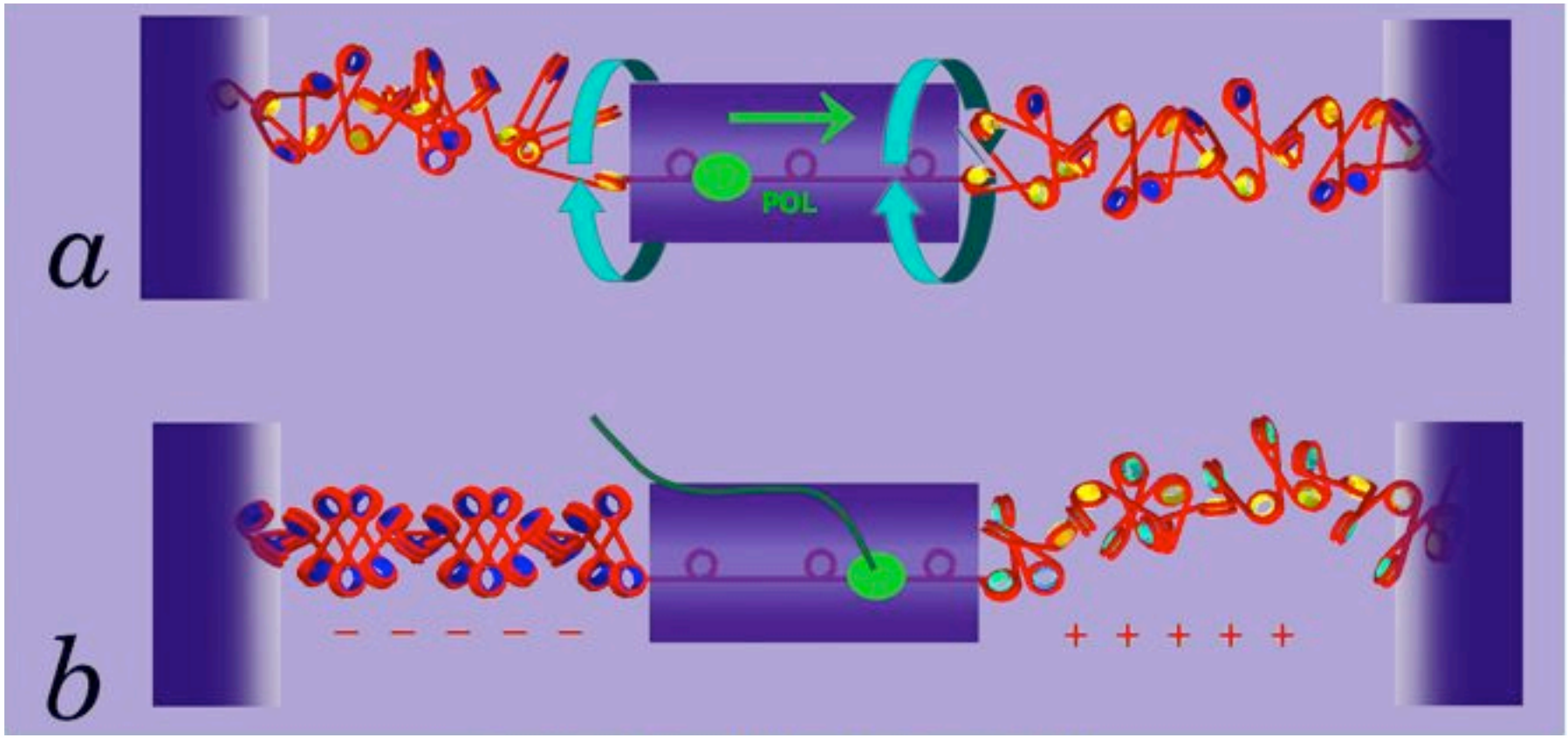
- **Maria Barbi** (UPMC)
- **Annick Lesne** (CNRS)
- **Jean-Marc Victor** (CNRS)
- **Julien Mozziconacci** (doc 2001-2004,
  postdoc ANR 2006–2008)
- **Hua Wong** (doc 2005-2008)
- **Fabien Paillusson** (doc 2007-2010)
- **Christophe Becavin** (doc 2007-2010)
- **Christophe Lavelle** (postdoc 2003-2004)

Experimental data fit for different numbers of nucleosome



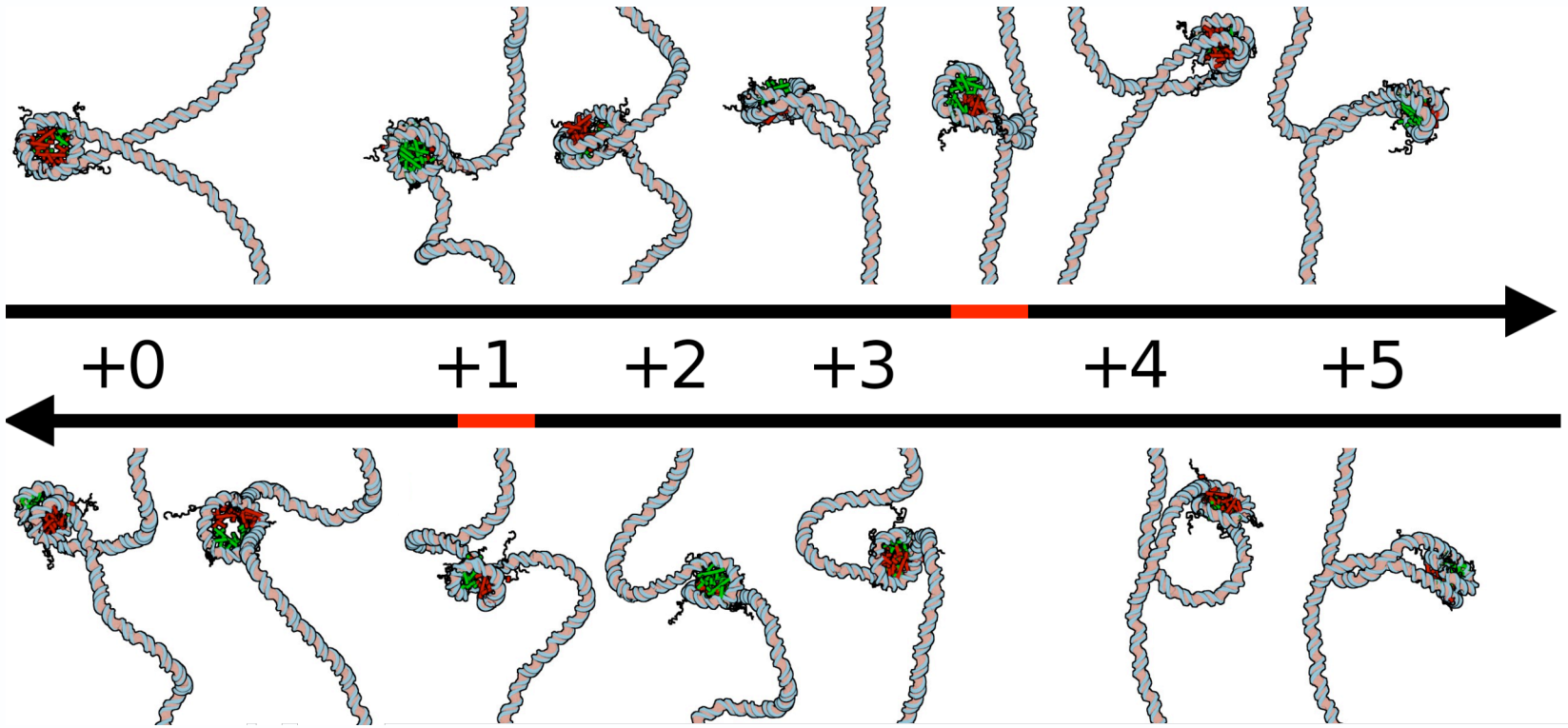
Bancaud et al, NSMB 2006

The three states acts as a topological buffer



(Bancaud et al, NSMB 2006)

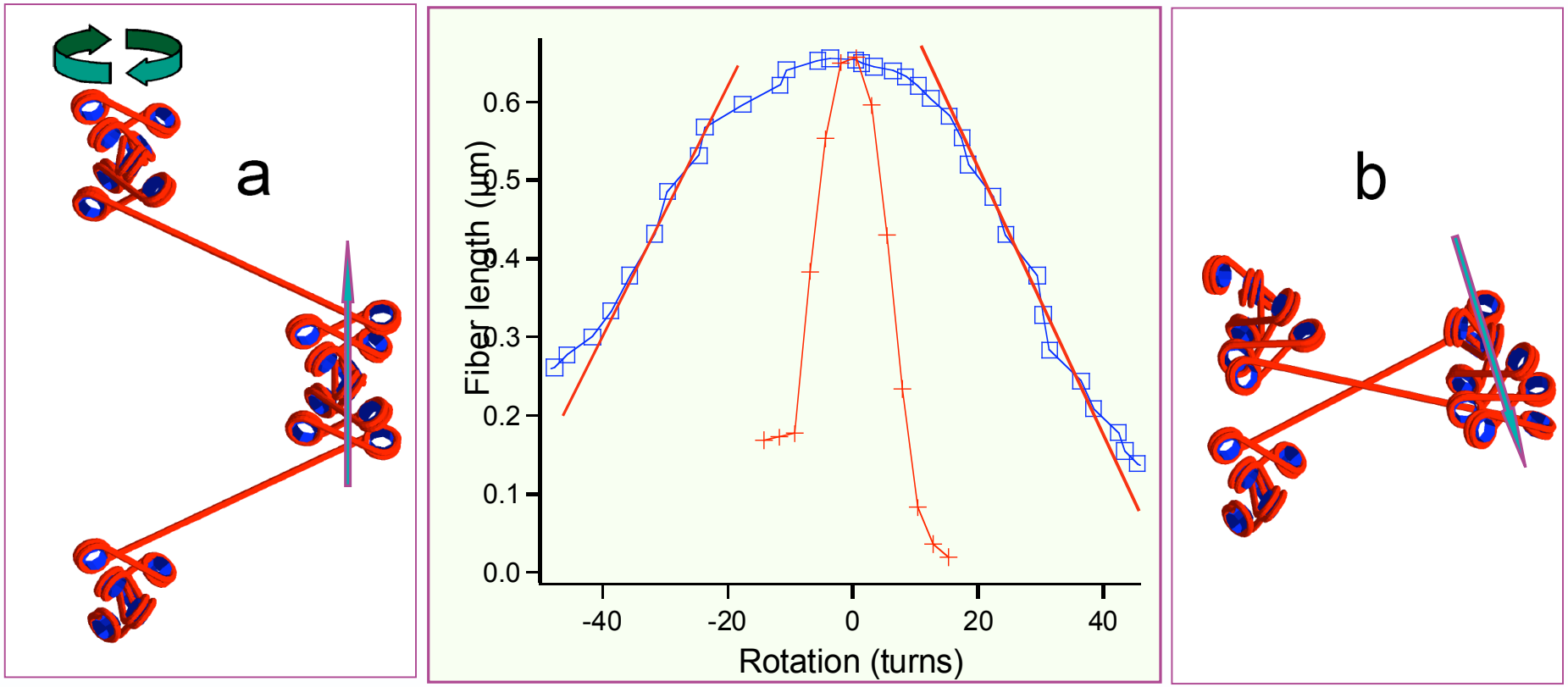
Looking at the transition path



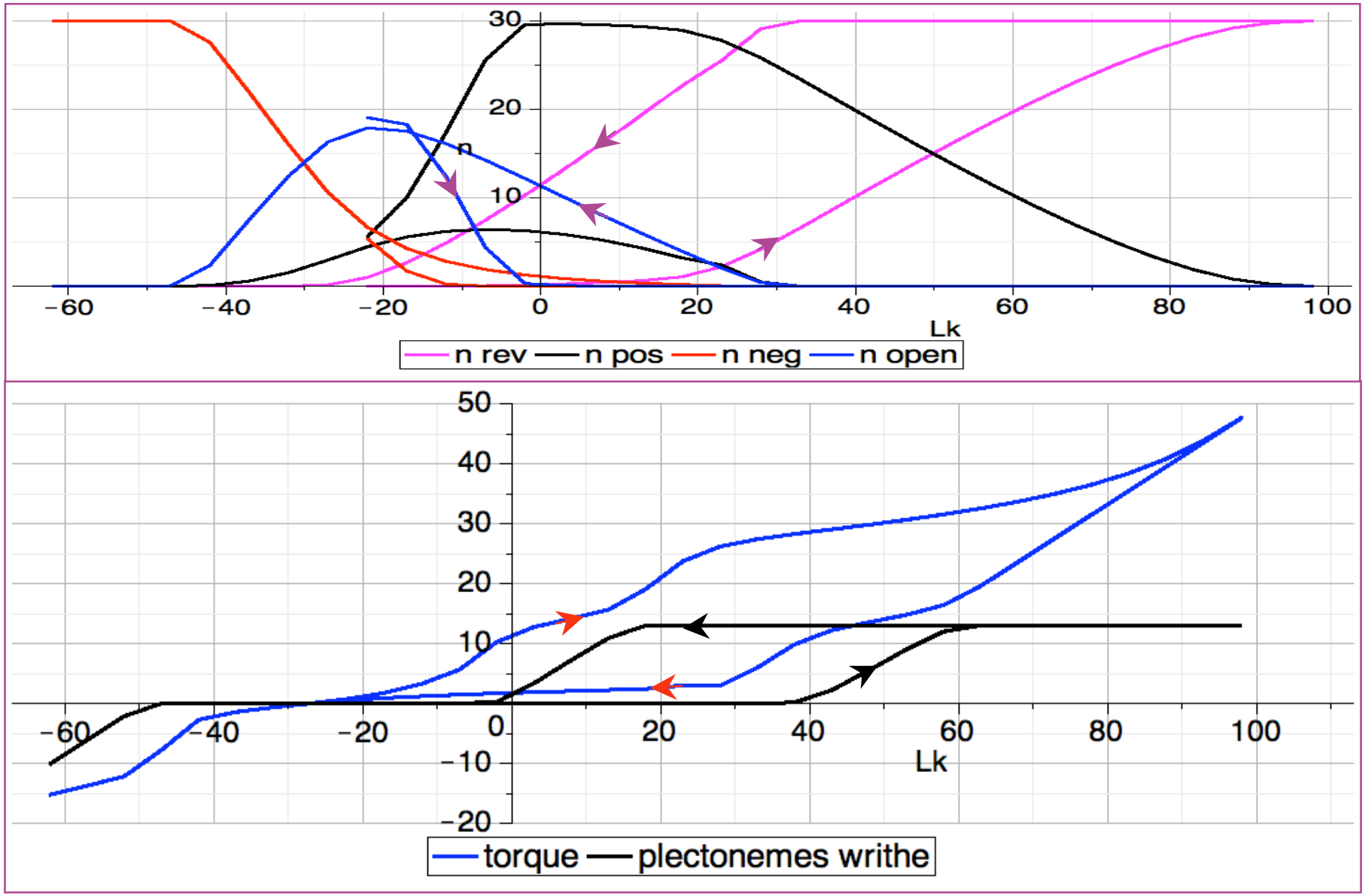
Plectonemes formation

plectonemes initiated thanks to fiber defects via "mini-fiber" inversion:

slope: $2 \cdot \langle L_{Minifiber} \rangle / turn$ where $\langle L_{Minifiber} \rangle = n \cdot \langle d \rangle / (N - n + 1)$

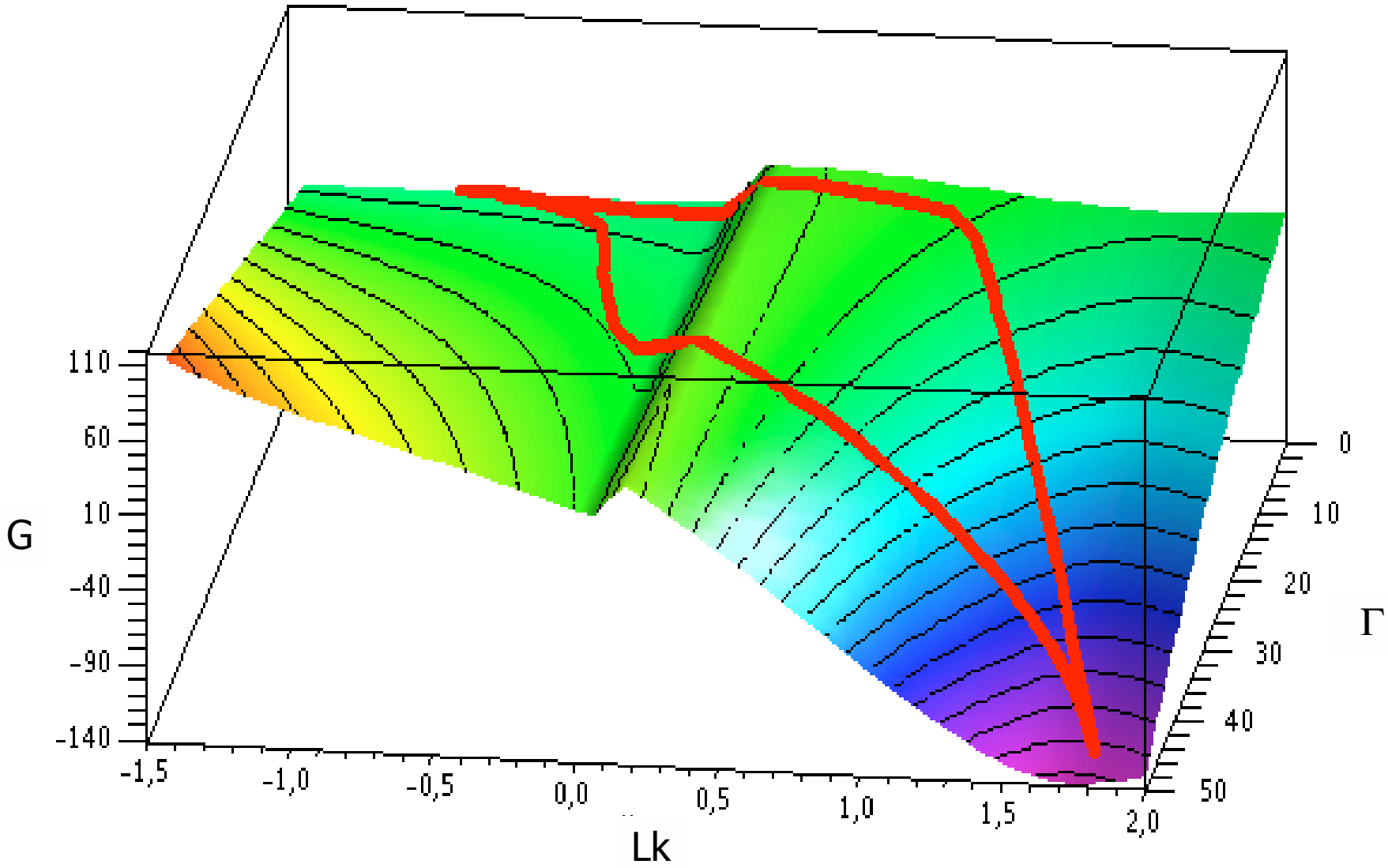


measuring the torque via the fit



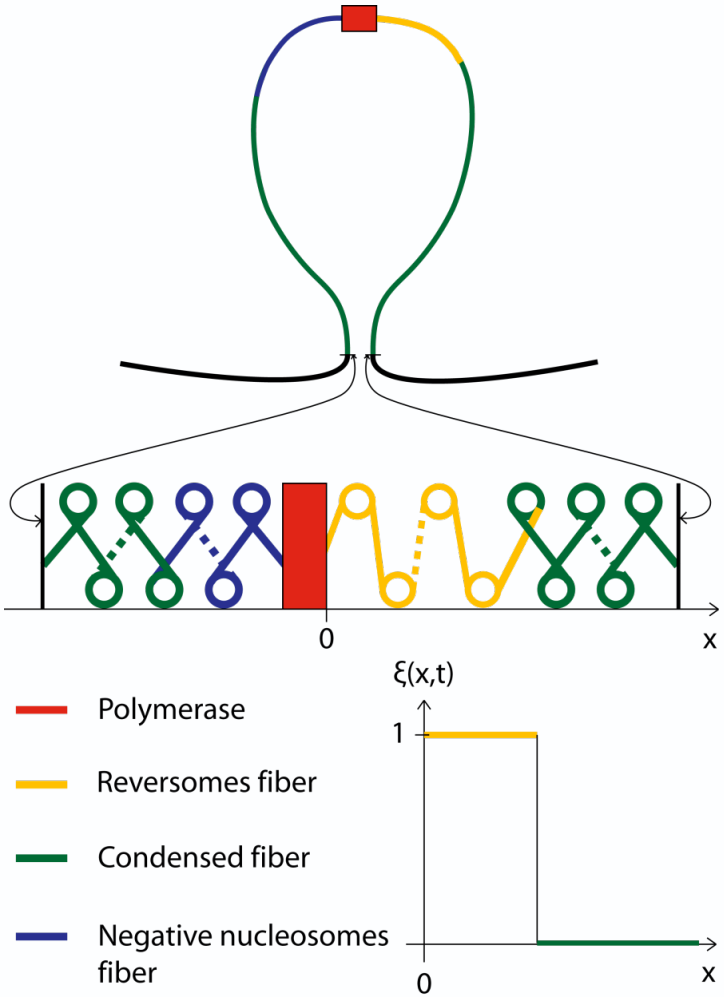
the applied torque is a model parameter which depends on Lk

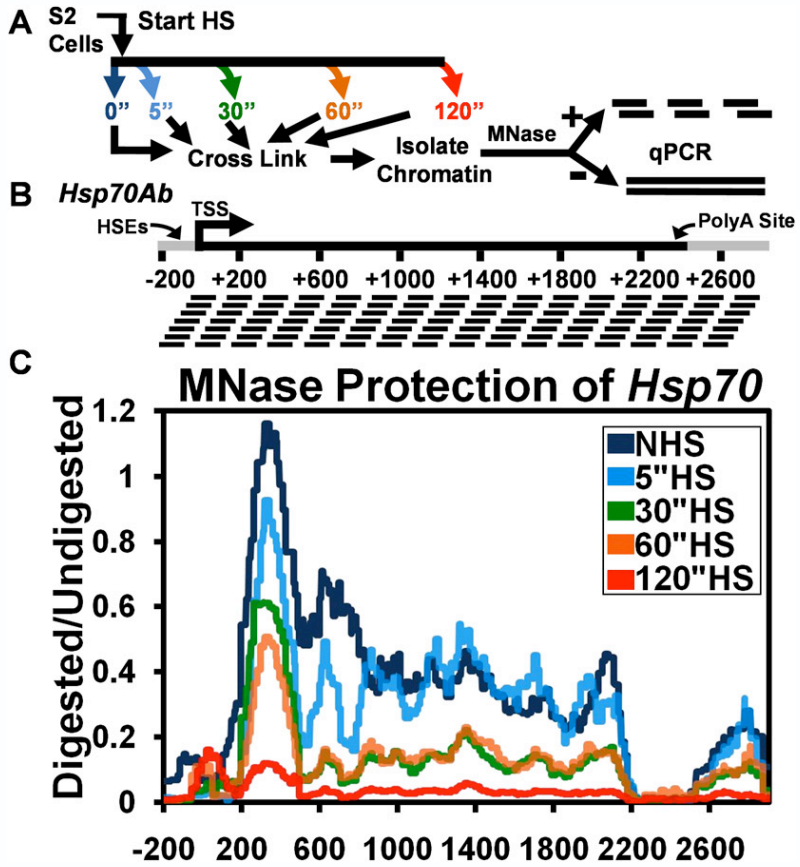
The hysteresis cycle on the energetic landscape



A reversome wave?

RNA Pol II { torque > 5 pN.nm; speed ~ 20 bp/s } ⇒ ~2 turns/s ⇒ ~1 reversome/s ⇒ ~200 bp/s





A wave of nucleosome disruption (Petesh and Lis, Cell 2008)