The Polymer Physics of DNA

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In order to perform its tasks, the cell uses

- Sequence
- Elastic properties
- Topological properties
- Statistical properties
- and tons of other properties , ...

of DNA

J. Physique — LETTRES **42** (1981) L-433 - L-436 1er OCTOBRE **1981**, PAGE L-433

Classification
Physics Abstracts
05.40 — 64.75 — 82.70

Ring polymers in solution : topological effects

J. des Cloizeaux

Service de Physique Théorique, CEN-Saclay, Boîte Postale n° 2, 91190 Gif sur Yvette, France

(*Reçu le 1er juin 1981, accepté le 19 août 1981*)

Résumé. — On étudie les effets de contraintes topologiques sur les propriétés d'anneaux polymères en solution. Quand les anneaux sont courts et rigides, la nature de ces effets peut être aisément comprise et un résultat simple est donné ici. Quand les anneaux sont longs et flexibles, la situation est complexe et une analyse plus subtile est nécessaire. Heureusement des études mathématiques récentes concernant le nombre d'enlacements de deux courbes conduisent à un résultat significatif. Cette information permet de développer des arguments montrant que les contraintes topologiques produisent essentiellement un accroissement de l'interaction locale de volume exclu ; cet effet topologique pourrait donc être pris en compte dans le cadre des théories actuelles.

Abstract. — The effect of topological constraints on the properties of ring polymers in solution are studied. When the rings are short and rigid, the effects can easily be understood and a simple result is given here. When the rings are long and flexible, the situation is complex and a more subtle analysis is needed. Fortunately recent mathematical studies concerning the linking numbers of two curves lead to a significant result. This information is used to argue that the topological constraints produce essentially an increase of the local excluded volume interaction ; this topological effect could therefore be taken into account within the framework of current theories.

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Résur Quan est dc
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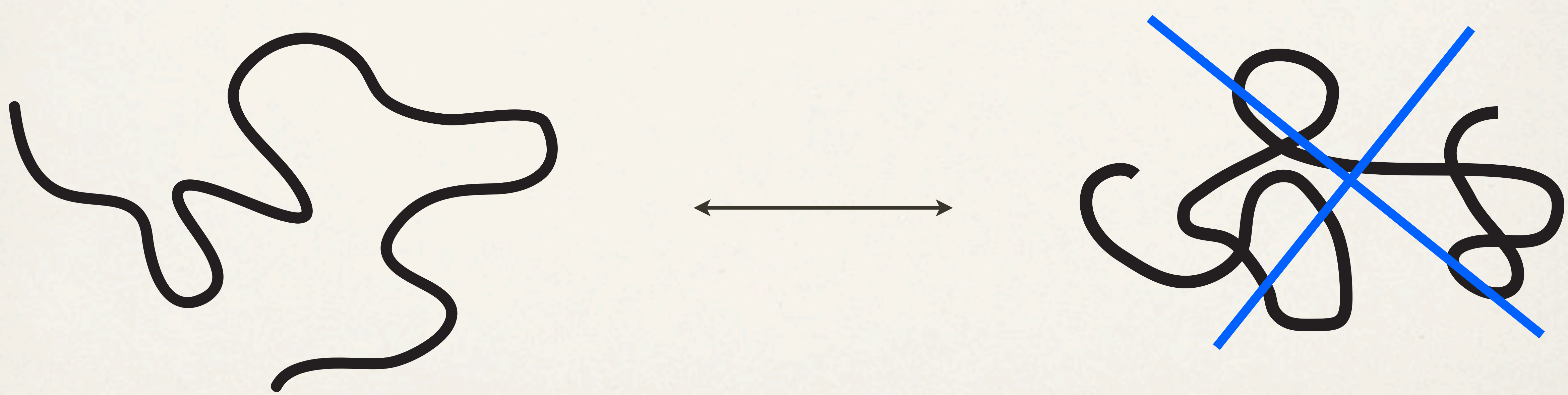
DNA is a Self-Avoiding Walk(SAW)

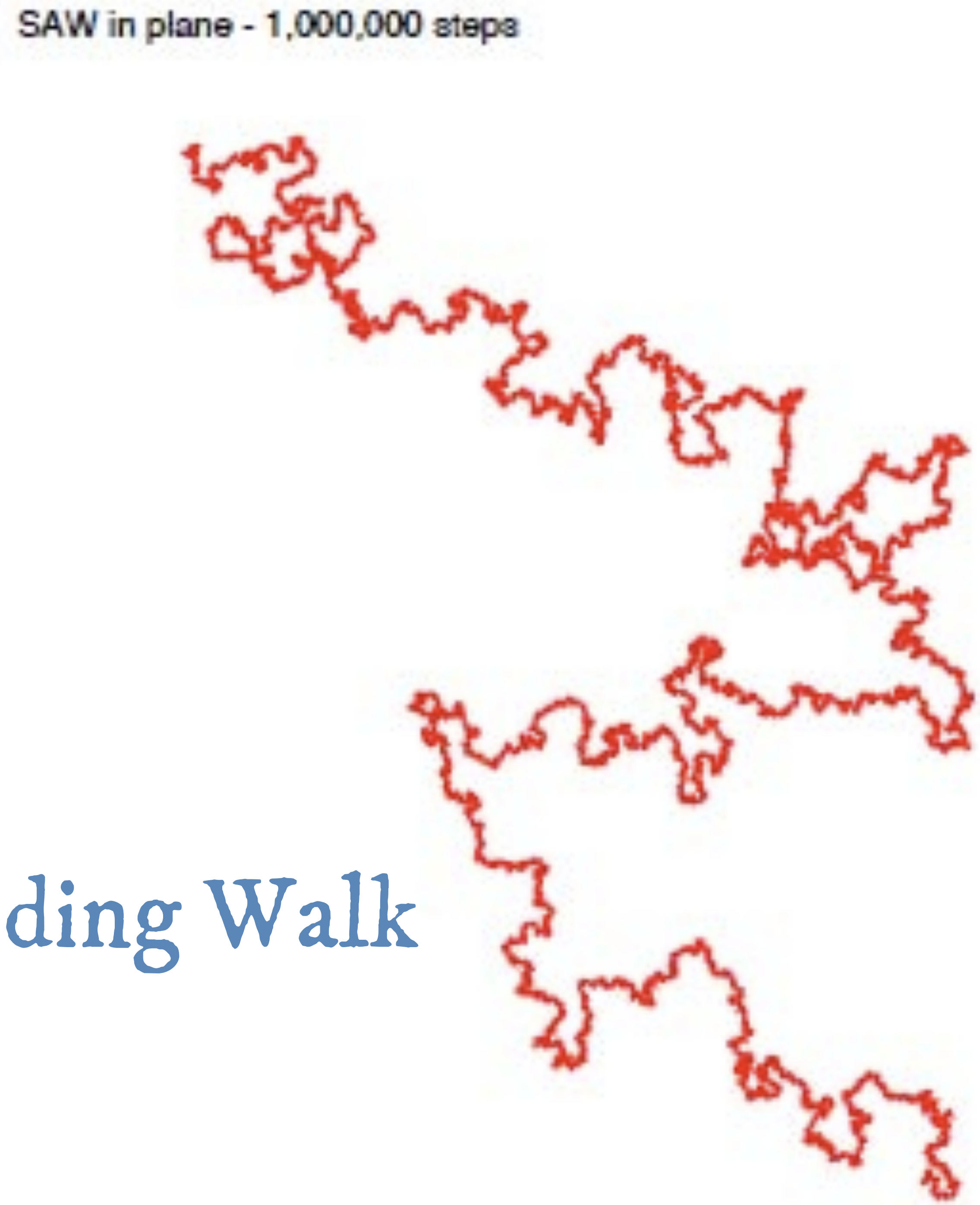
Good Solvent Conditions

SAW

Random Walk (RW)



Random Walk



Self-Avoiding Walk

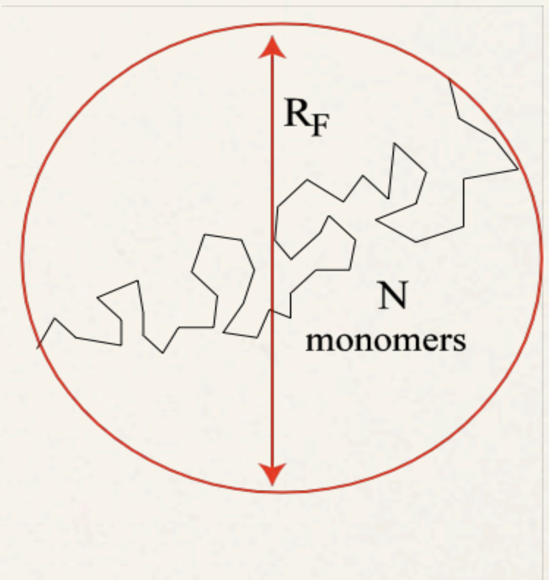
Universality Class		Theoretical Model	Physical System	Order Parameter
d=2	n=1	Ising Model in two dimen.	Adsorbed Films	Surface Density
	n=2	XY Model in two dimen.	Helium-4 films	Amplitude of superfluid phase
	n=3	Heisenberg Model in two dimen.		Magnetization
d>2	n=∞	"Spherical" Model	None	
d=3	n=0	Self-Avoiding random walk	Conformation of long polymers	Density of chain ends
	n=1	Ising Model in 3 dimen.	Uniaxial ferromagnet	Magnetization
			Fluid near a critical point	Density difference between phases
			Mixture of fluids near a consolute point	Concentration difference
			Alloys near a order-disorder transition	Concentration difference
	n=2	XY Model in 3 dimen.	Planar ferromagnet	Magnetization
			Helium-4 near superfluid transition	Amplitude of the superfluid phase
	n=3	Heisenberg model in 3 dimen.	Isotropic ferromagnet	Magnetization
d>=4	n=-2		none	
	n=32	Quantum chromodynamics	Quarks bound in protons, etc	

Universality and Universality Classes: behavior depends only from d and n

$$d=1;\ \nu=1.00;\quad \xi=\xi_o L$$

$$d=2;\ \nu=0.75;\quad \xi=\xi_o L^{0.750}$$

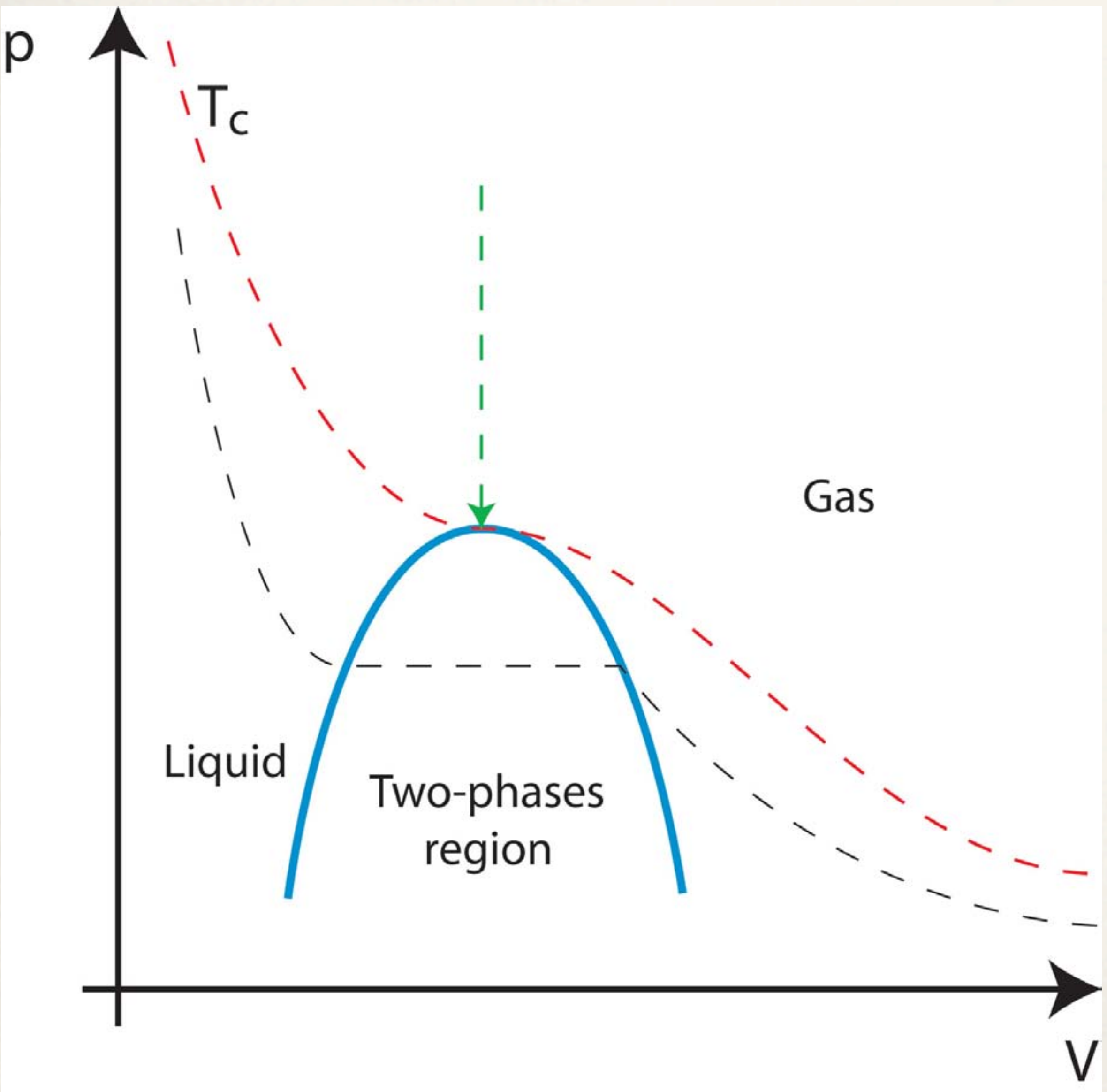
$$d=3;\ \nu=0.588;\ \xi=\xi_o L^{0.588}$$

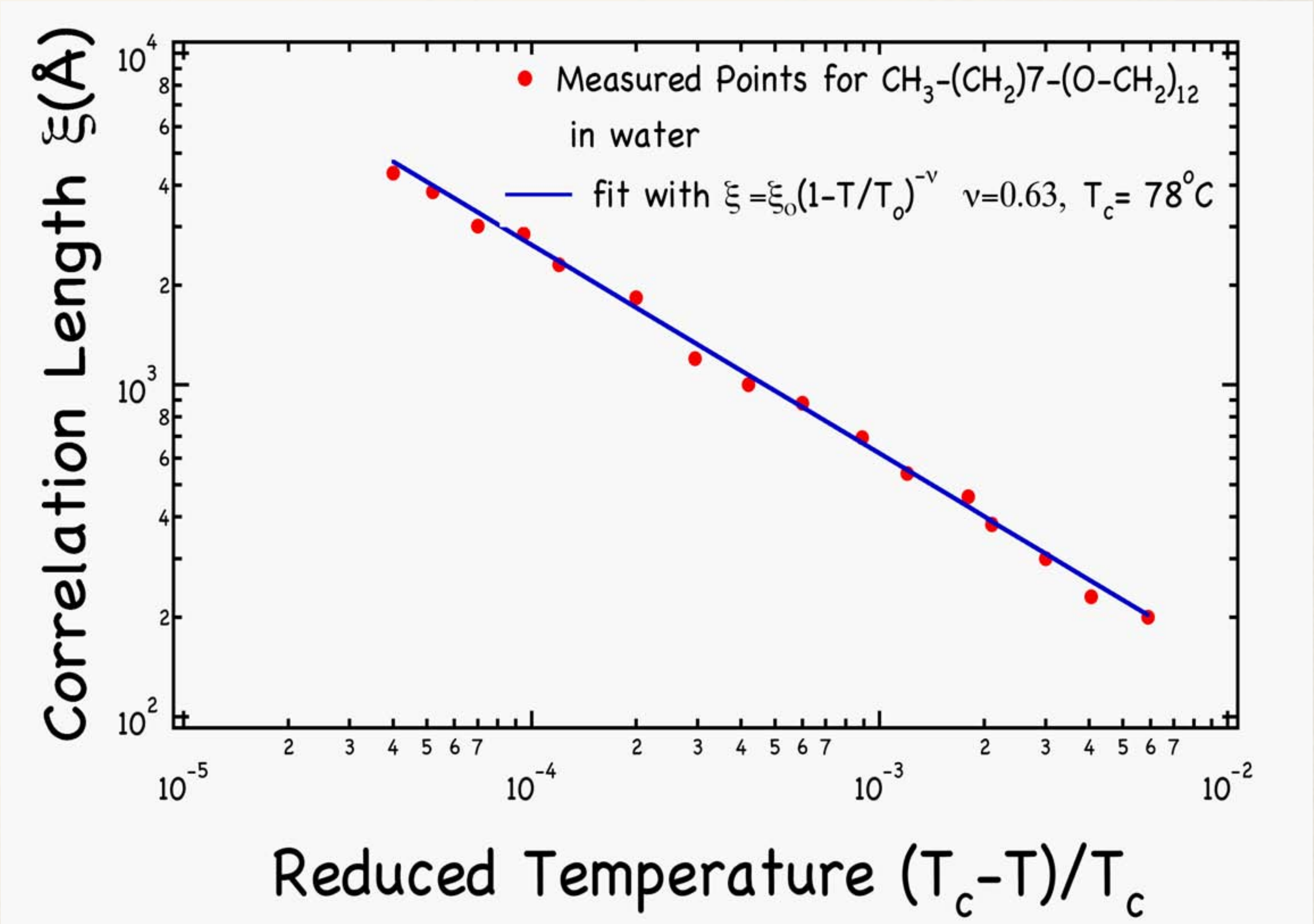


from K. Wilson, 1974

This power law behavior is very similar to critical phenomena near a second order phase transition:

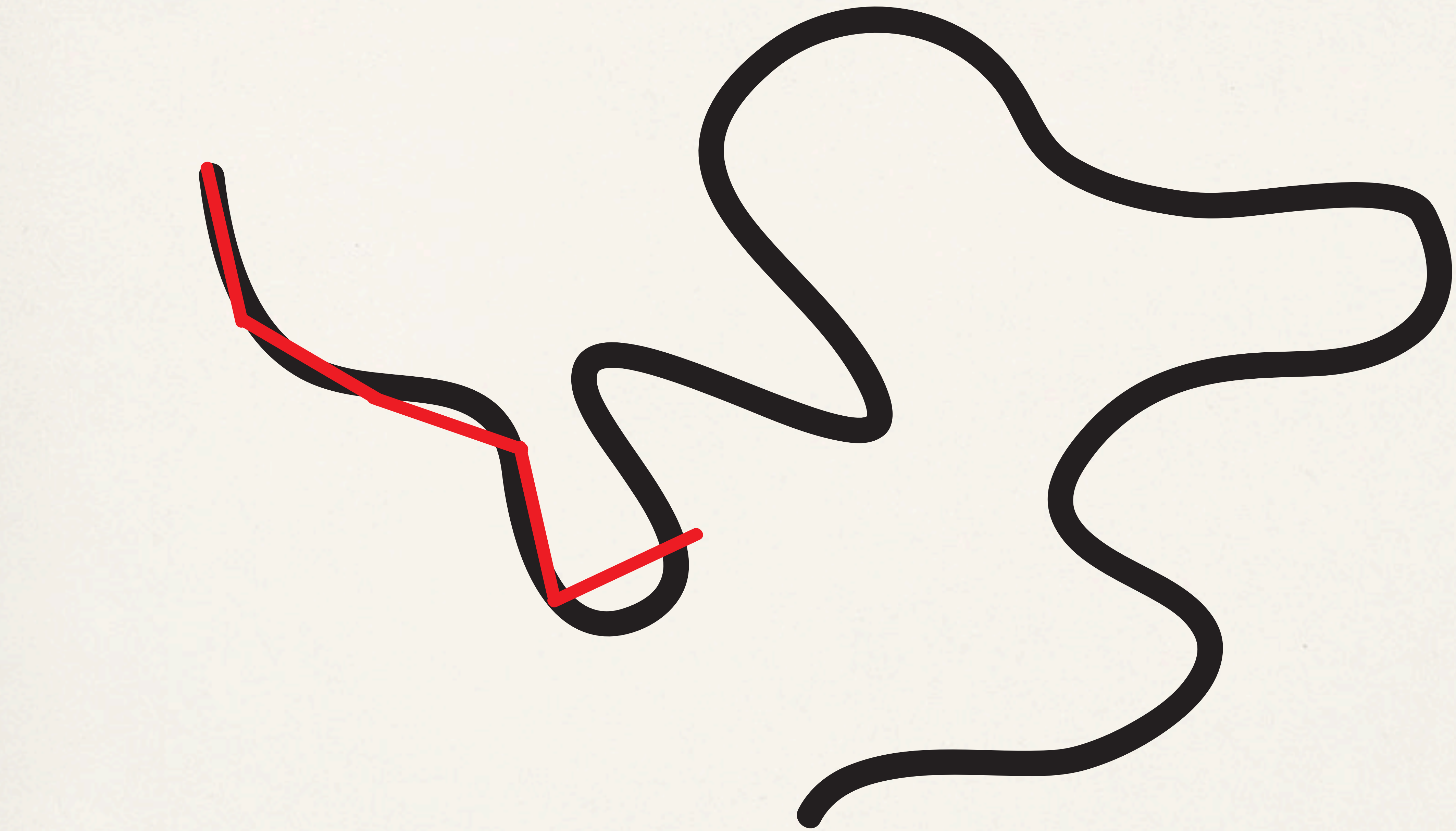
i) gas-liquid phase transition
ii) ferromagnet
phase separation
of binary solutions





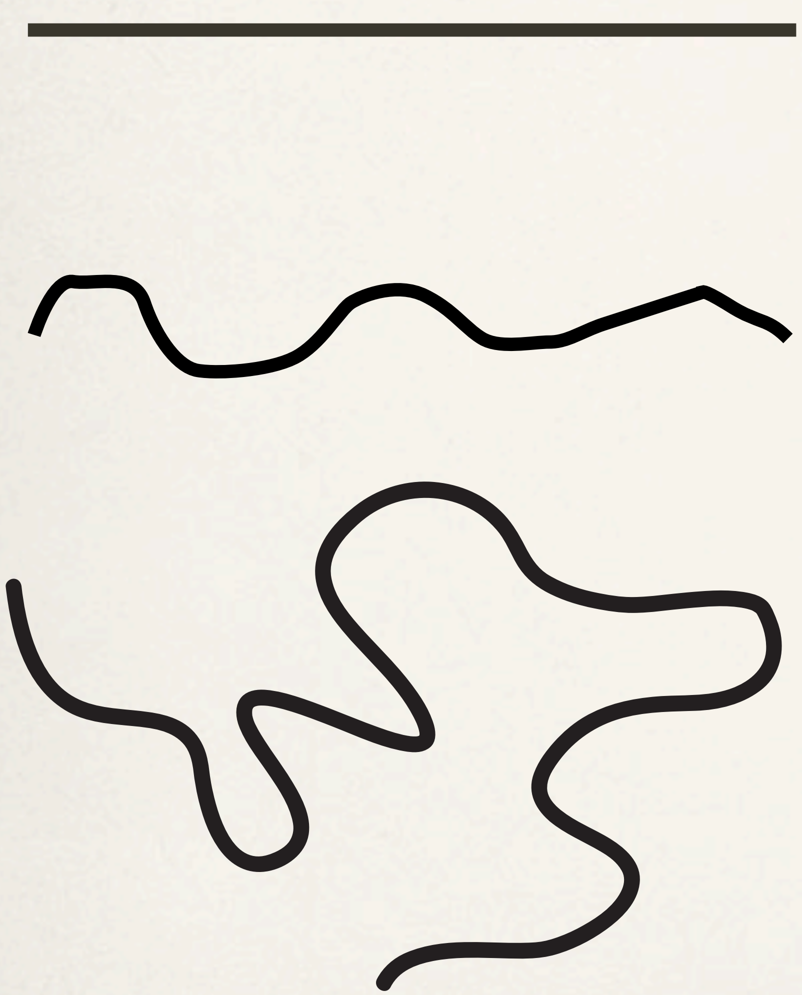
Dietler et al., PRL 88(1988) 1852

DNA in a Thermal Bath



Persistence Length $\ell_p = \frac{EI}{k_B T} \quad \left(I_{disk} = \frac{1}{4}\pi R^4 \right)$

DNA in a Thermal Bath



Length Scale	Elastic Constants	Temperature
Short (< ℓ_p)	Stiff (E big)	T = 0 K
Medium (~ ℓ_p)	Semiflexible	T > 0 K
Large (>> ℓ_p)	Very flexible	T >> 0 K

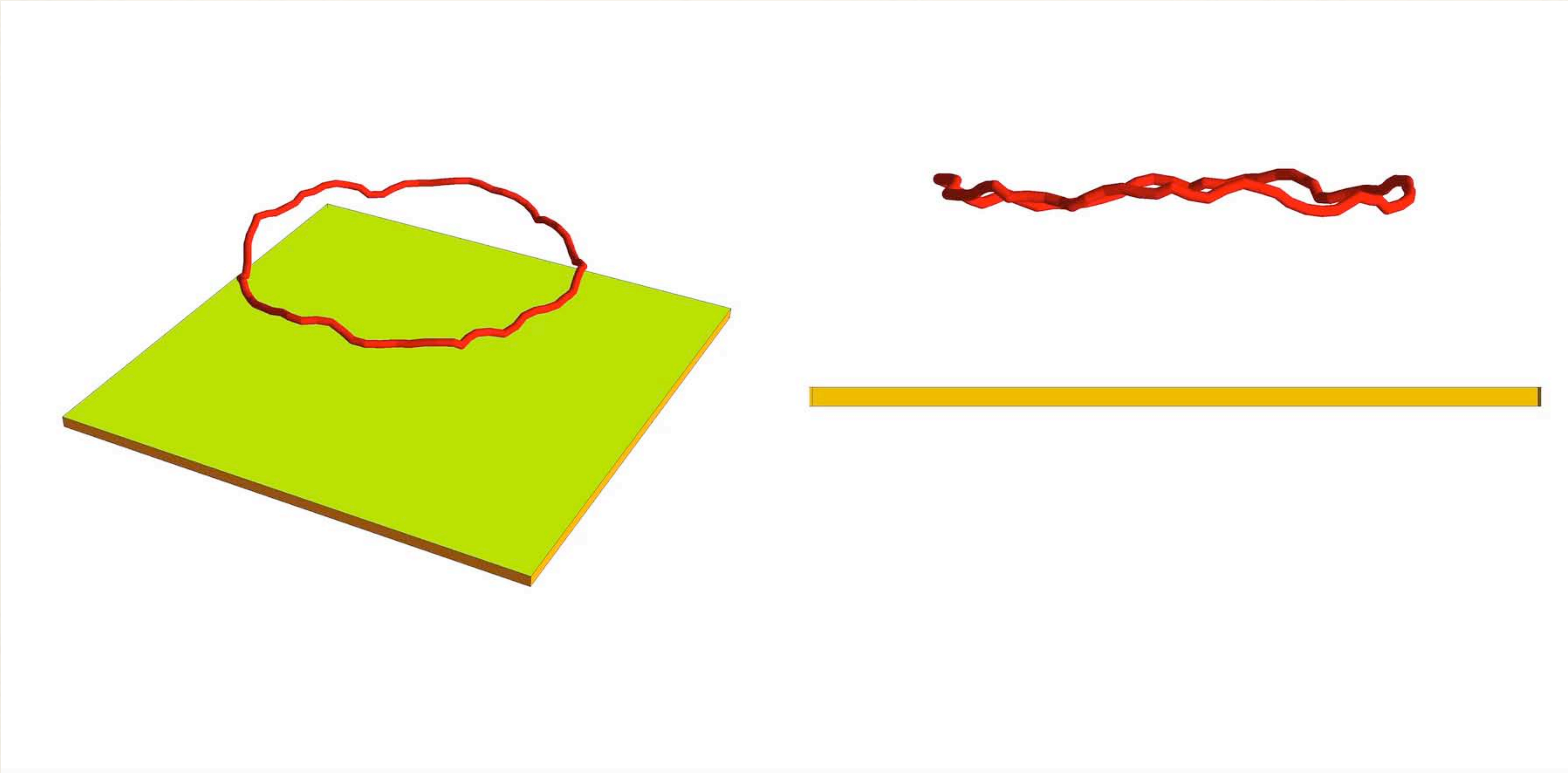
$$Persistence\ Length\ \ell_p = \frac{EI}{k_B T}$$

Methods :

- ☑ Imaging of DNA by Atomic Force Microscopy
- ☑ Tracing the DNA molecules
- ☑ Statistical Properties in 2 D:
  - ☑ End-to-End Distance
  - ☑ Correlation Function
  - ☑ Distributions

Atomic force microscopy

- DNA deposition on mica in $MgCl_2$ solution
- Technique ensures 2D equilibration of DNA



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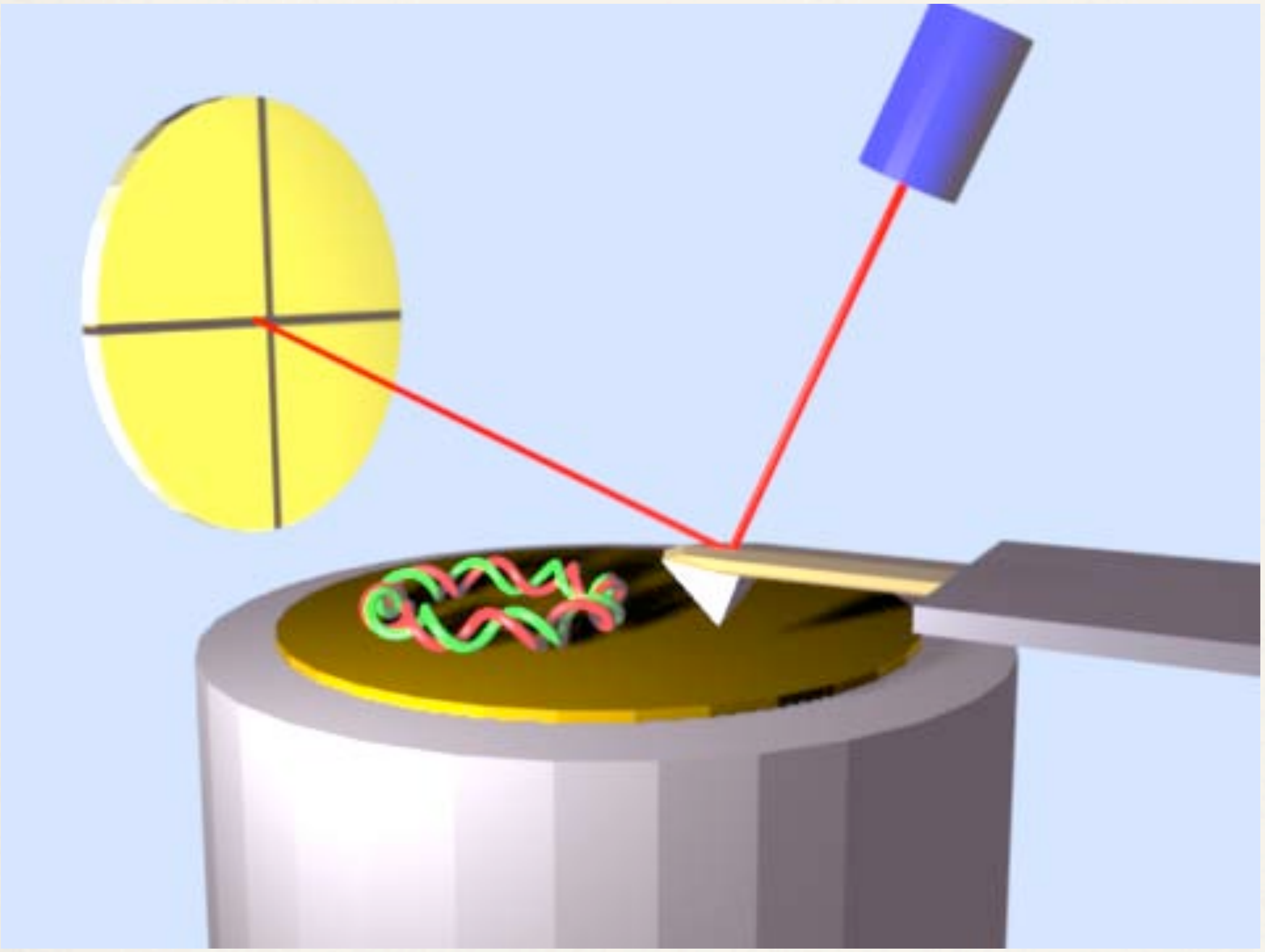

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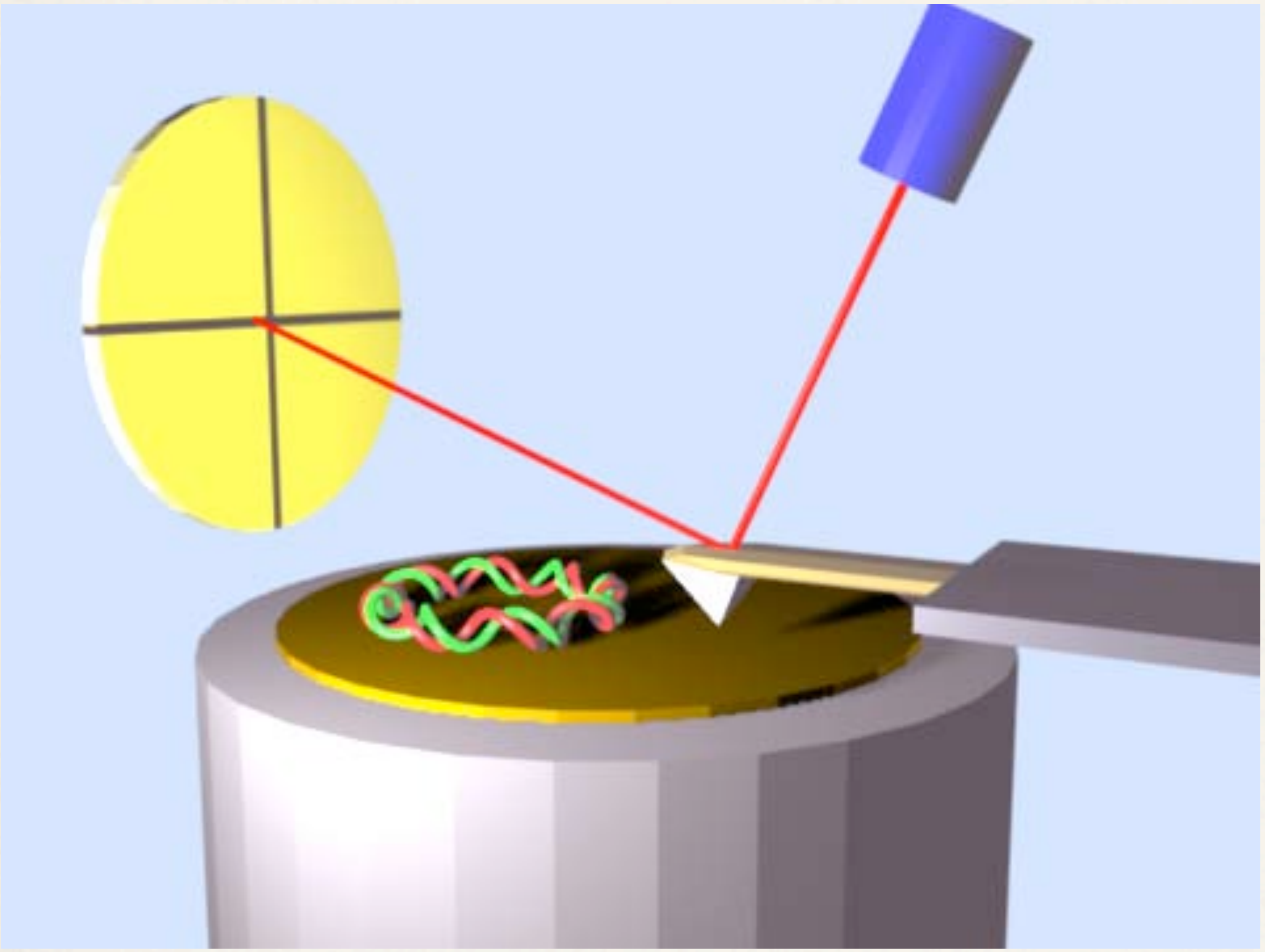

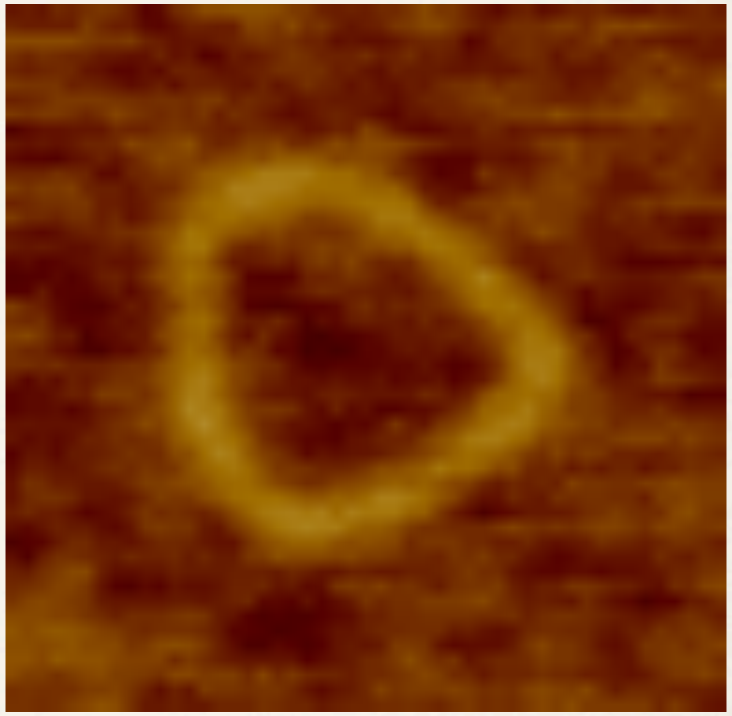

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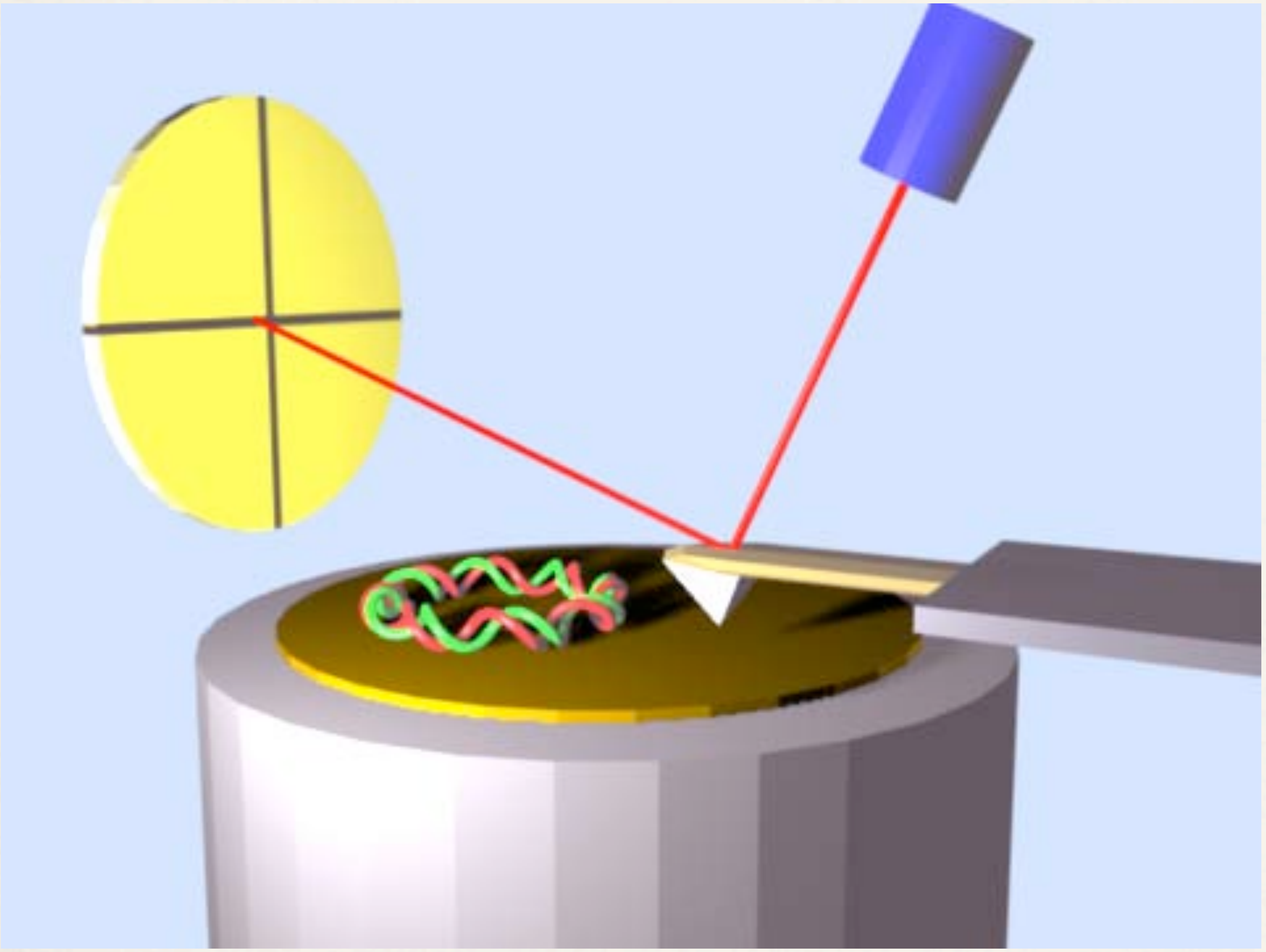

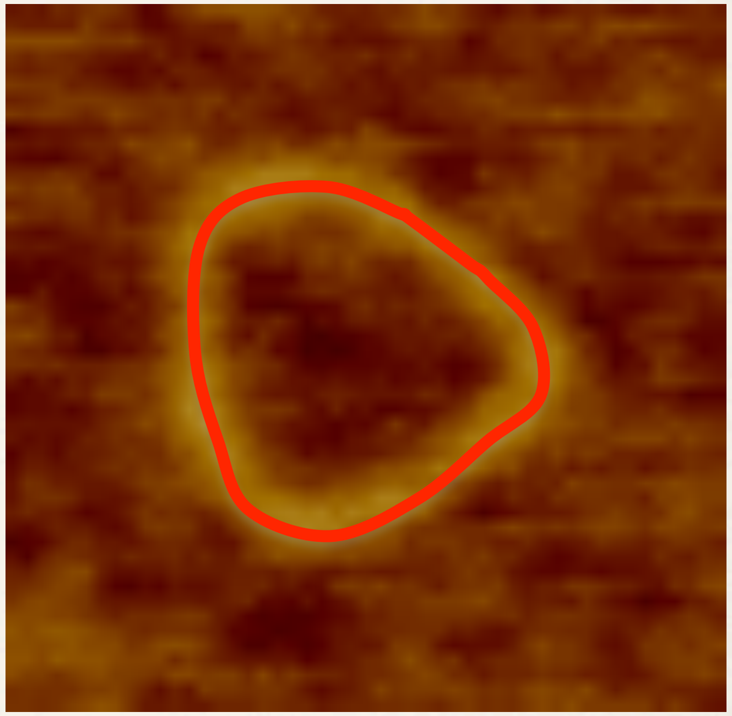

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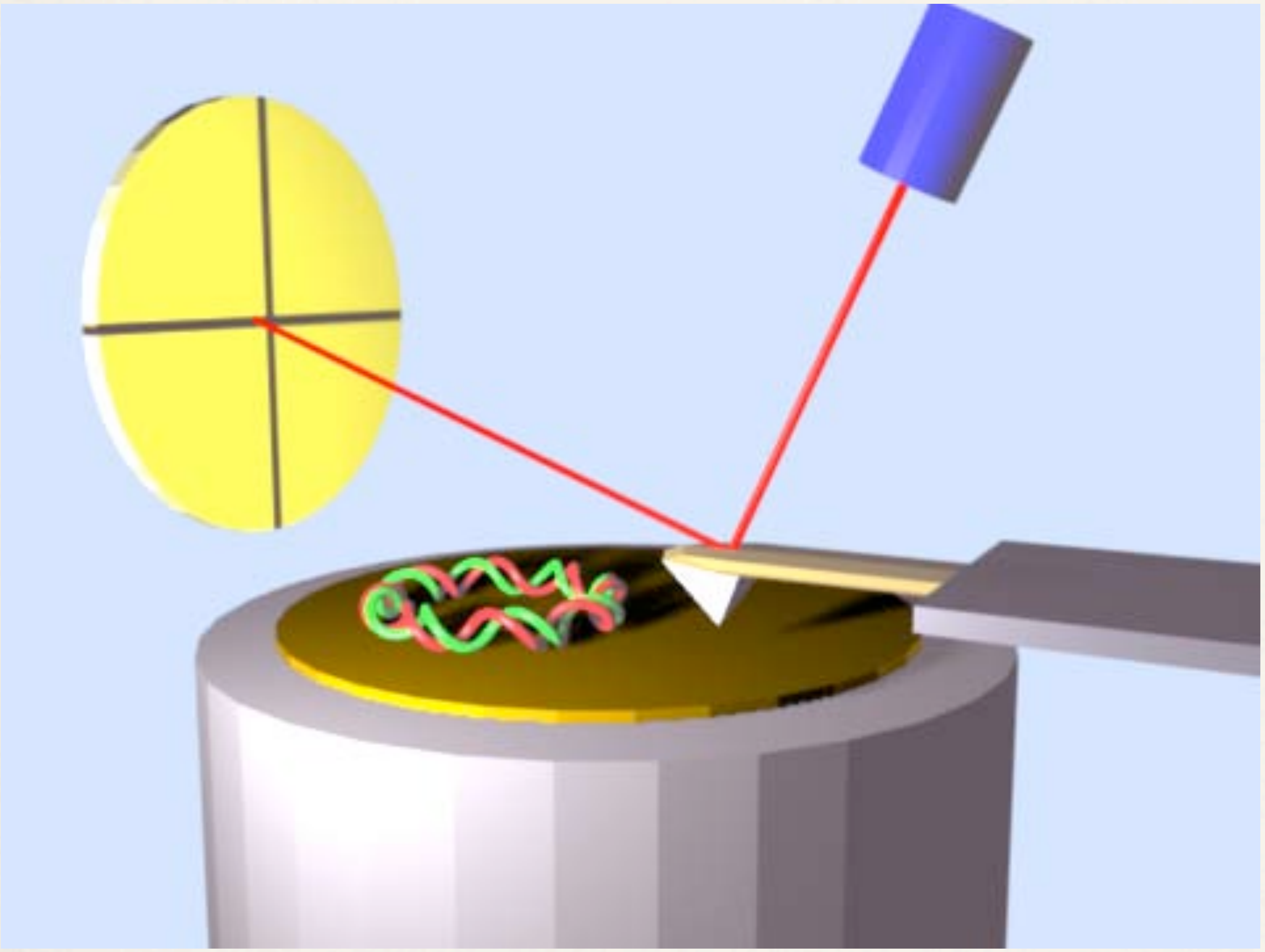
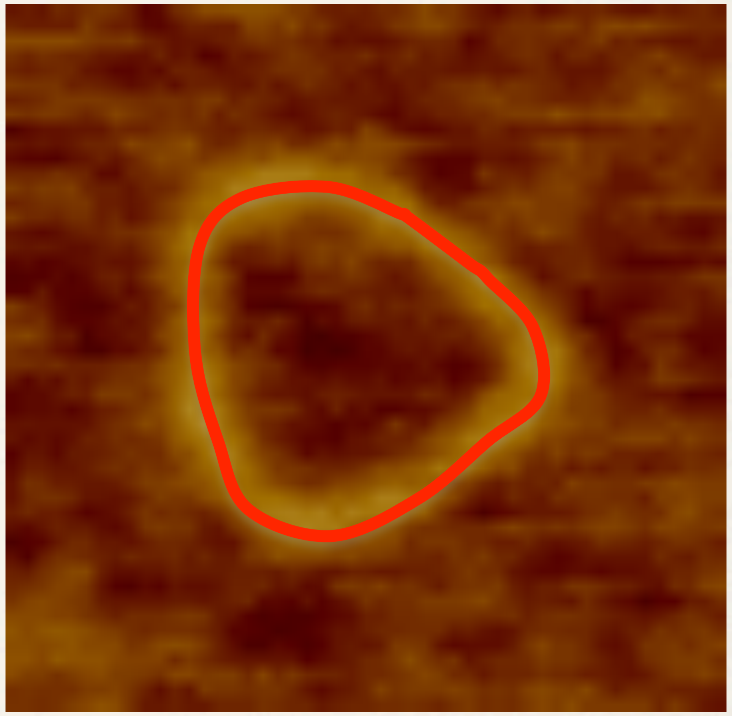
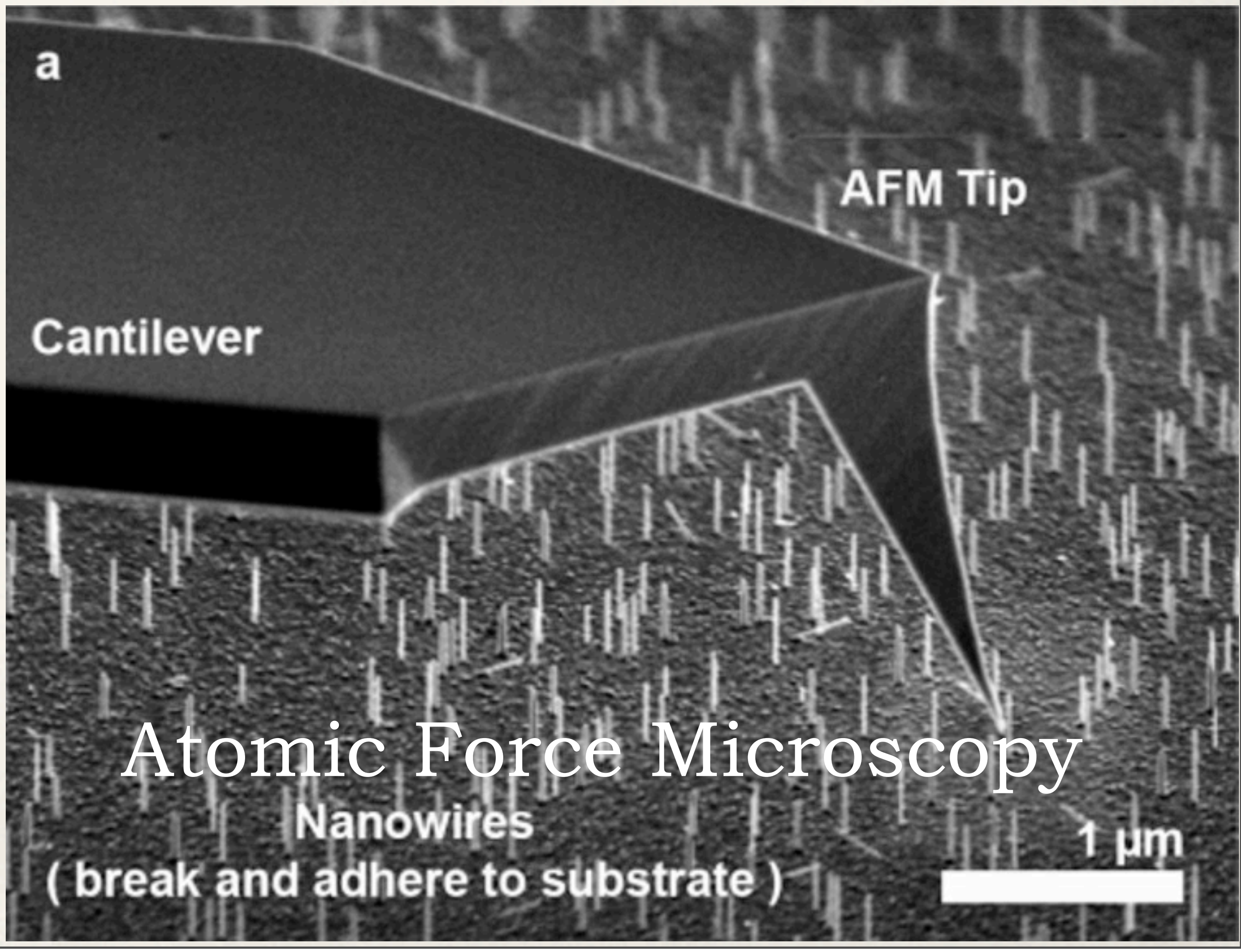
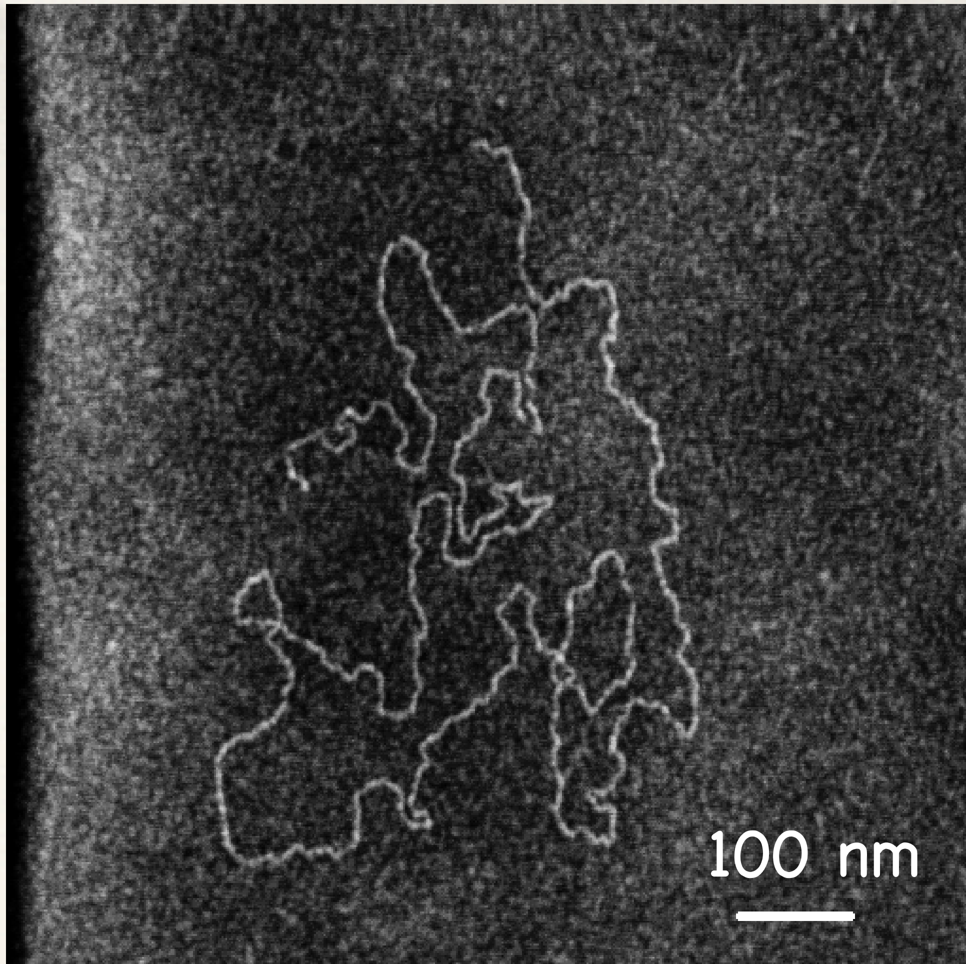


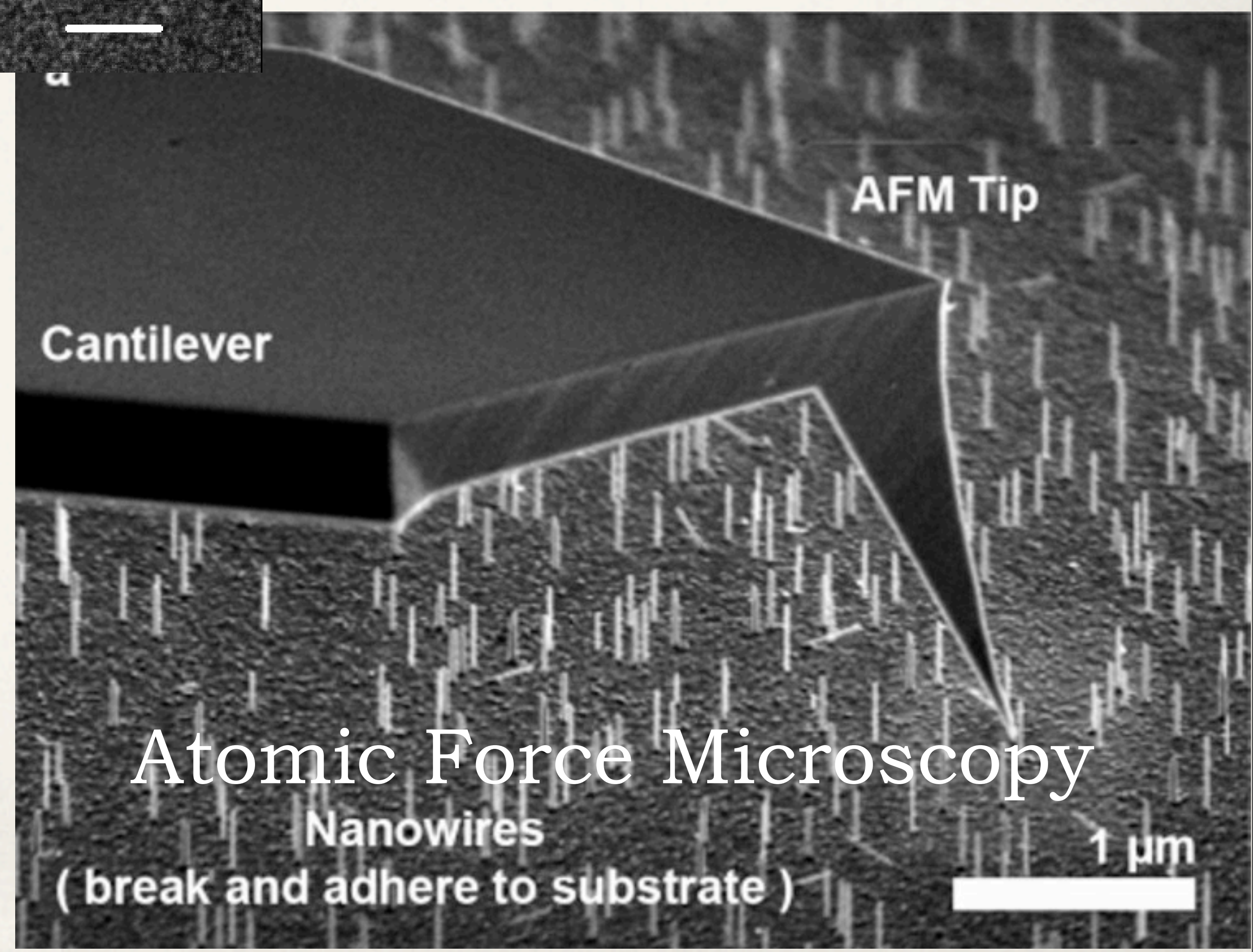


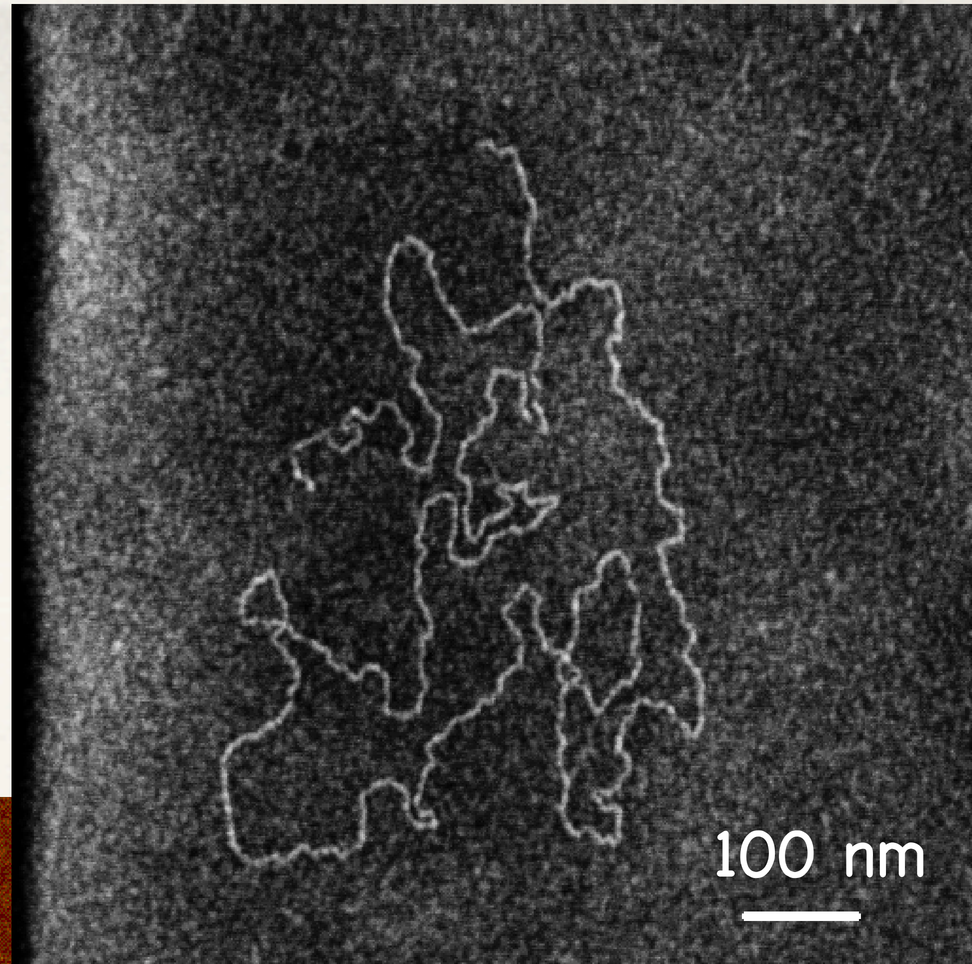
Molecular paths extracted from images

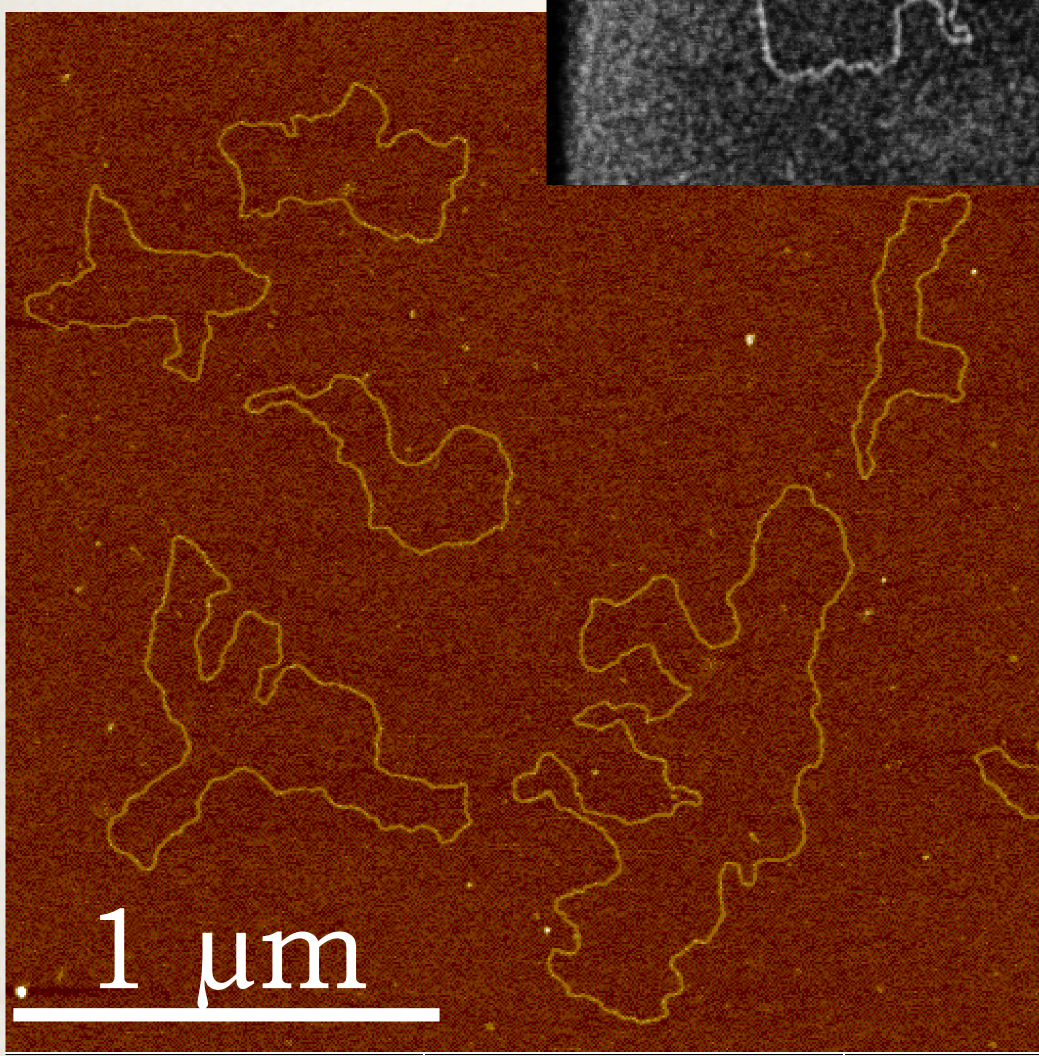

a
AFM Tip
Cantilever
Atomic Force Microscopy
Nanowires
(break and adhere to substrate)
1 μm

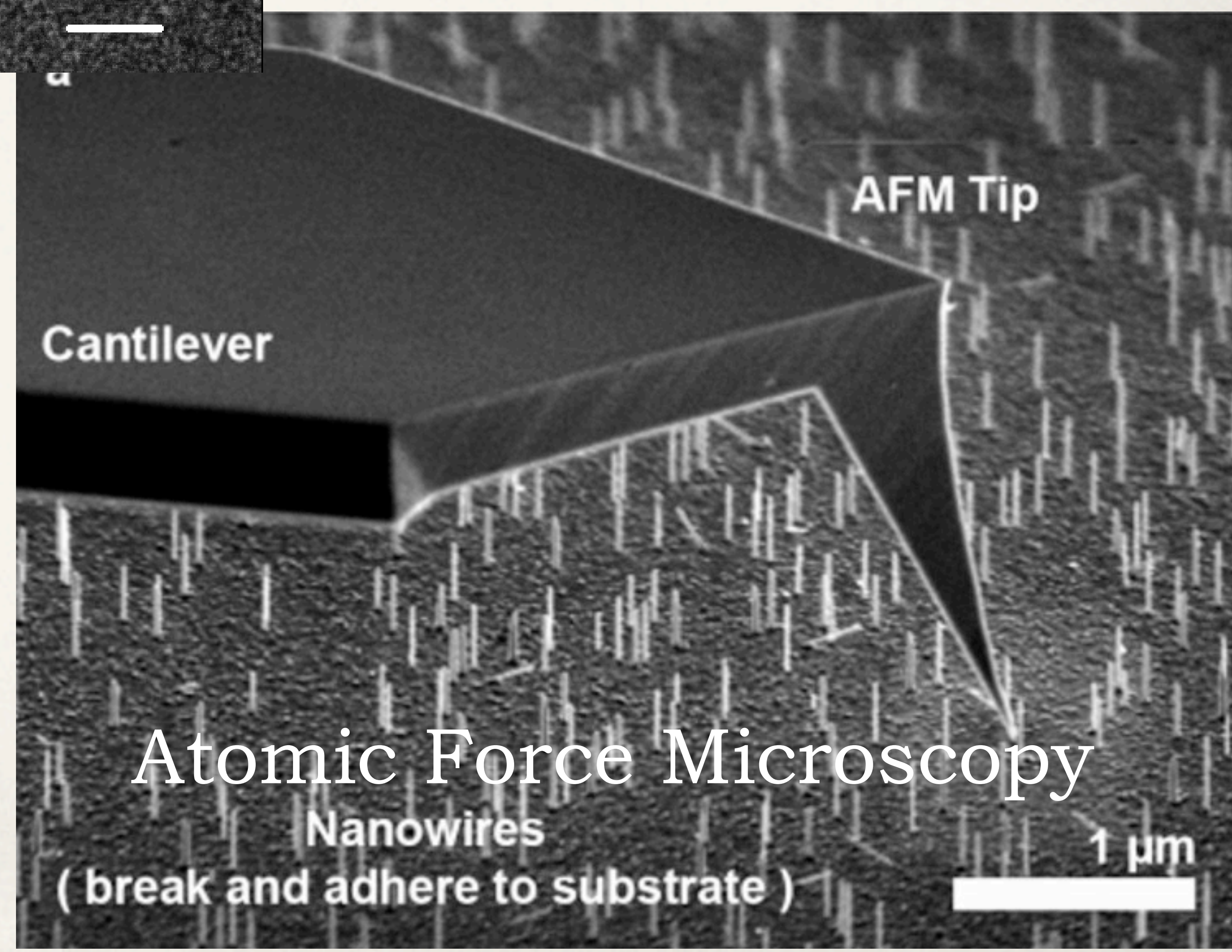


Atomic Force Microscopy




100 nm


1 μm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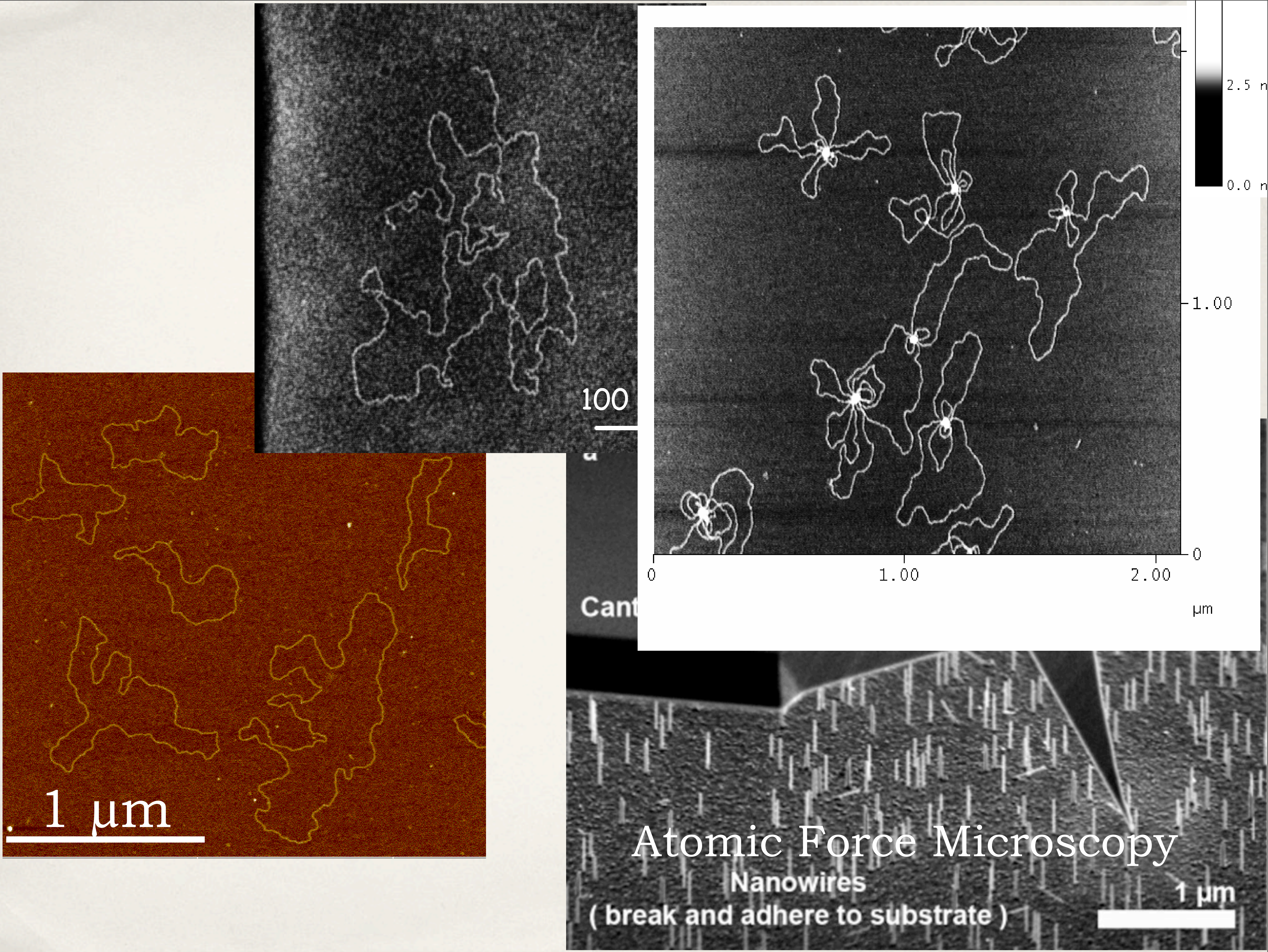


Atomic Force Microscopy

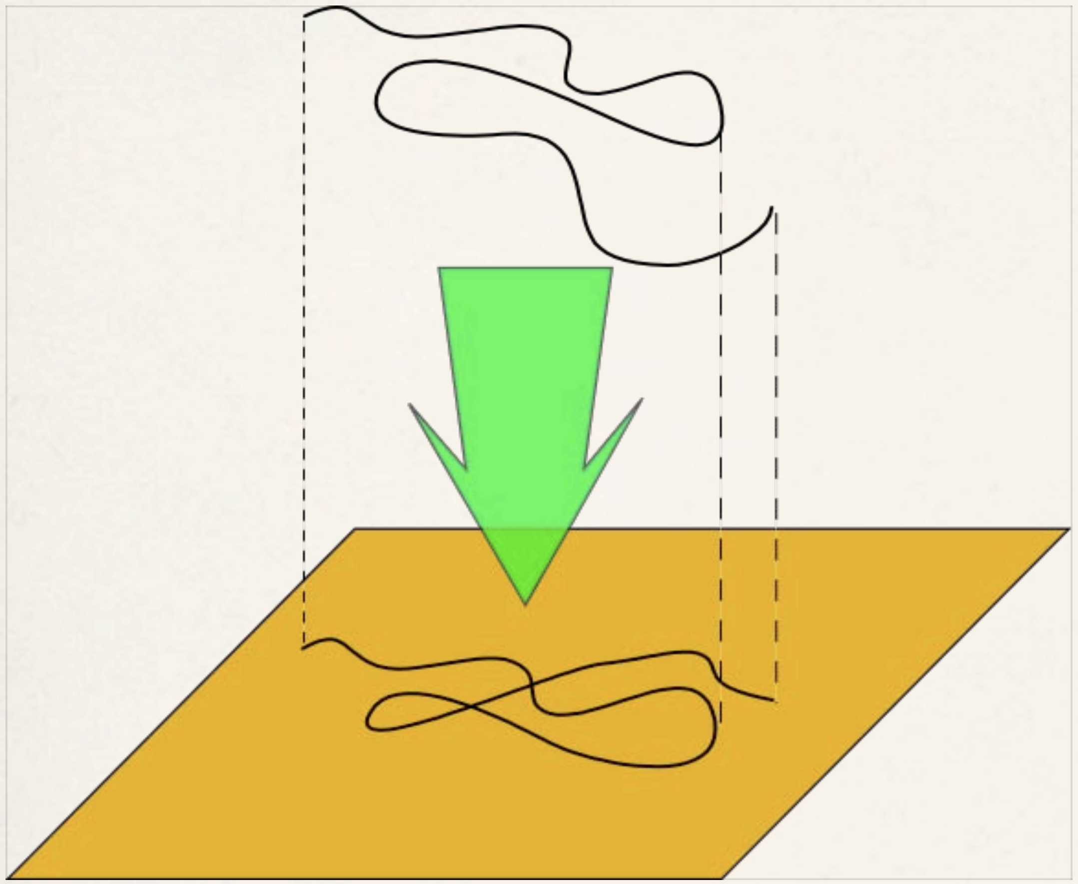
Deposition

APTES

Mg^{2+} or “GM”

Deposition

APTES



Trapping

Strong interaction

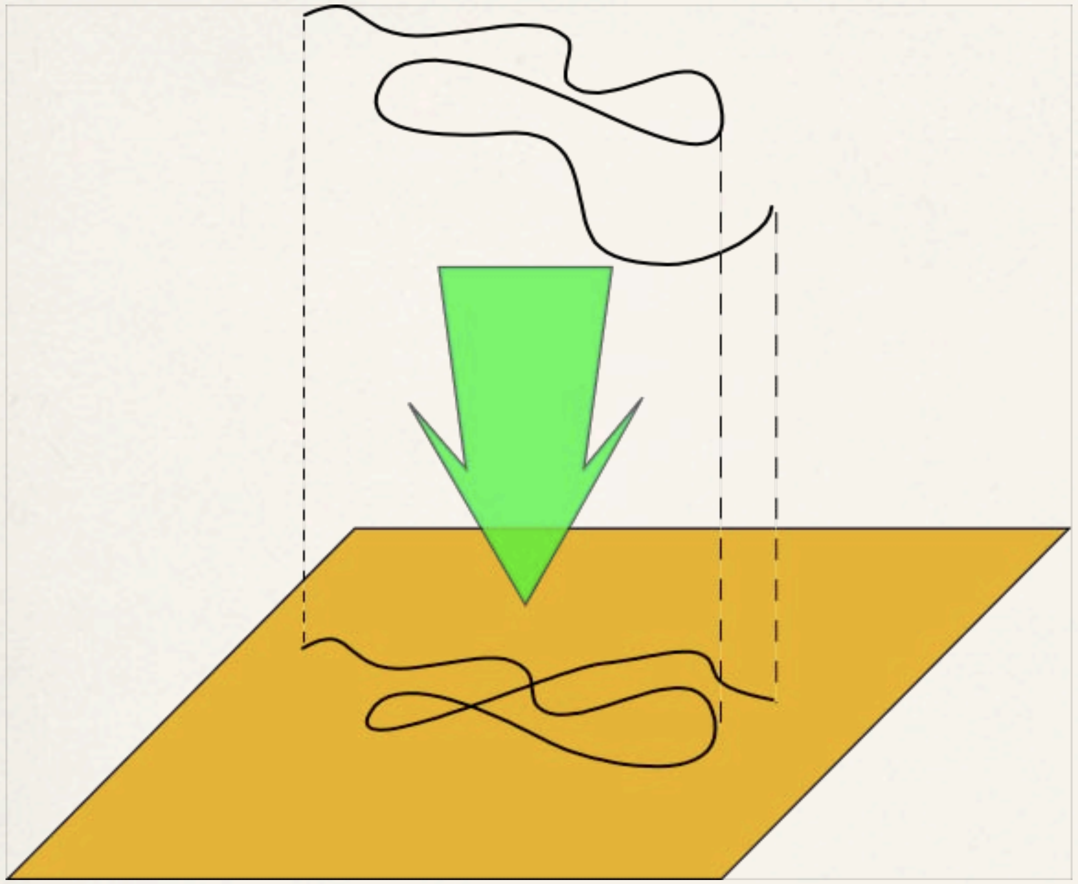
DNA-surface

$U_{int} >> k_B T$

Mg^{2+} or "GM"

Deposition

APTES



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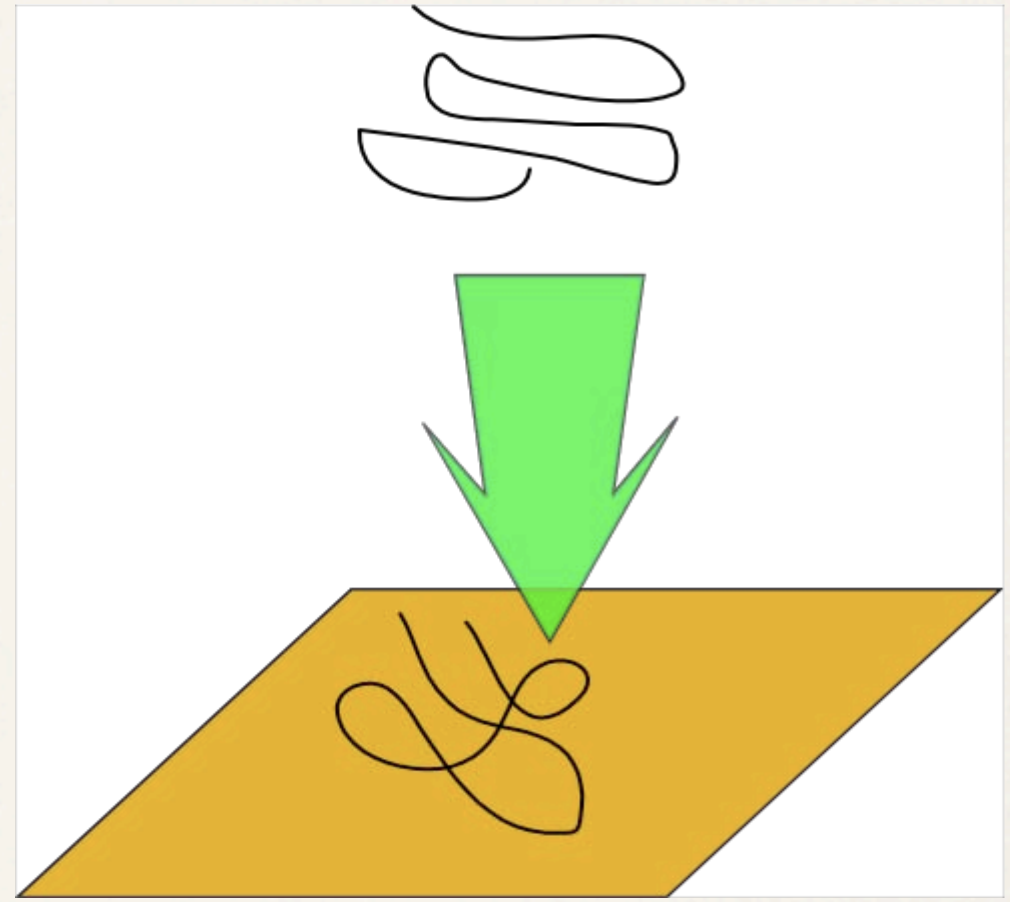


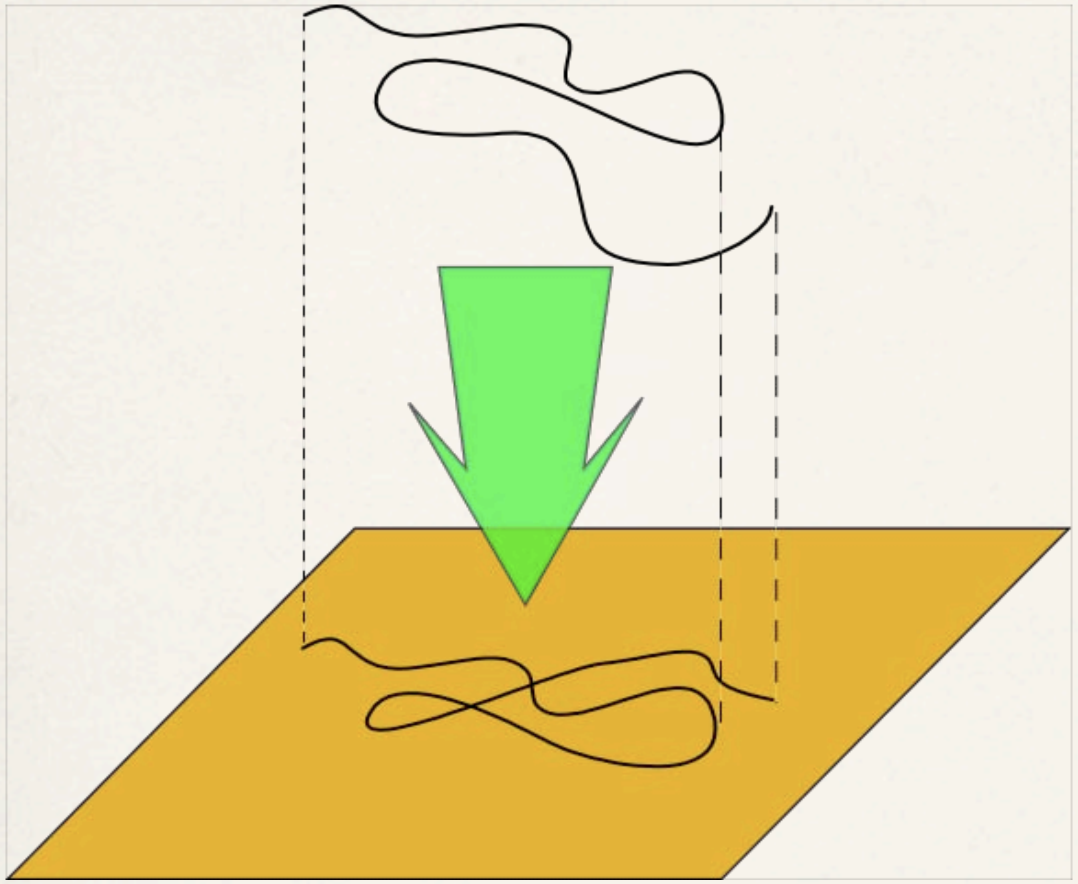
Equilibration

Weak interaction DNA-surface

$U_{int} \leq k_B T$

Deposition

APTES



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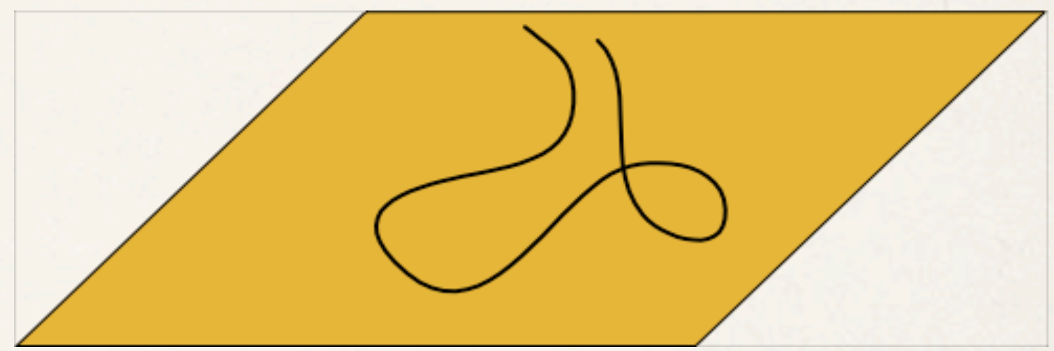

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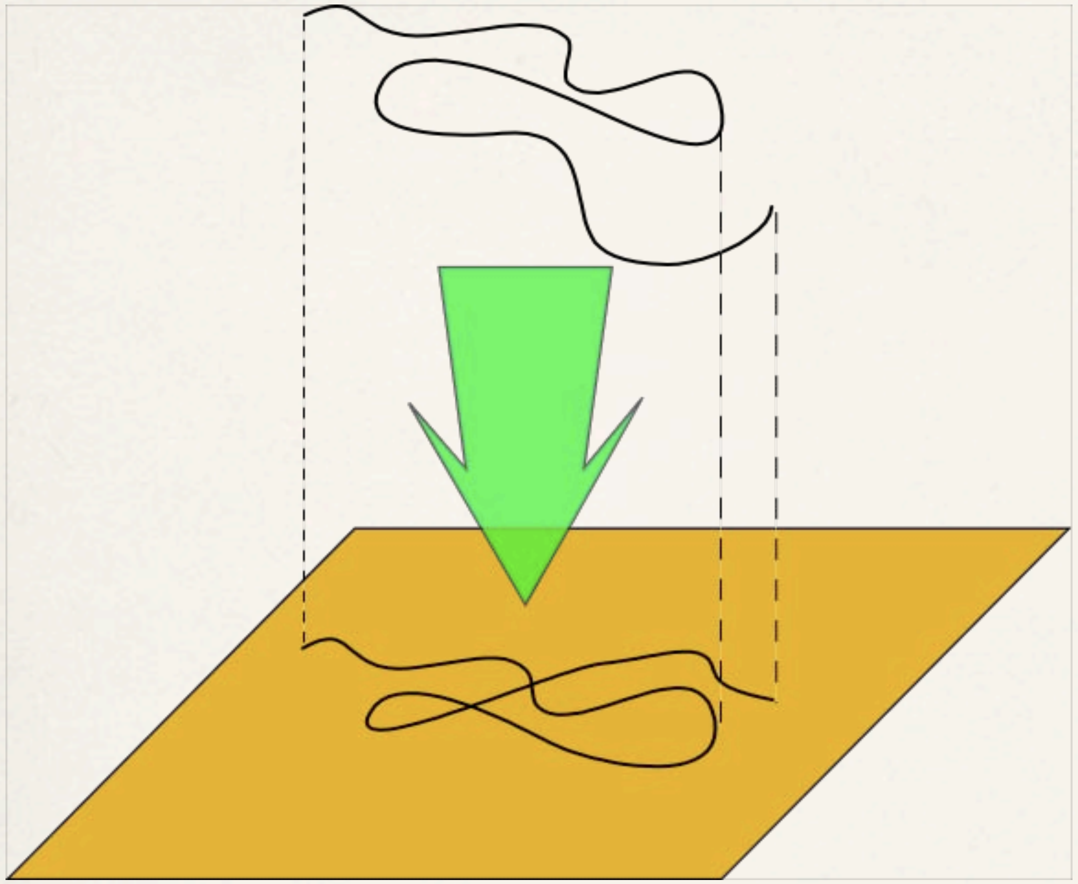

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Strong interaction DNA-surface

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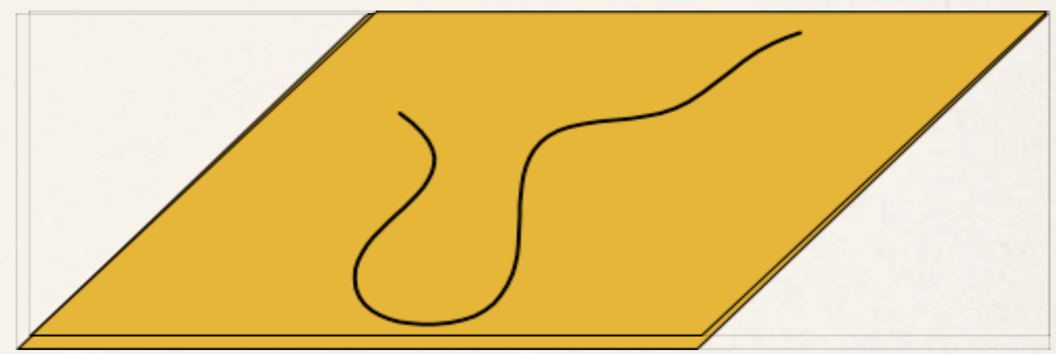
Mg^{2+} or "GM"



Equilibration

Weak interaction DNA-surface

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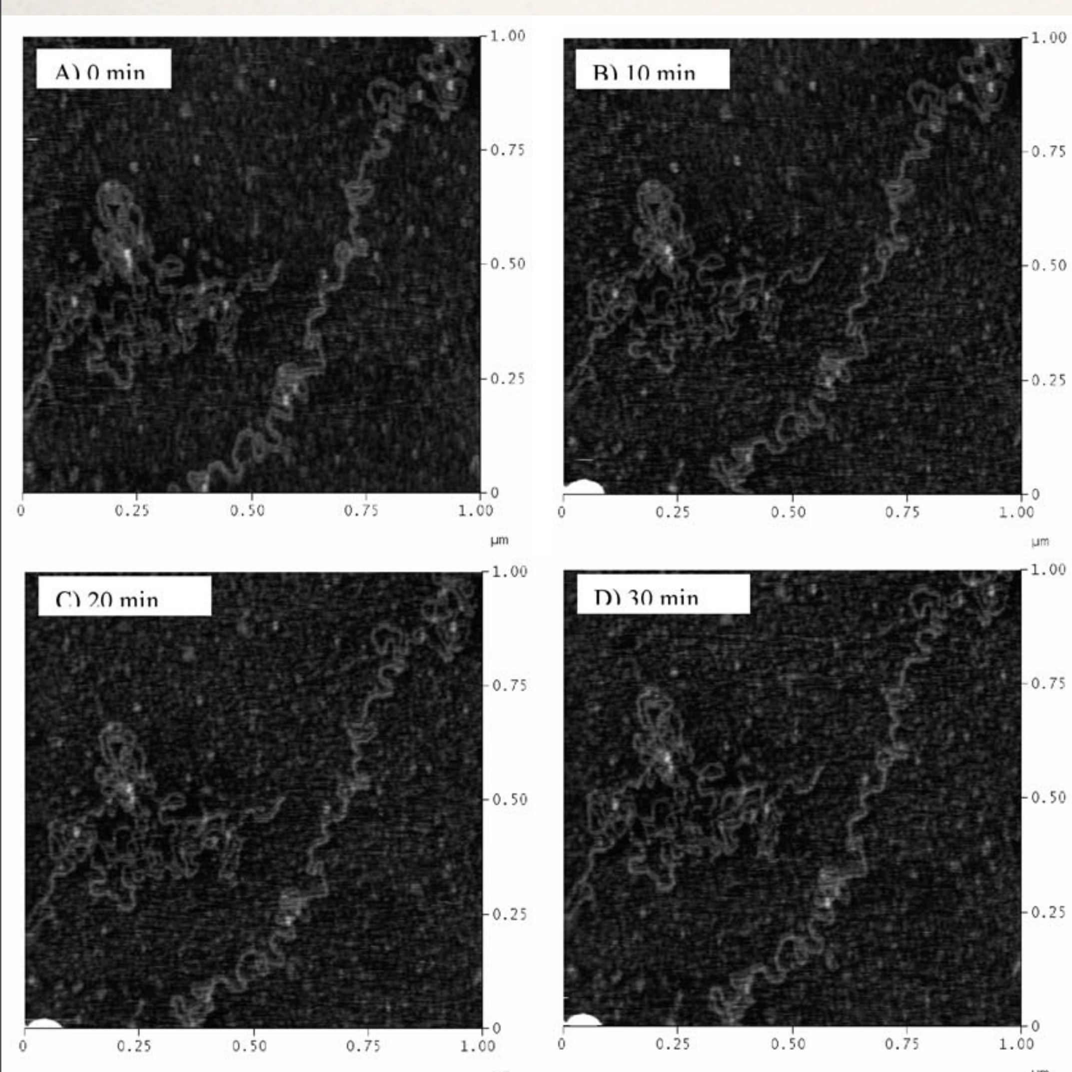
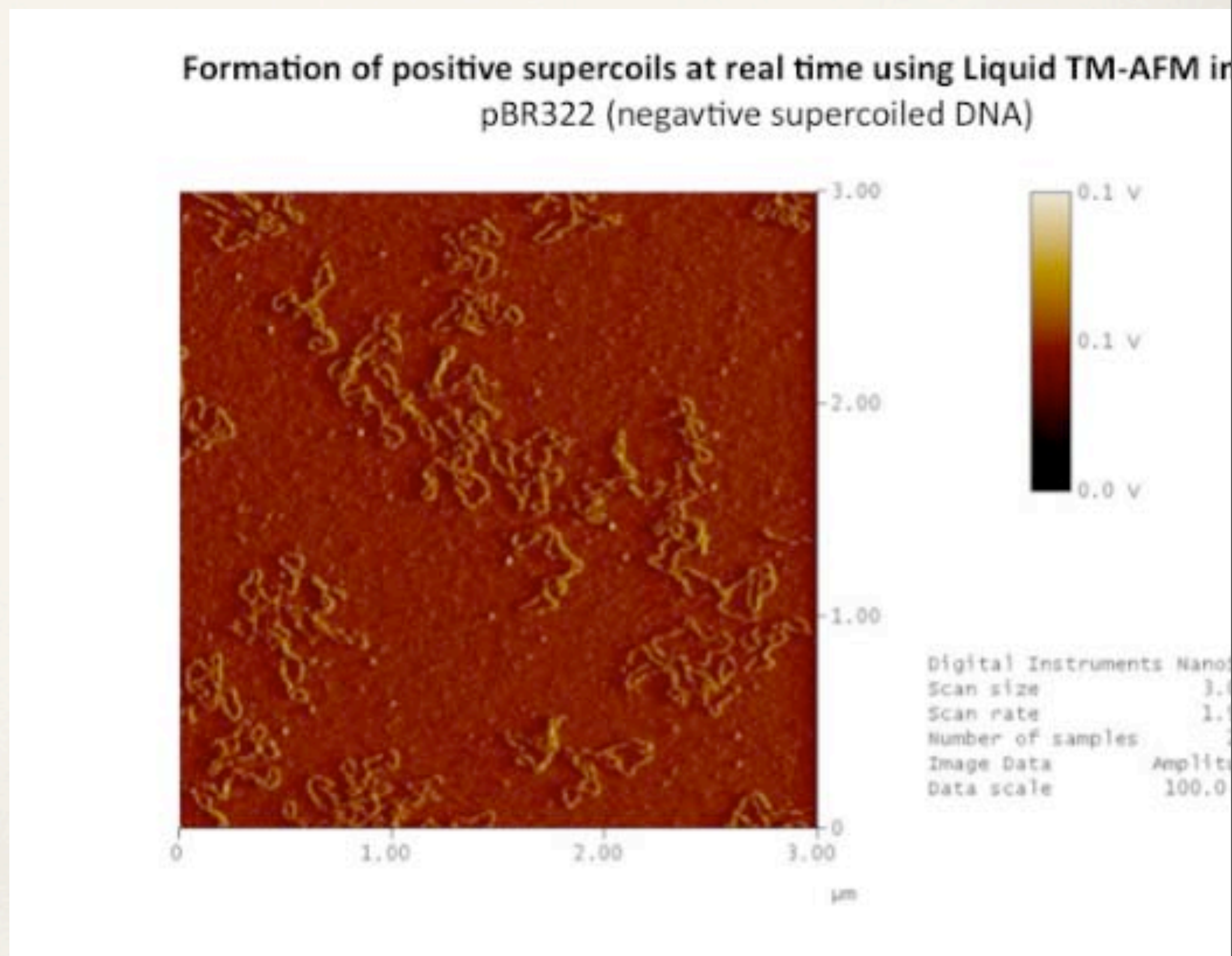
Strong vs Weak Absorption





Strong vs Weak Absorption

Trapping

Strong interaction

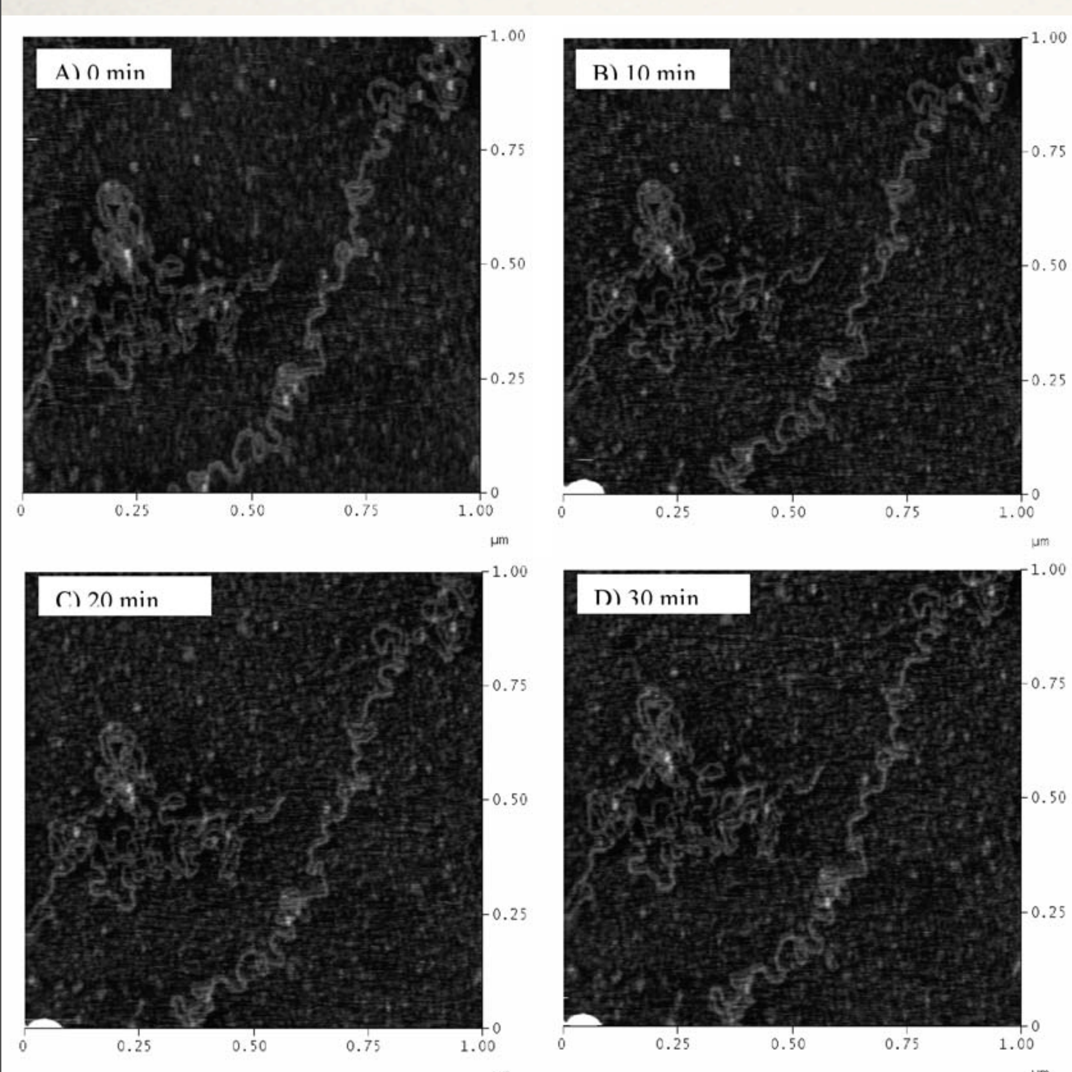
DNA-surface

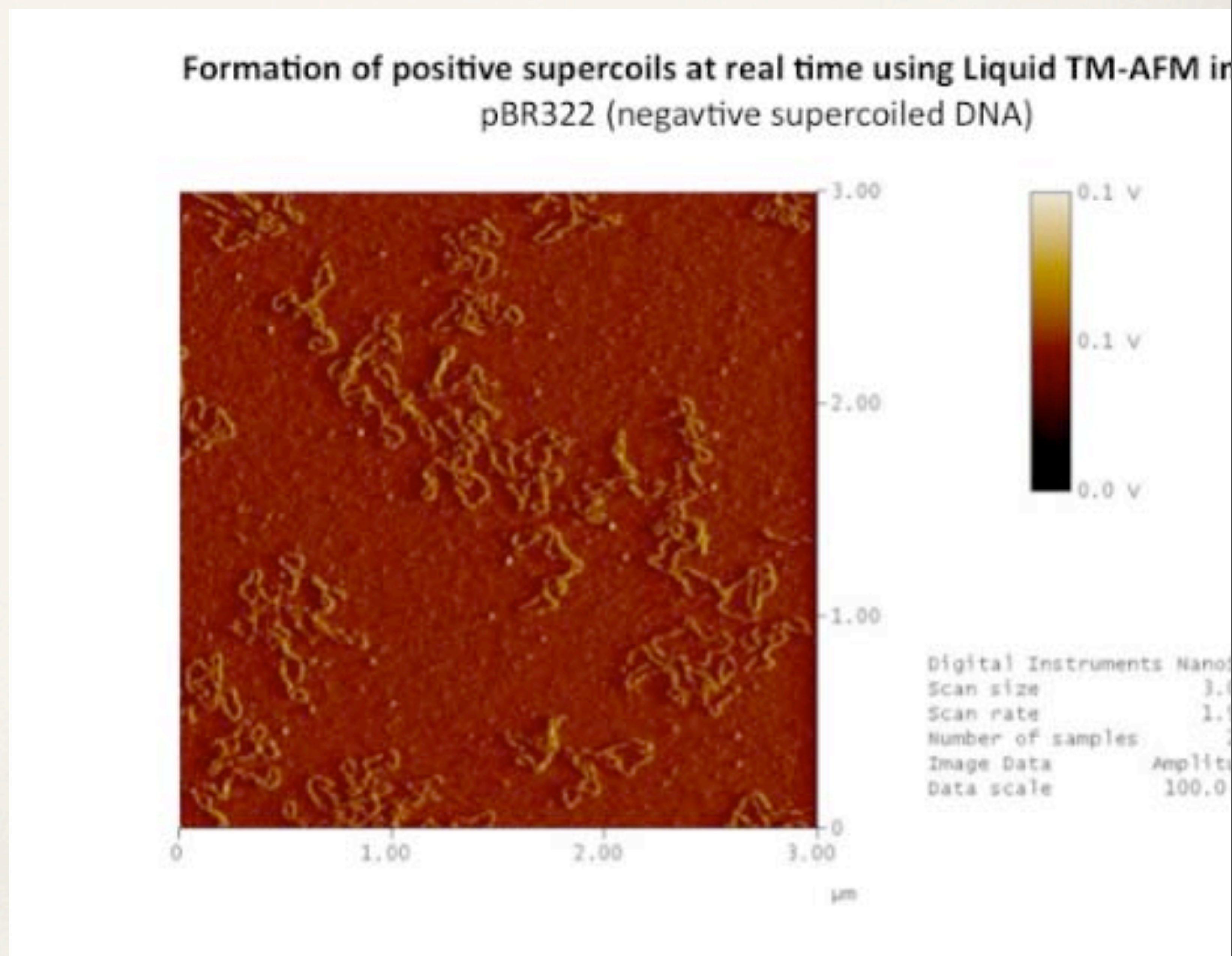
$U_{int} >> k_B T$

Equilibration

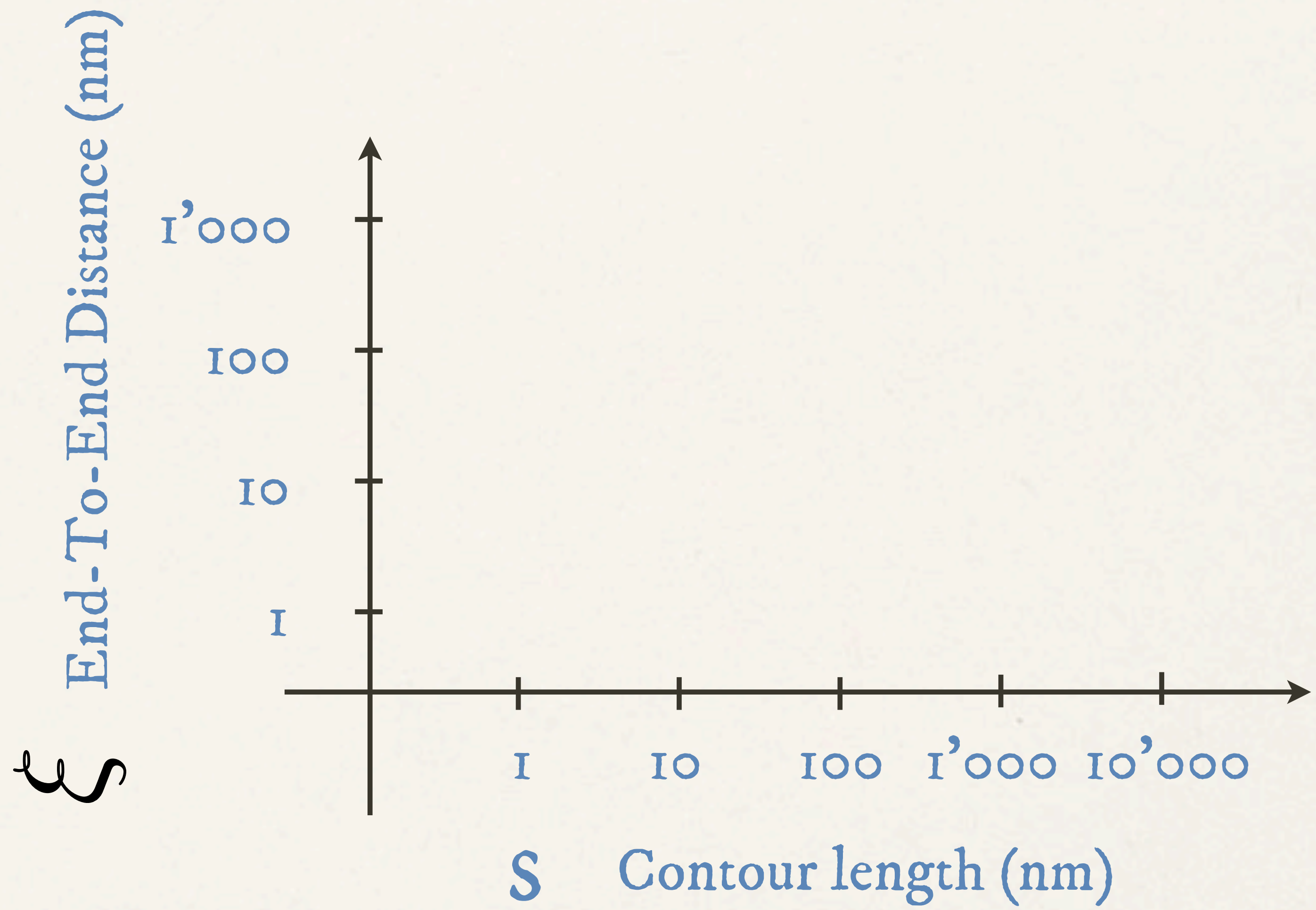
Weak interaction DNA-surface

$U_{int} \leq k_B T$





End-to-End Distance



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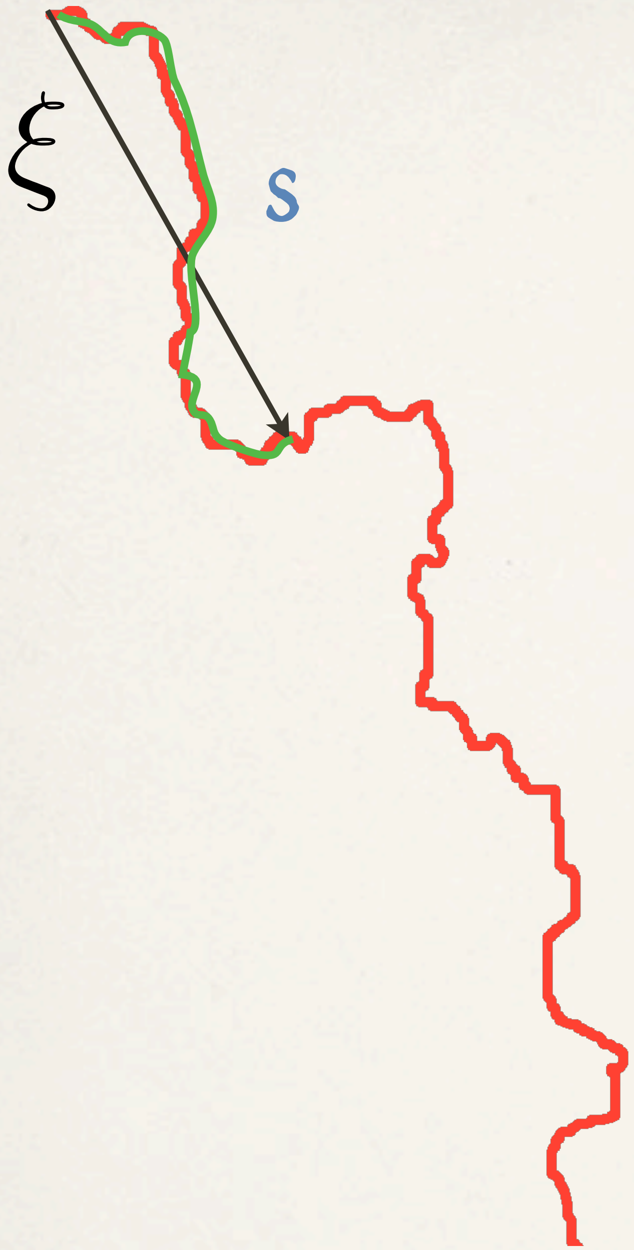

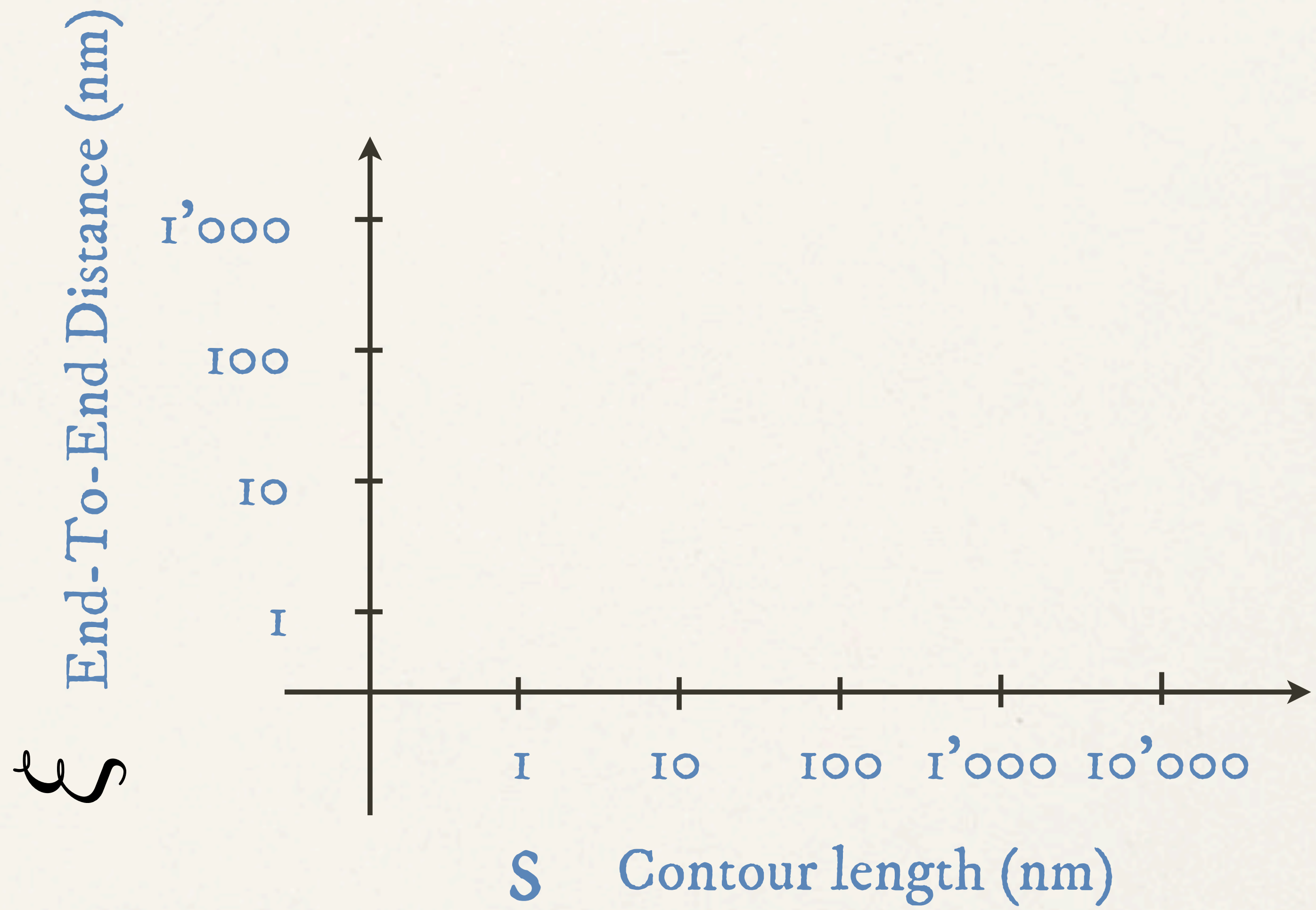

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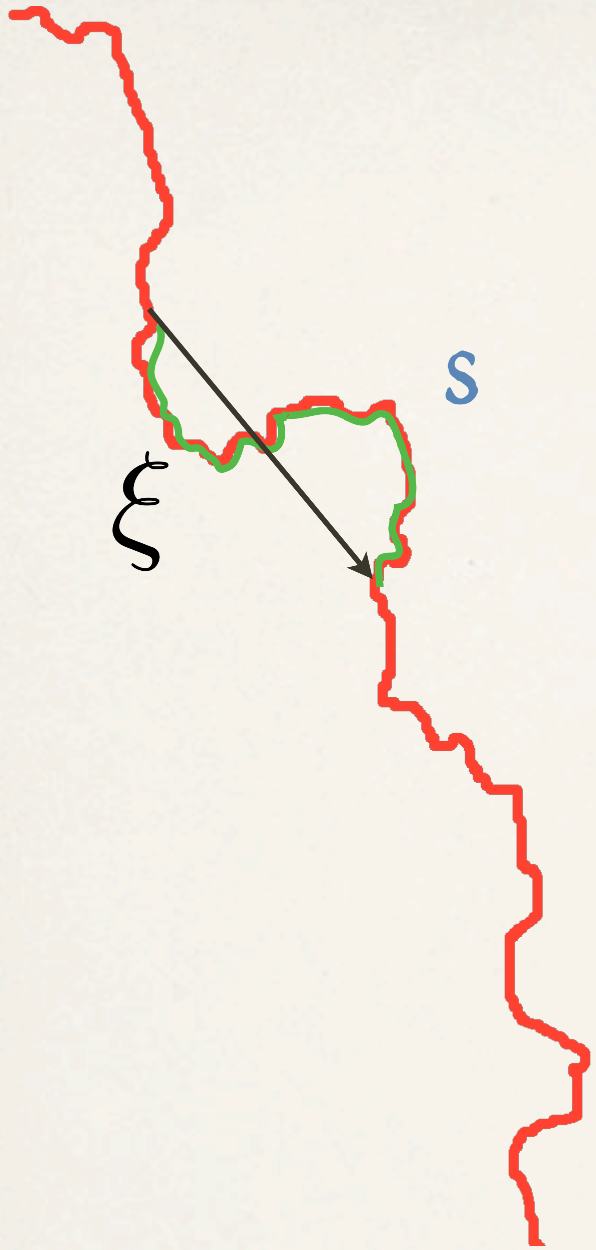

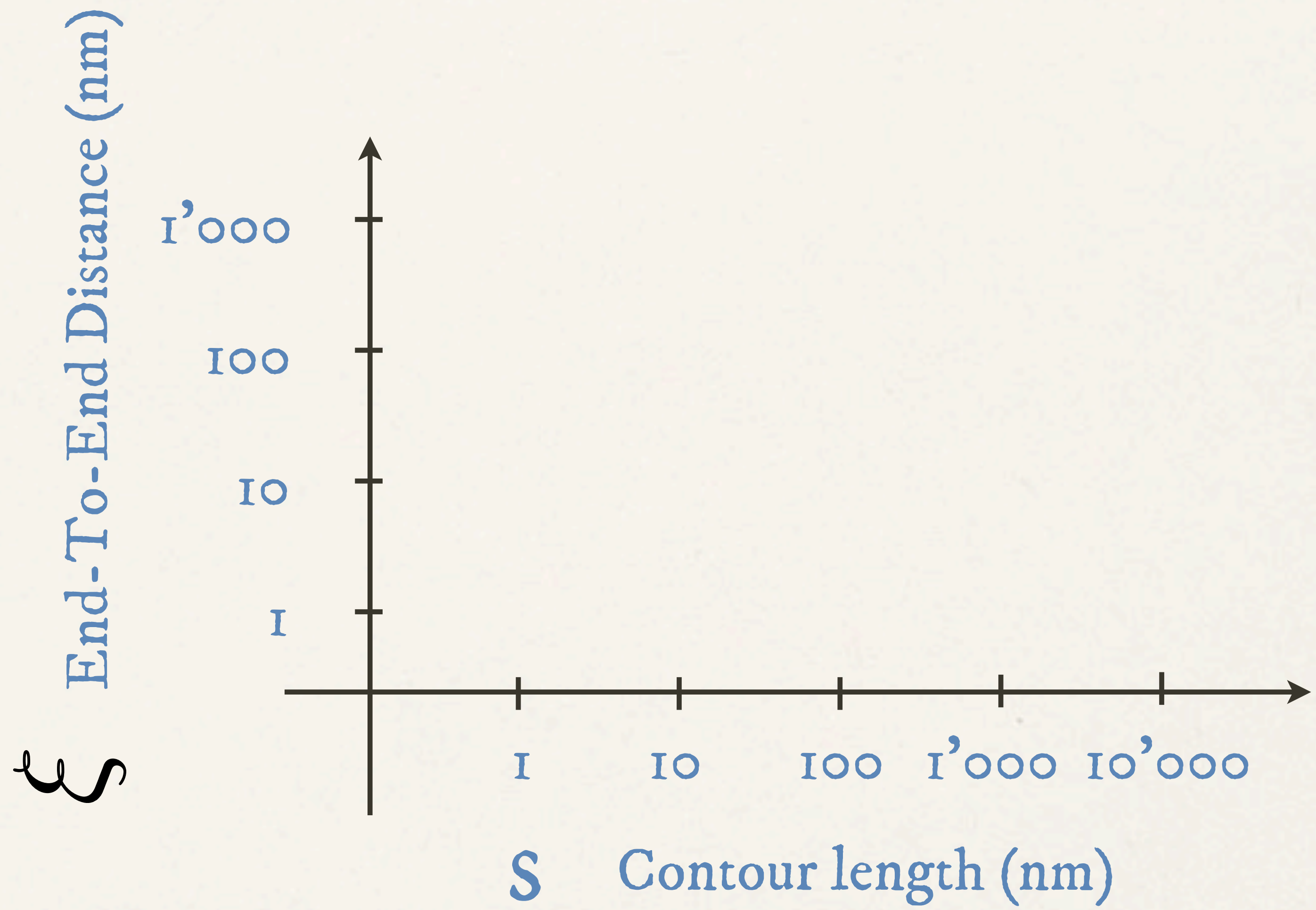

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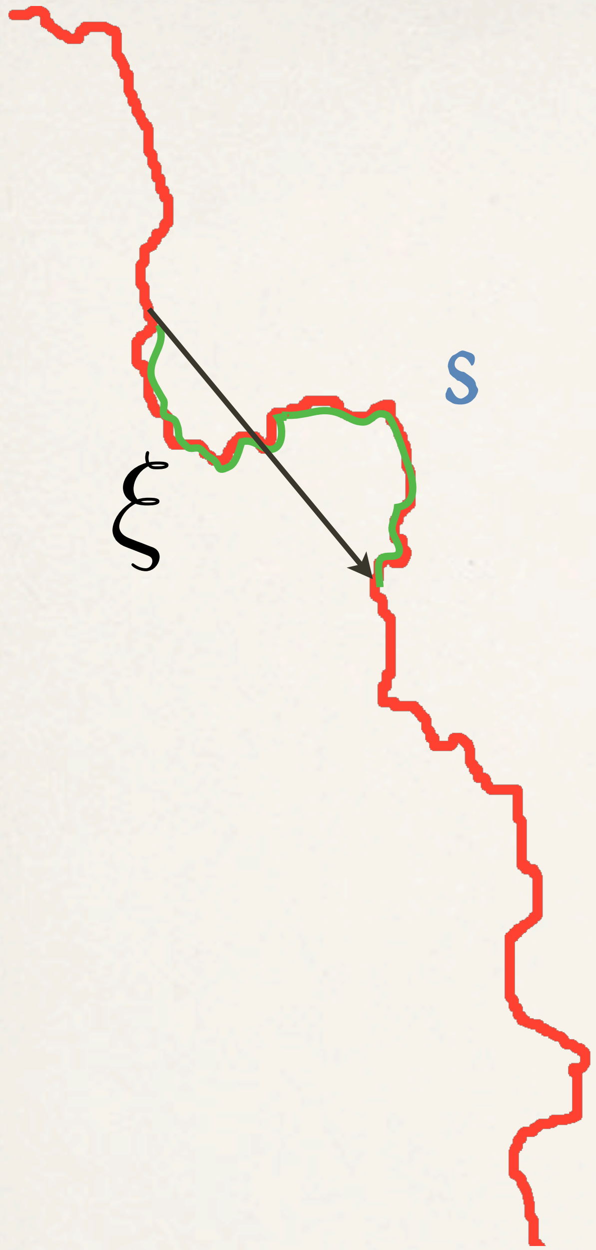

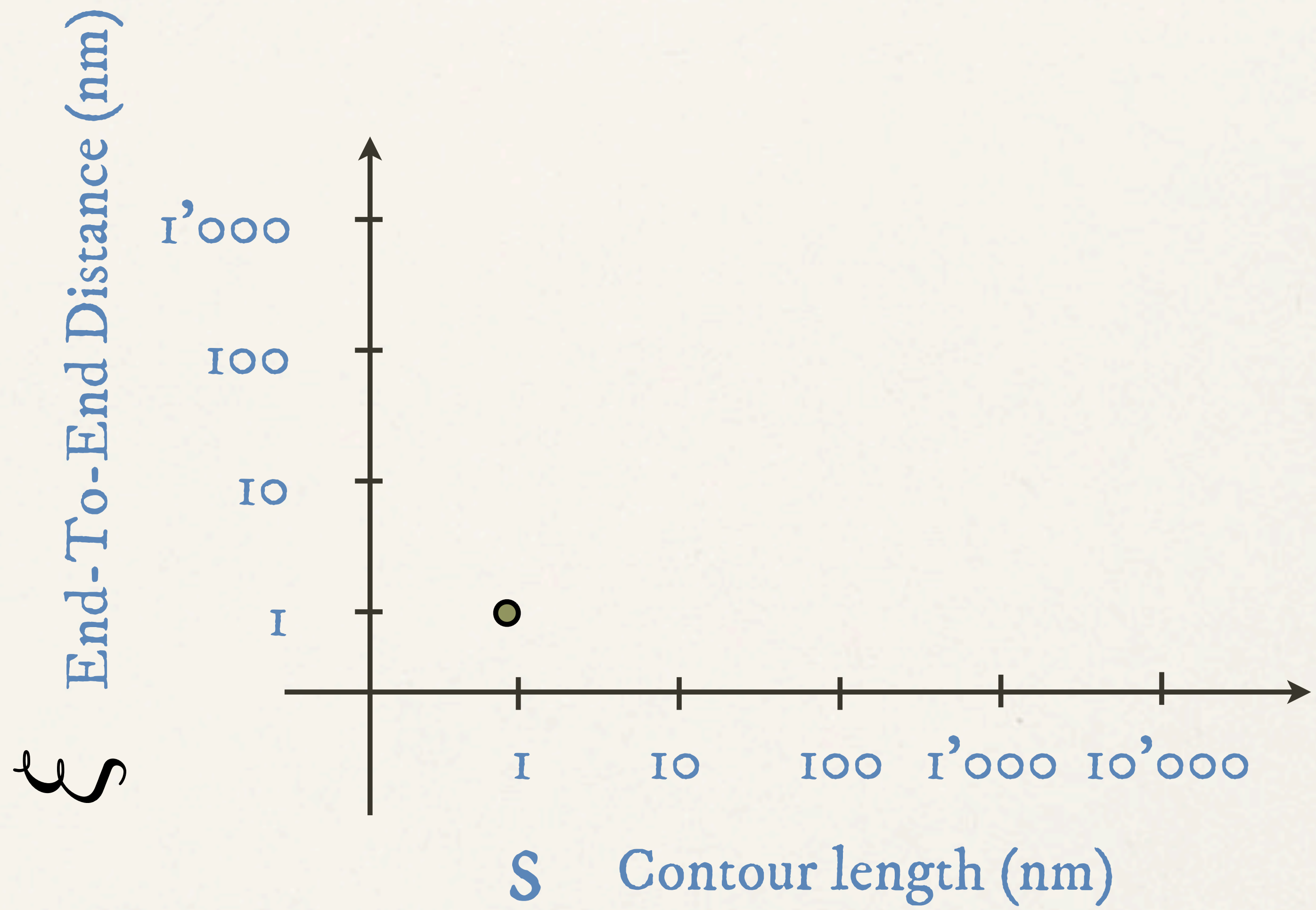

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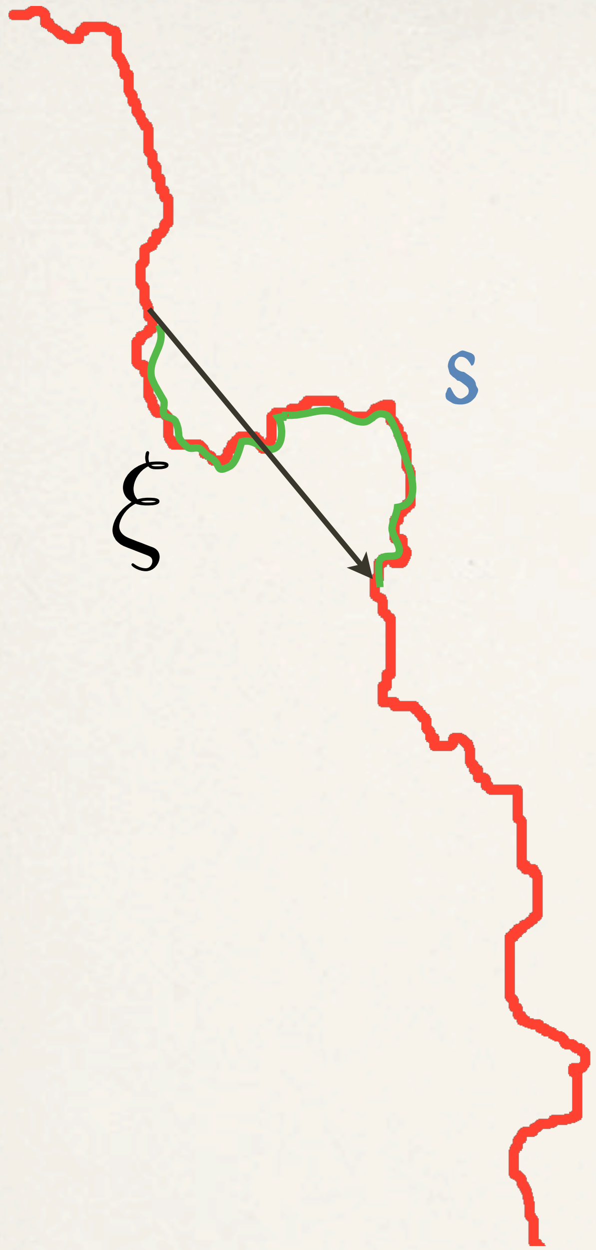

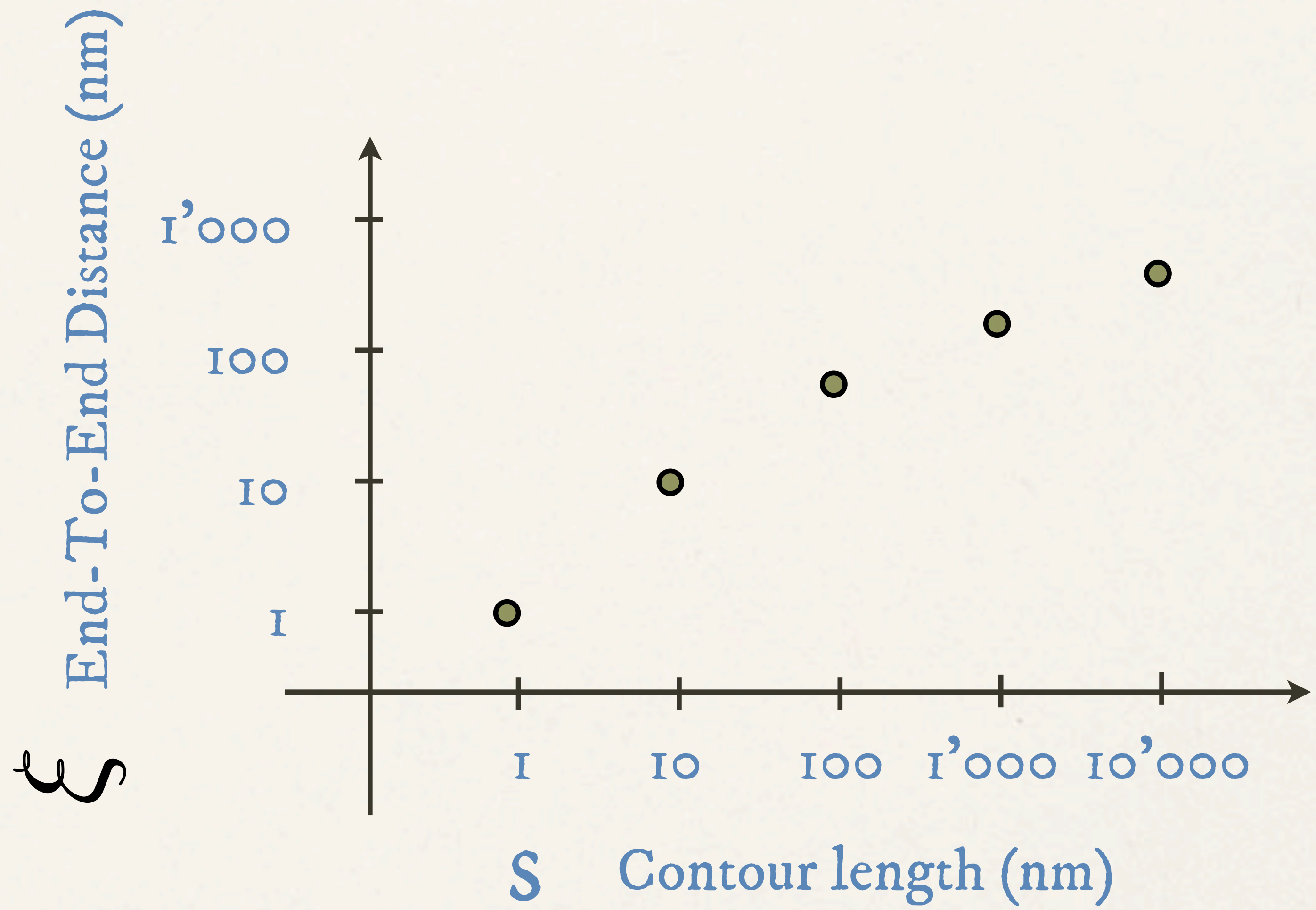

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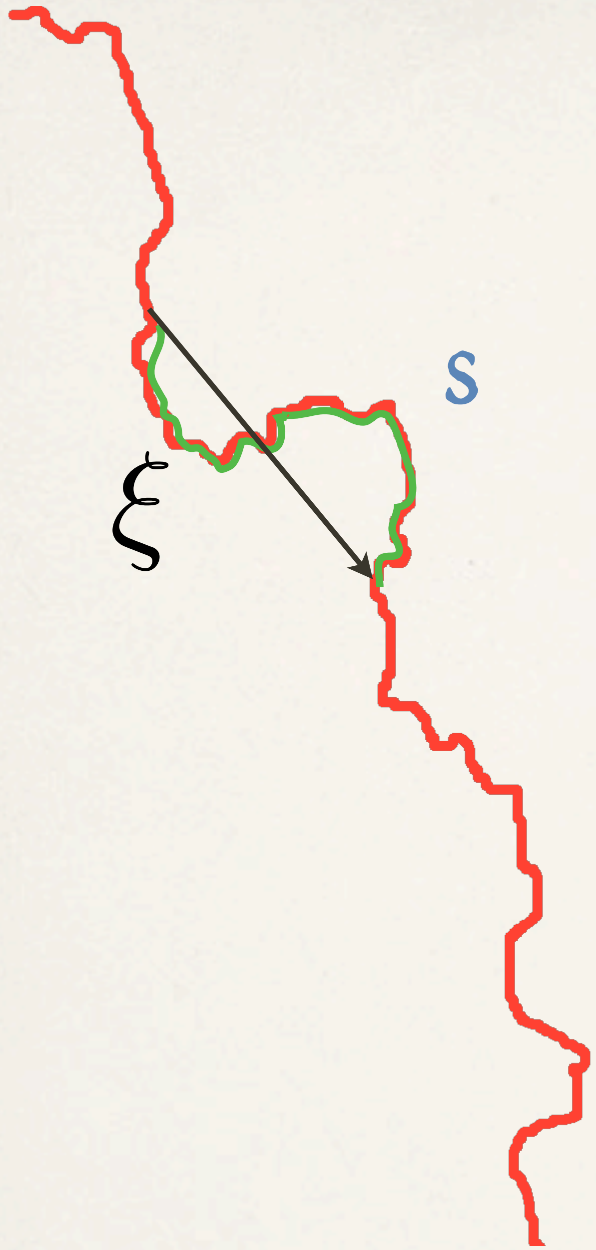

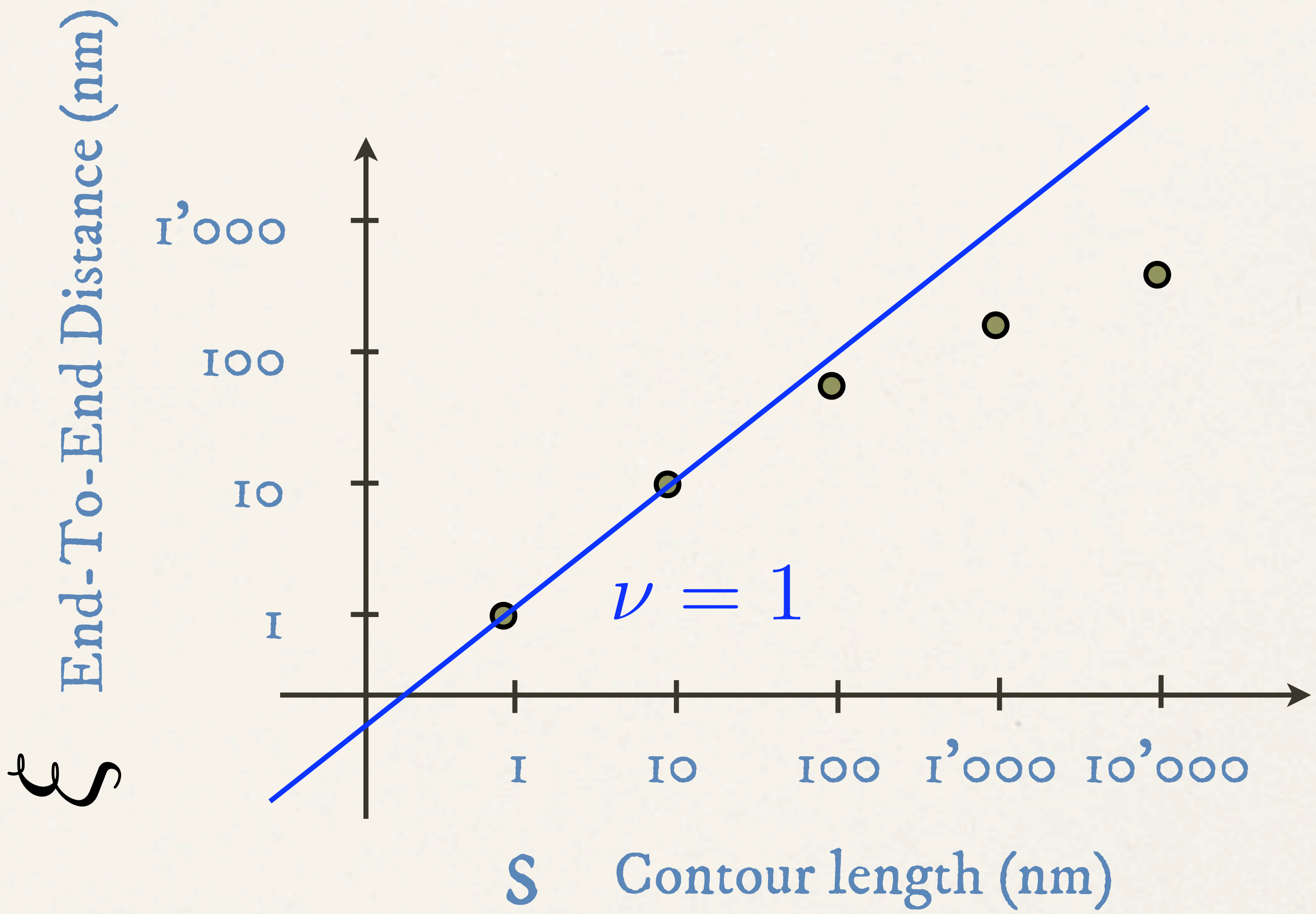

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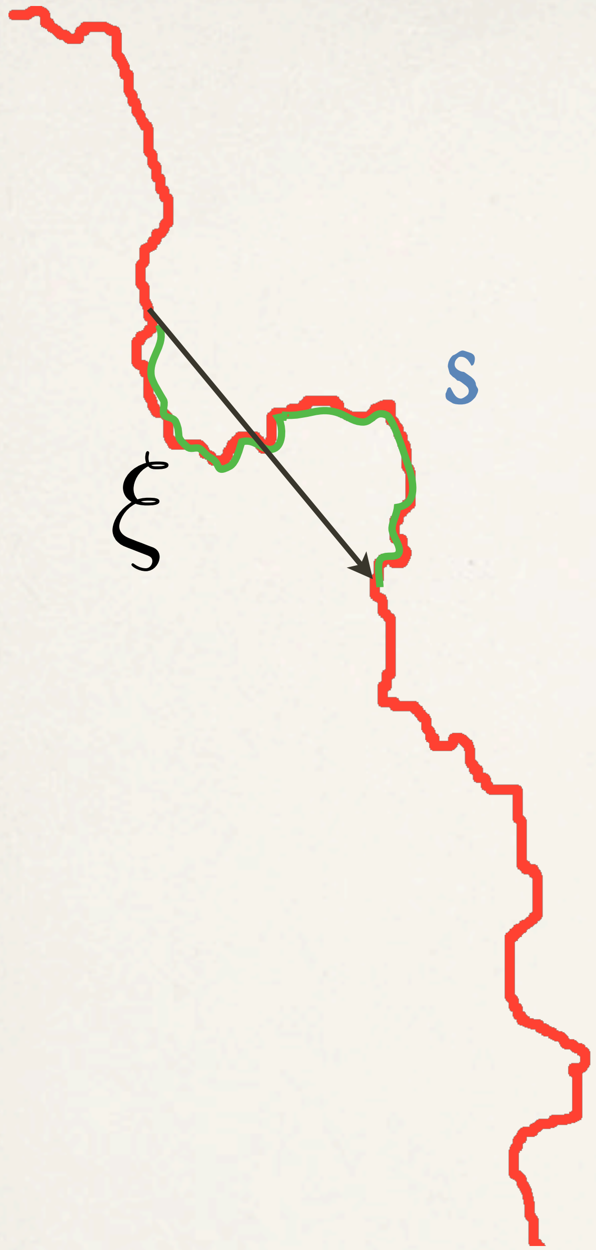
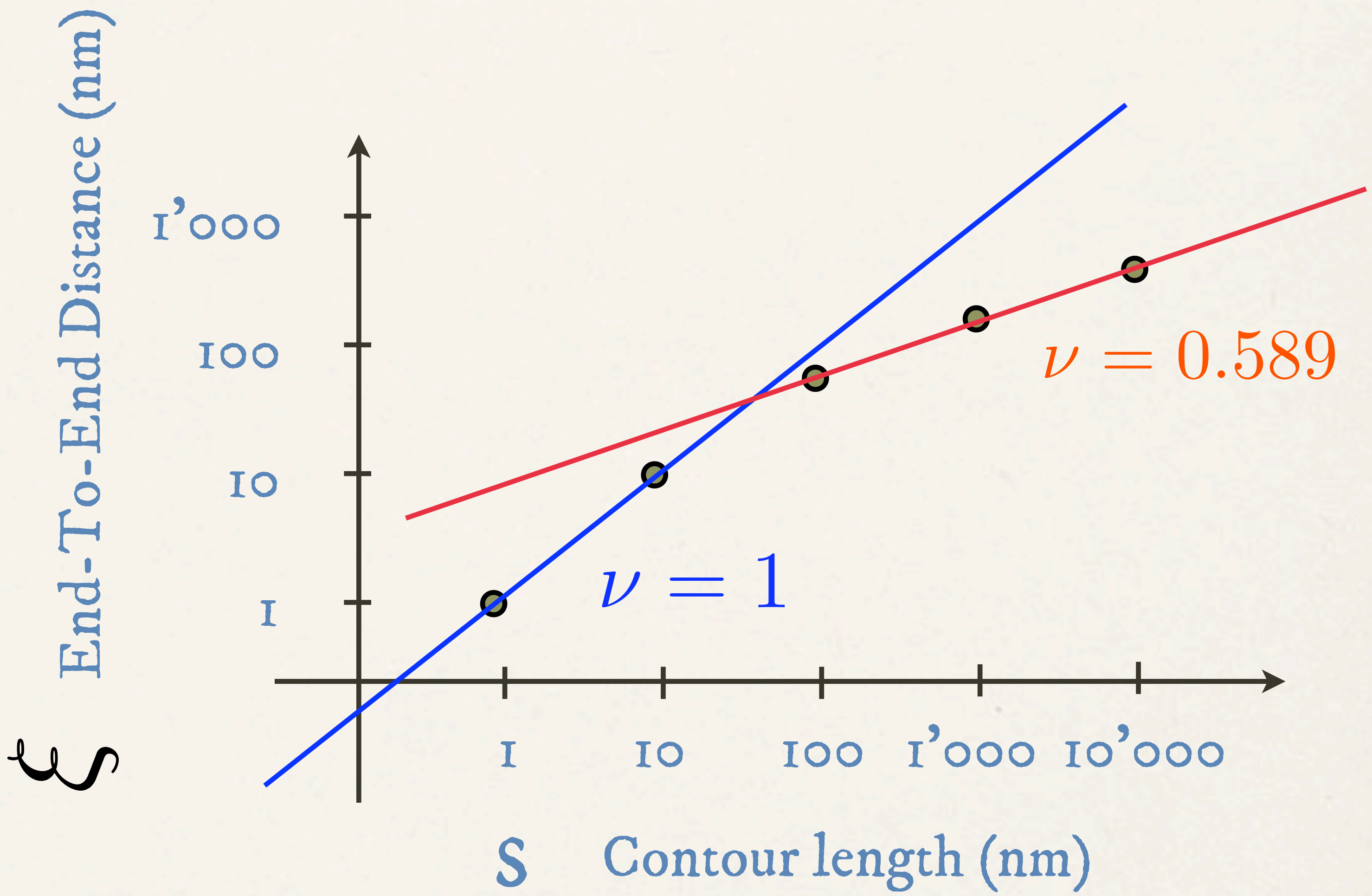




$$\xi \sim s^{\nu}$$

$$R_G \sim s^{\nu}$$

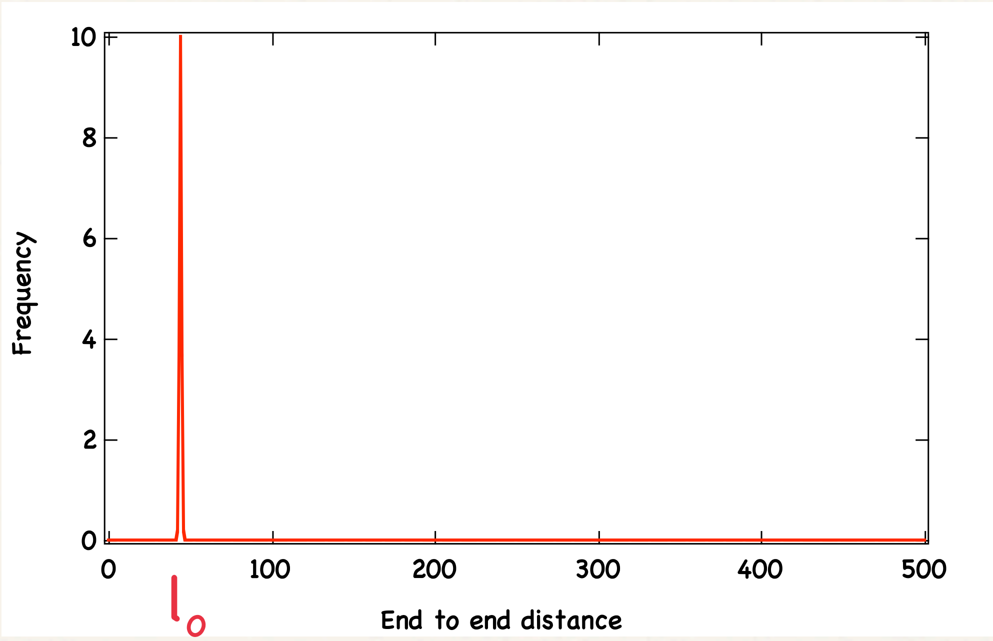
Distribution Functions

Distribution Functions

Perfectly rigid polymer of total length l_o

l_o

End-to-end distribution

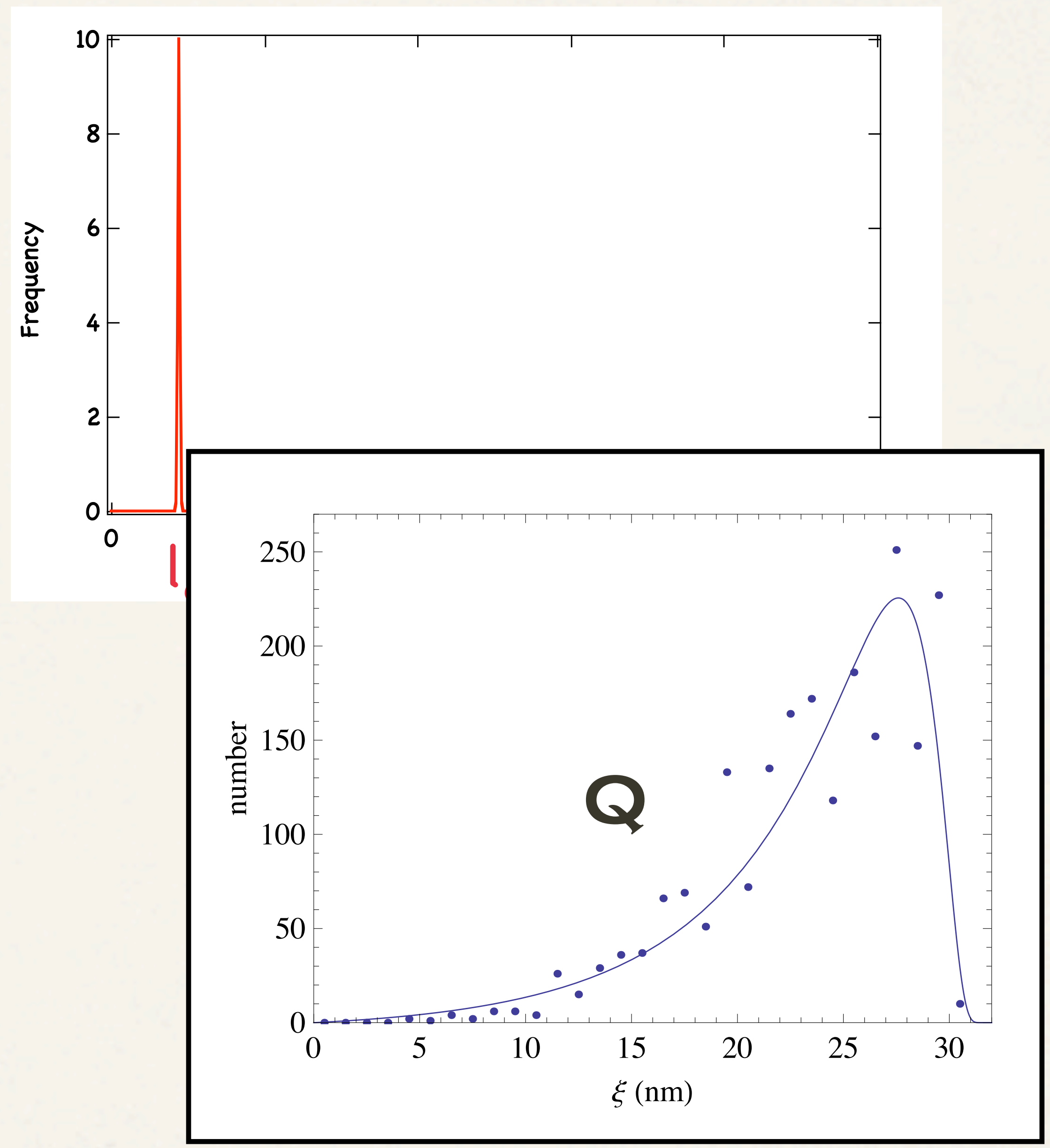


Distribution Functions

Perfectly rigid polymer of total length l_o

l_o

End-to-end distribution



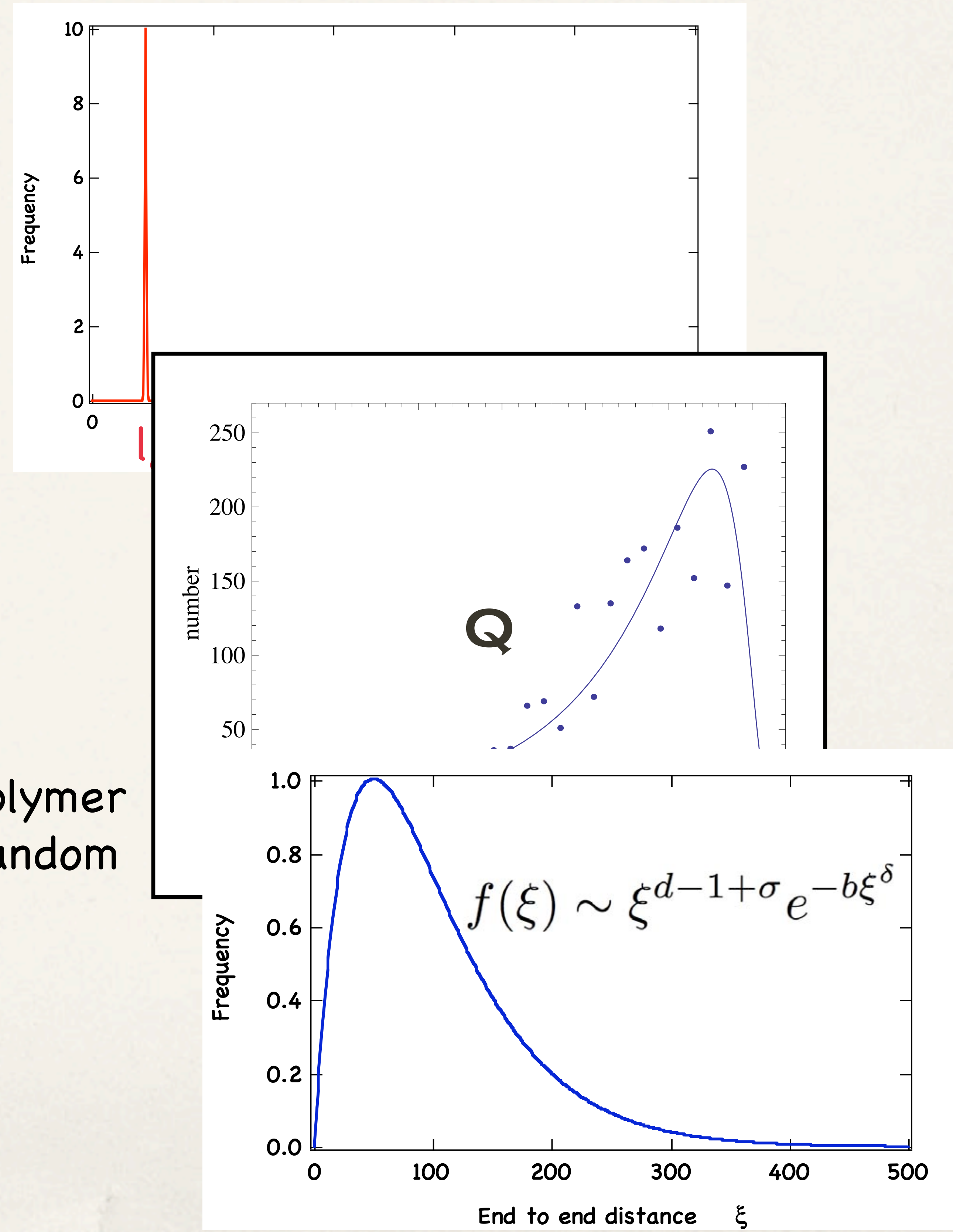
Semi-flexible polymer of total length l_o

Distribution Functions

Perfectly rigid polymer
of total length l_o

l_o

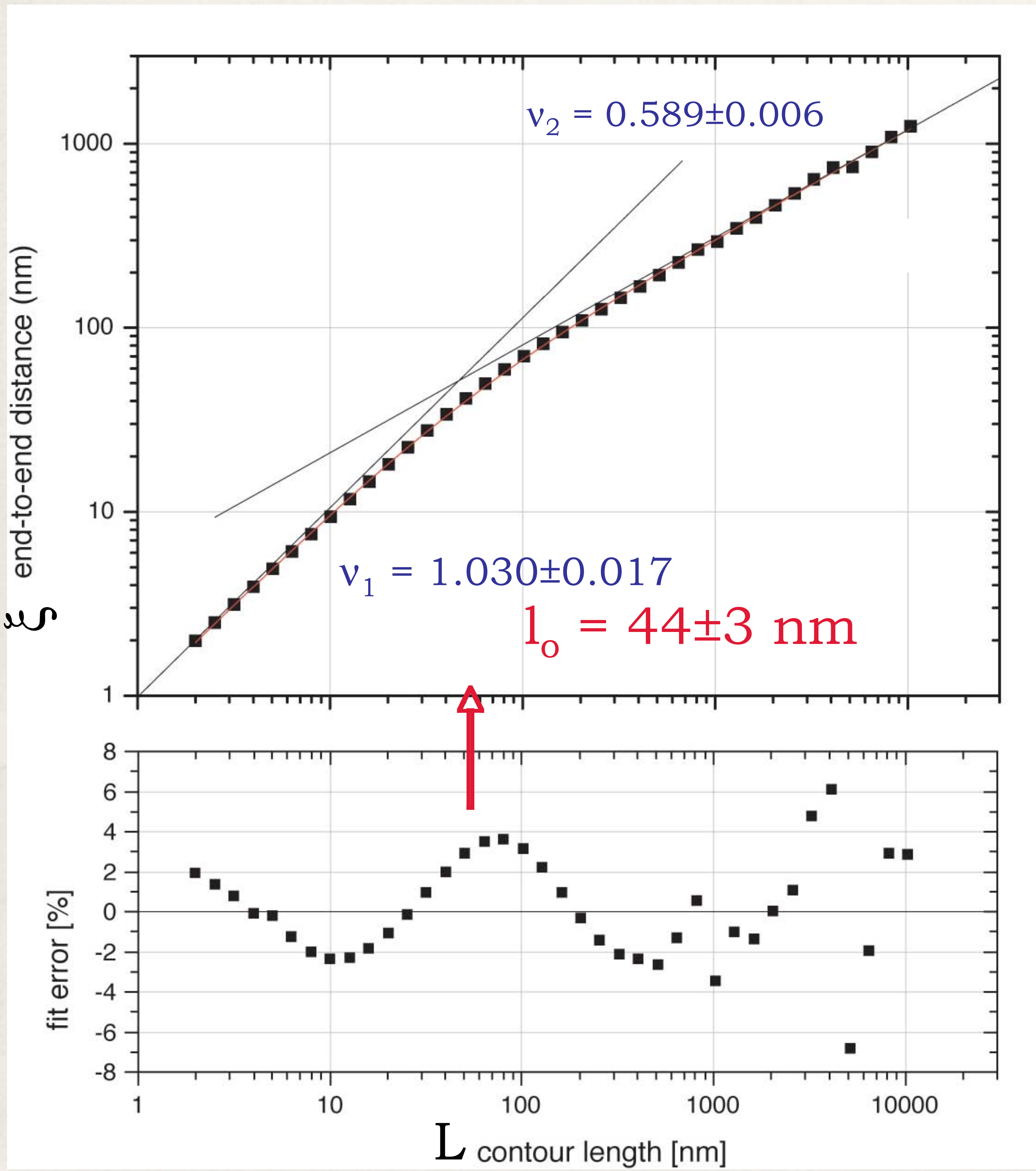
End-to-end distribution



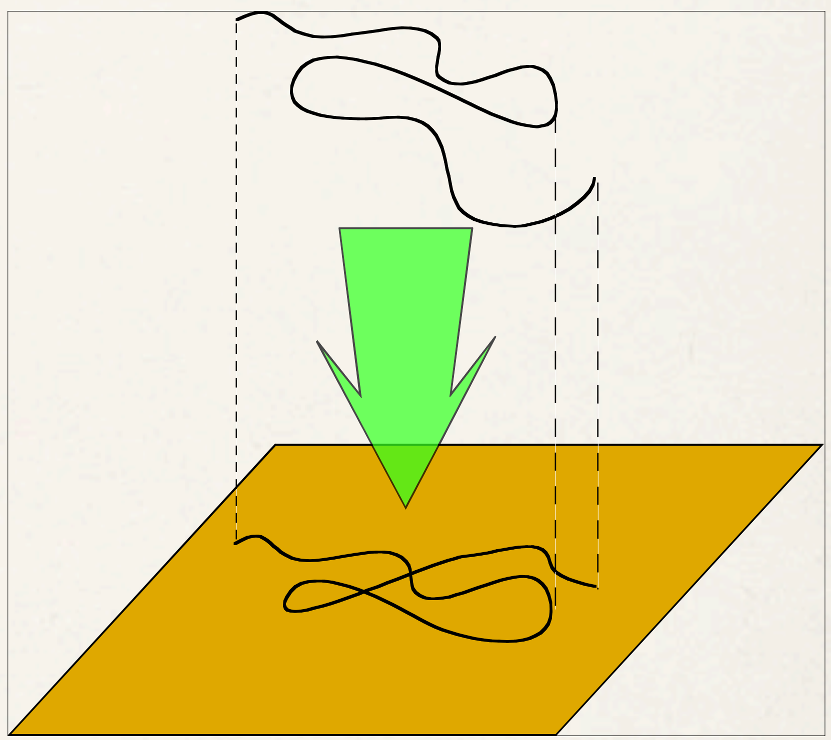
Semi-flexible polymer
of total length l_o

Perfectly flexible polymer
of total length L (Random Walk)

Previous Results on Linear DNA



$$\xi = \xi_o \left(\frac{L}{l_o}\right)^{\nu_1} \left(1 + \frac{L}{l_o}\right)^{\nu_2 - \nu_1}$$



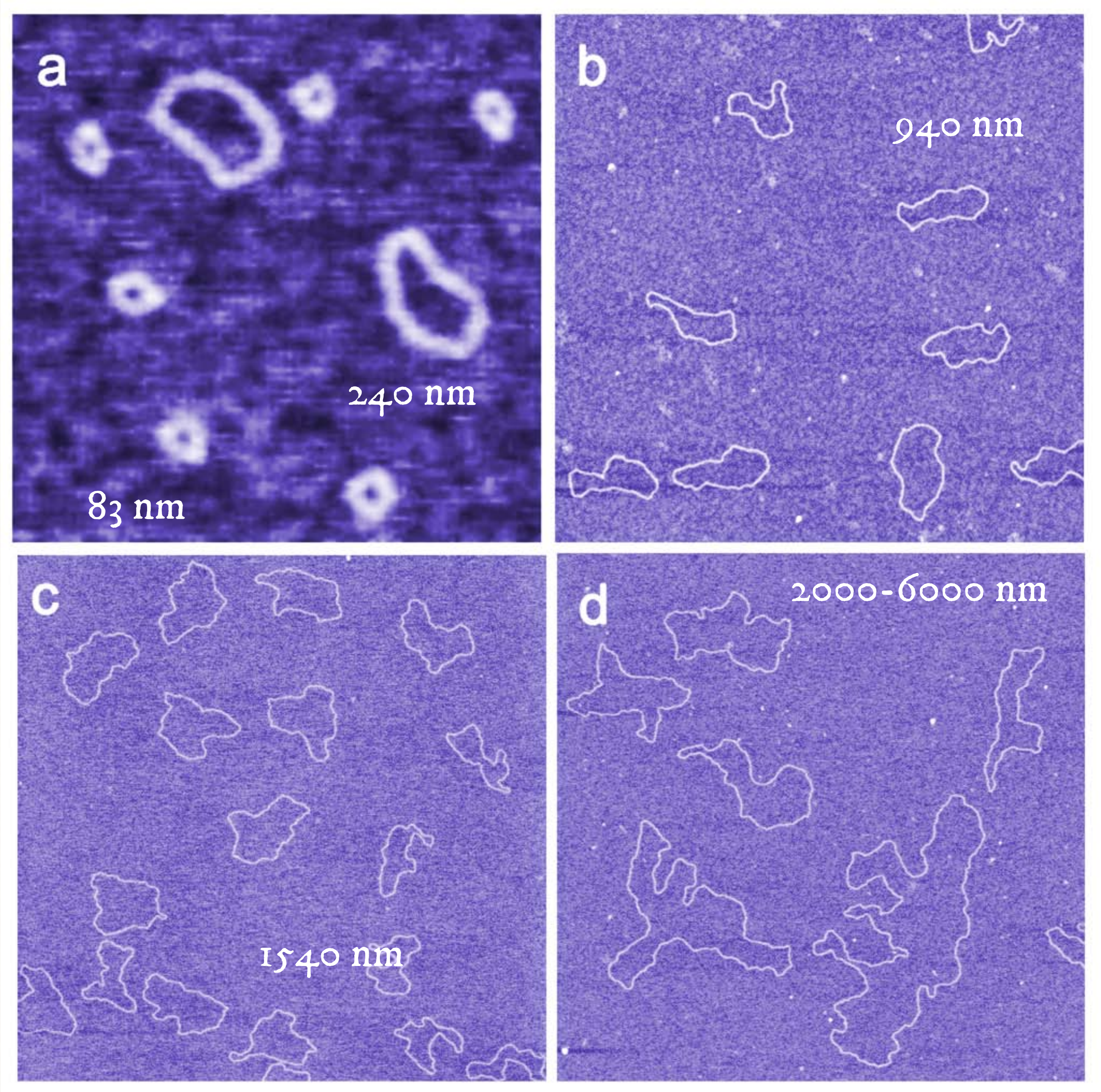
Trapping

Strong interaction DNA-surface

$U_{int} >> k_B T$

[Valle, Favre, De Los Rios, Rosa and Dietler, PRL, **95** 158105 (2005)]

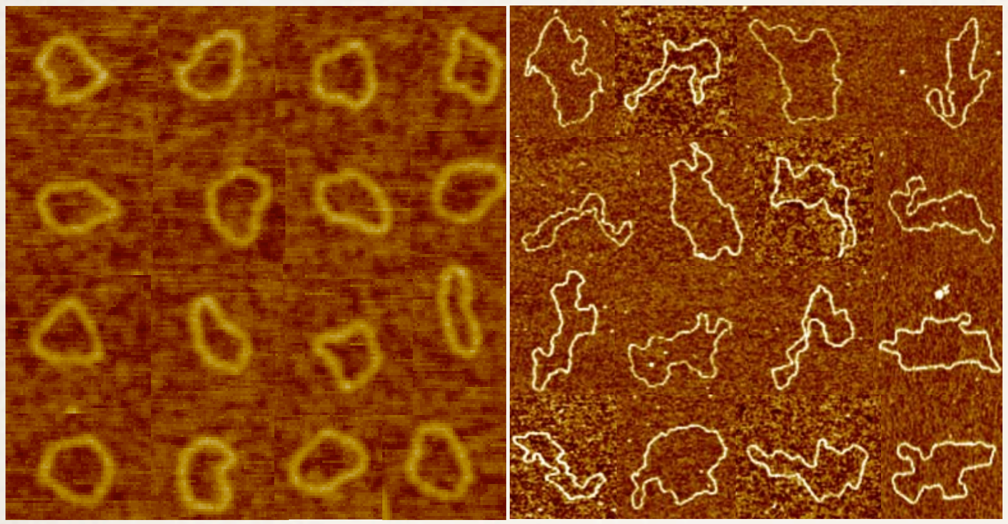
Circular dsDNA in 2D

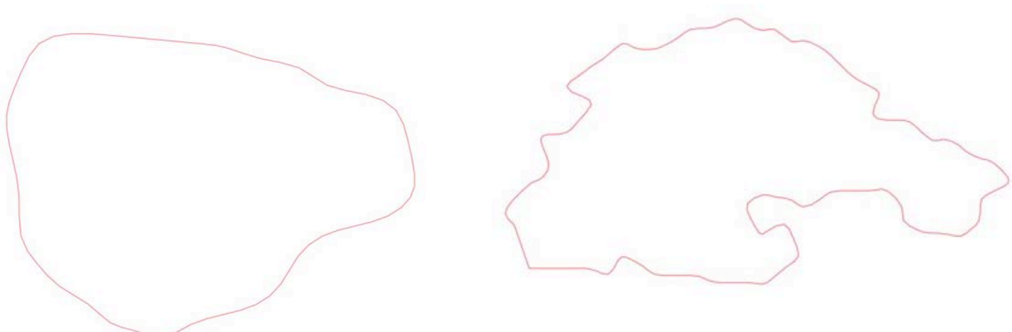


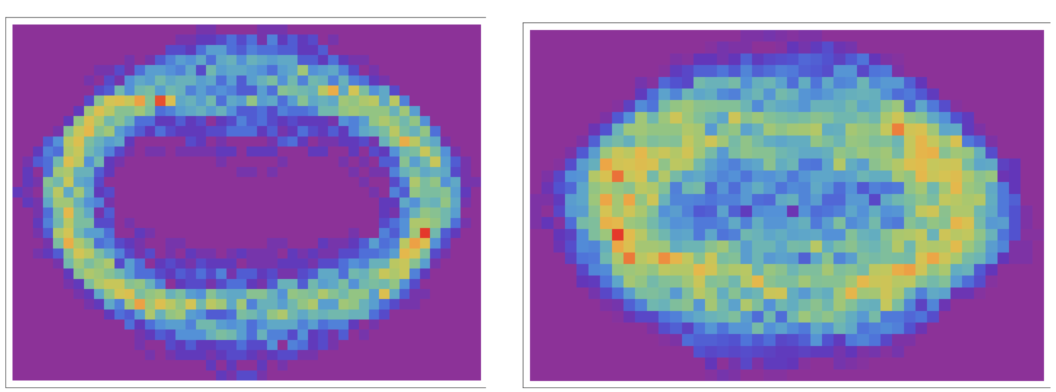
Witz et al., PRL, 101, (2008) 148103.

Shape of ring polymers

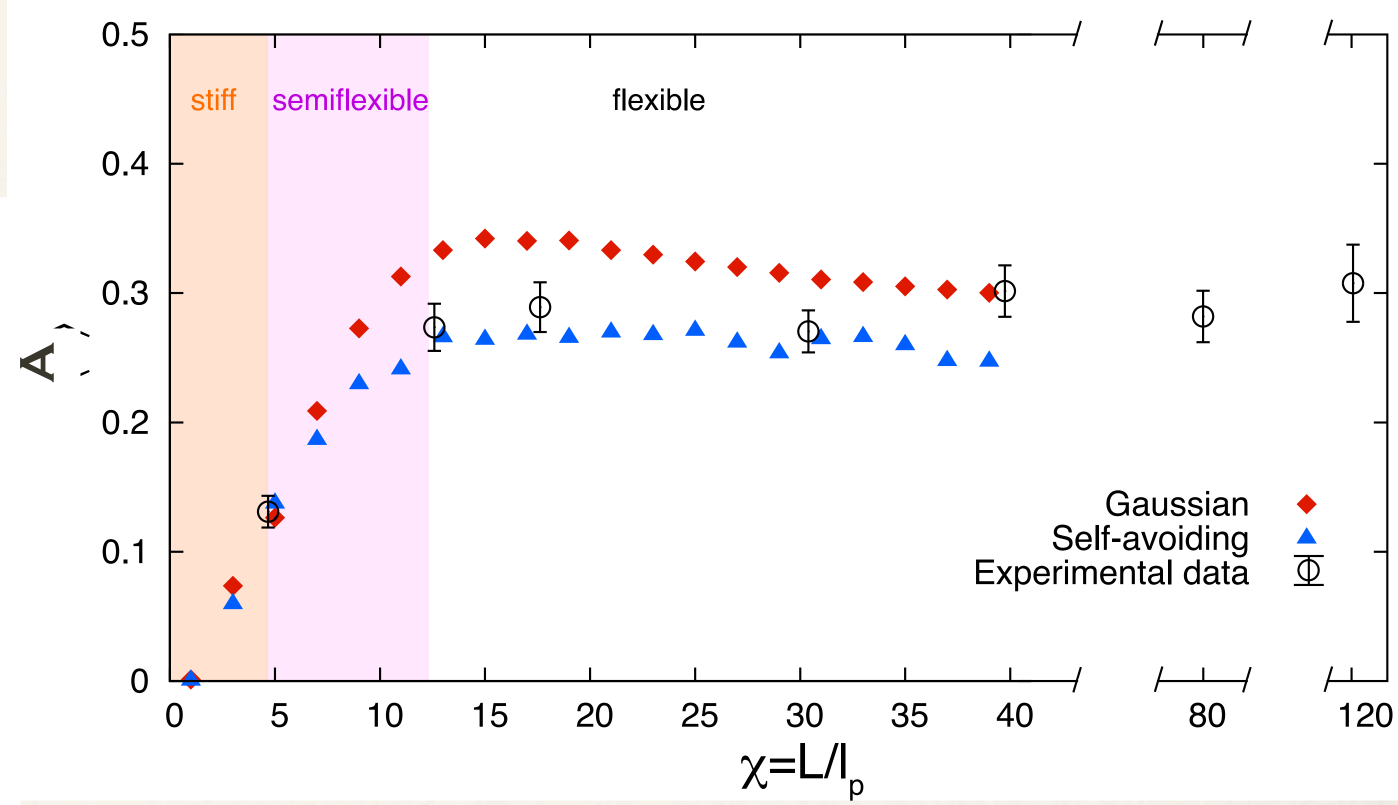
230 nm ring 2 microns ring







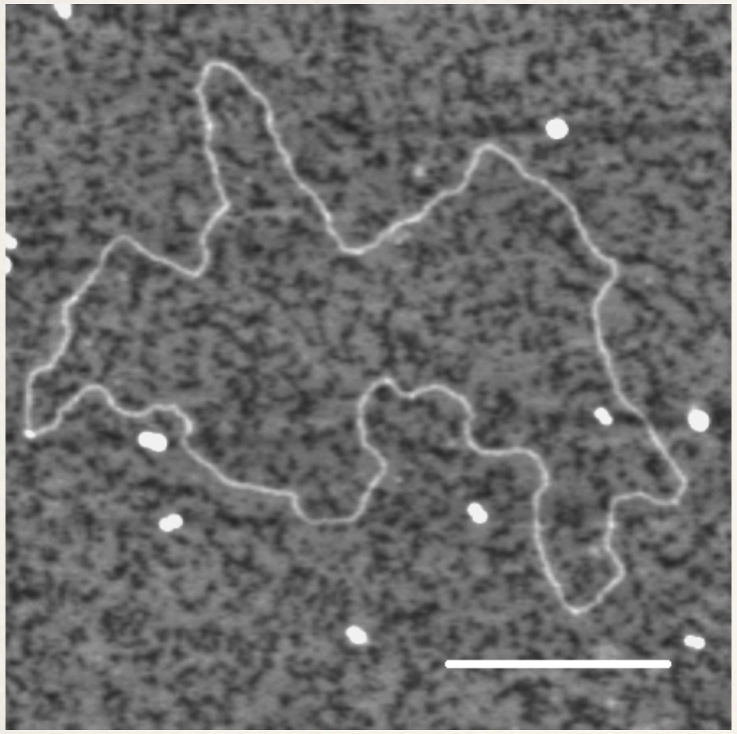
- Short rings adopt elliptical shapes, with a breathing movement. No SAW effects
- Long rings are also clearly elliptical. SAW effects appear



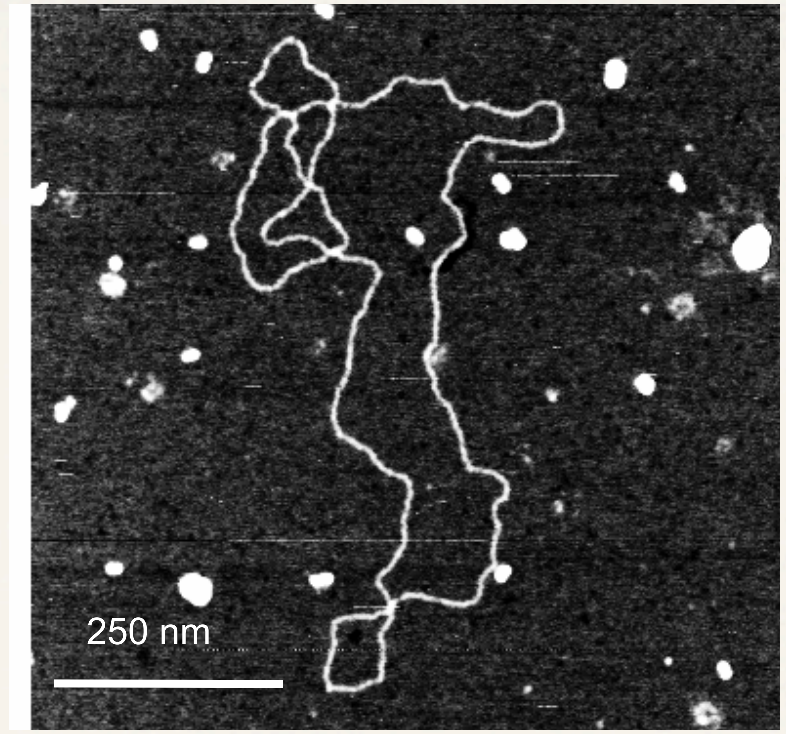
- SAW effects appear in the semiflexible regime
- Good agreement between numerical and experimental data

Drube F., Alim K., Witz G., Dietler, G. and Frey E., Nano Lett. 10, 1445-1449 (2010)

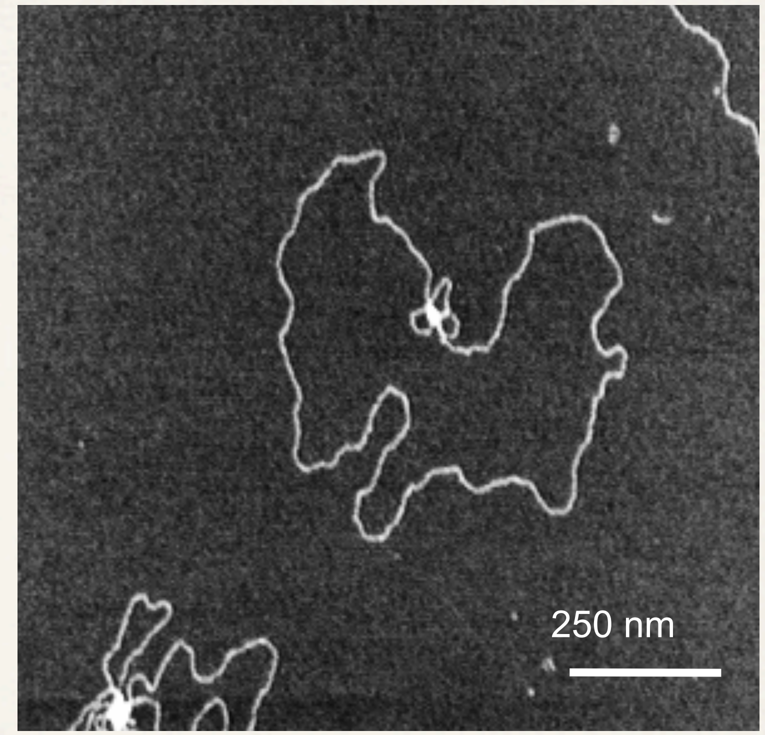
Weak Adsorption: 2D Knots



Unknot



Simple

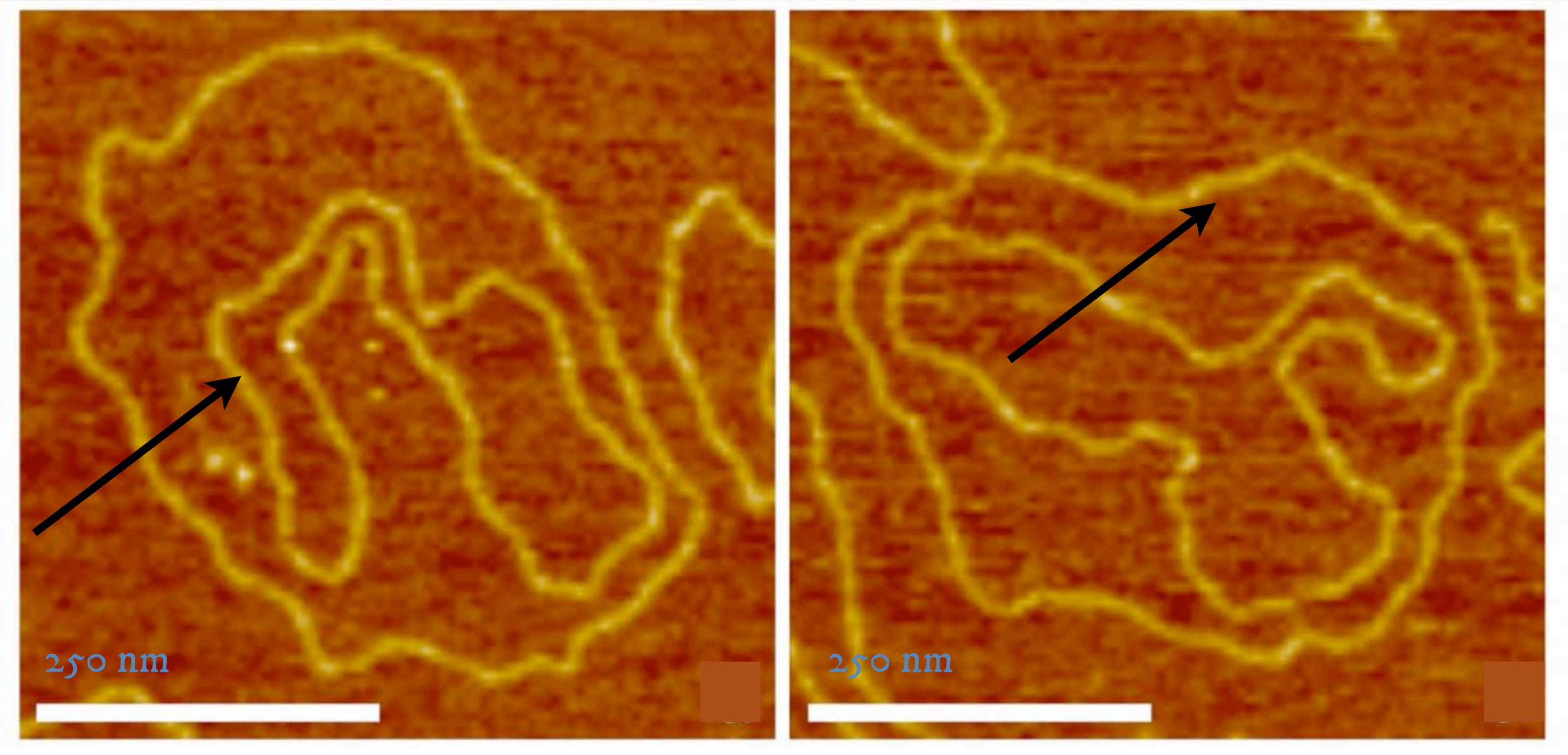


Complex

Weak adsorption		
	d_f	$\nu = 1/d_f$
Unknots	1.491 ± 0.037	0.670 ± 0.017
Simple knots	1.530 ± 0.065	0.654 ± 0.028
Complex knots	1.541 ± 0.086	0.650 ± 0.036

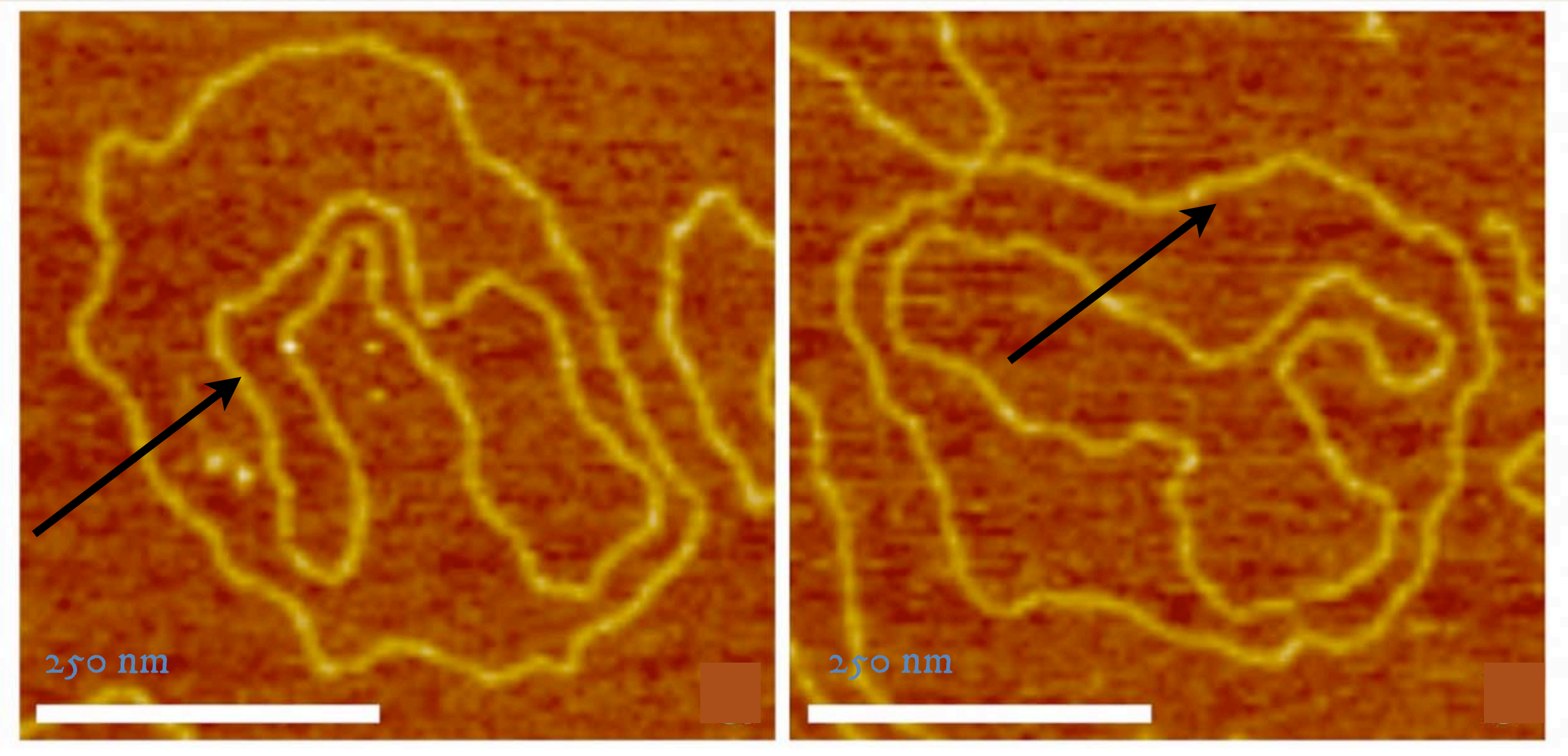
Ercolini et al., PRL, 98, 058102 (2007)

Polymer confinement



Witz G., Rechendorff, K., Adamcik, J. and Dietler, G., *PRL, to appear.*

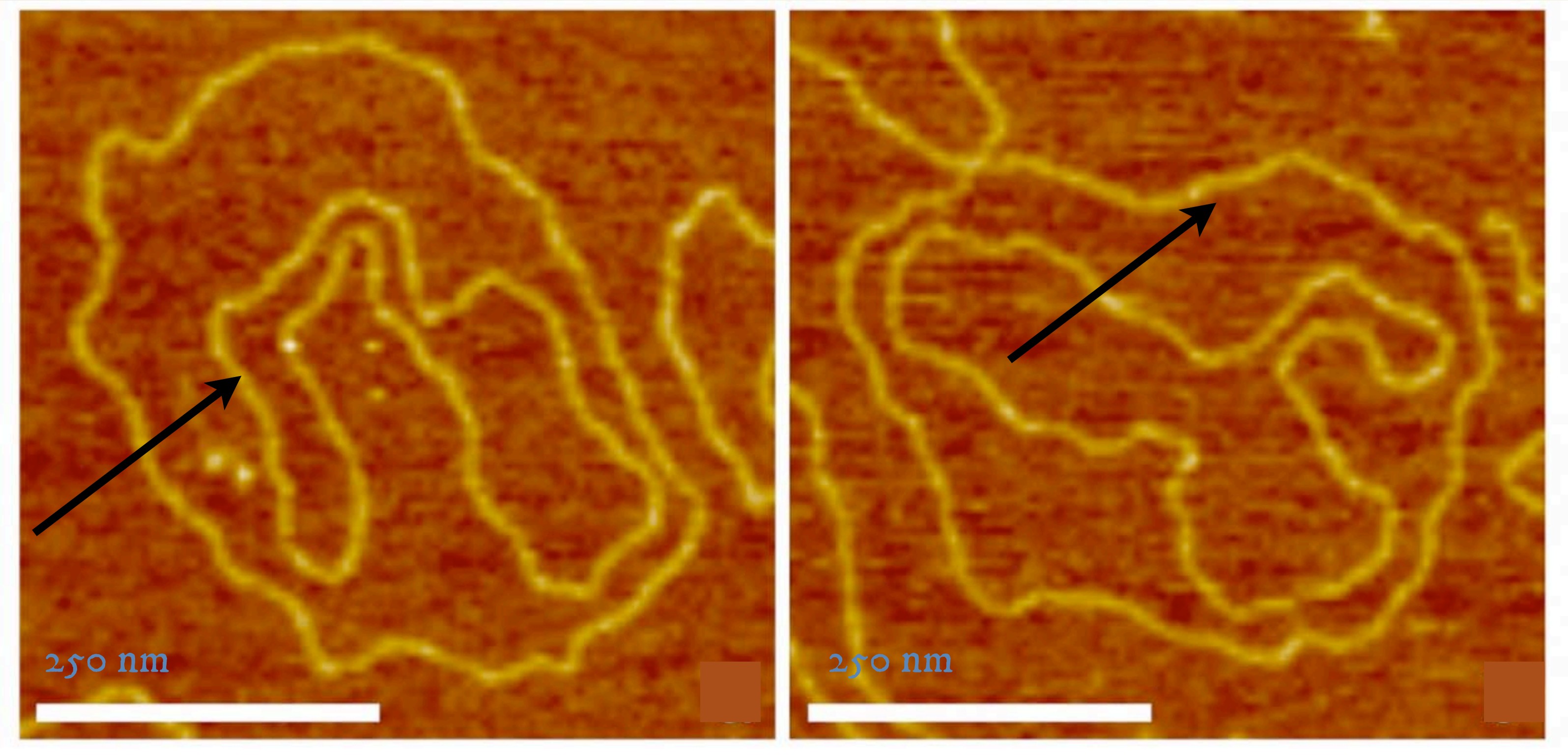
Polymer confinement



- Polymer confinement generally studied by fluorescence microscopy
- AFM offers much higher resolution

Witz G., Rechendorff, K., Adamcik, J. and Dietler, G., *PRL, to appear.*

Polymer confinement



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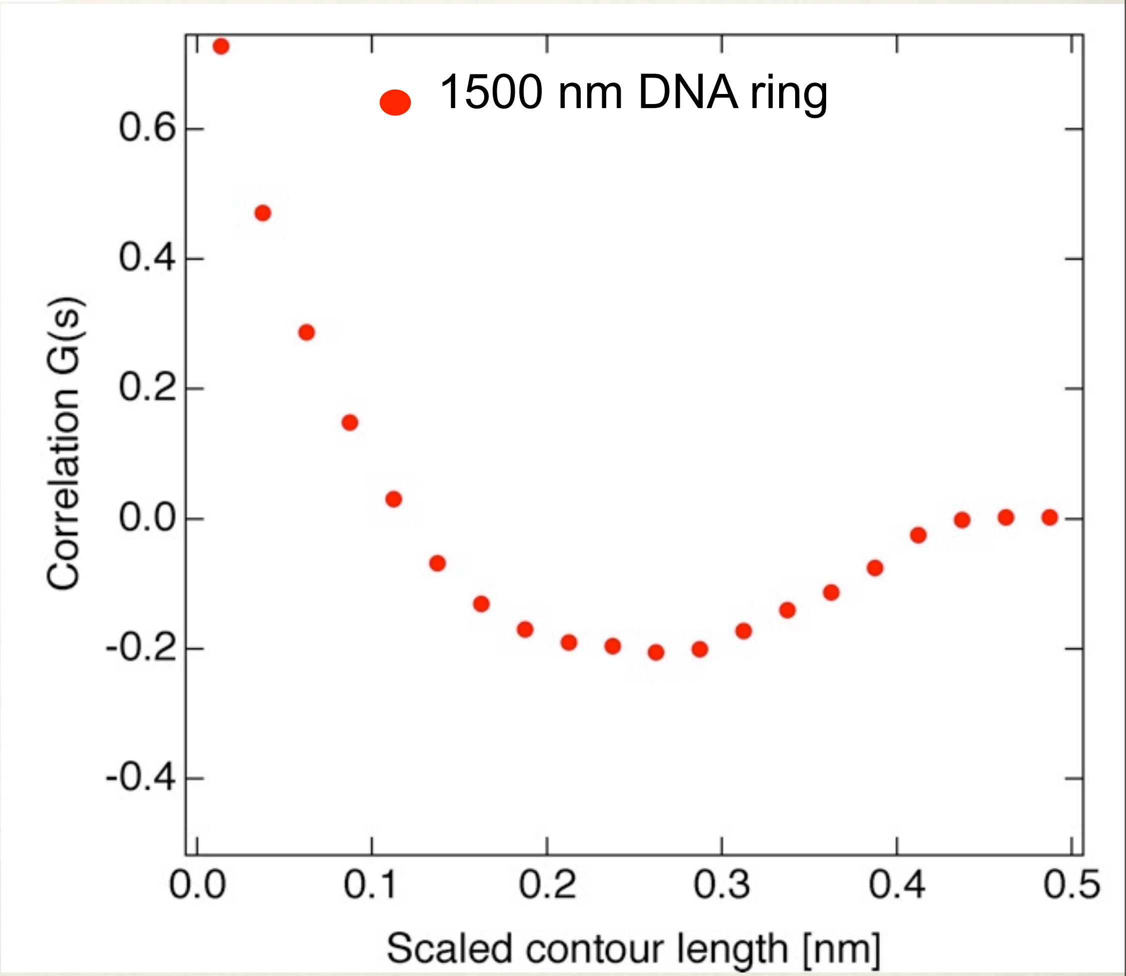
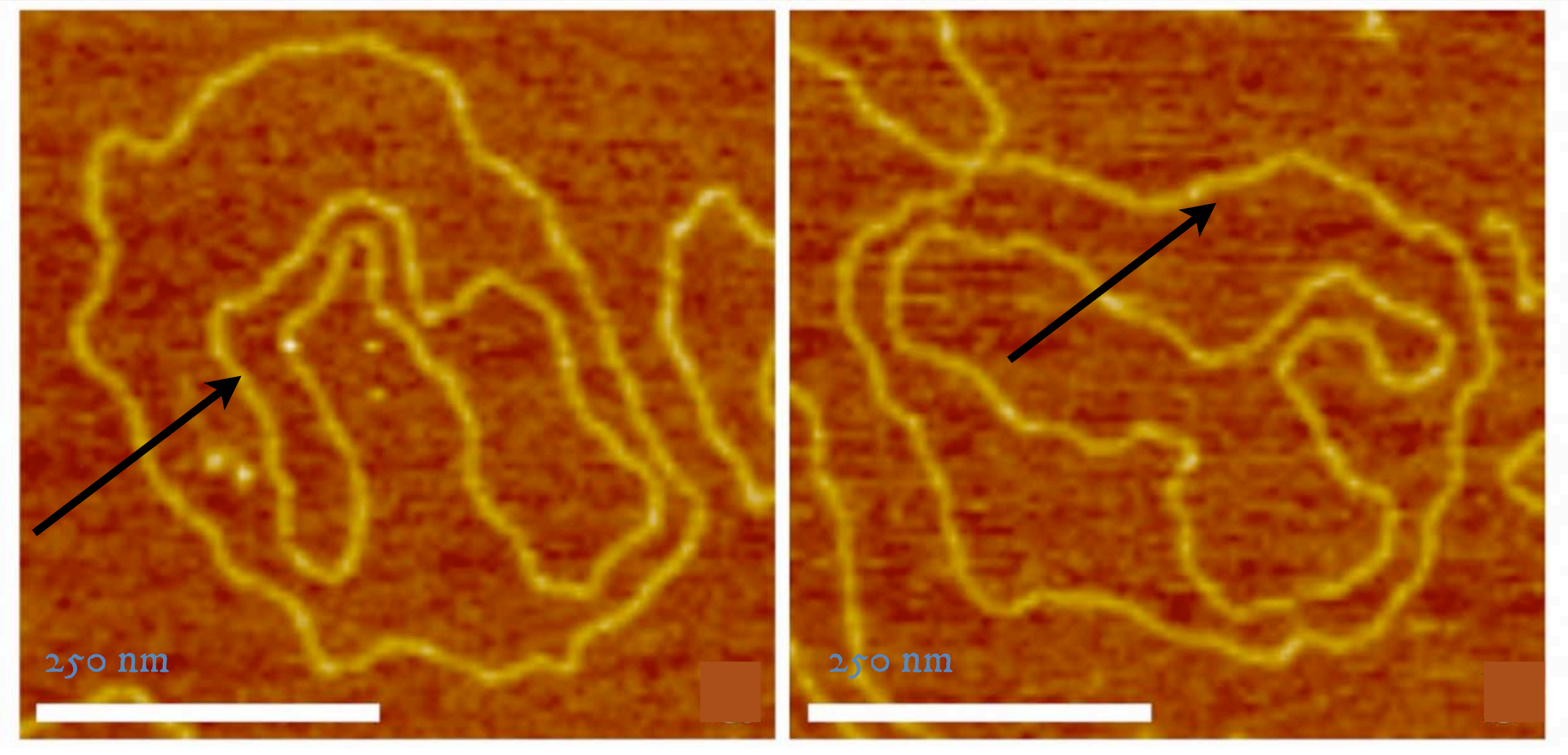


Witz G., Rechendorff, K., Adamcik, J. and Dietler, G., *PRL, to appear.*

Polymer confinement



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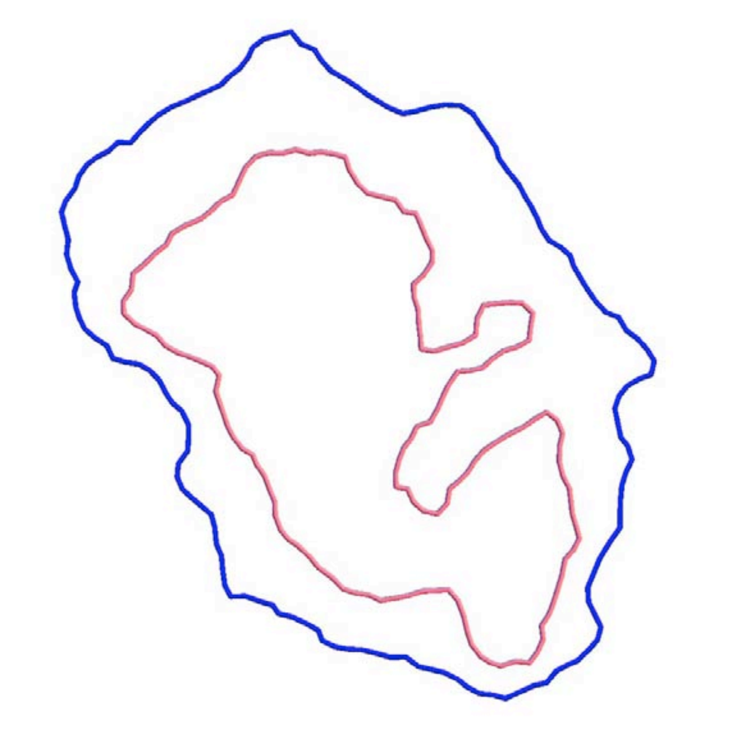
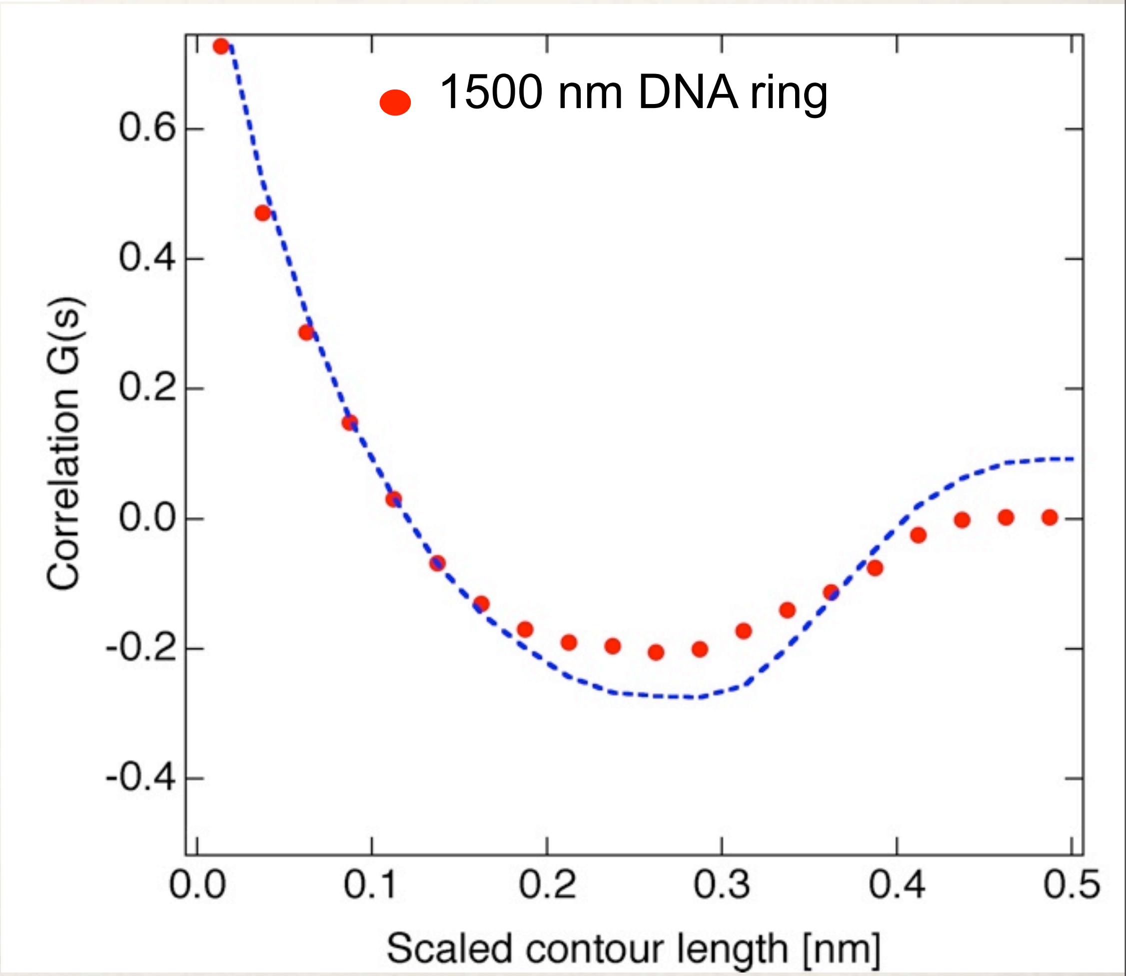
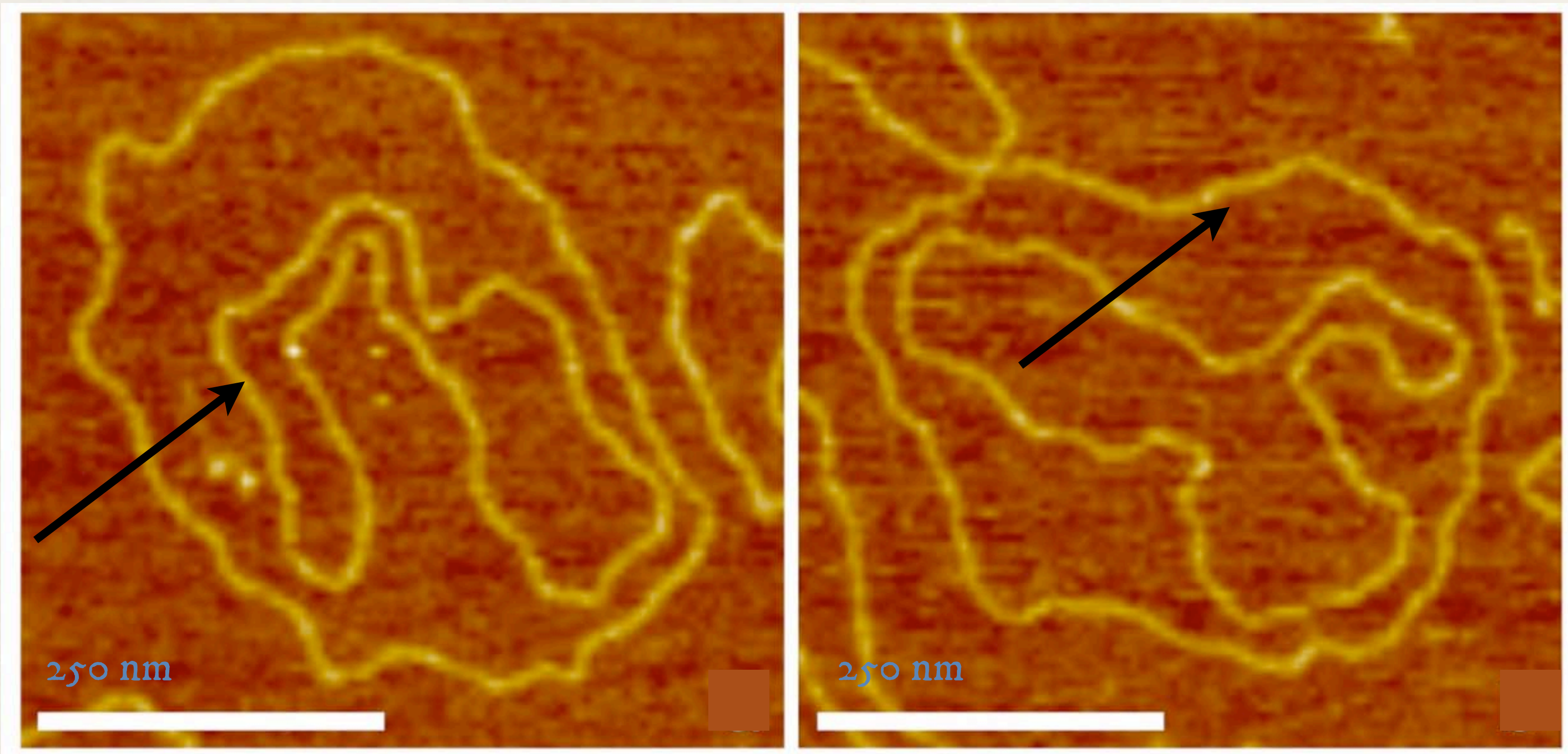


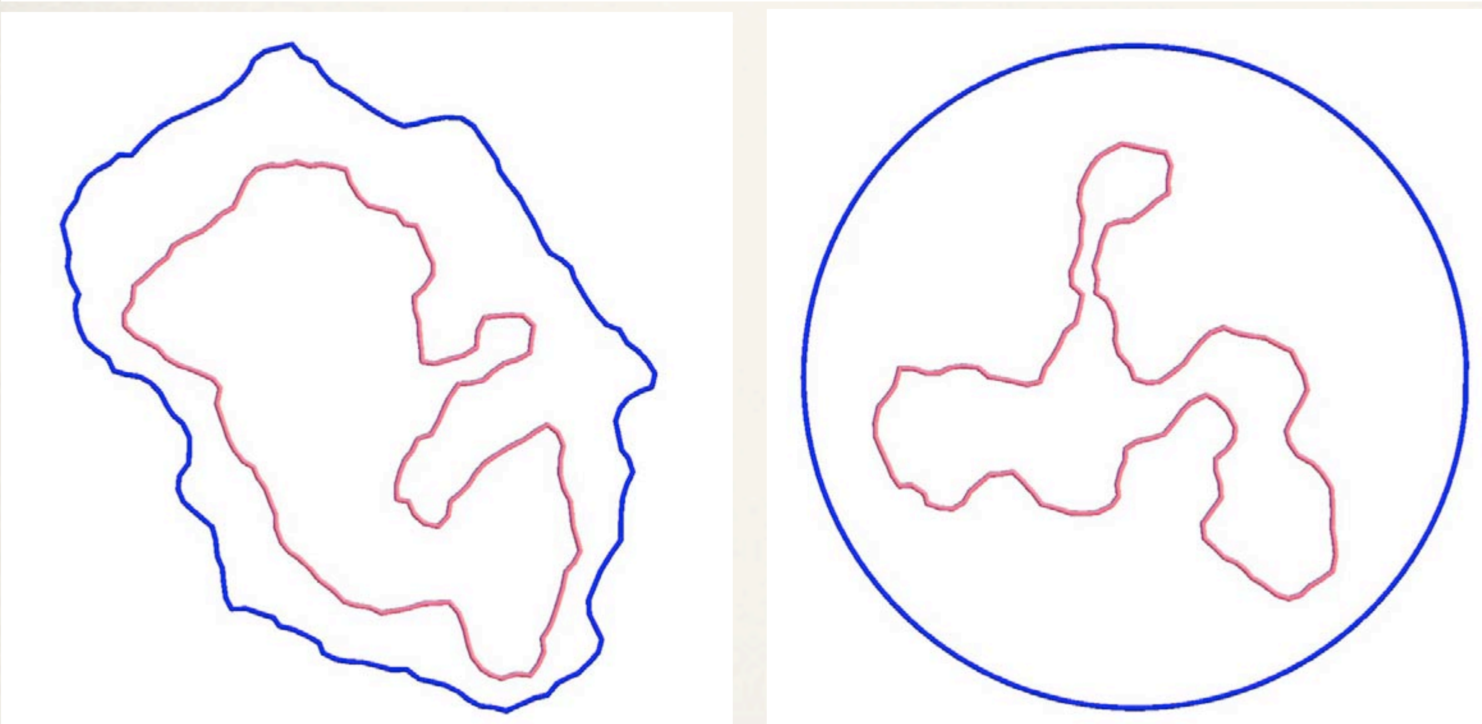


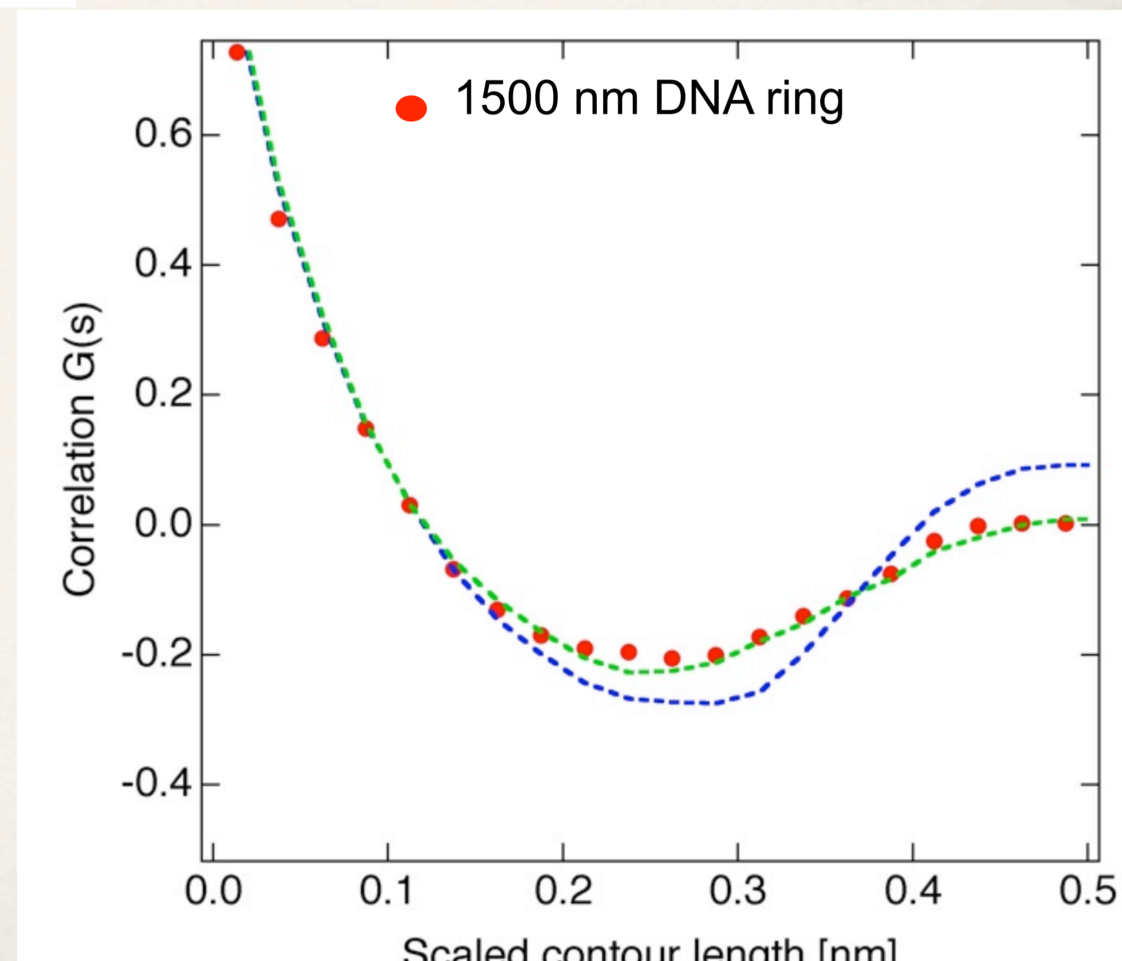
Witz G., Rechendorff, K., Adamcik, J. and Dietler, G., *PRL, to appear.*

Polymer confinement



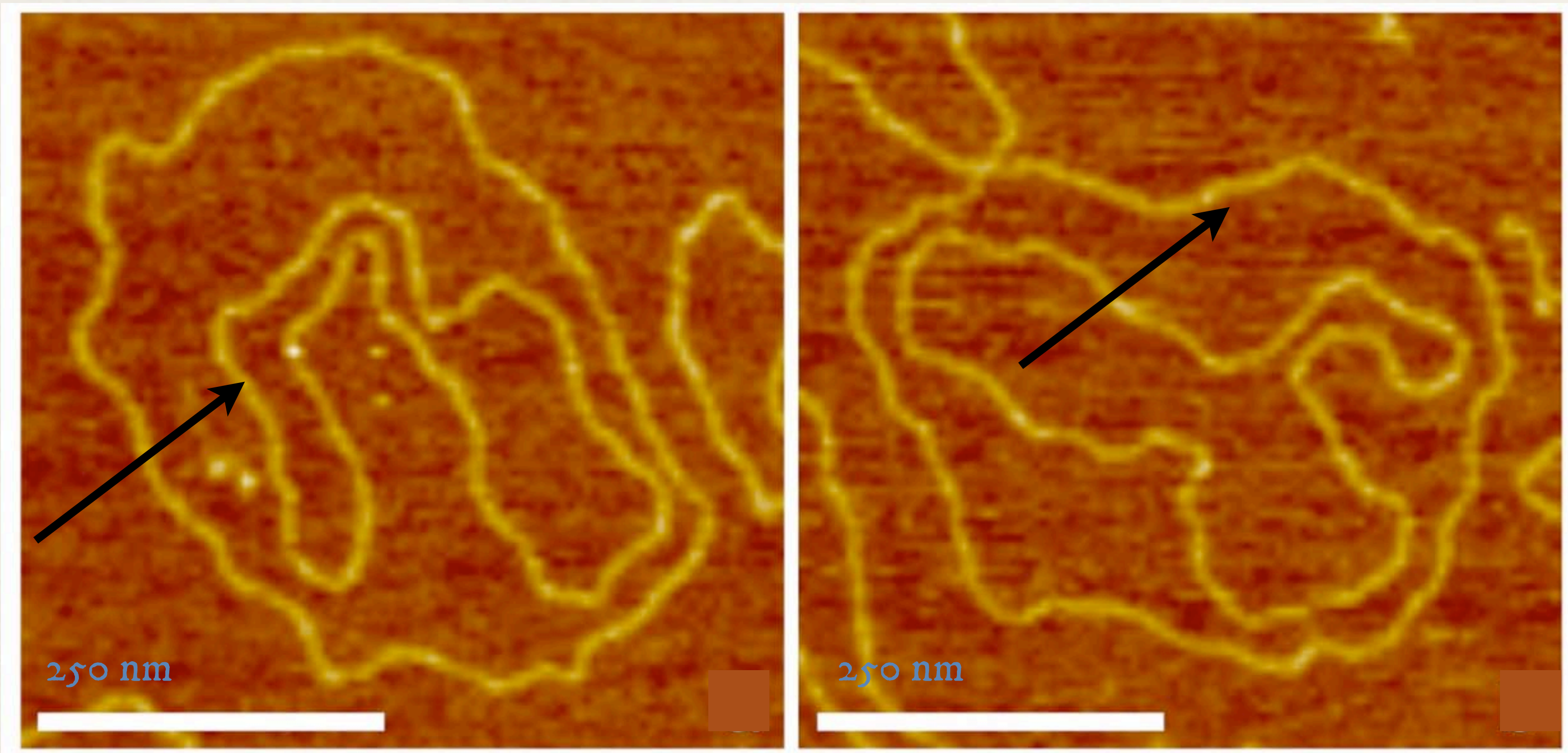
- Polymer confinement generally studied by fluorescence microscopy
- AFM offers much higher resolution



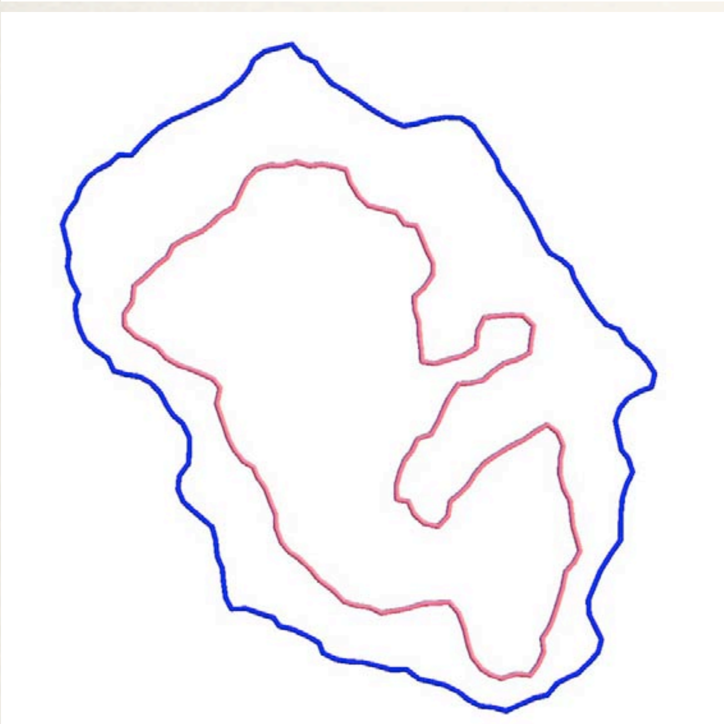


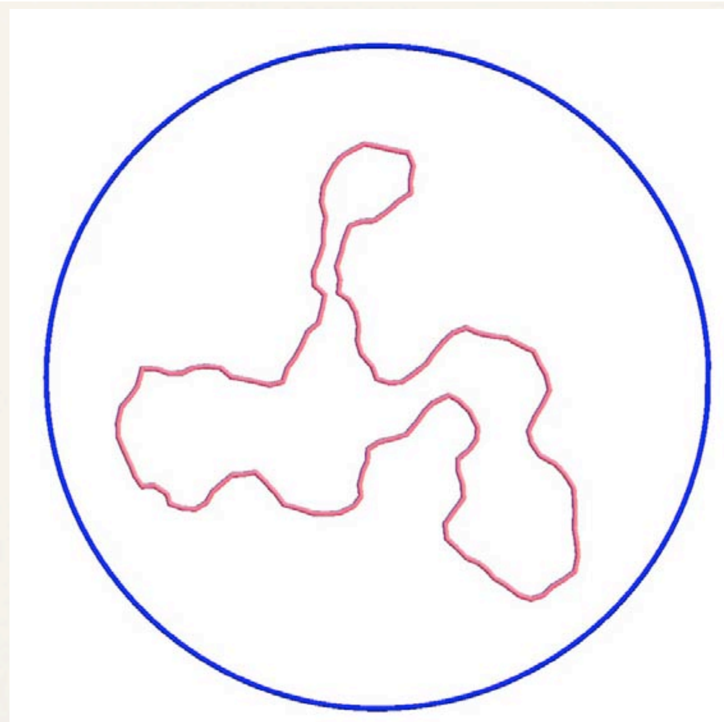
Witz G., Rechendorff, K., Adamcik, J. and Dietler, G., *PRL, to appear.*

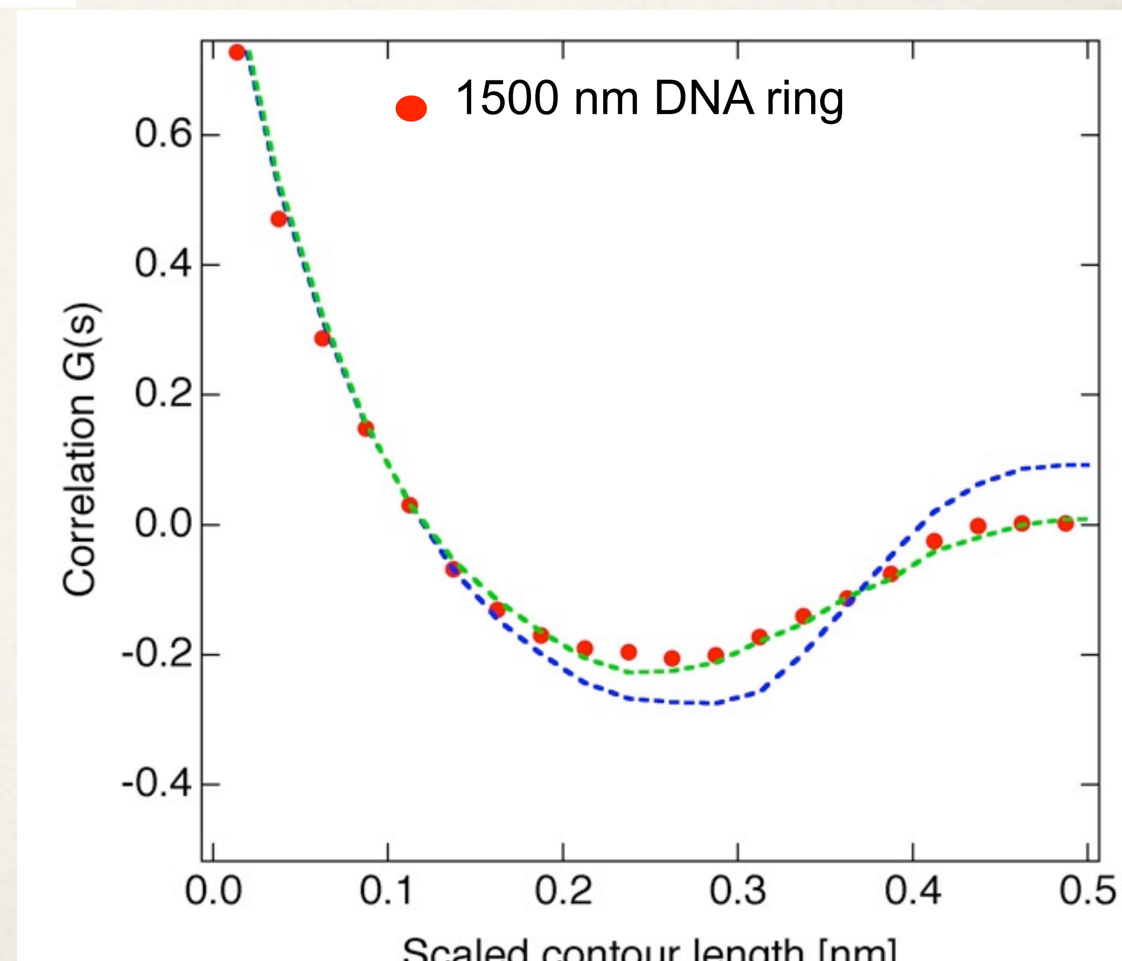
Polymer confinement



- Polymer confinement generally studied by fluorescence microscopy
- AFM offers much higher resolution
- Experimental system close to ideal 2D polymer confinement



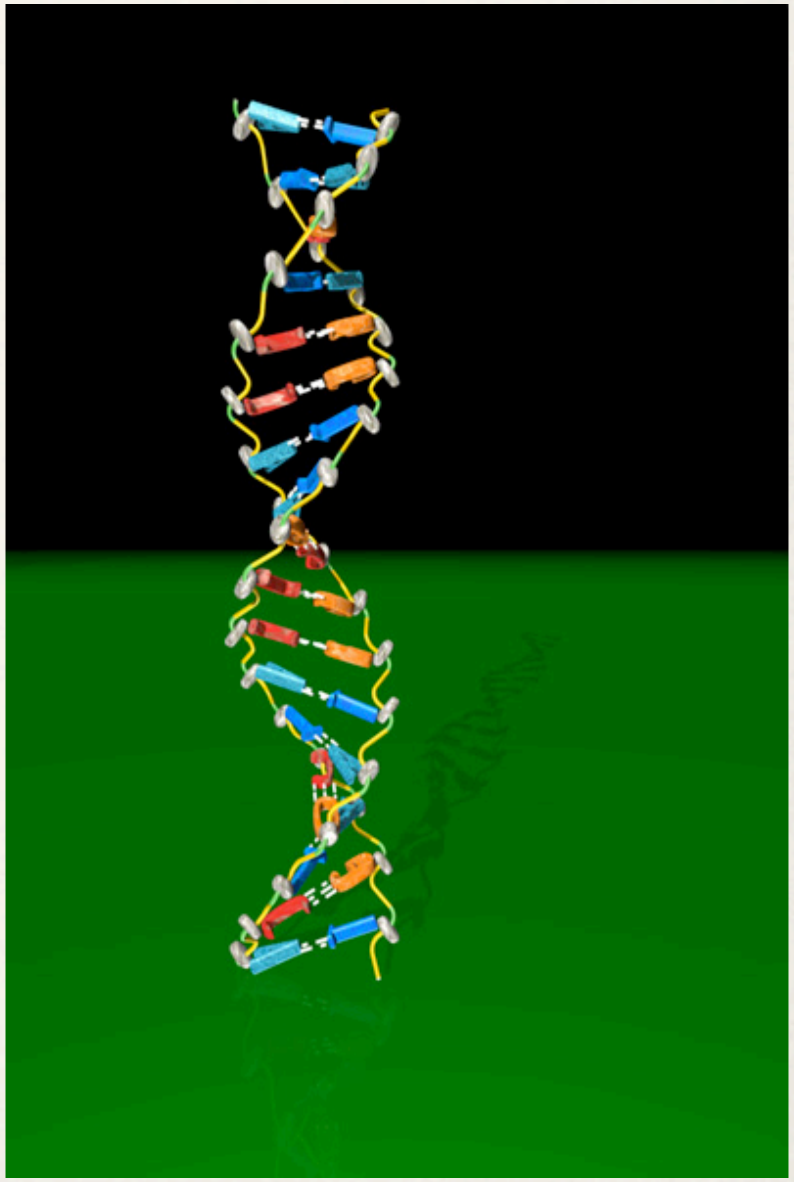




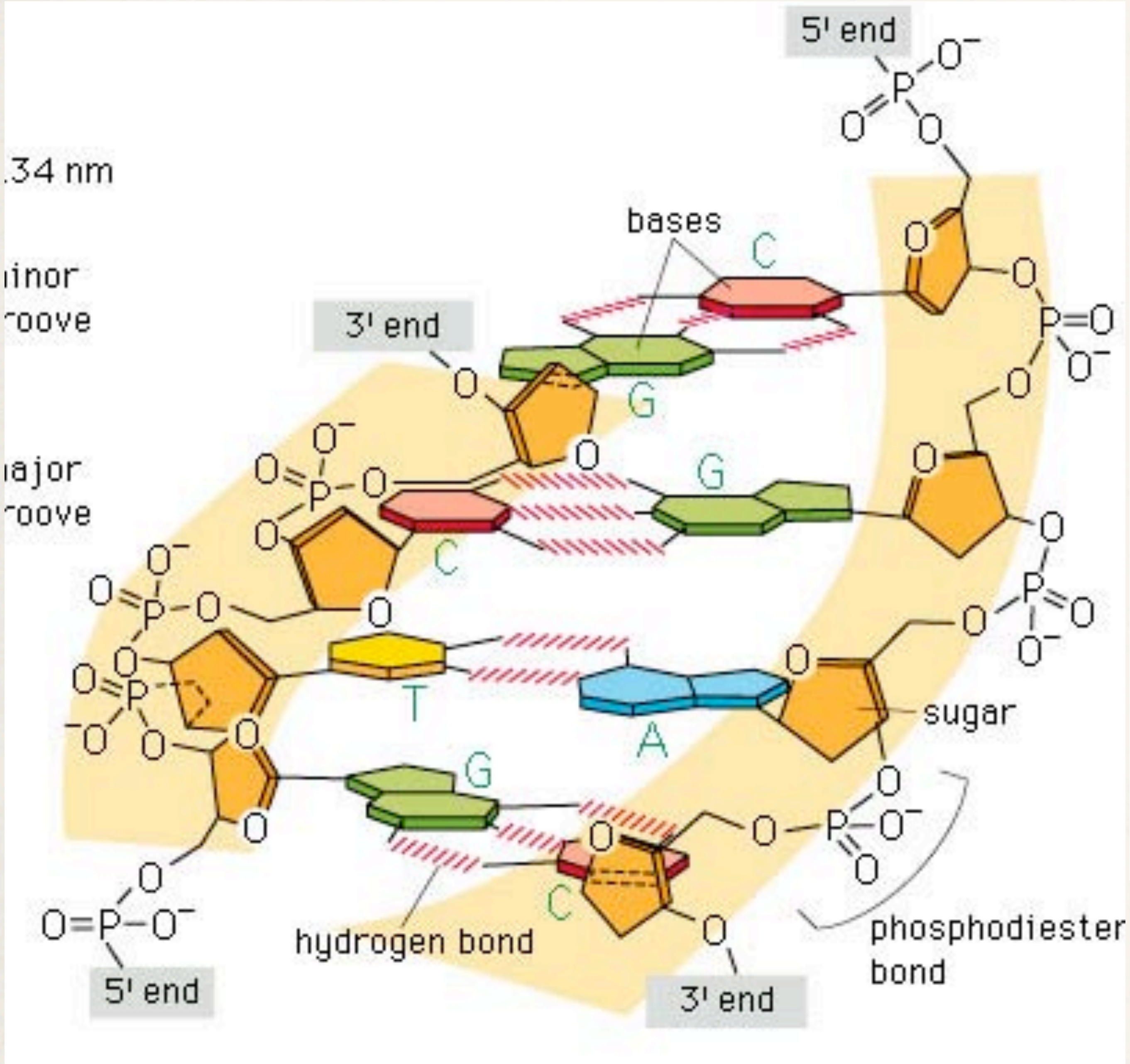
Witz G., Rechendorff, K., Adamcik, J. and Dietler, G., *PRL, to appear.*

The Gauss Integral and the control of gene expression

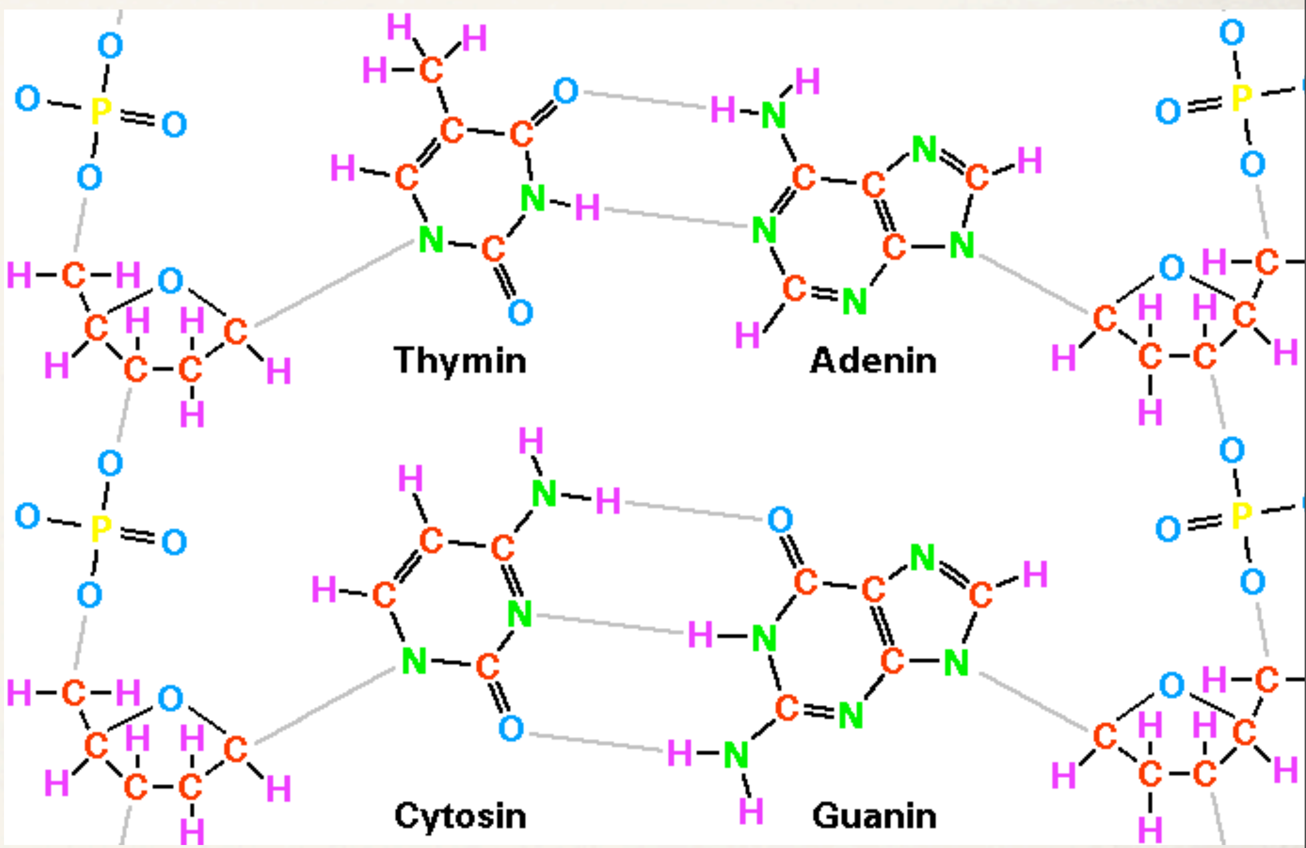
DNA Model



DNA base pairs



T = A

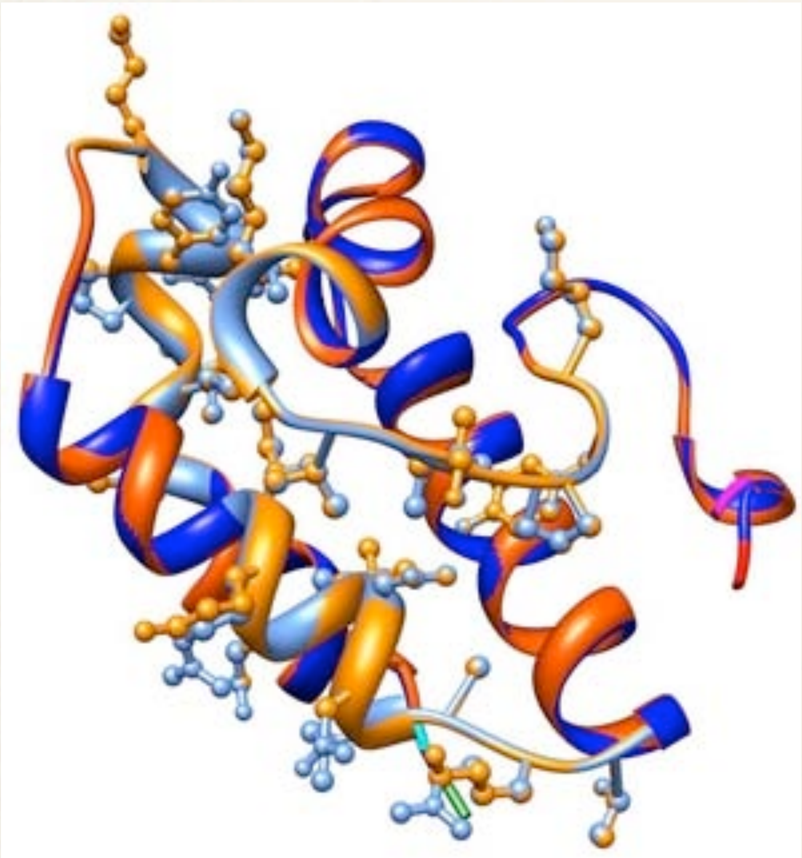


C ≡ G

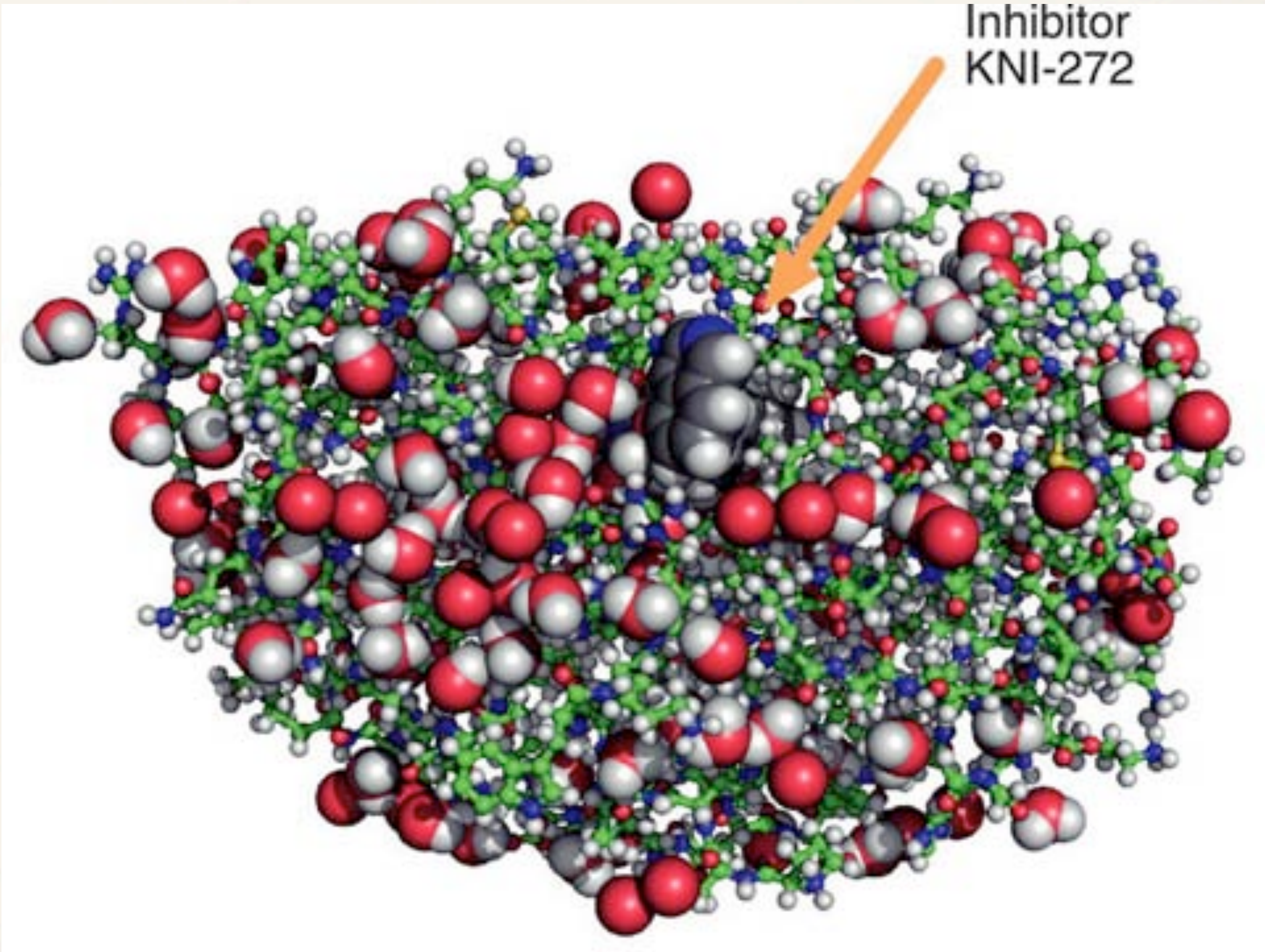
3 DNA base pairs code for one amino acid in a protein

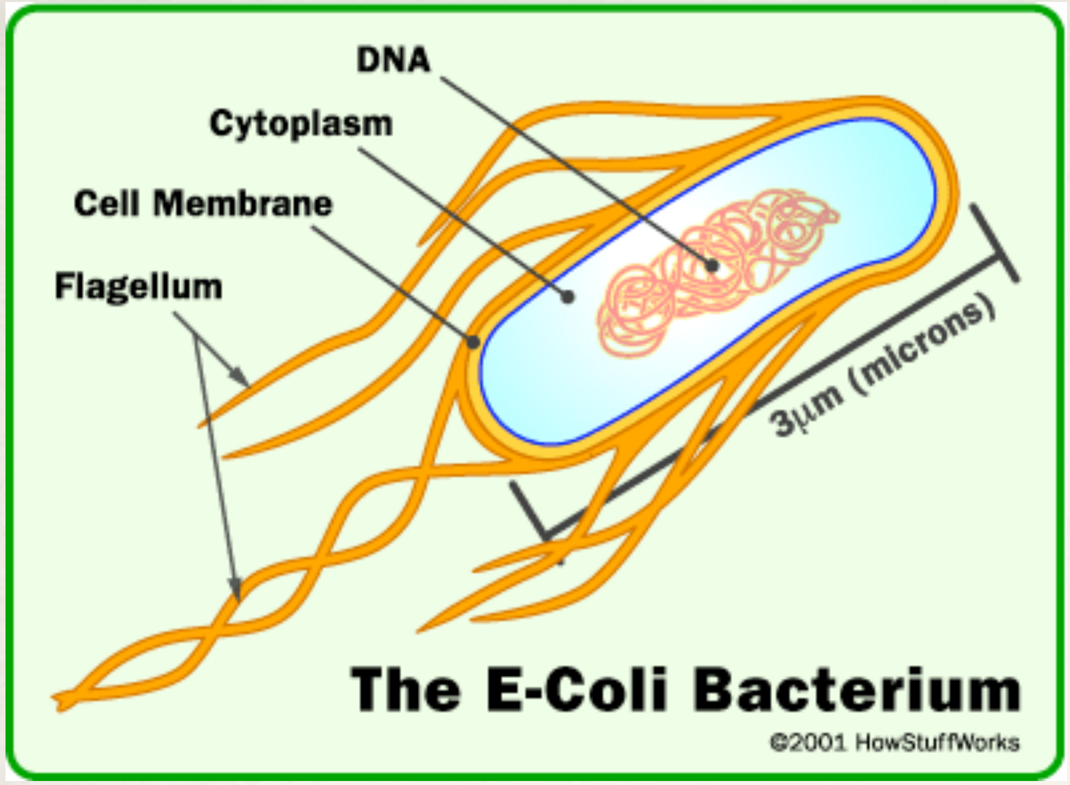
UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys
UUC	Phe	UCC	Ser	UAC	Tyr	UGC	Cys
UUA	Leu	UCA	Ser	UAA	Stp, Gln[3]	UGA	Stp,Trp[4,5],Cys[6],SeC[7]
UUG	Leu	UCG	Ser	UAG	Stp, Gln[3]	UGG	Trp
CUU	Leu	CCU	Pro	CAU	His	CGU	Arg
CUC	Leu	CCC	Pro	CAC	His	CGC	Arg
CUA	Leu	CCA	Pro	CAA	Gln	CGA	Arg
CUG	Leu, Ser[1]	CCG	Pro	CAG	Gln	CGG	Arg, Usp[8]
AUU	Ile	ACU	Thr	AAU	Asn	AGU	Ser
AUC	Ile	ACC	Thr	AAC	Asn	AGC	Ser
AUA	Ile, Usp[2]	ACA	Thr	AAA	Lys	AGA	Arg, Usp[9]
AUG	Met	ACG	Thr	AAG	Lys	AGG	Arg
GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly
GUC	Val	GCC	Ala	GAC	Asp	GGC	Gly
GUA	Val	GCA	Ala Res[10]	GAA	Glu	GGA	Gly
GUG	Val	GCG	Ala	GAG	Glu	GGG	Gly

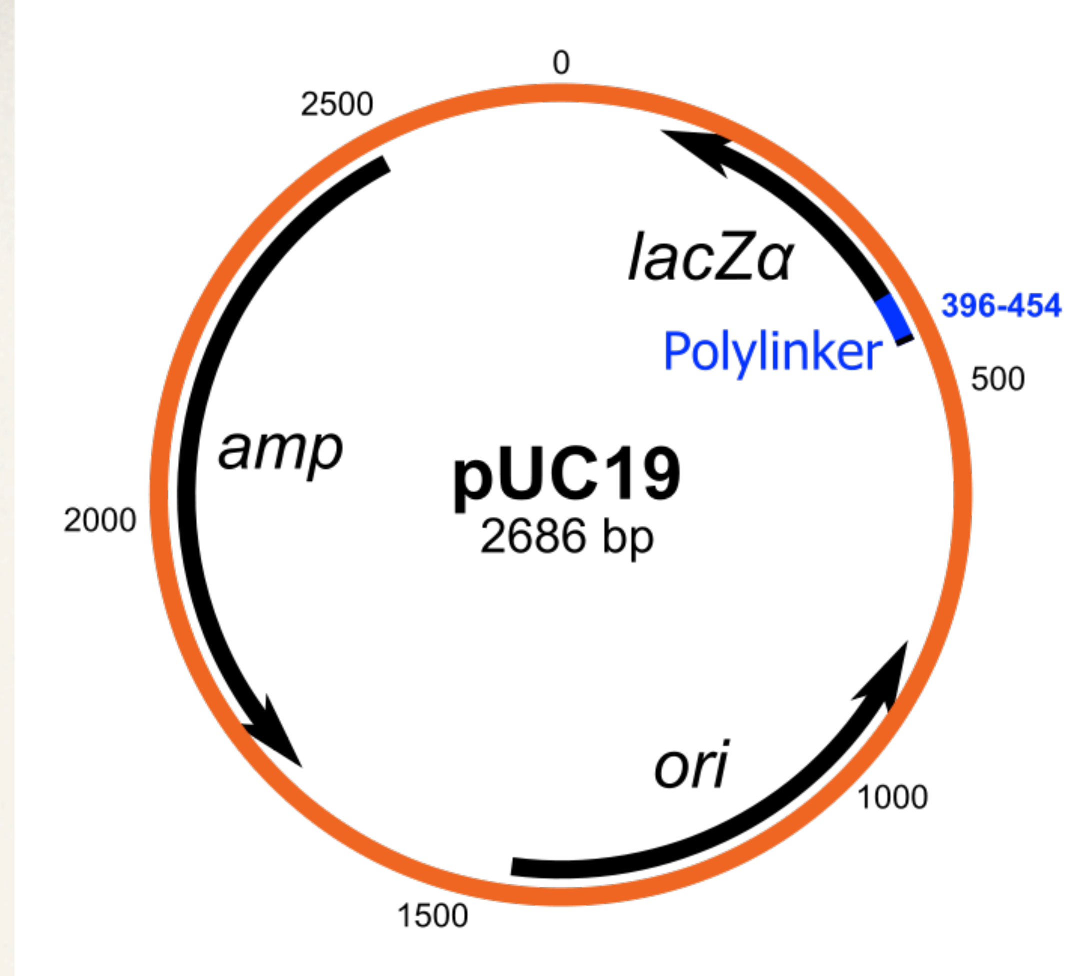
The cells use this codons to synthetize the proteins

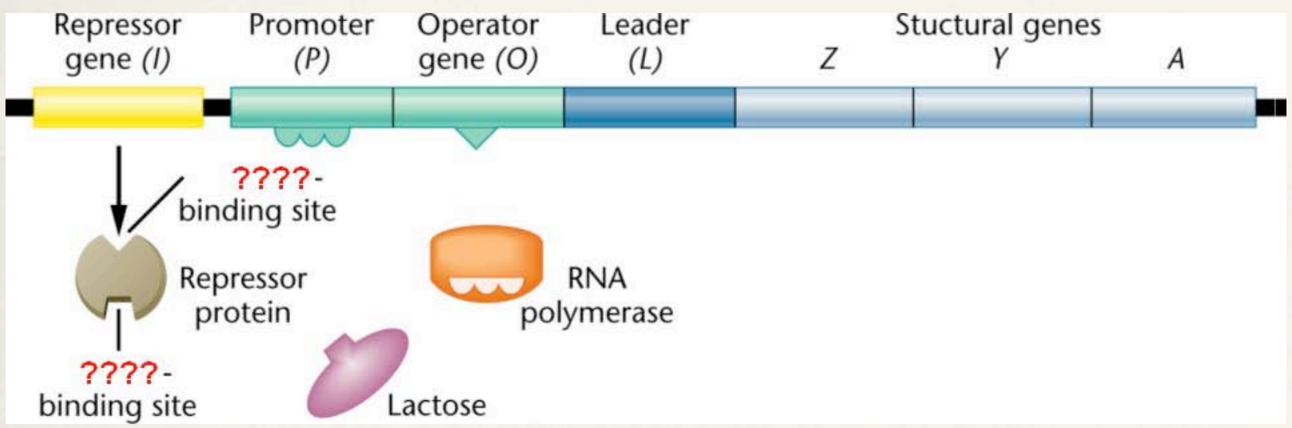


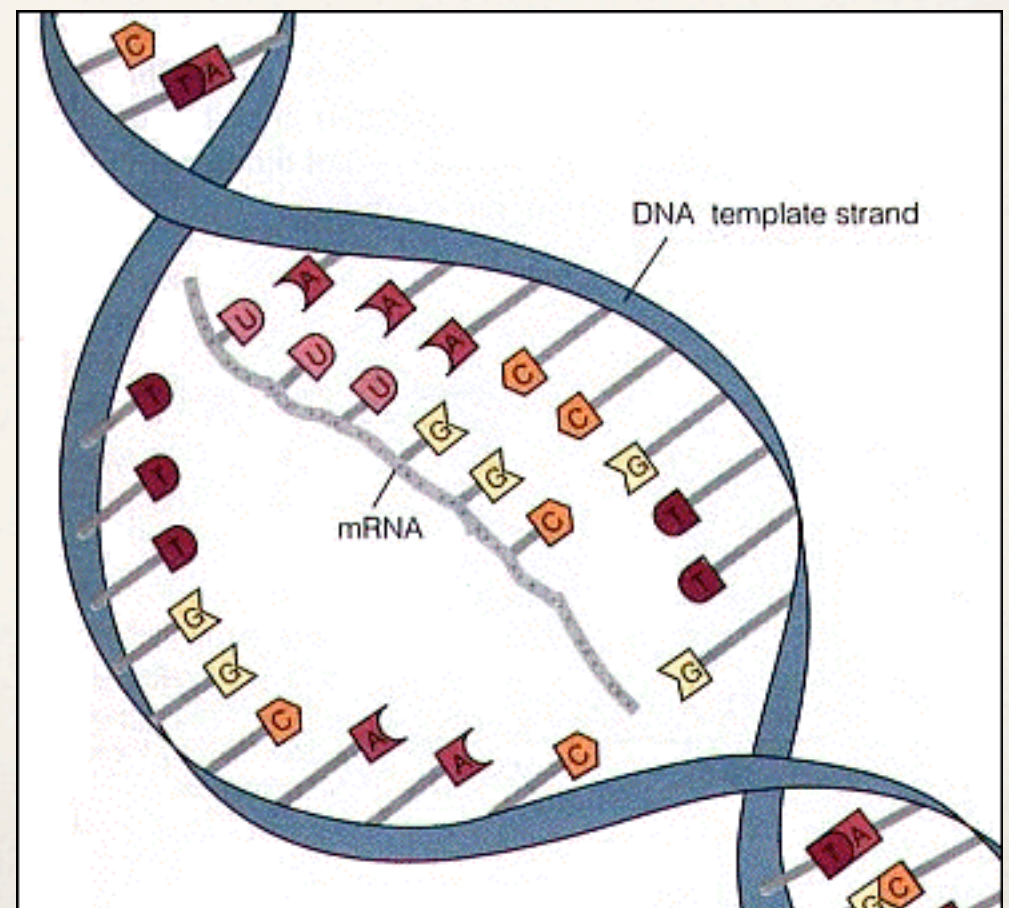
Wine Protein




DNA
Cytoplasm
Cell Membrane
Flagellum
3µm (microns)
The E-Coli Bacterium
©2001 HowStuffWorks


0
2500
500
2000
1000
1500
lacZα
396-454
Polylinker
amp
pUC19
2686 bp
ori


Repressor gene (I)
Promoter (P)
Operator gene (O)
Leader (L)
Stuctural genes
Z
Y
A
????-binding site
Repressor protein
????-binding site
RNA polymerase
Lactose


DNA template strand
mRNA

1. Denaturation temperature is 70 C !

1. Denaturation temperature is 70 C !

2. How life can work at 37 C?

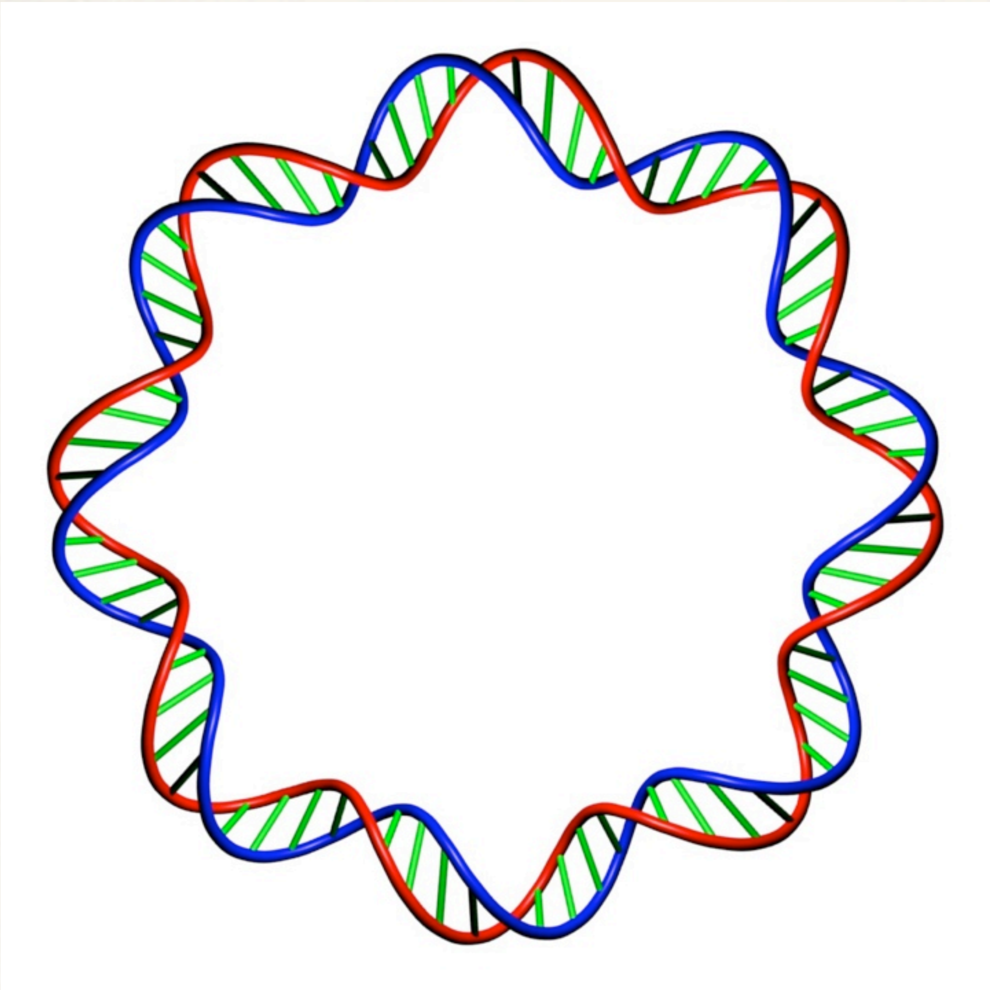
1. Denaturation temperature is 70 C !

2. How life can work at 37 C?

3. Did Nature a mistake?

Here topology and the Calugareanu-White-Fuller Theorem comes into play

$$Lk(R) = Tw(R) + Wr(R)$$

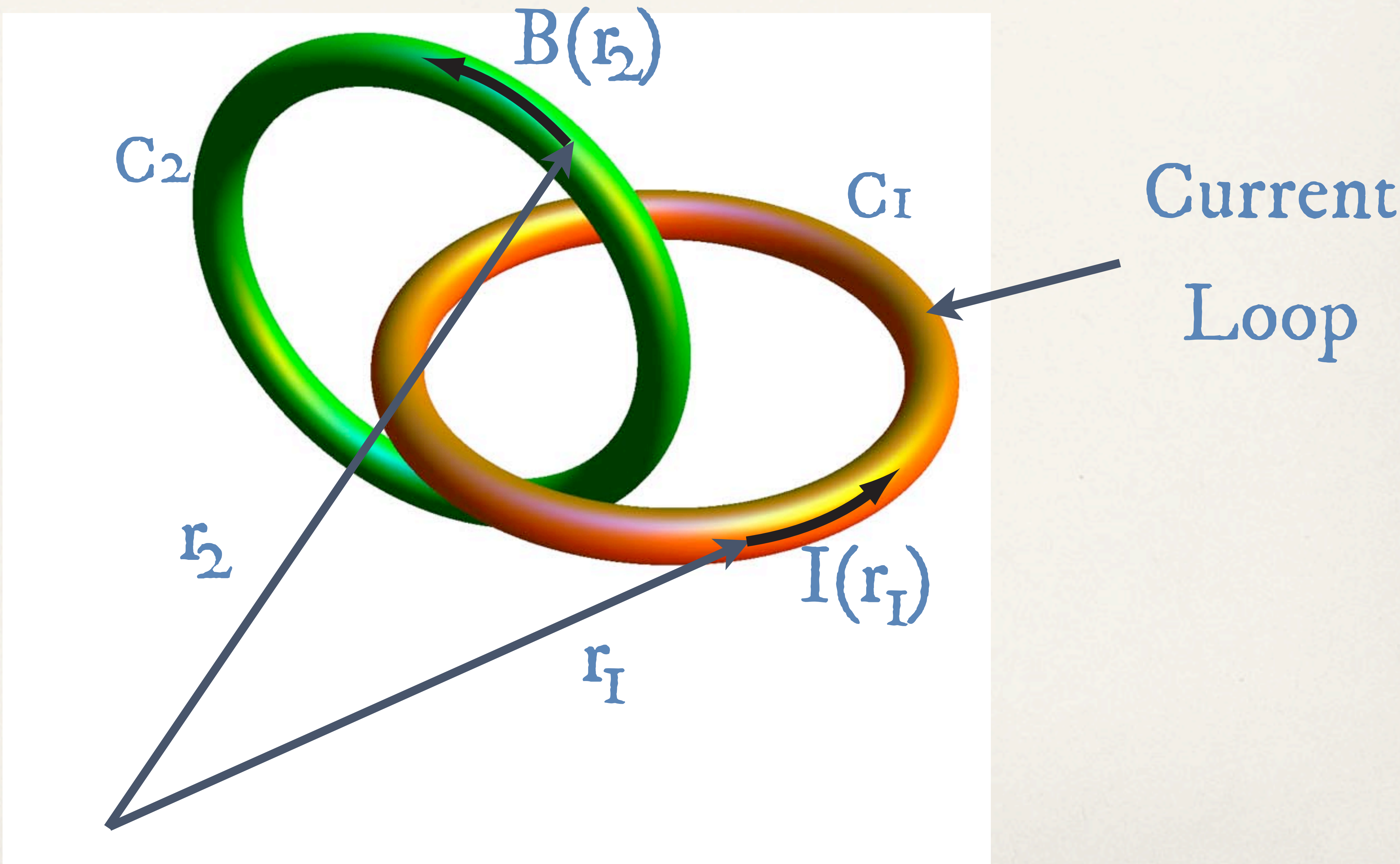


Lk = Linking Number

Tw = Twist

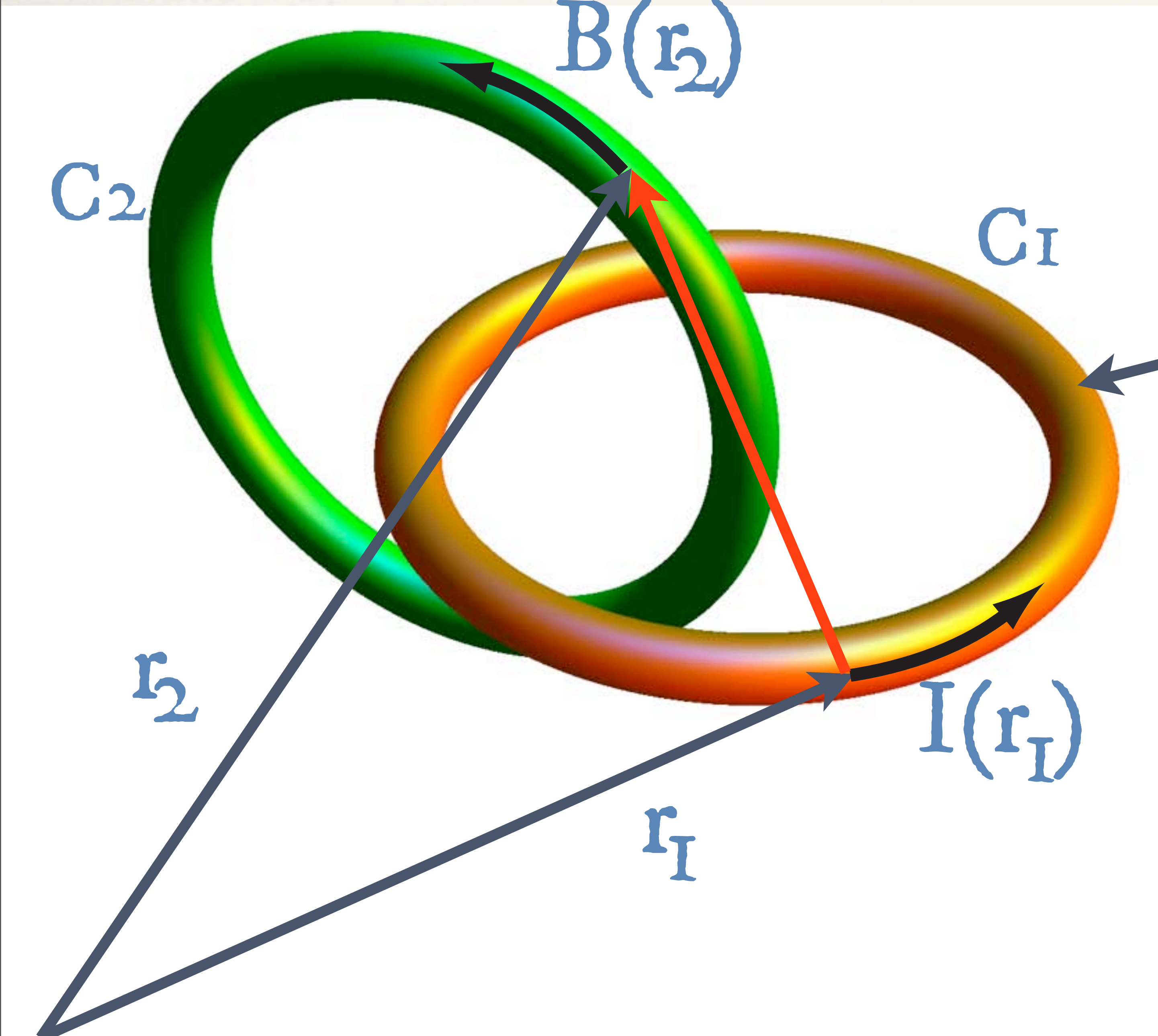
Wr = Writhe

The Gauss-Integral & the linking number of two curves



Biot-Savart's Law + Ampère's Law

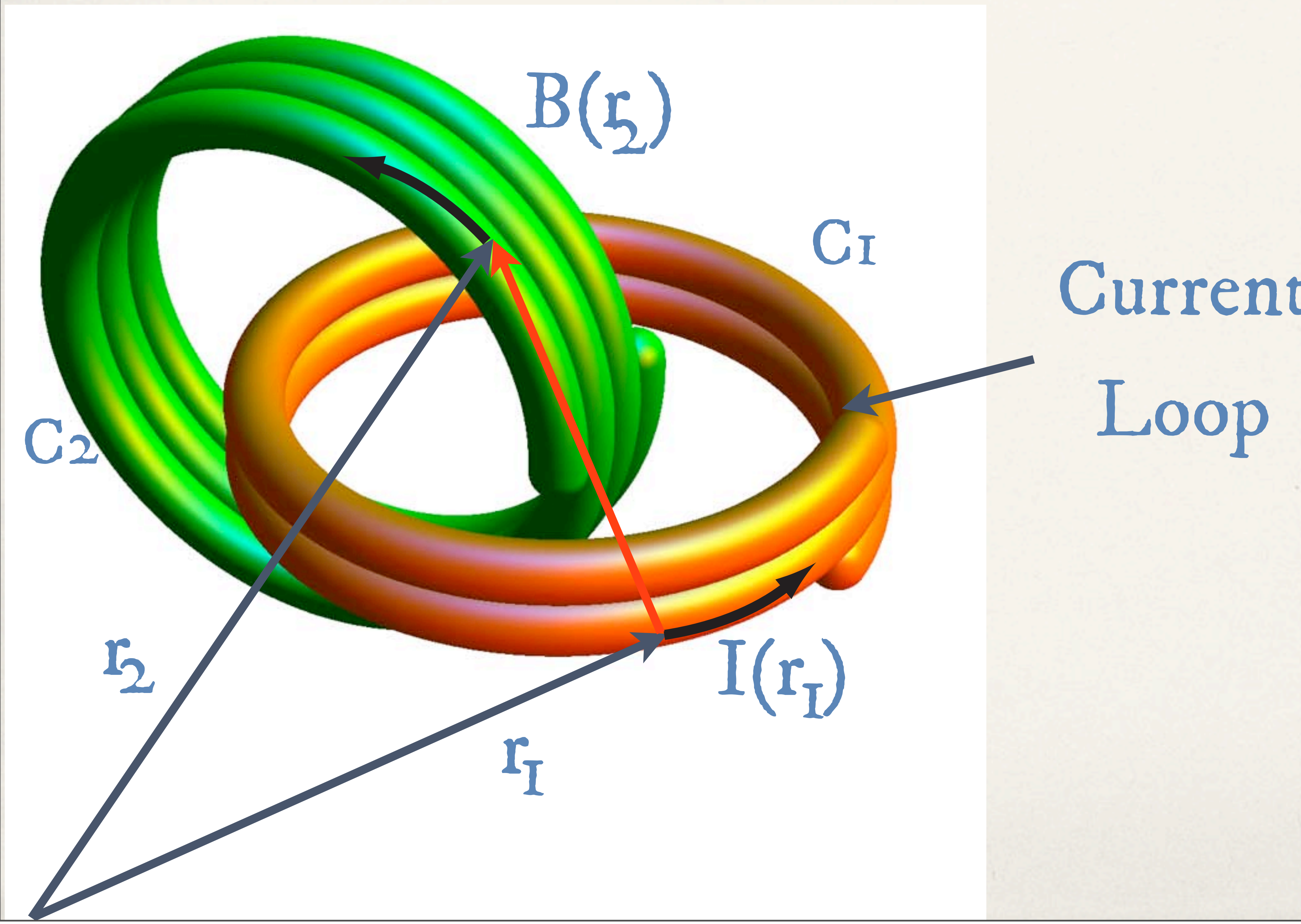
$$Lk(C_1, C_2) = \frac{1}{4\pi} \oint_{C_2} \oint_{C_1} \frac{(\vec{r}_1 - \vec{r}_2) \times d\vec{r}_1 \cdot d\vec{r}_2}{|\vec{r}_1 - \vec{r}_2|^3}$$



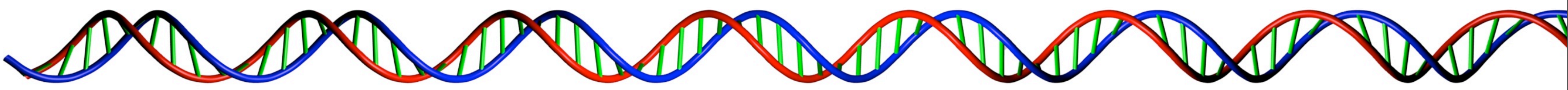
Current Loop

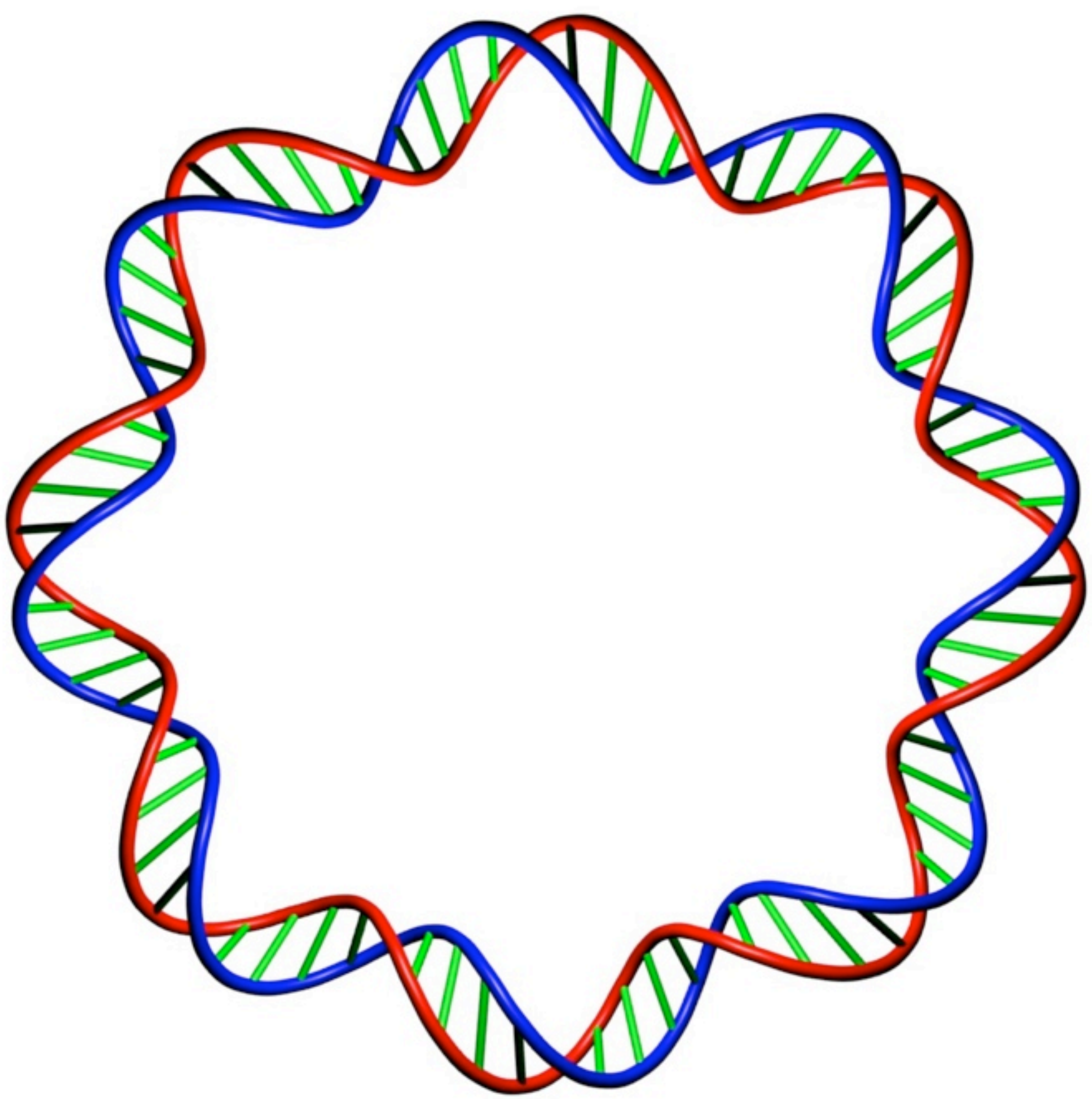
Biot-Savart's Law + Ampère's Law

$$Lk(C_1, C_2) = 3 \times 2 = 6$$



DNA double helix

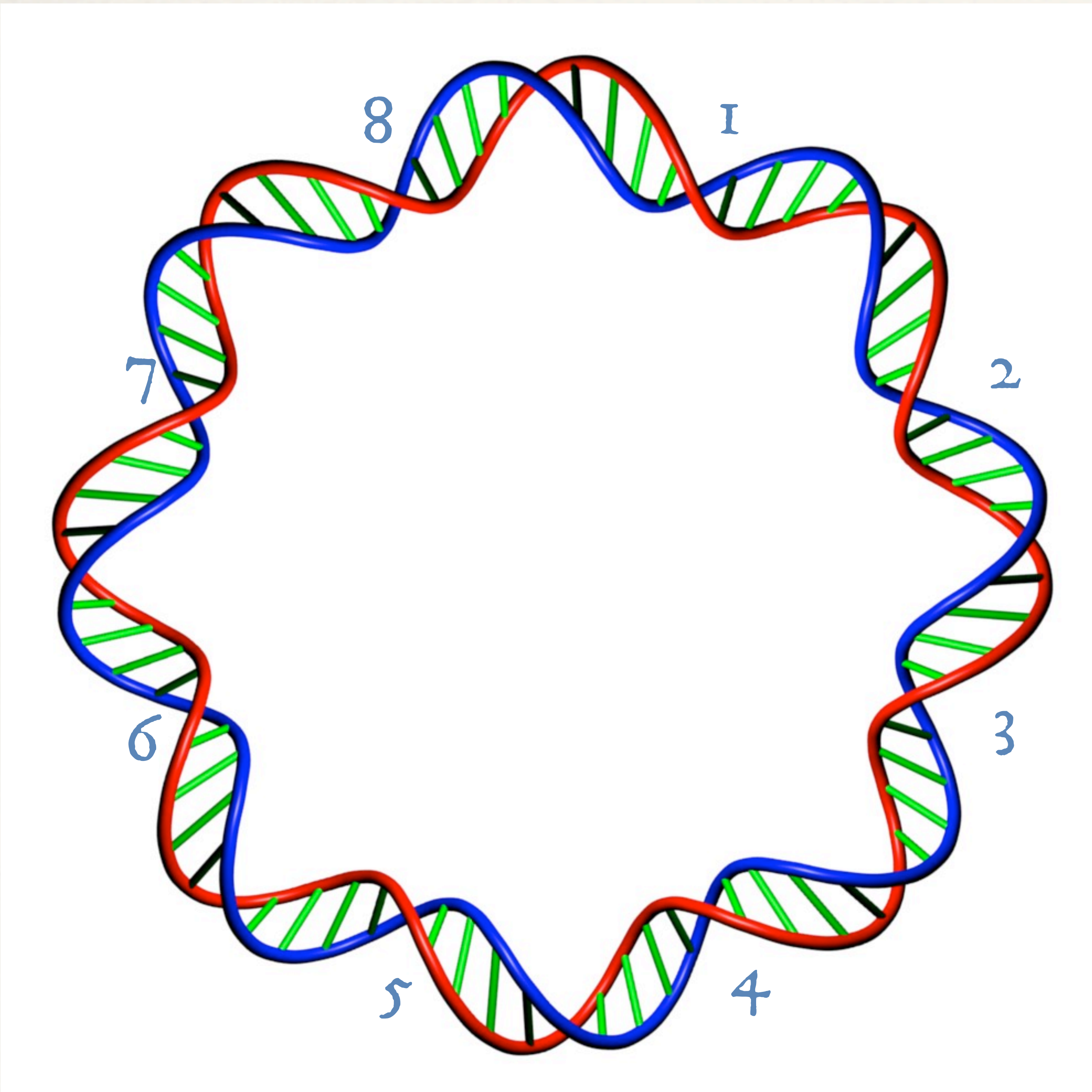


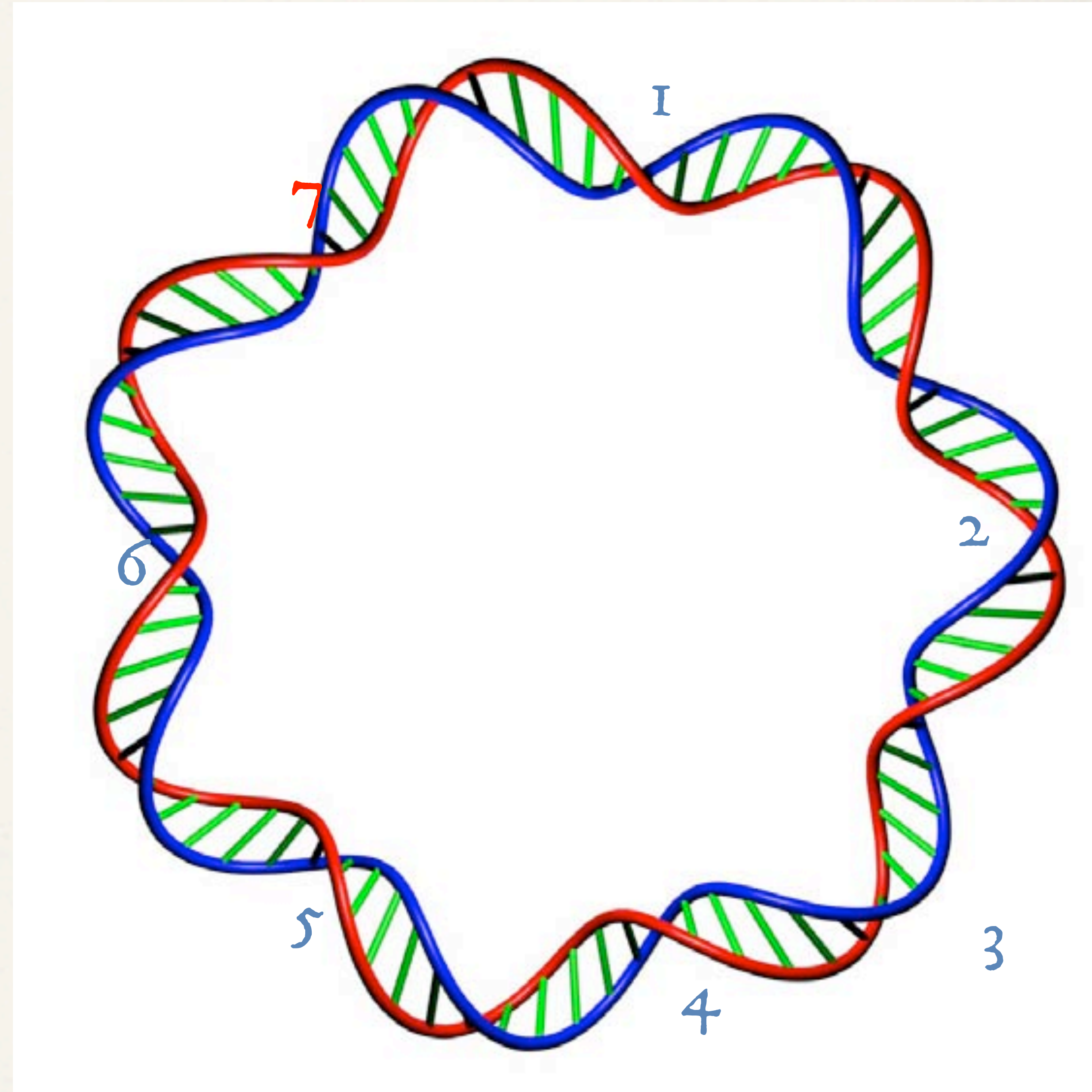


$$Lk(C_1, C_2) = Tw = \frac{N_{base\ pairs}}{10.4}$$

$$Lk(C_1, C_2) = Tw$$
$$= 2686/10.4 = 258$$

Topology of DNA





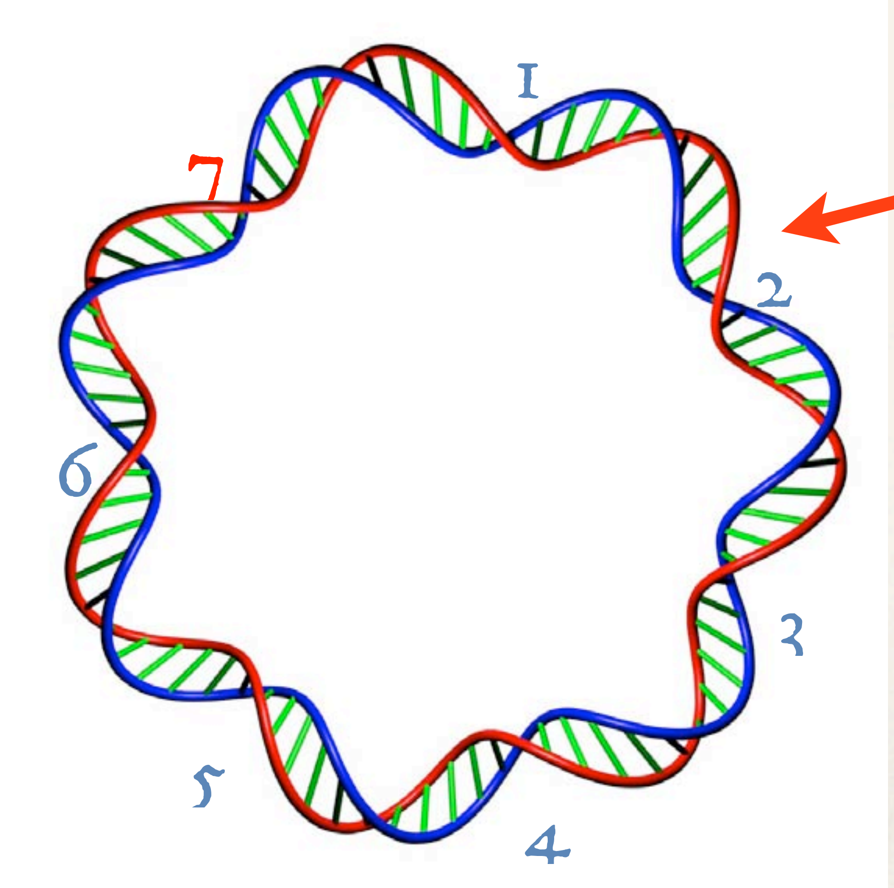
Ideal B-form DNA
(here 10.4 bp/turn)

Underwound DNA
(here 11.4 bp/turn)

Topology of DNA

Torsion or Bending ?

Torsion



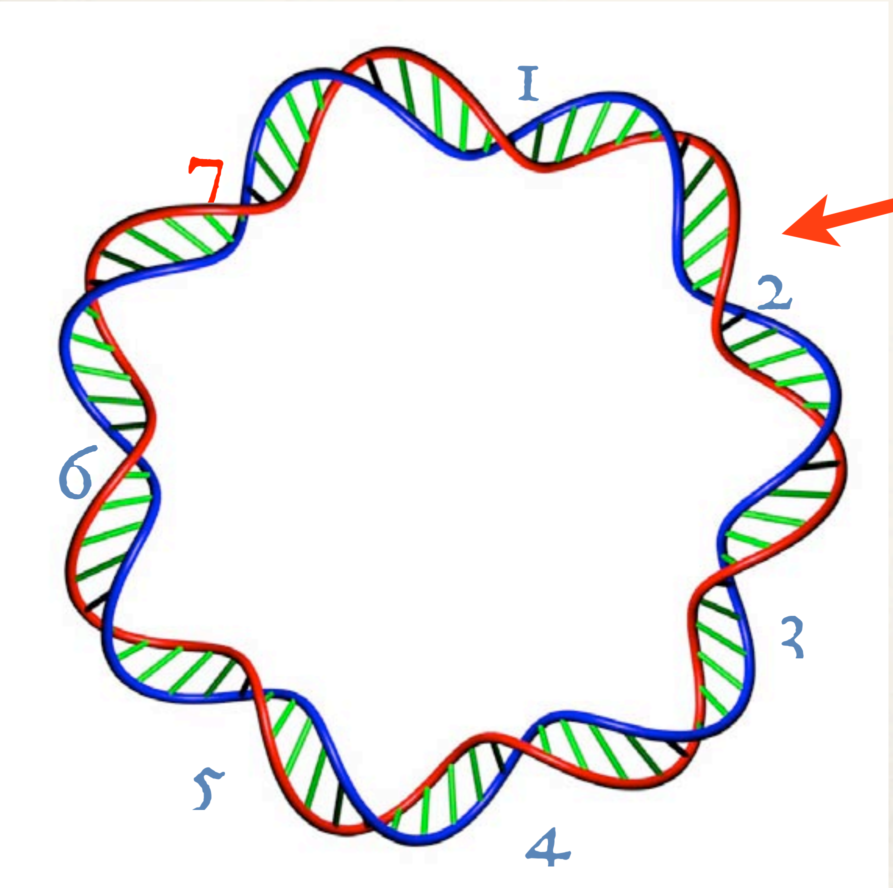
7 twists

Topology of DNA

Torsion or Bending ?

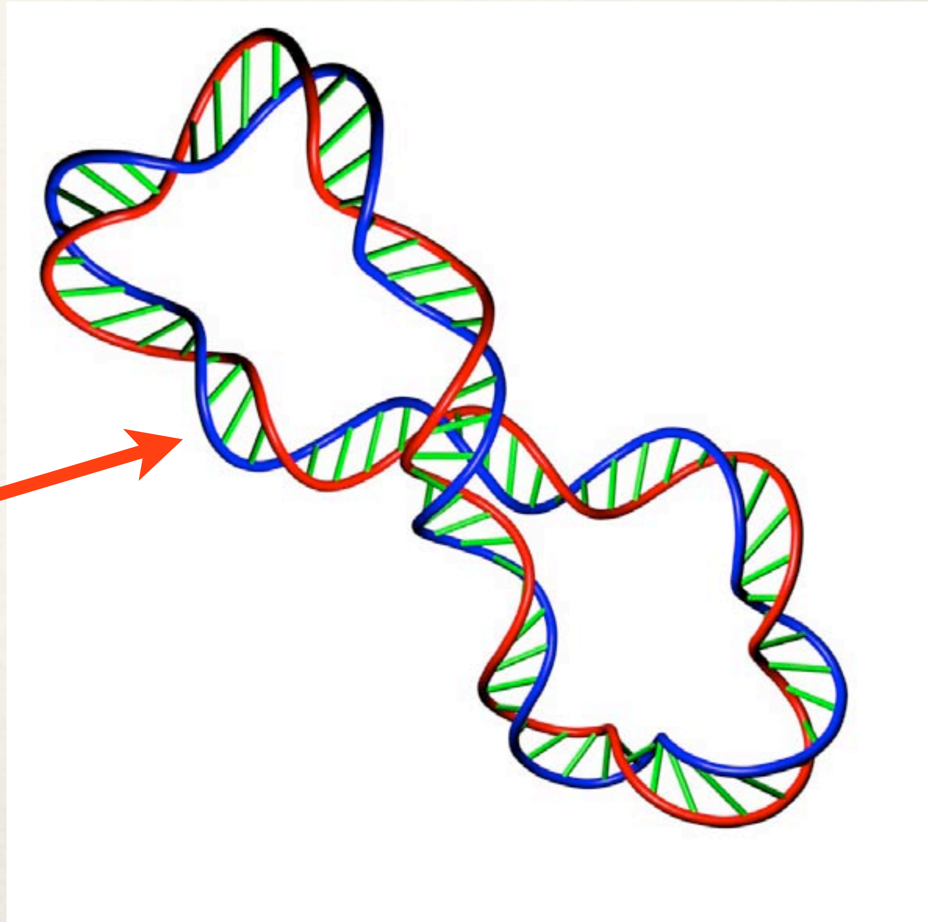
Relaxation of torsional stress

Torsion → Bending



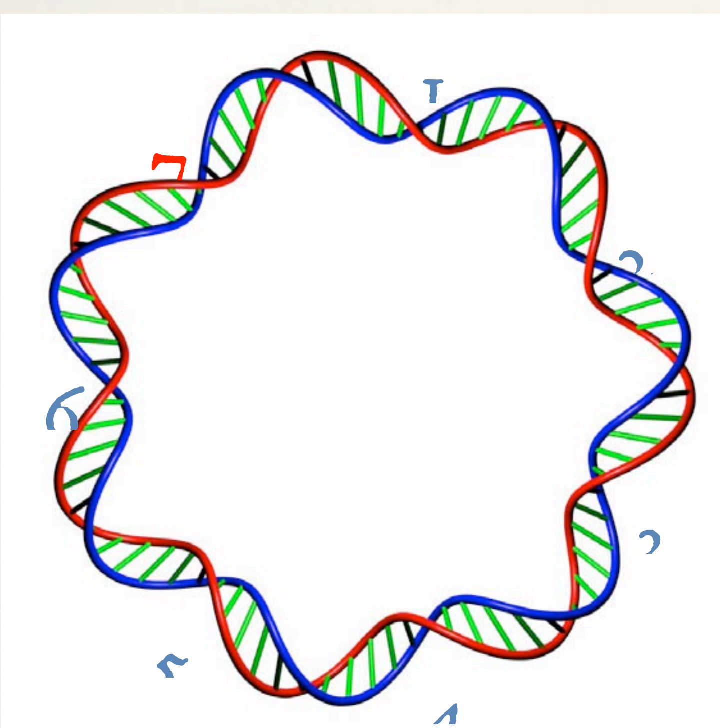
7 twists

8 twists



Here topology and the Calugareanu-White-Fuller Theorem comes into play

$$Lk(R) = Tw(R) + Wr(R)$$



Tw=7

Wr=0

Tw=8

Wr=-1

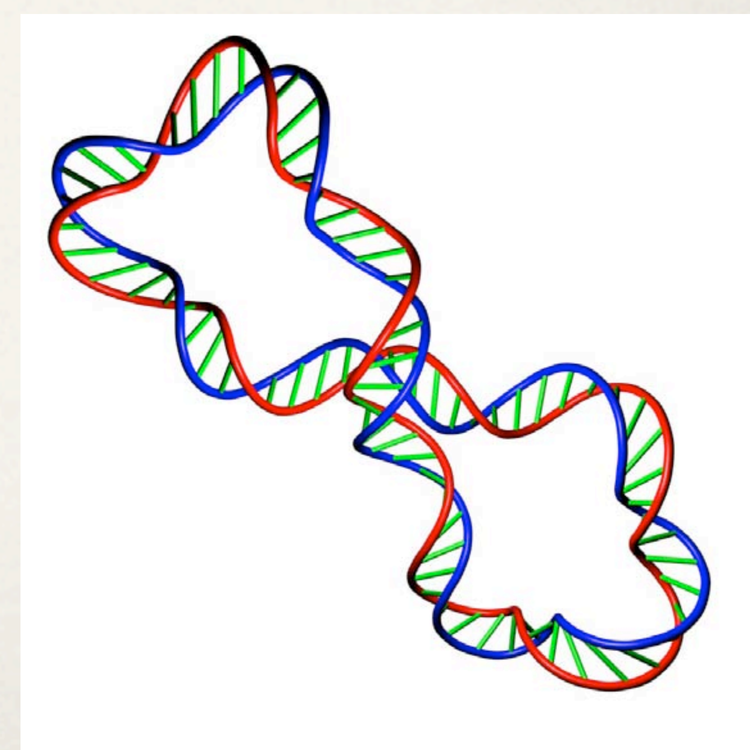
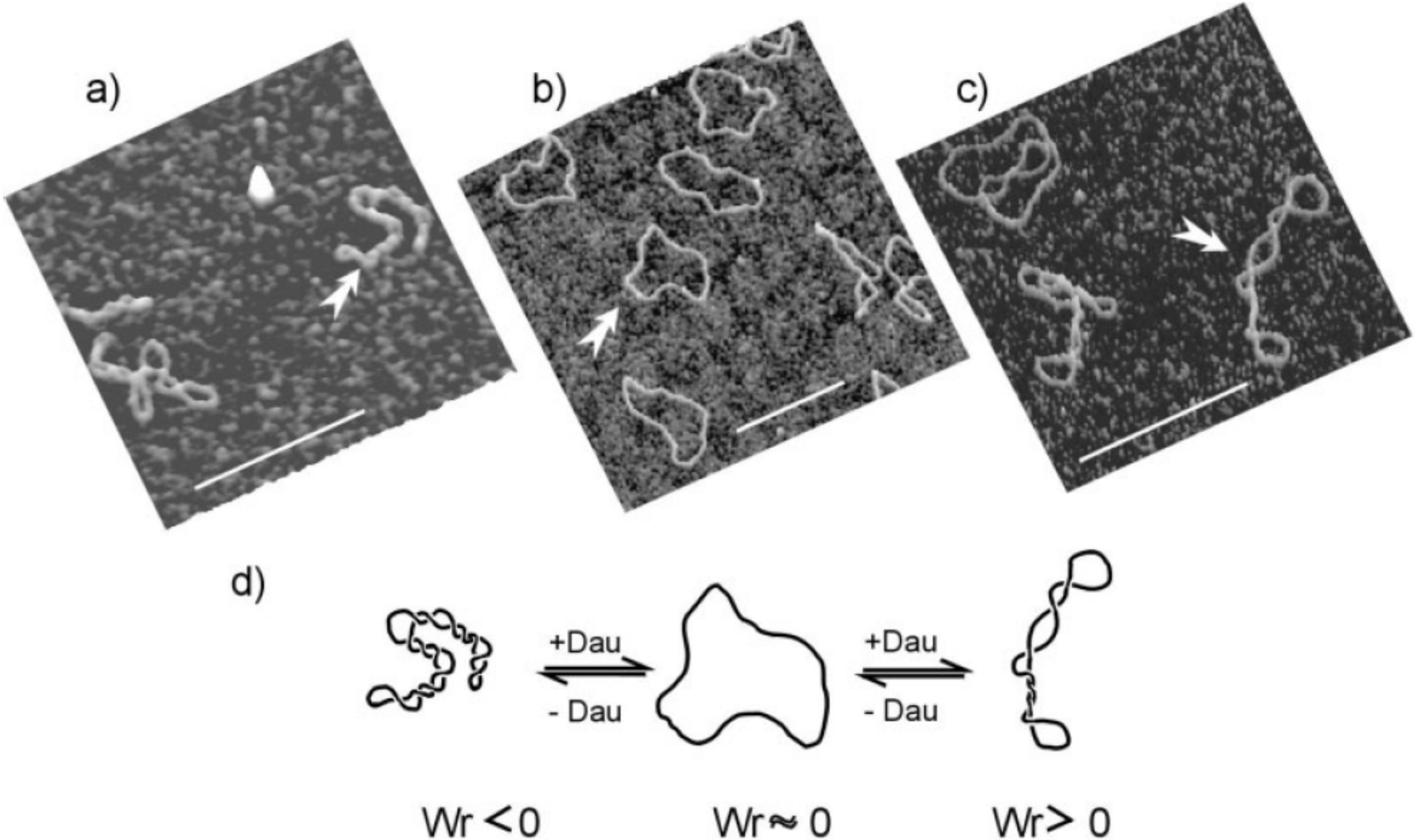
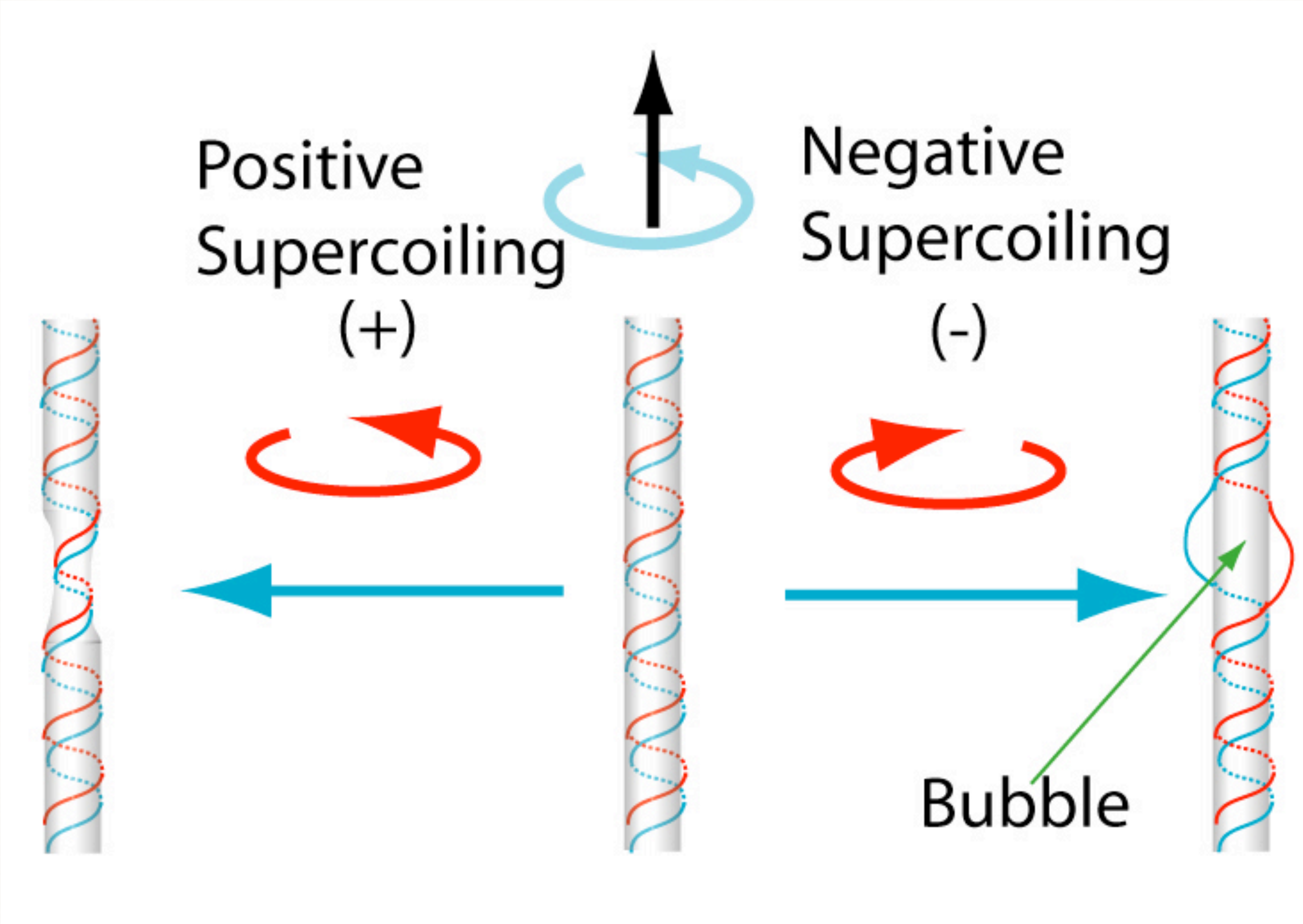


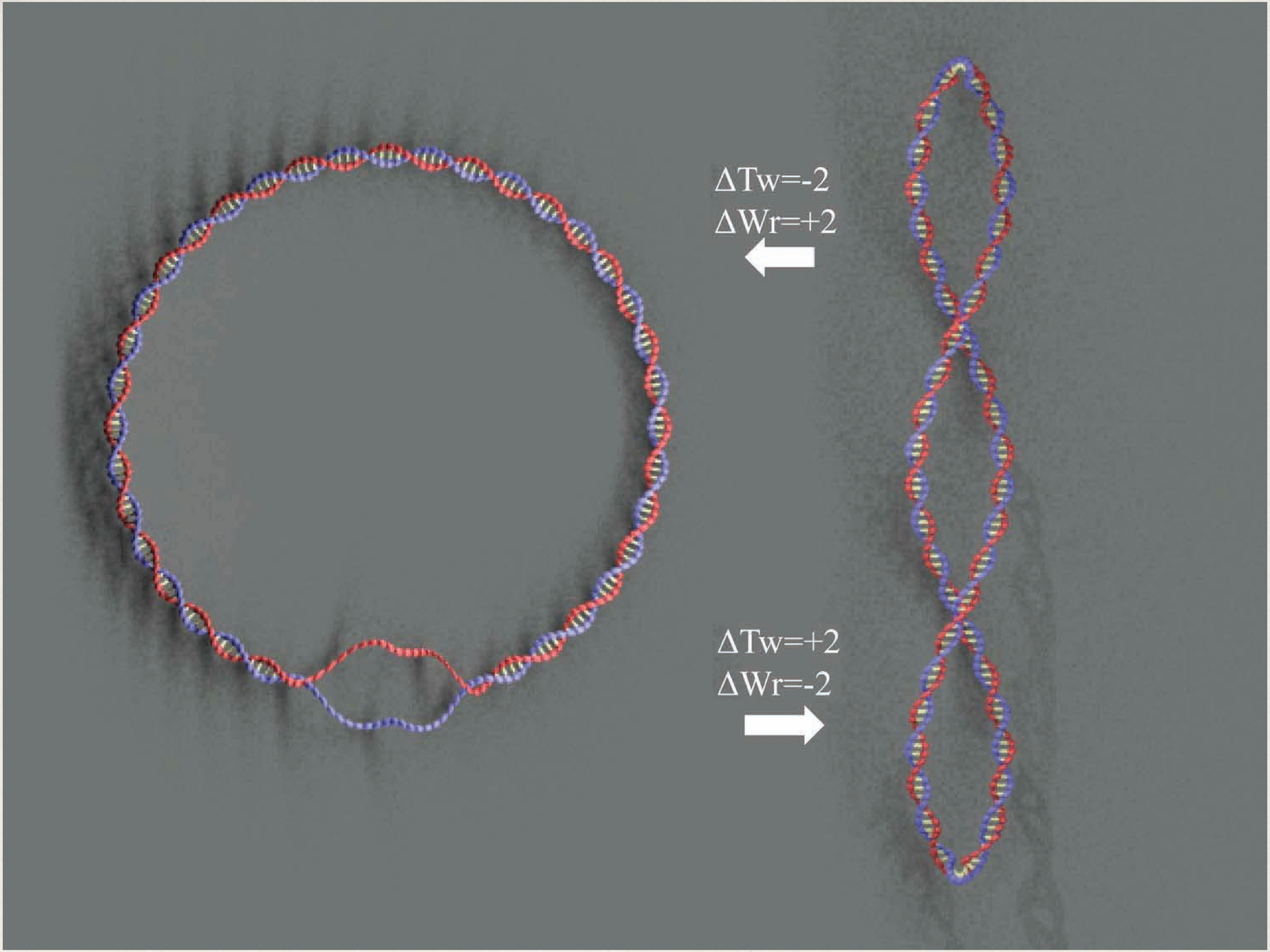
Illustration of the conservation of Lk

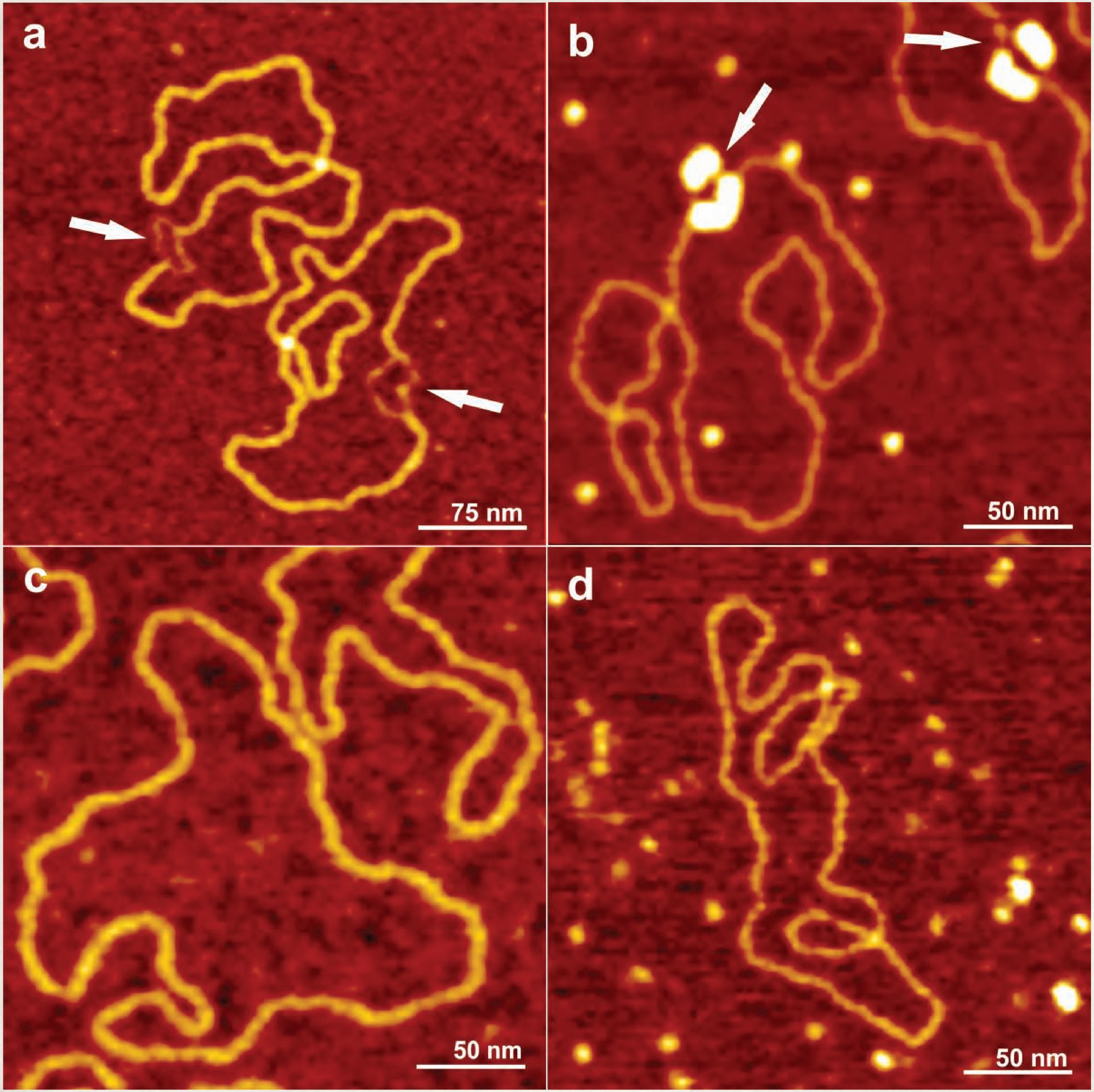
Viglasky et al., Electrophoresis, 24, 1703 (2003)



Effect of supercoiling




ΔTw=-2
ΔWr=+2
ΔTw=+2
ΔWr=-2



pUC19

2686 bp=

878 nm

Tw=258

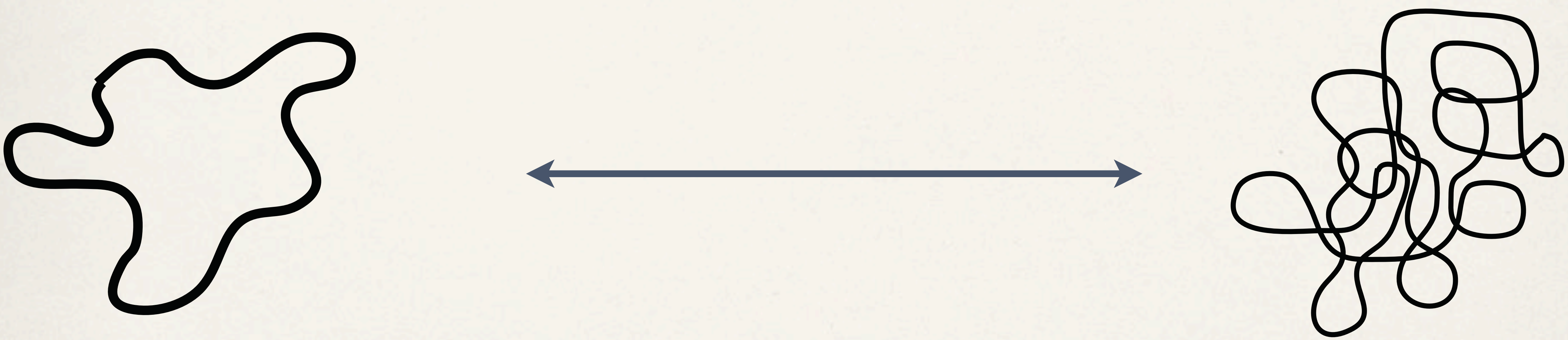
Conservation of the linking number

B-Form DNA of pUC19 = relaxed DNA -- $Tw = 258$

But Nature has chosen $Lk = 242$ (-6%)

Calugareanu-White-Fuller : $Lk = Tw + Wr$

$Lk = 242 = 258 + Wr$ ---- $Wr = -16$



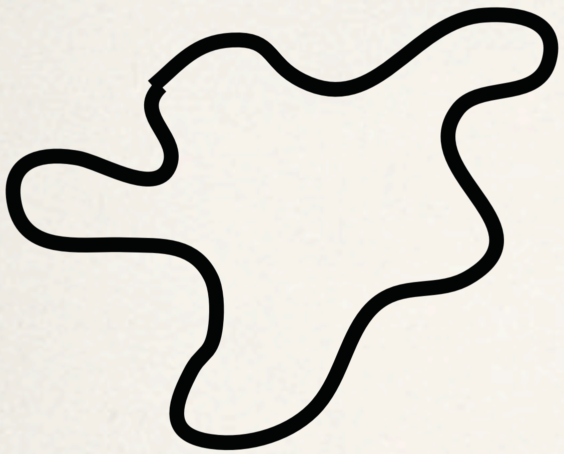
$Tw=242$; $Wr=0$

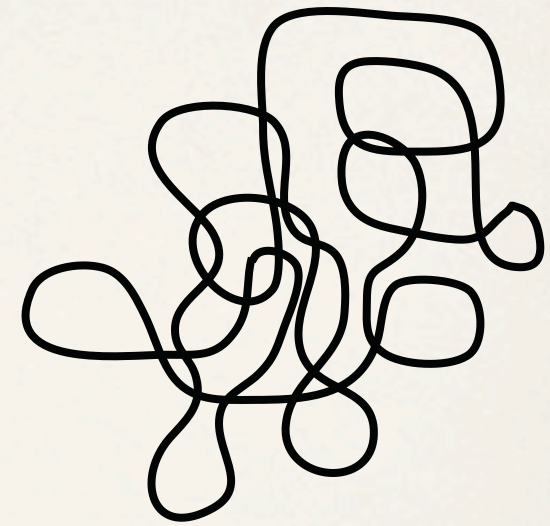
A lot of torsional energy

$Tw=258$; $Wr=-16$

Mostly bending energy

Conservation of the linking number



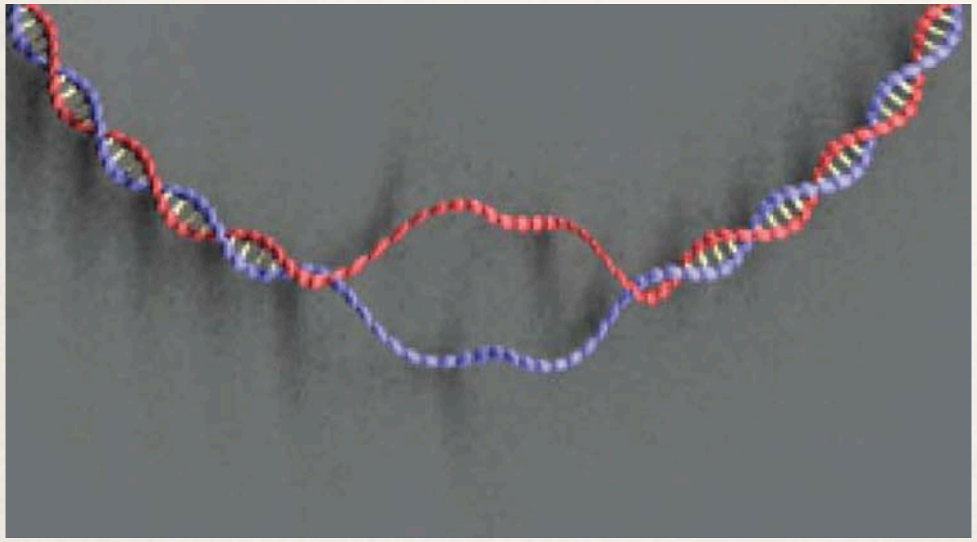


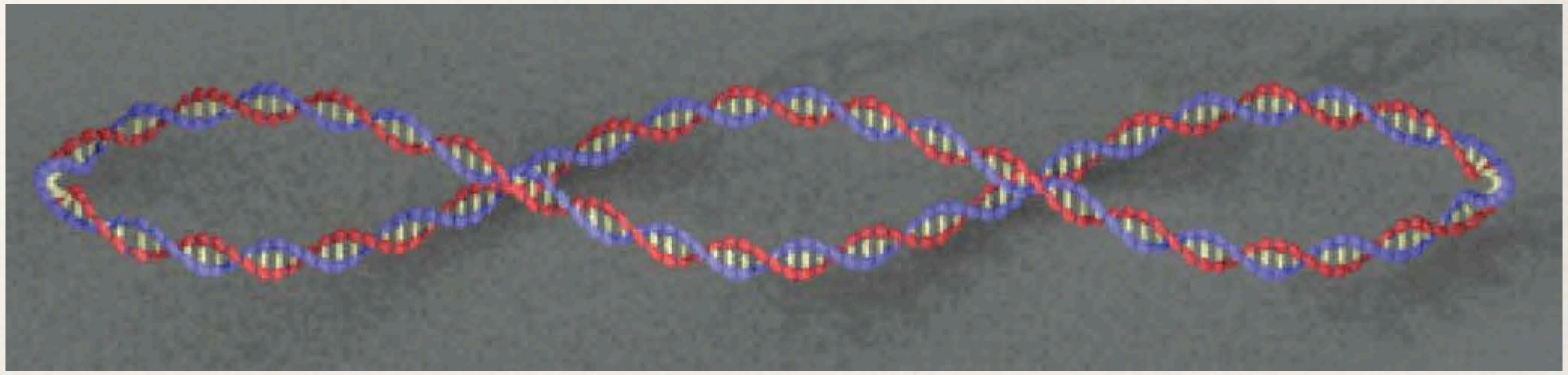
Tw=242 ; Wr=0

A lot of torsional energy

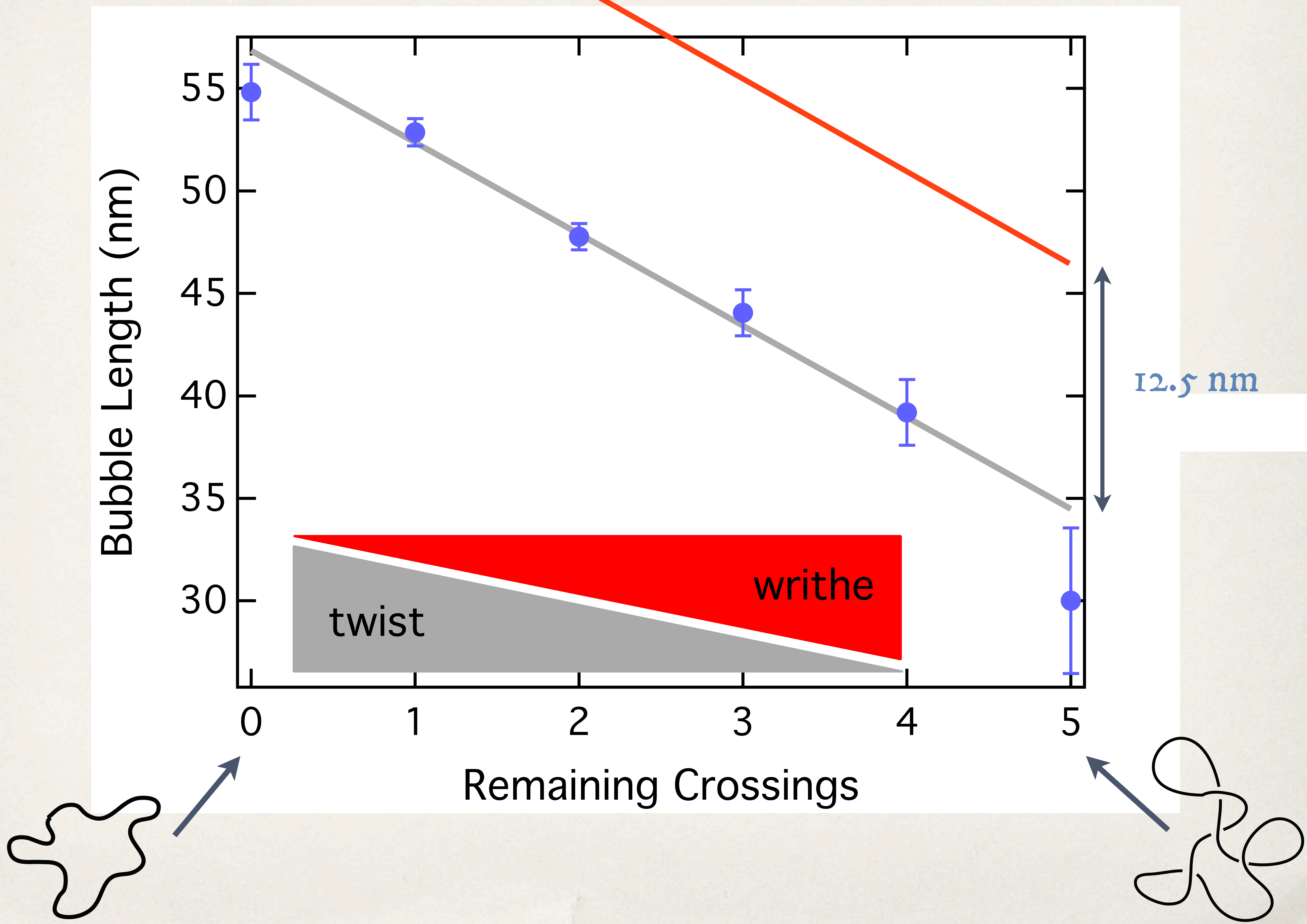
Tw=258 ; Wr=-16

Mostly bending energy





Experiments with pUC19

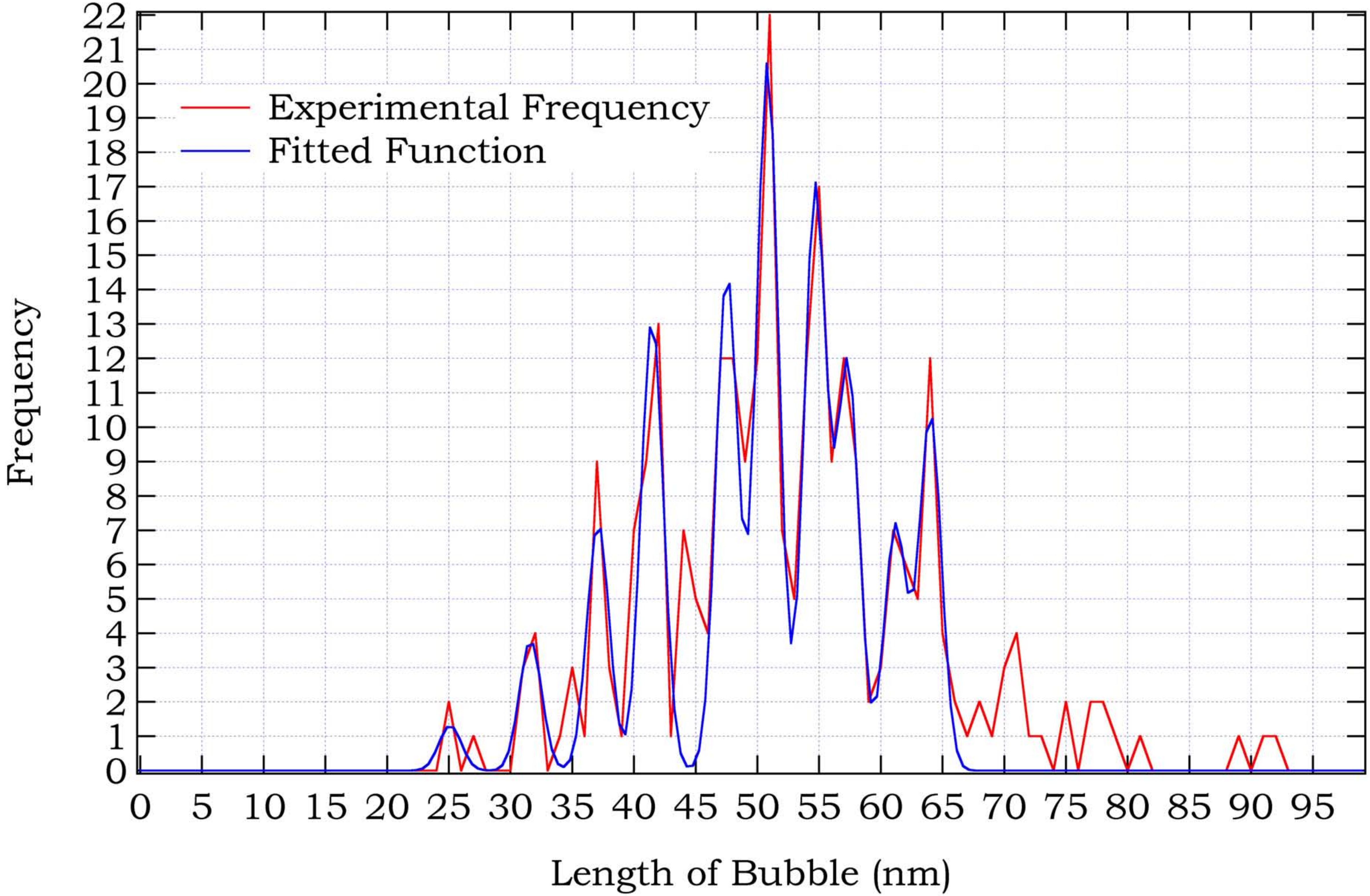


Theoretical prediction (R. Metzler)

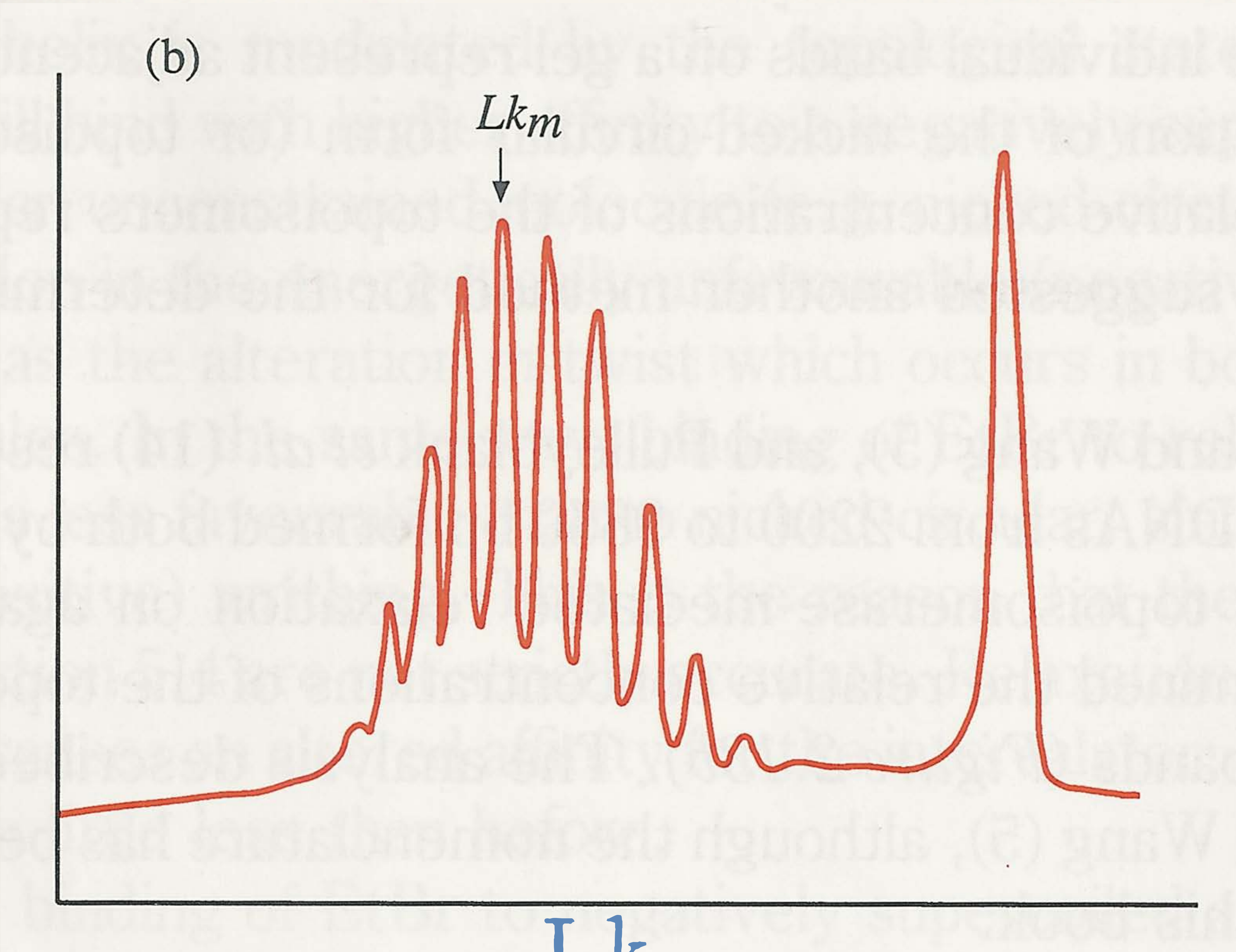
$$b(\mathrm{Wr}) = -\frac{N l_s}{\mathrm{Lk}_0}|\mathrm{Wr}| + |\sigma| N l_s - \frac{l_d l_s N^3}{4\pi^2 C_{tw} \mathrm{Lk}_0^2}\overline{\varepsilon}$$

pUC19 (2686 bp)

Distribution of Bubble Lengths for a Mixture of Topoisomers



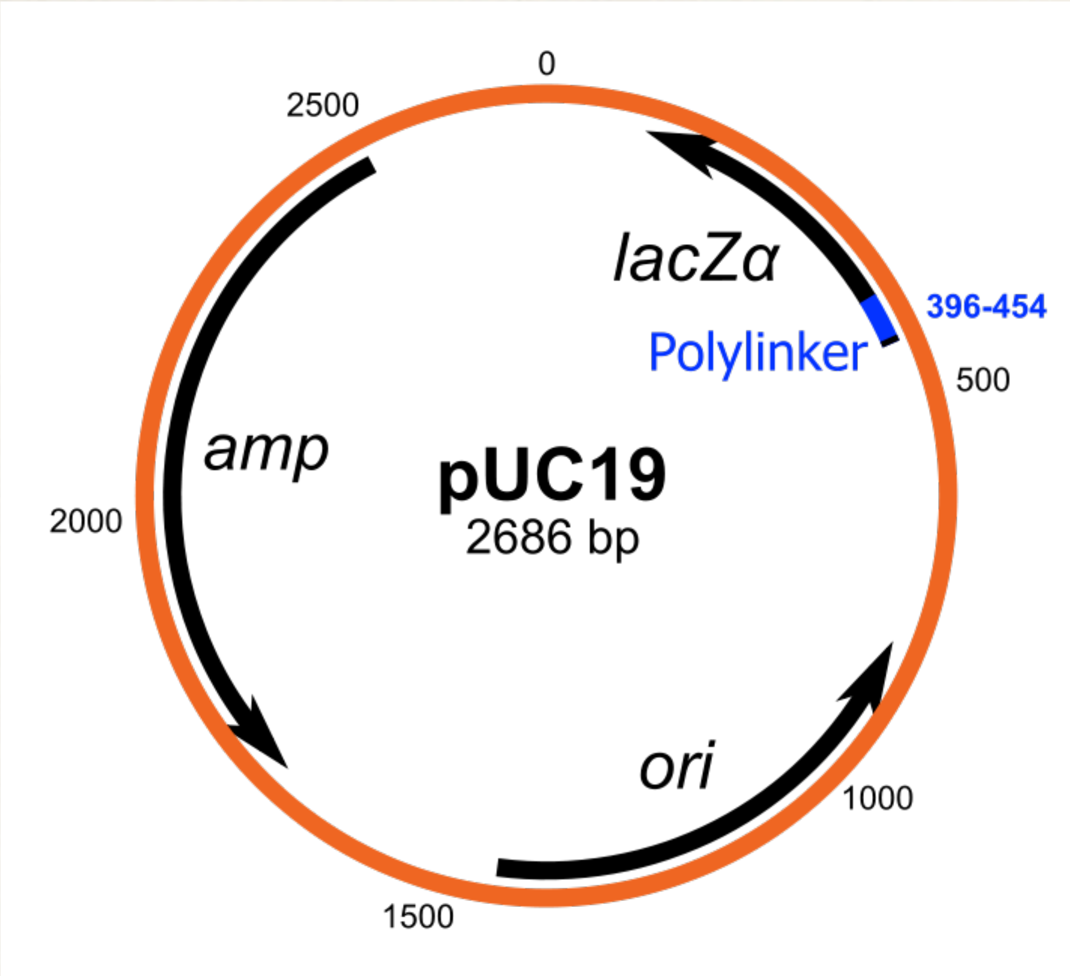
Topoisomers Distribution for PM2 Plasmid (9850 bp)



Lk

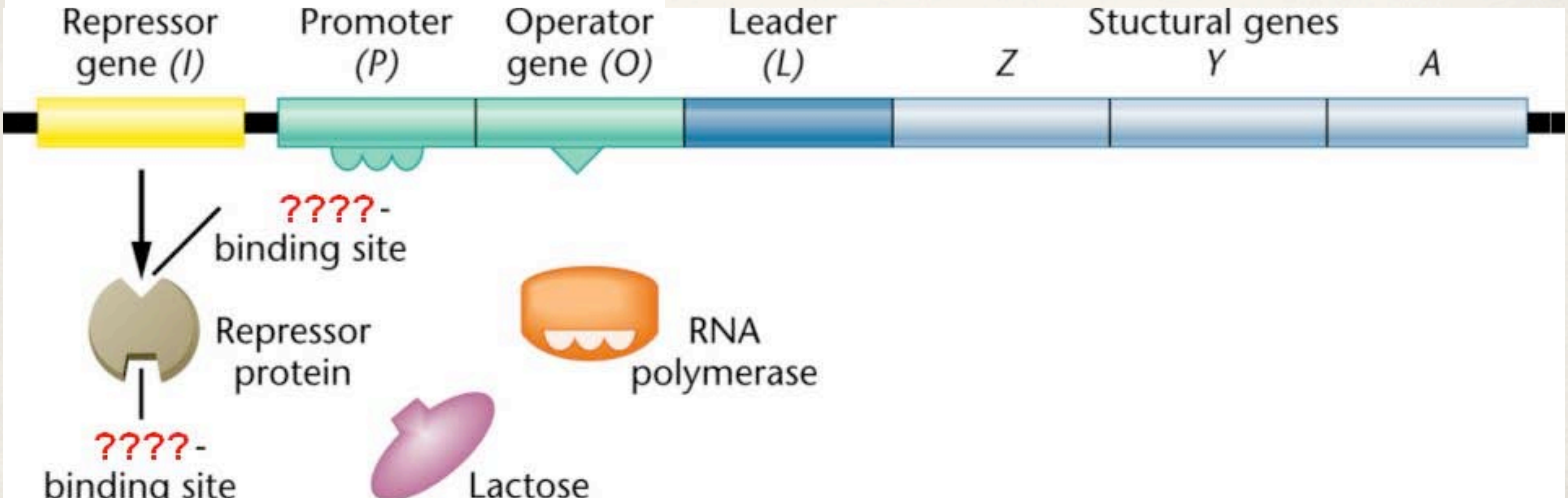
From Depew & Wang, PNAS, 72, 4275 (1975)

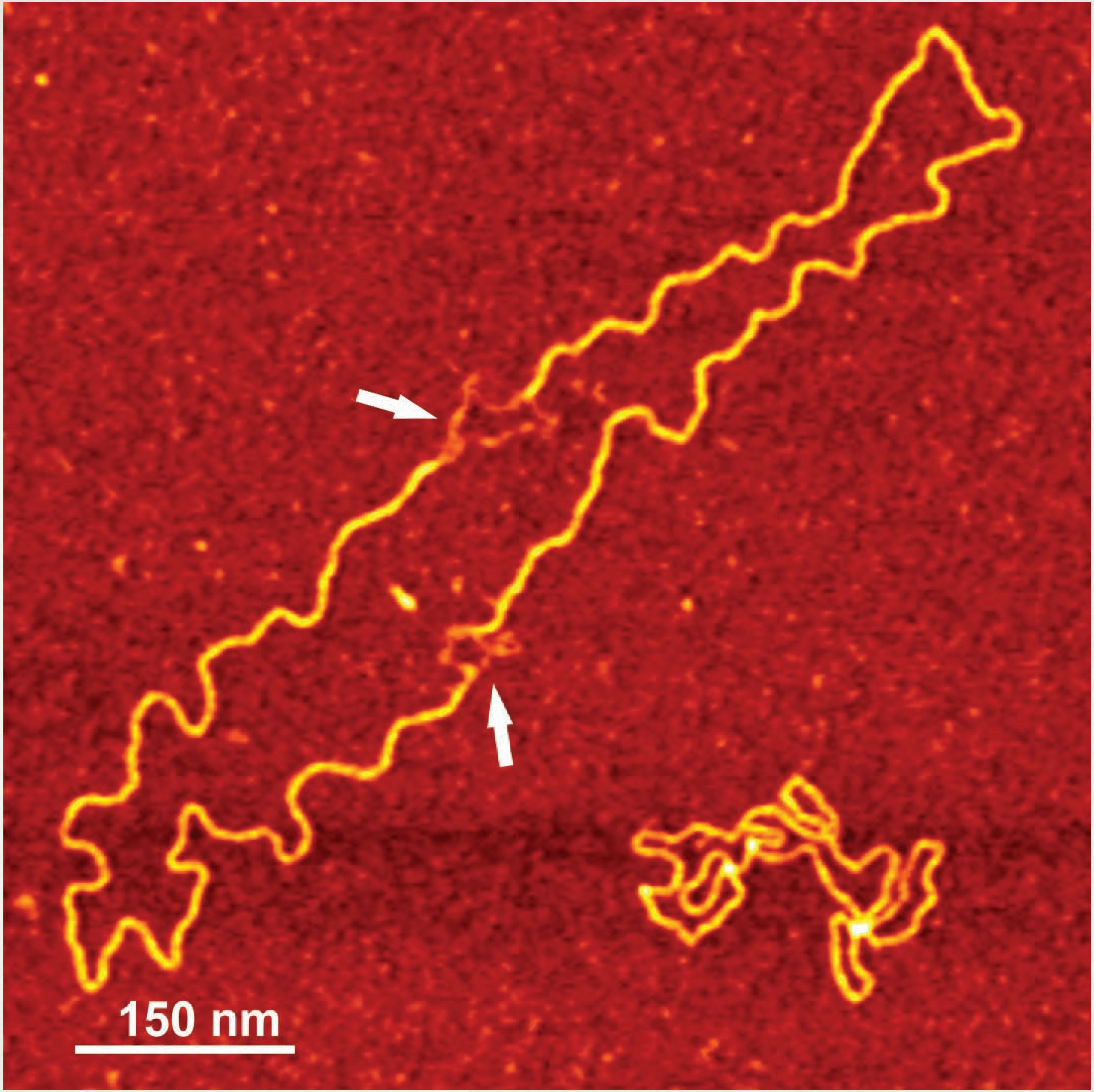
Why only one bubble?



TATA Box

TATATA----




150 nm

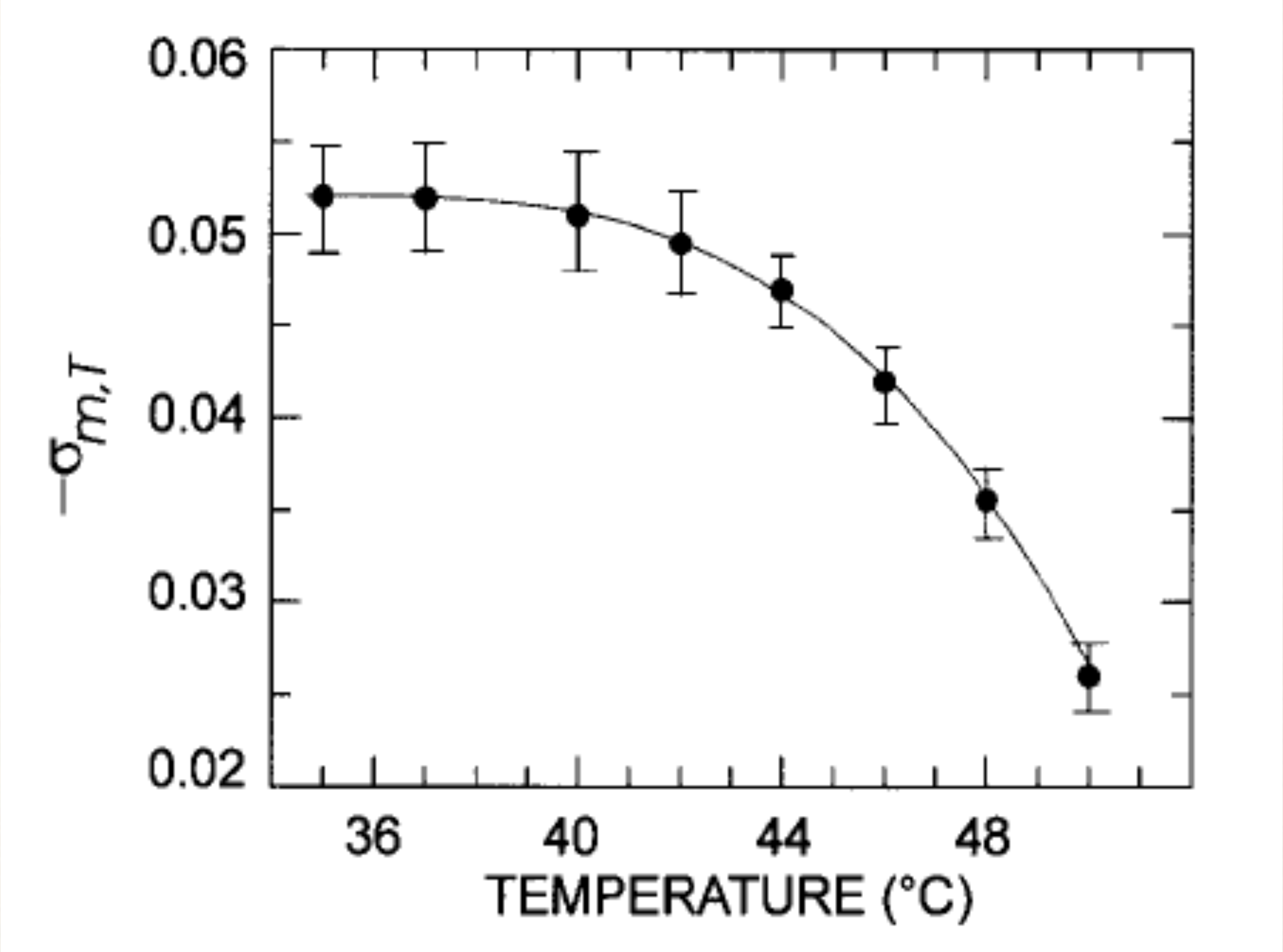
What happen if the temperature is raised?

The opening of the double helix will be promoted!

How will the cell react ?

Temperature dependence of the linking number

Reduction of the underwinding



Adamcik et la., Electrophoresis, 23, 3300 (2002)

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