Magnetic tweezer experiments as a benchmark for models of DNA-DNA electrostatic interaction

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joint work with:
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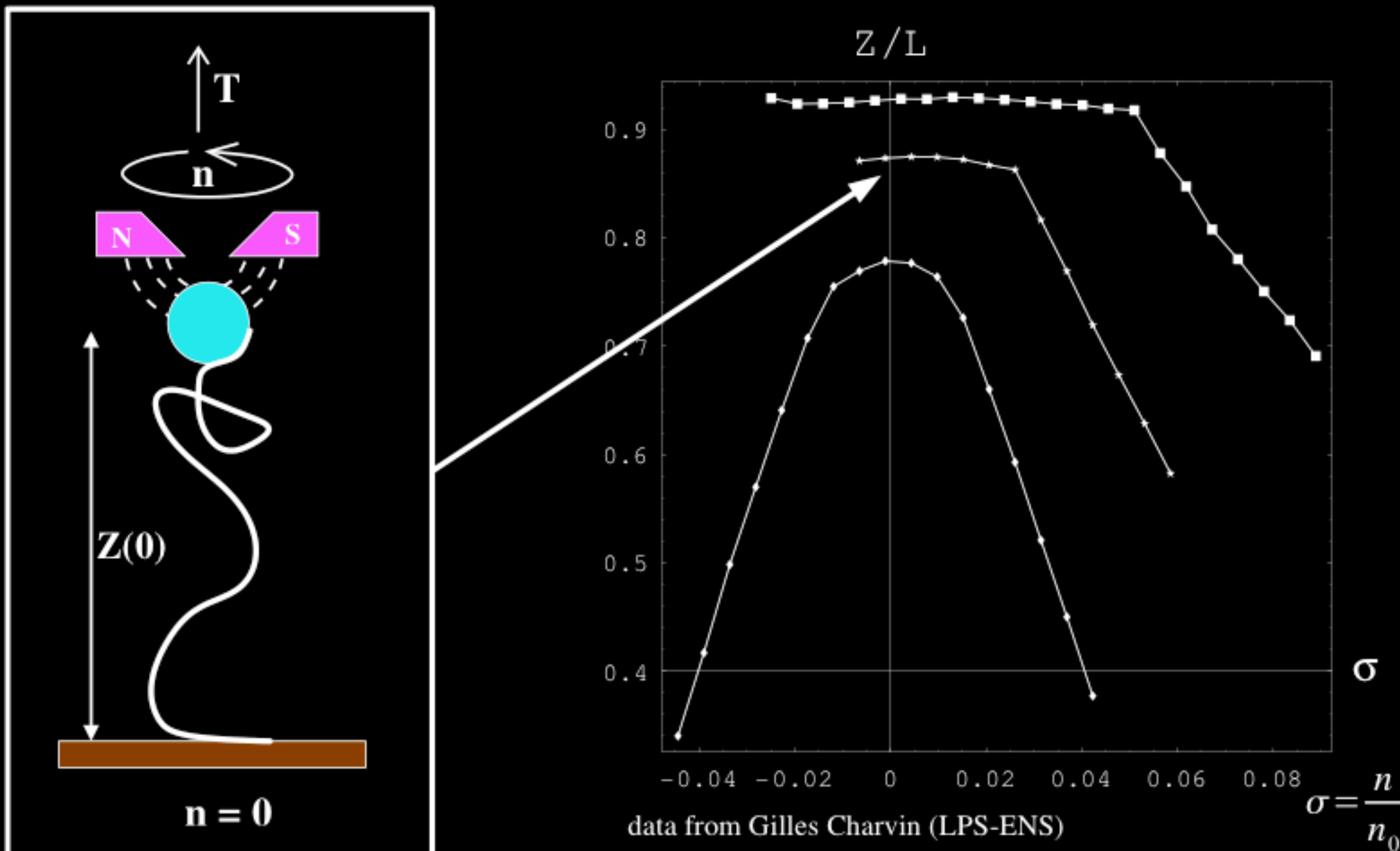
Why study DNA mechanical properties ?

mechanical properties influence biology of the cell

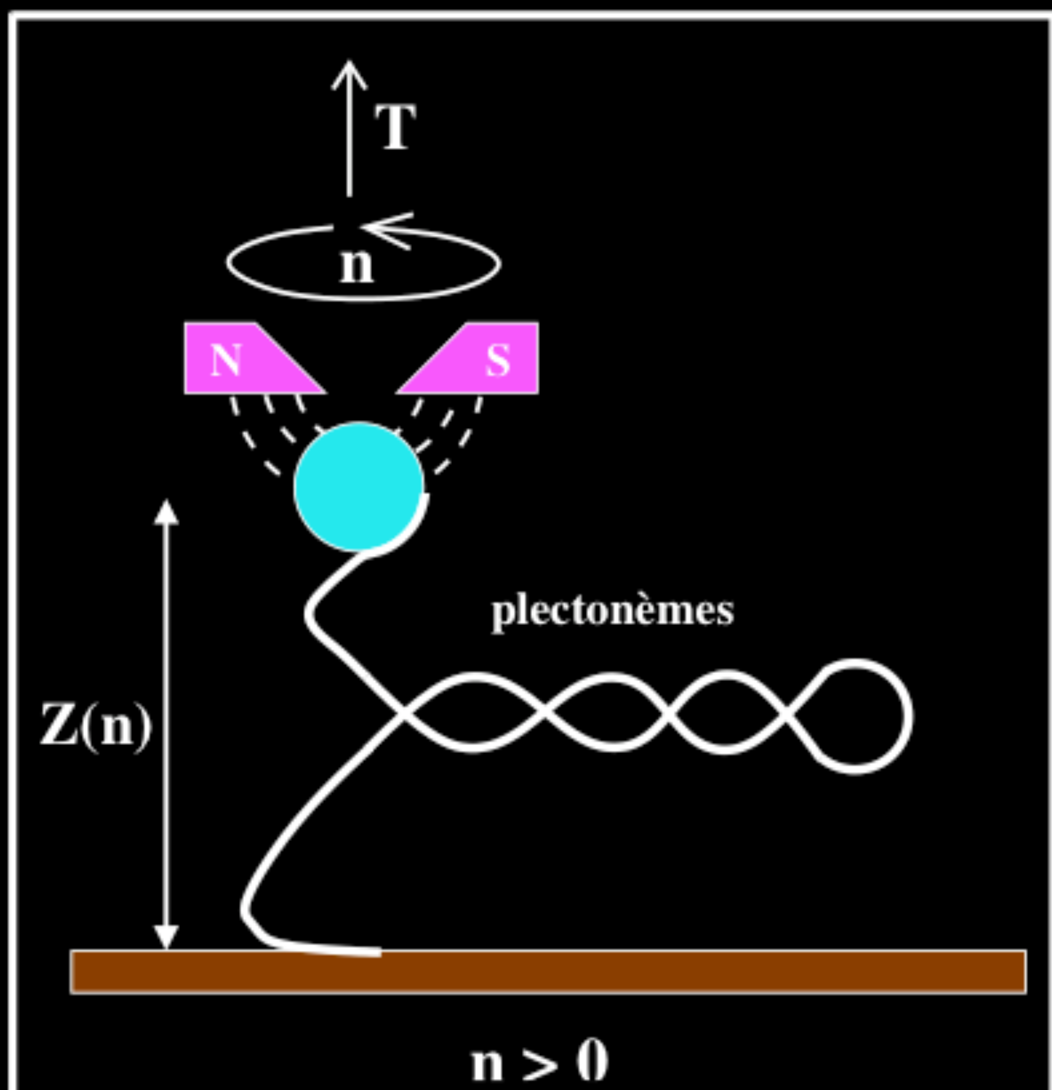
- 2 meters of DNA in a 10 micron wide nucleus
- ejection from viral capside
- transcription (RNApolymerase is torque dependent)
- protein binding is strain dependent, or induces strain on DNA
- chromatin compaction/decompaction (cell division)

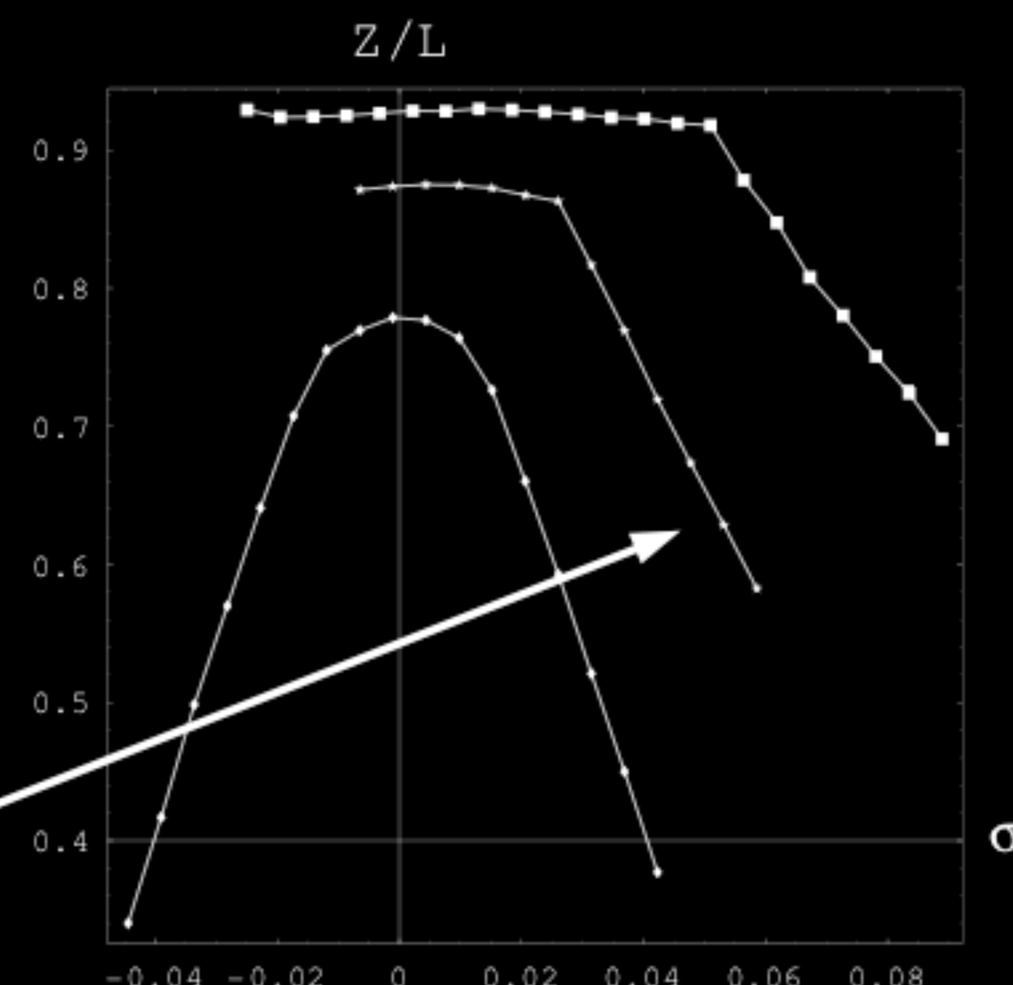
Pulling and twisting DNA



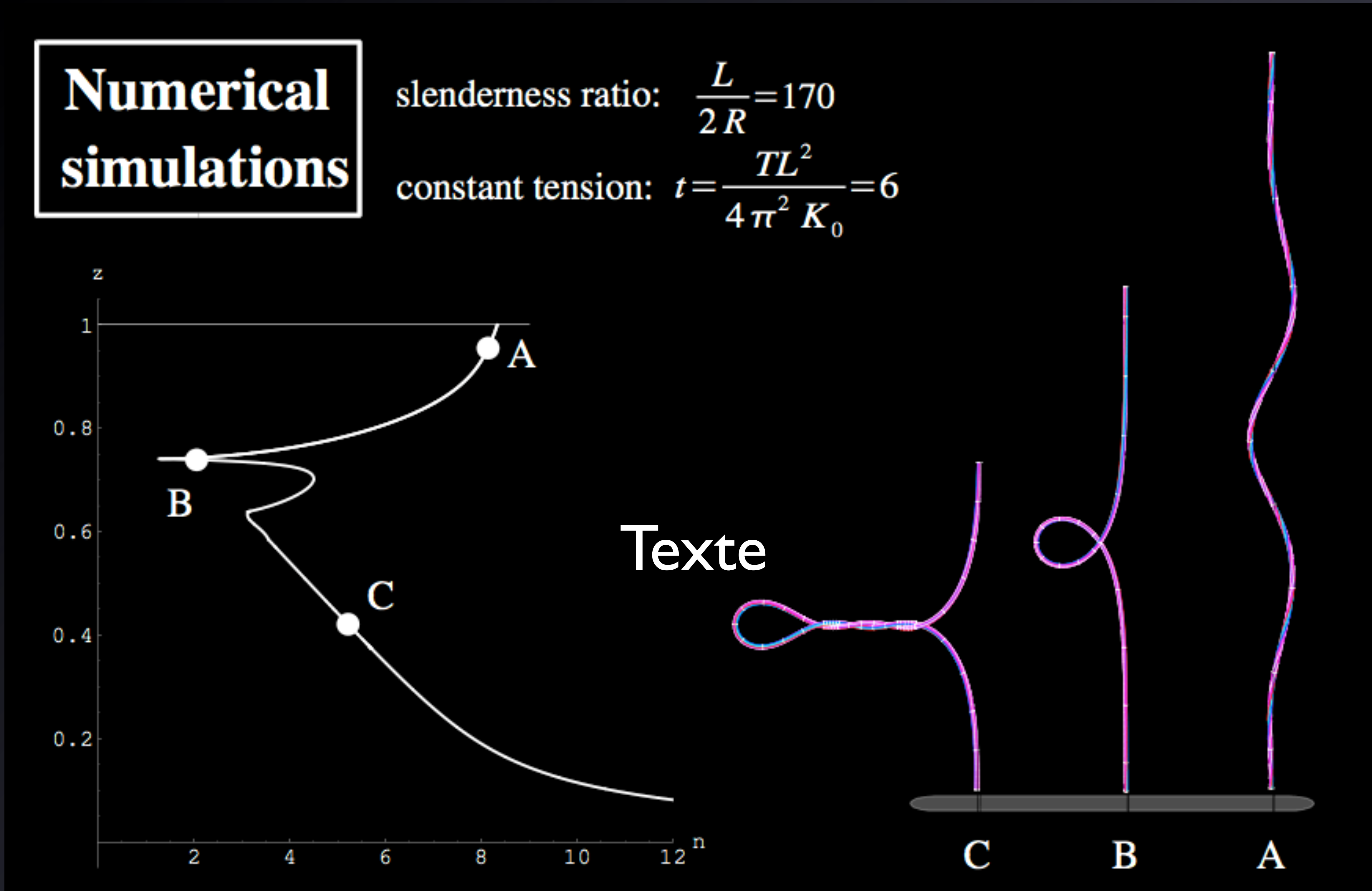
data from Gilles Charvin (LPS-ENS)

Pulling and twisting DNA



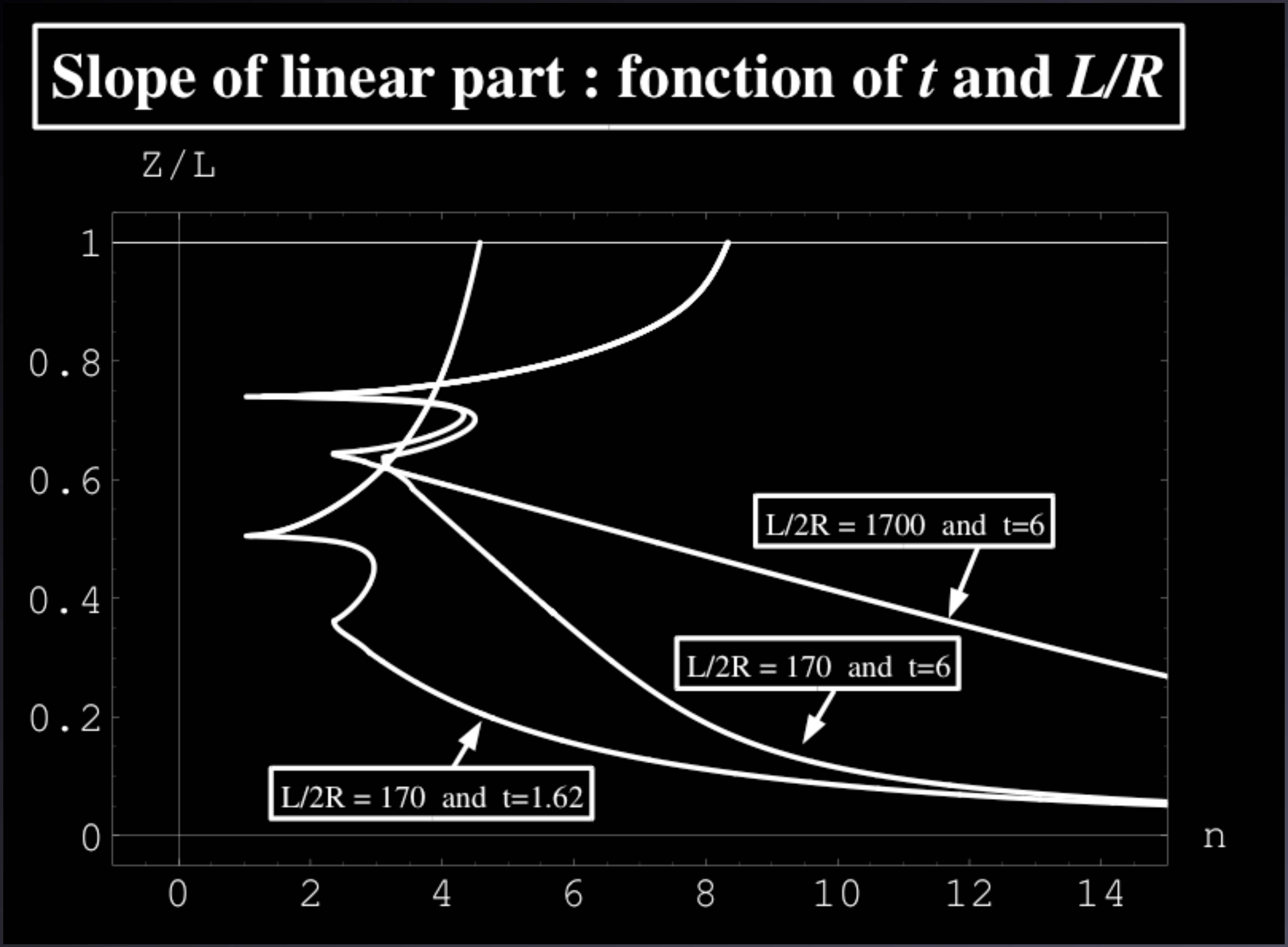


data from Gilles Charvin (LPS-ENS) $\sigma = \frac{n}{n_0}$

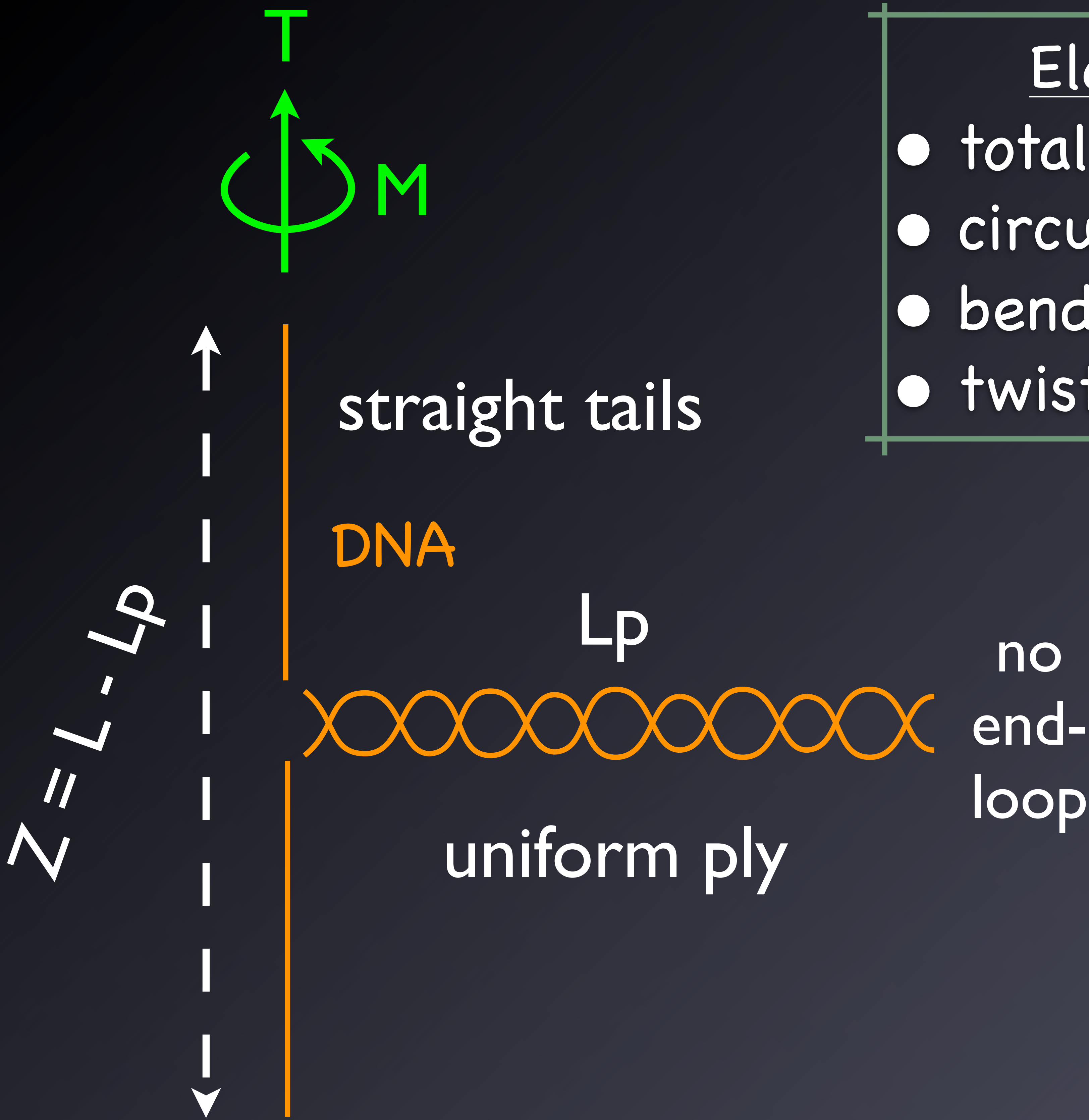


(based on Swigon+Coleman model for contact in Kirchhoff rods)

S. Neukirch, "Extracting DNA … ", Phys. Rev. Lett. **93** (2004)


Slope of linear part : fonction of t and L/R
Z/L
1
0.8
0.6
0.4
0.2
0
0
2
4
6
8
10
12
14
n
L/2R = 1700 and t=6
L/2R = 170 and t=6
L/2R = 170 and t=1.62

Analytical model for plectonemic DNA



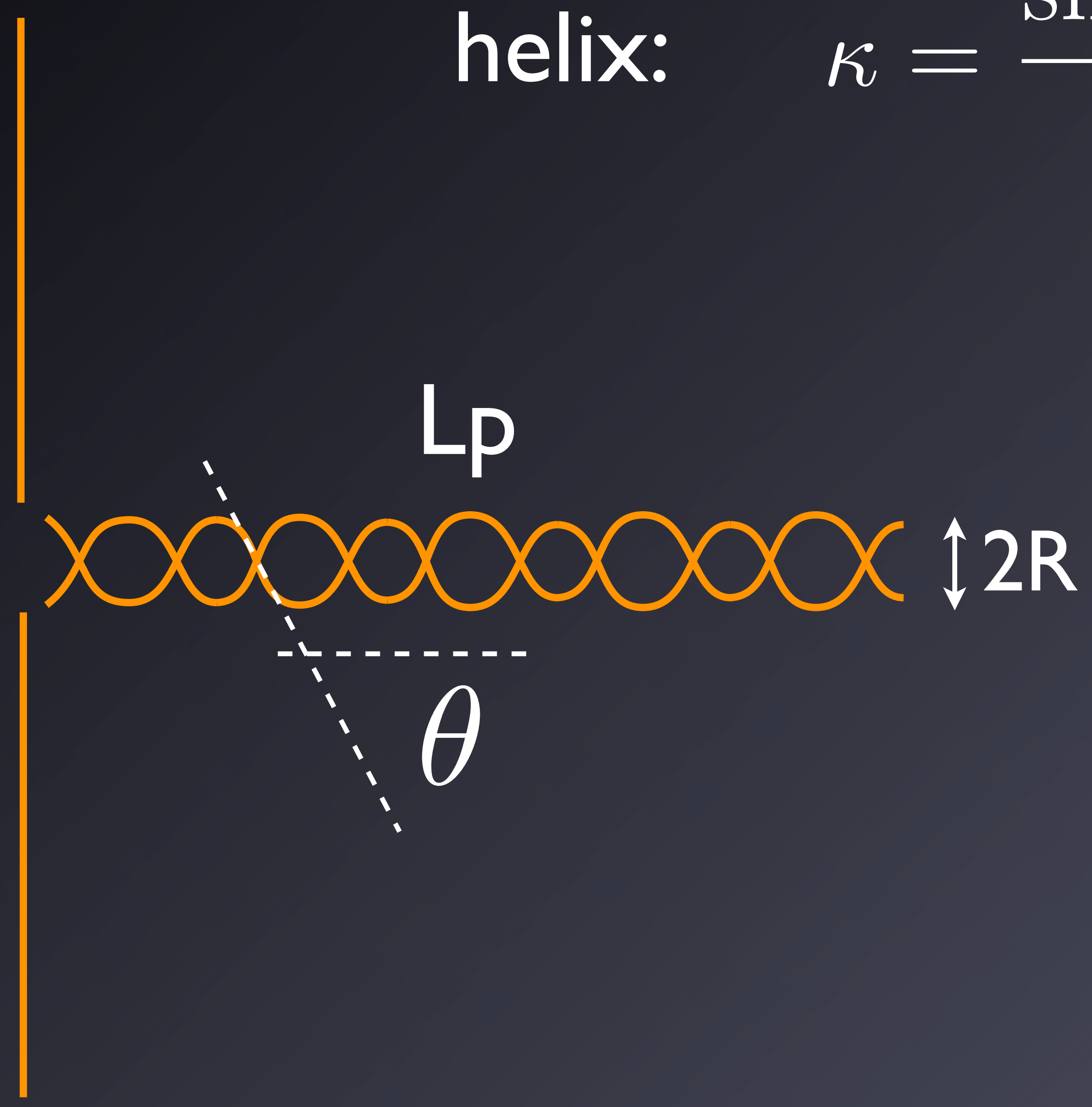
<u>Elastic rod</u> with :

- total length L
- circular cross-section R_0
- bending rigidity K_0
- twist rigidity K_3

Energy formulation: elastic strain energy

bending: $V = \frac{1}{2} K_0 \kappa^2 L_p$

helix: $\kappa = \frac{\sin^2 \theta}{R}$ (uniform)

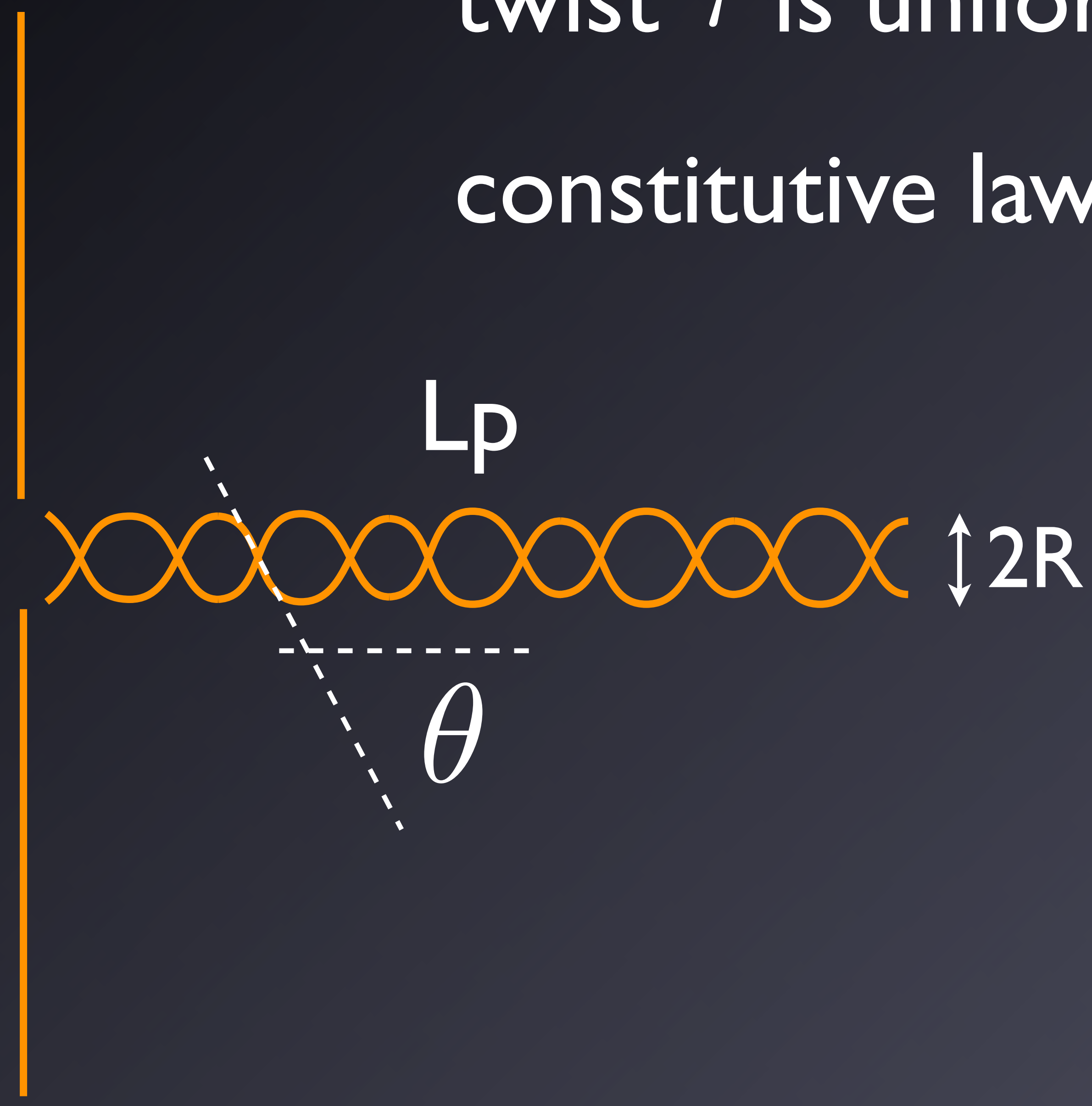


Energy formulation: elastic strain energy

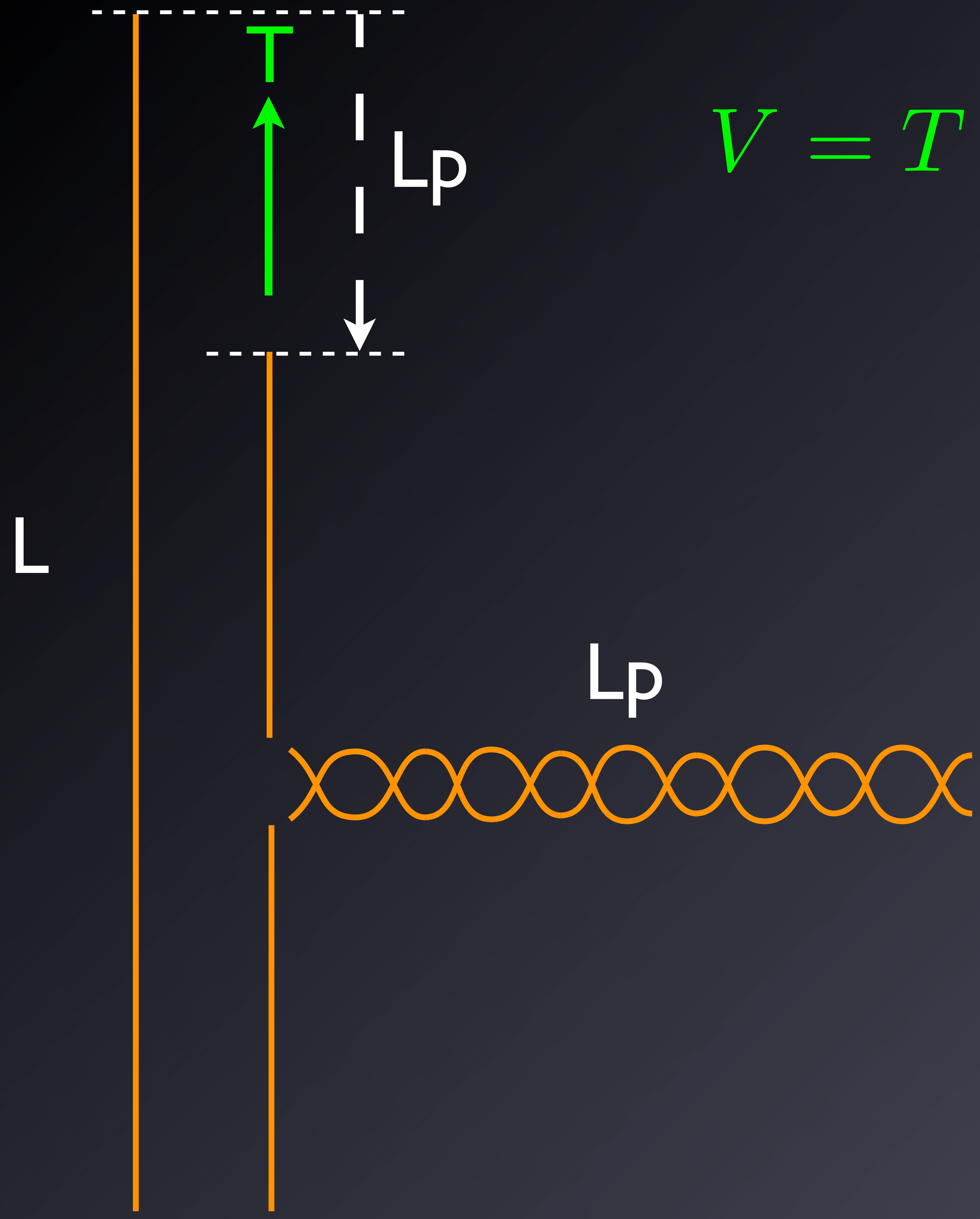
twisting: $V = \frac{1}{2} K_3 \tau^2 L$

twist τ is uniform along the rod

constitutive law: $M = K_3 \tau$



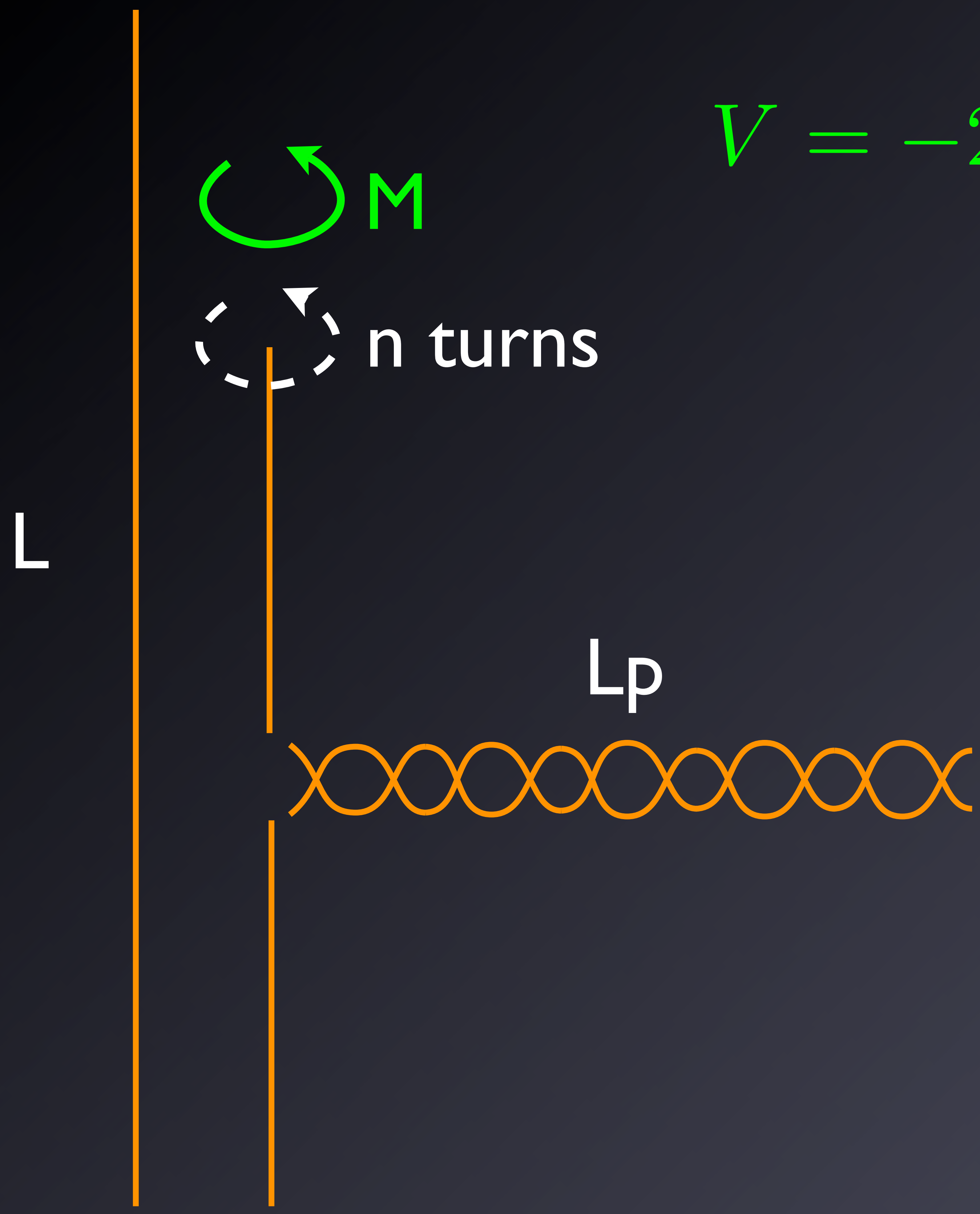
Energy formulation: work of external loads



$$V = T\ L_p$$

Energy formulation: work of external loads

$$V = -2\pi n M$$



Energy formulation: self-interaction

hard-wall (contact)
=> constraint:

$$V = \lambda\,(R - R_0)$$

long-range:
~ electrostatics

- S. Leikin
- D. Stitger
- Debye-Hukel
- G. Manning
- ...

$$V = L_p\,U(\theta, R)$$

Energy formulation: equilibrium

$$V = \frac{1}{2}K_0\frac{\sin^4\theta}{R^2}L_p + \frac{1}{2}K_3\tau^2 L + T\ L_p - 2\pi n M + \left(\begin{array}{c}\lambda\ (R-R_0)\\ \text{or}\\ L_p\ U(\theta,R)\end{array}\right)\ ,$$

$$\text{where } n = Lk = Tw + Wr = \frac{1}{2\pi}\left(\tau L + \frac{\sin 2\theta}{2R}L_p\right)\ .$$

$$V = V[\theta, R, L_p]$$

Euler-Lagrange equations : $\left(\frac{\partial V}{\partial\theta}, \frac{\partial V}{\partial R}, \frac{\partial V}{\partial L_p}\right) = 0$

Energy formulation: results (hard-wall)

$$0 = \left(\frac{\partial V}{\partial \theta}, \frac{\partial V}{\partial R}, \frac{\partial V}{\partial L_p} \right) \Rightarrow$$

tension

$$T = \frac{K_0}{R_0^2} \sin^4\theta \left(\frac{1}{2} + \frac{1}{\cos 2\theta} \right),$$

numerical simulations

$$T = \frac{K_0}{R_0^2} (1.66\,\theta^4)$$

contact pressure

$$p \left(= \frac{\lambda}{L_p} \right) = \frac{K_0}{R_0^3} \frac{\sin^4\theta}{\cos 2\theta}$$

torque

$$M = \frac{2K_0}{R_0} \frac{\cos\theta \sin^3\theta}{\cos 2\theta}$$

N. Clauvelin, B. Audoly, S. Neukirch, Macromolecules (2008)

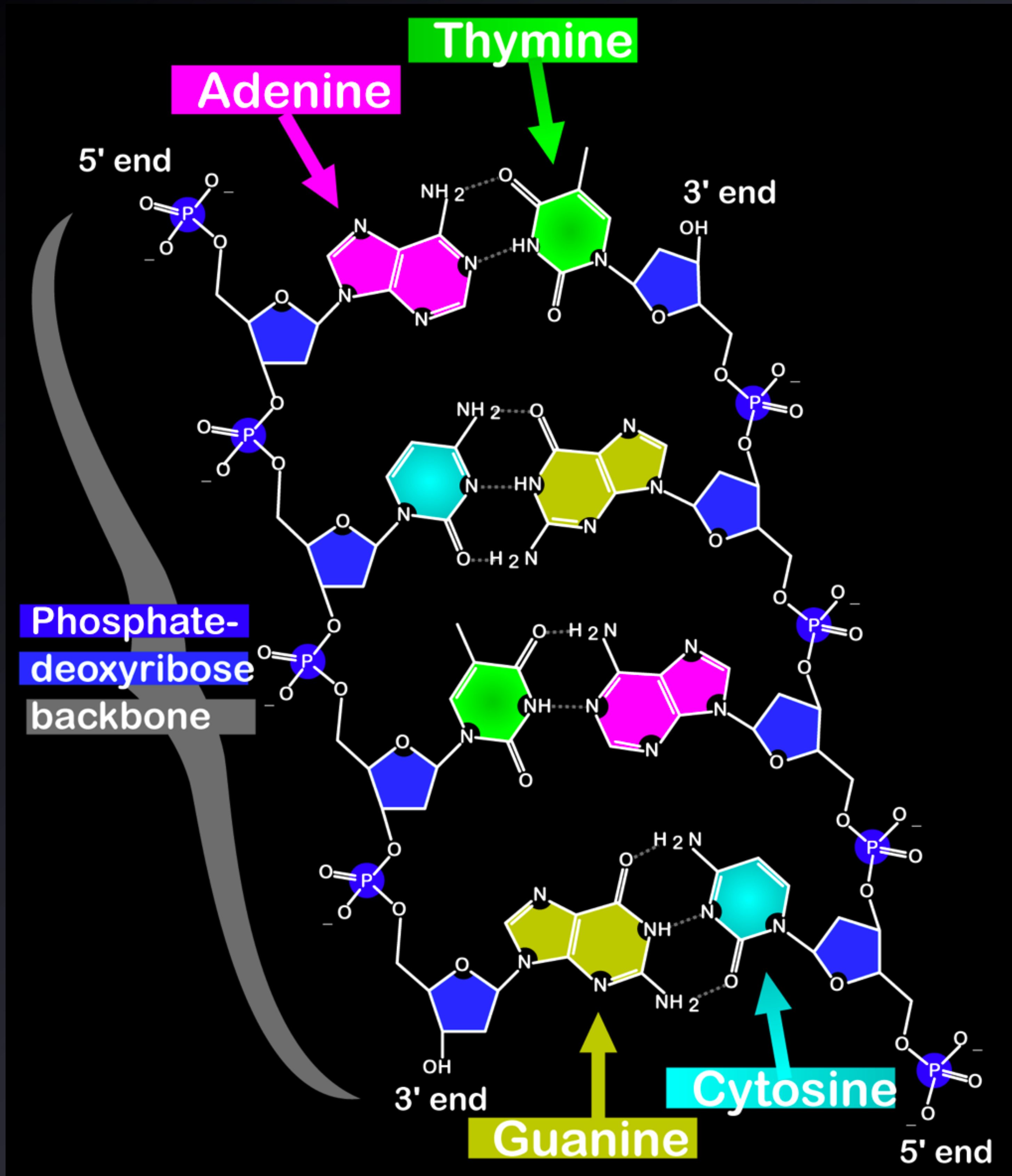
Energy formulation: results (long-range)

$$0 = \left(\frac{\partial V}{\partial \theta}, \frac{\partial V}{\partial R}, \frac{\partial V}{\partial L_p} \right) \Rightarrow \begin{cases} T = \dfrac{K_0}{2R^2} \sin^4\theta - R\dfrac{\partial U}{\partial R} - U(R,\theta) \\ M = \dfrac{2K_0}{R} \dfrac{\sin^4\theta}{\sin 2\theta} - \dfrac{2\,R^2}{\sin 2\theta}\dfrac{\partial U}{\partial R} \\ M = \dfrac{2K_0}{R} \dfrac{\cos\theta \sin^3\theta}{\cos 2\theta} + \dfrac{R}{\cos 2\theta}\dfrac{\partial U}{\partial \theta} \end{cases}$$

Once U(θ,R) is given,
3 equations for
3 unknowns (R, θ, M)

DNA electrostatics

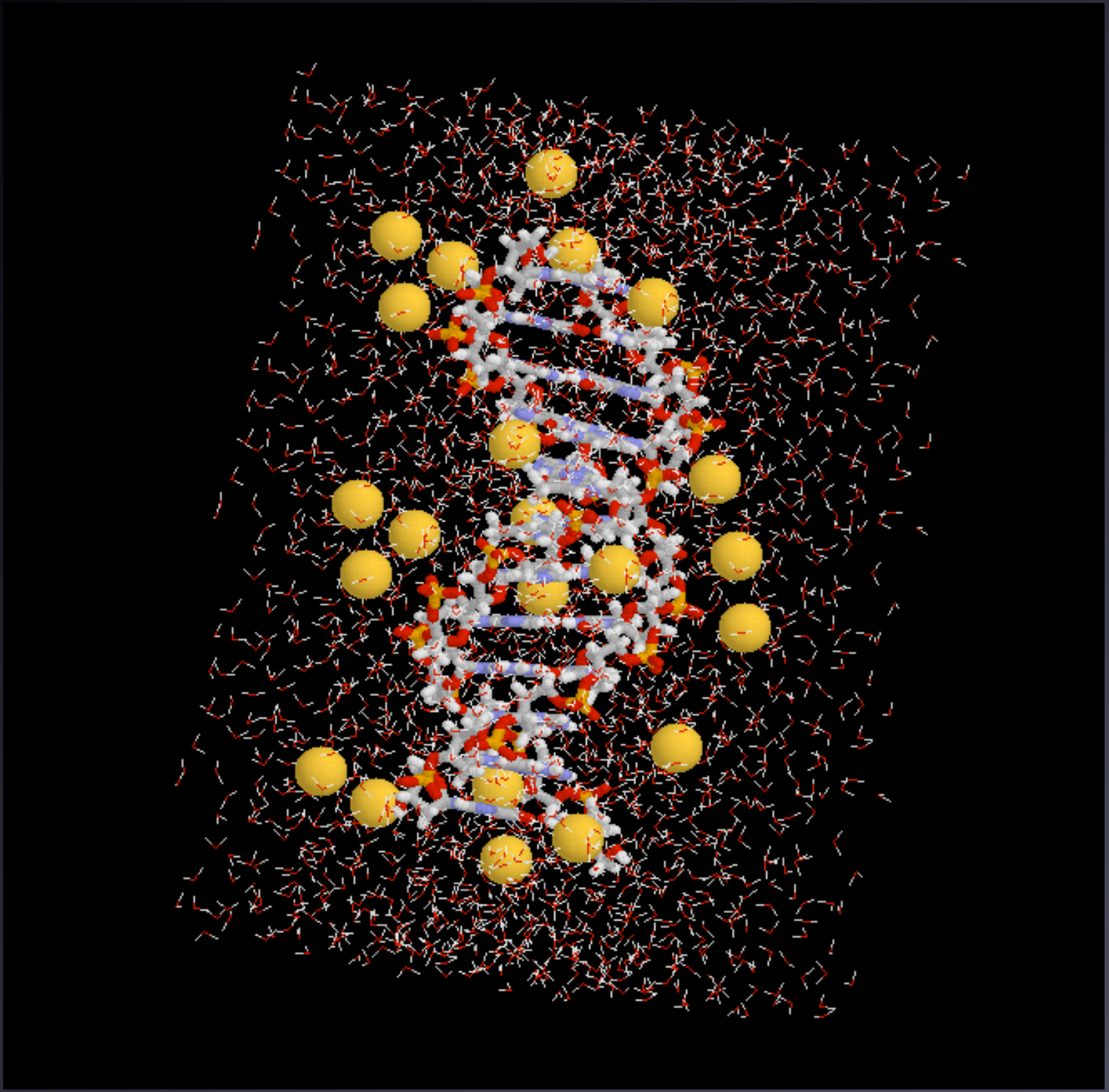
Wikipedia



2 e^- per base-pair

<=> 1 e^- / 0.17 nm

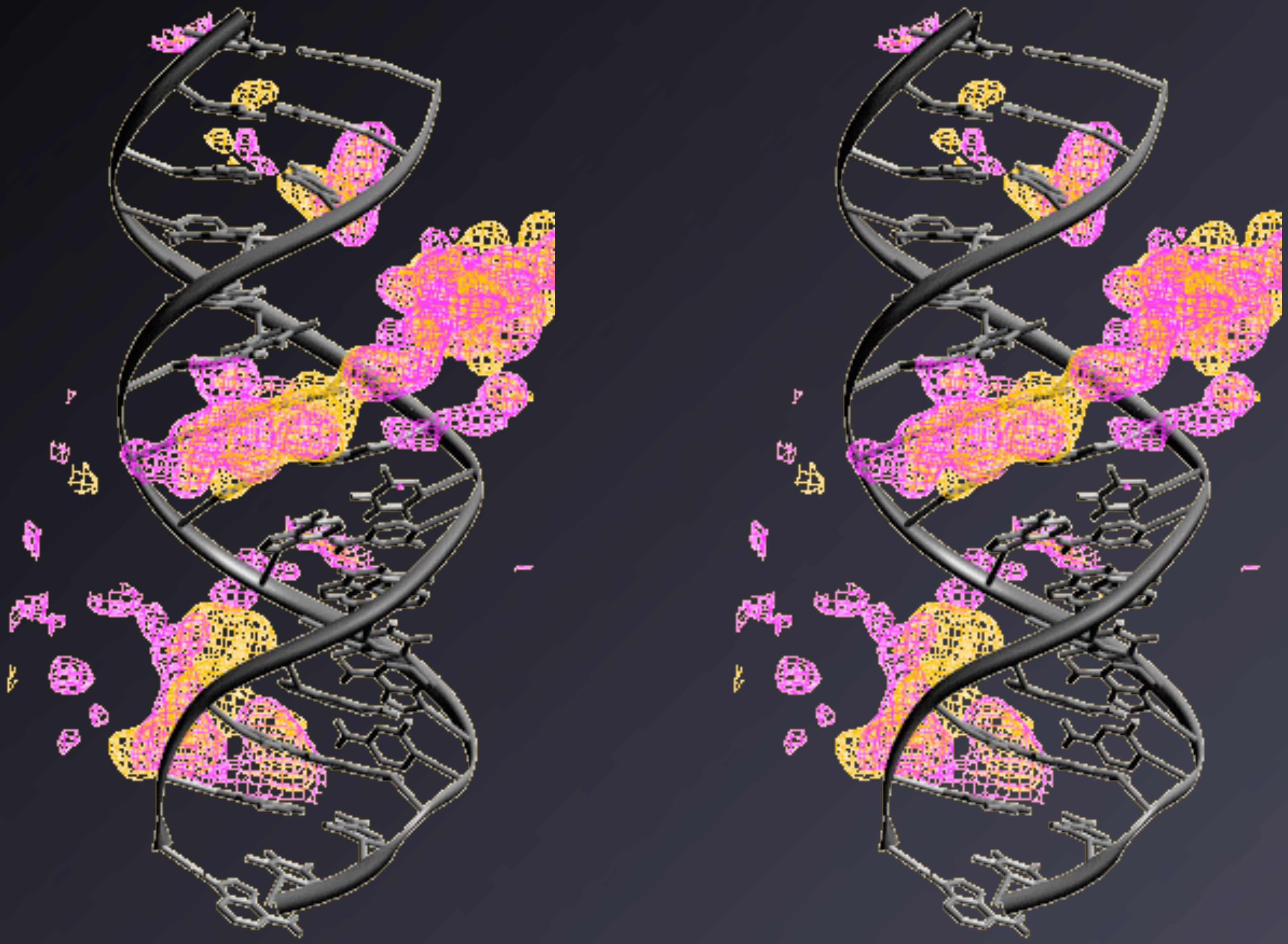
DNA electrostatics



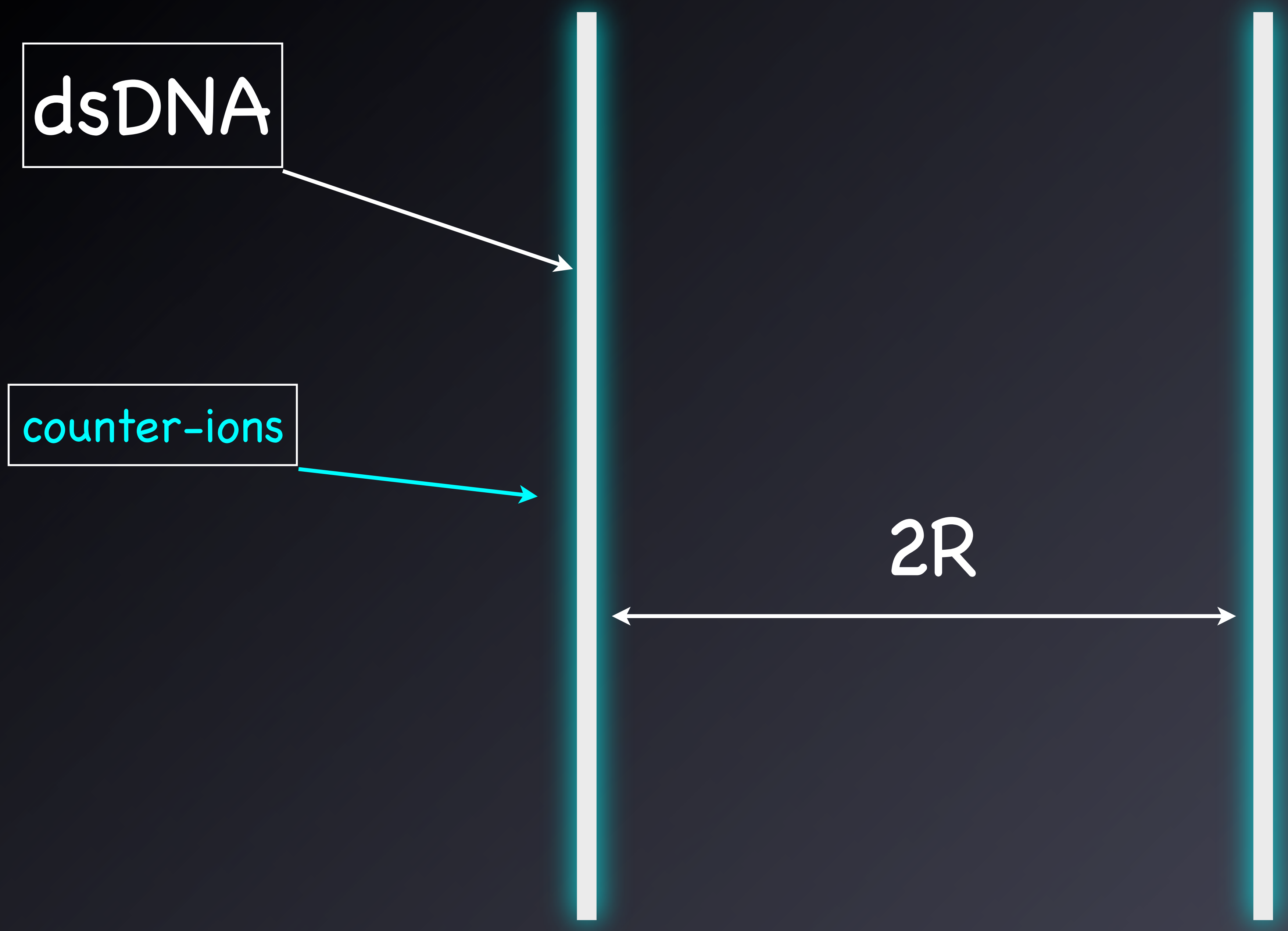
Alexander MacKerell
www.psc.edu

DNA electrostatics

Alexandre Bonvin
www.nmr.chem.uu.nl



DNA electrostatics : Poisson-Boltzmann



effective charge (10mM): $\nu = 1.38/L_B \quad (m^{-1})$

$$L_B = \frac{e^2}{\epsilon KT}$$

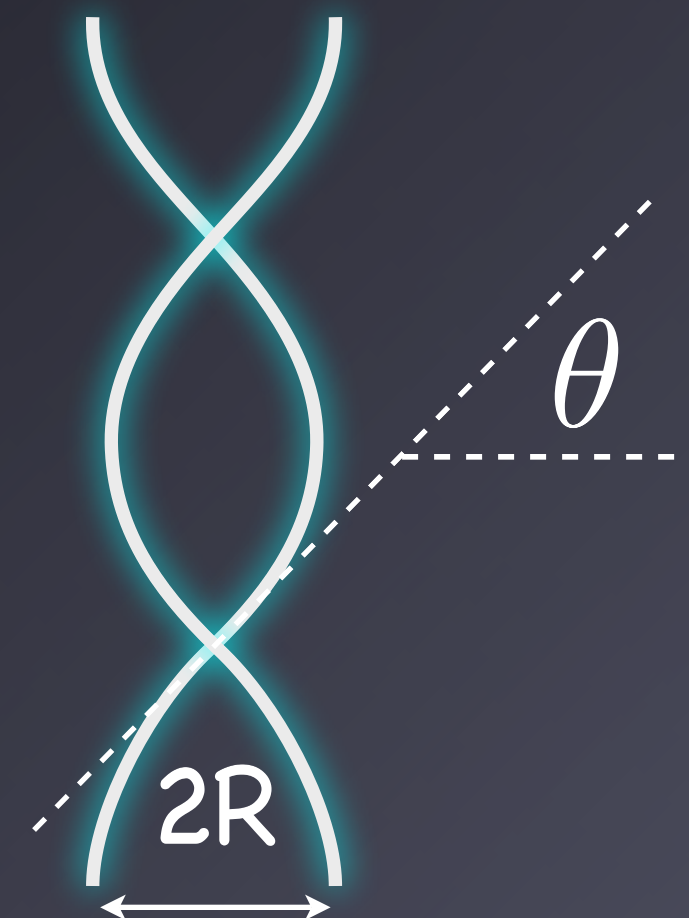
DNA electrostatics : Poisson-Boltzmann

$$U(R,\theta) = \frac{1}{2} kT\nu^2 L_B \sqrt{\frac{\pi}{\kappa R}} e^{-2\kappa R} \cdot \phi(\theta)$$ (per unit length)

κ : Debye

$$L_B = \frac{e^2}{\epsilon KT}$$

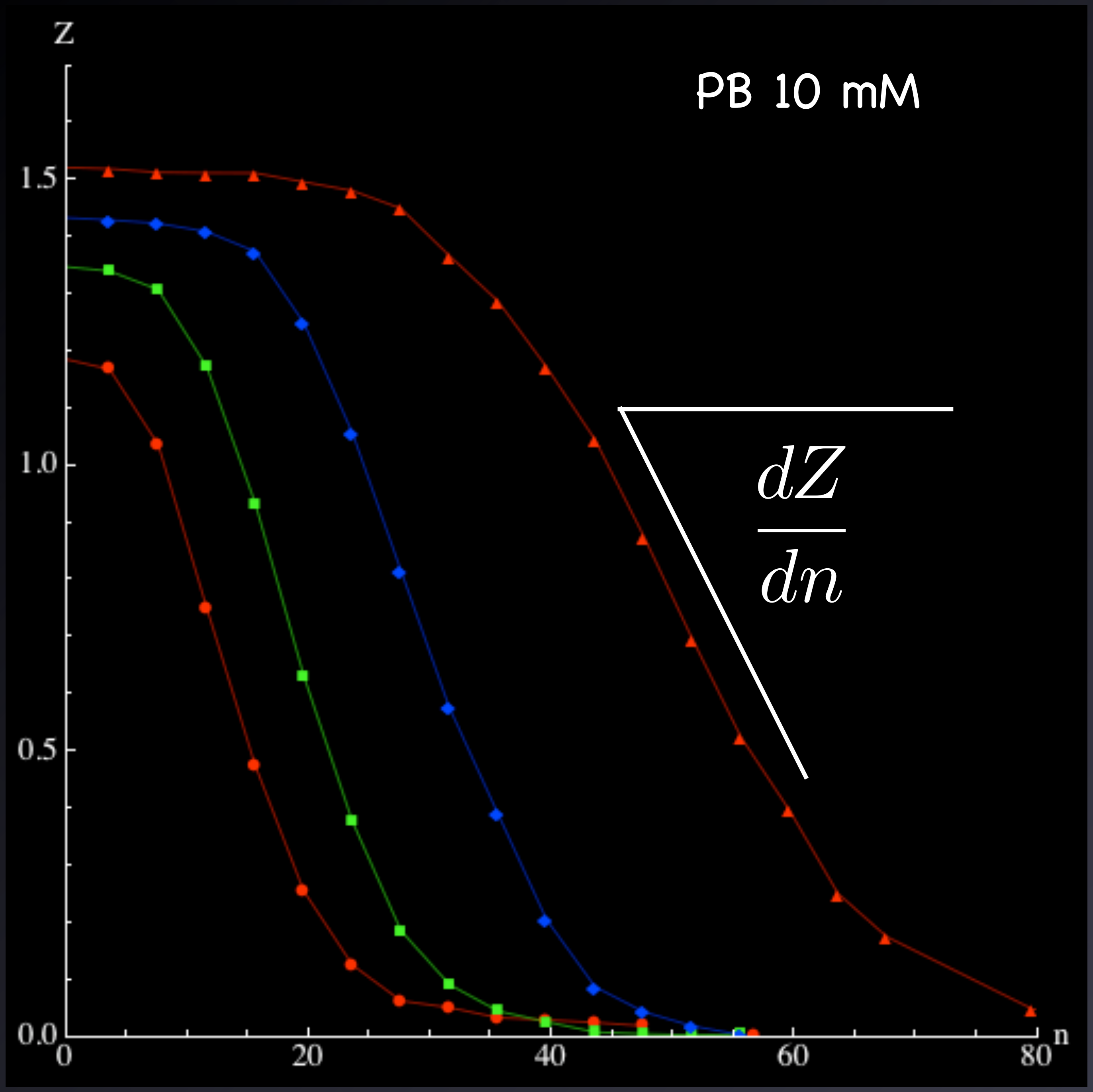
$$\phi(\theta) = 1$$



$$\phi(\theta) = 1 + 0.83 \tan^2\theta + 0.86 \tan^4\theta$$

J. Ubbink, T. Odijk, Biophysical Journal (1999)

Results : comparison with experimental data



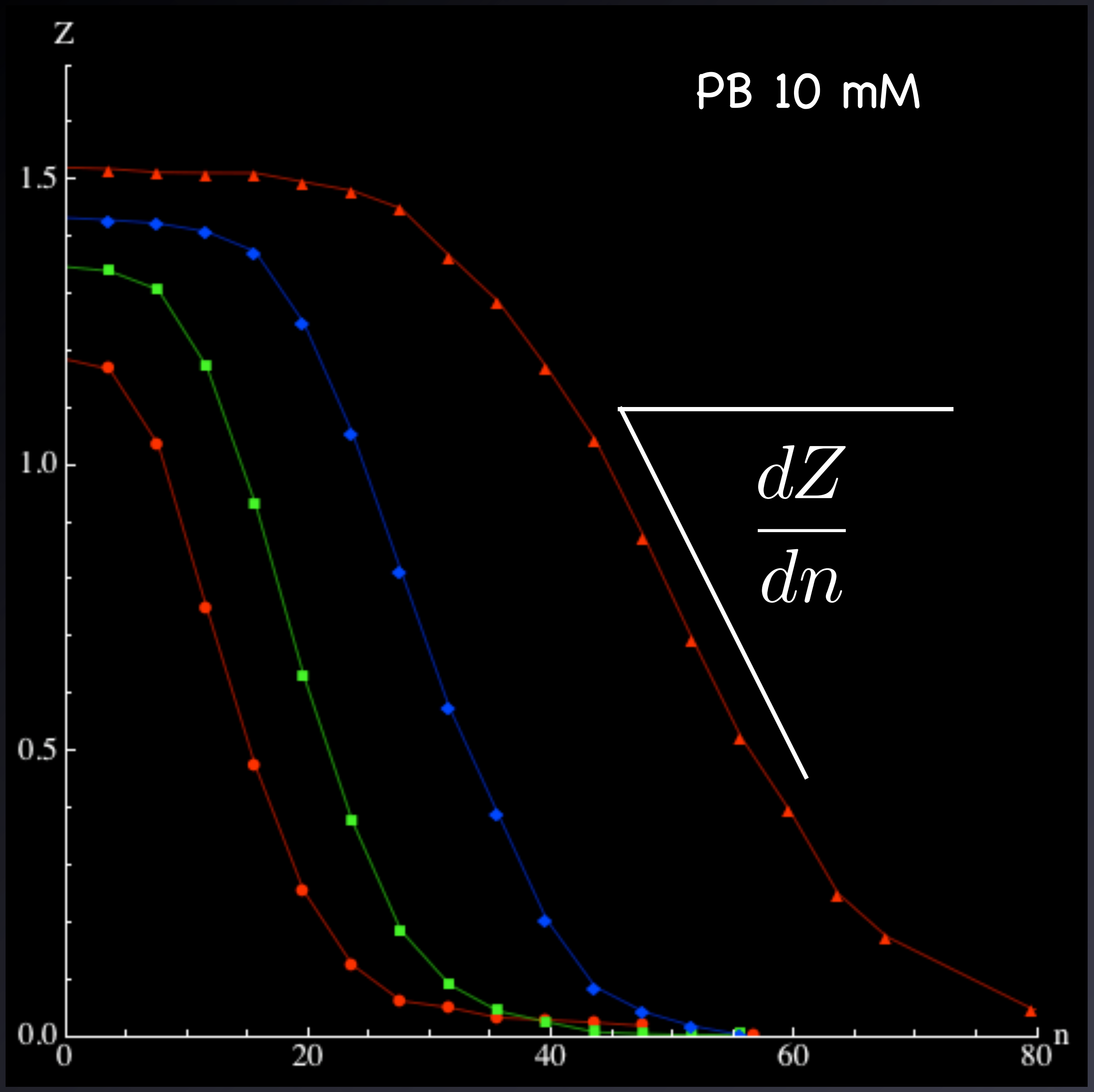
data from Gilles Charvin (ENS-Paris)

$$n = Lk = Tw + Wr$$

with Wr linear of z

$$\Rightarrow \frac{dZ}{dn} = \frac{4\pi R}{\sin 2\theta}$$

Results : comparison with experimental data



data from Gilles Charvin (ENS-Paris)

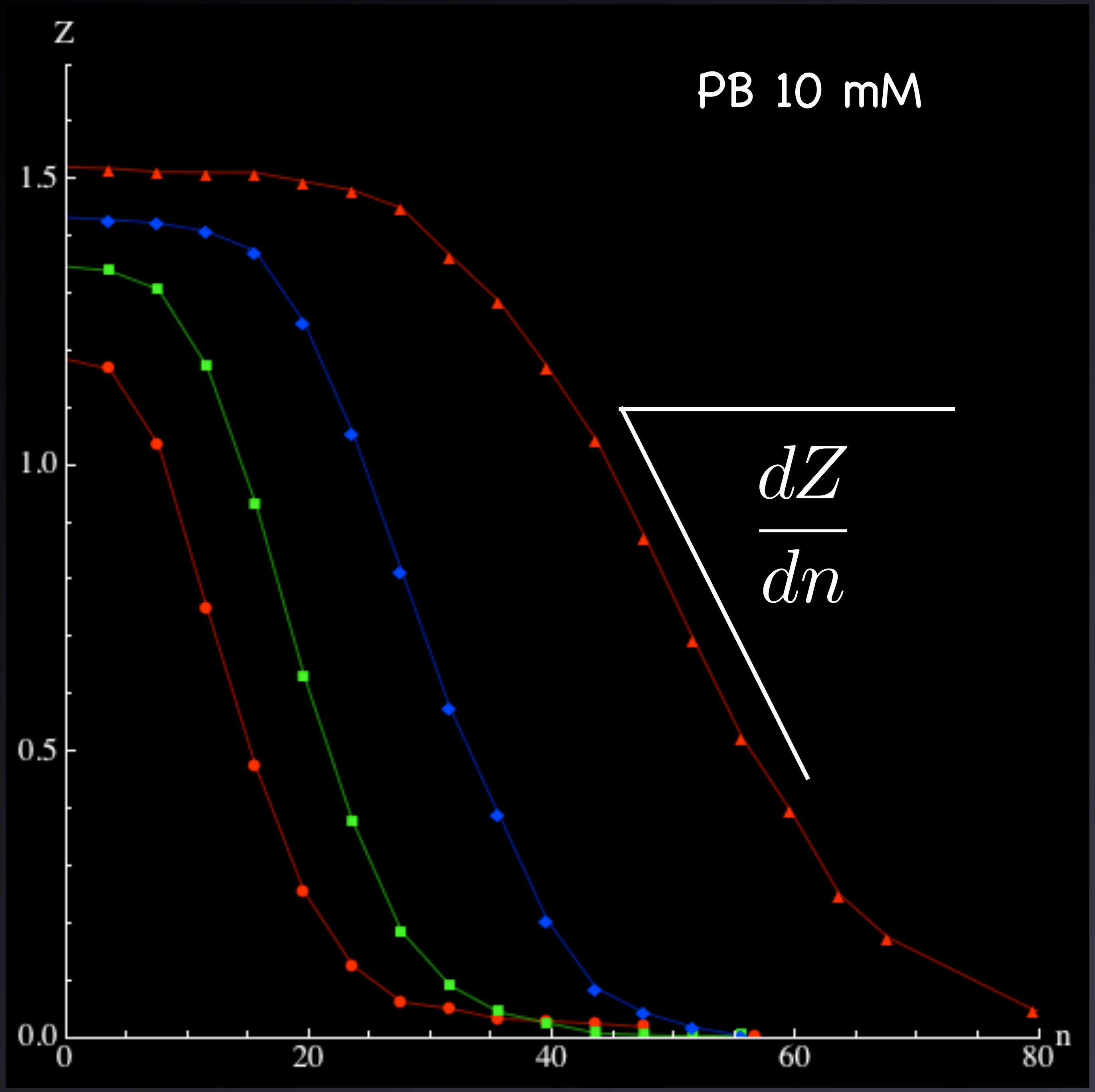
$$n = Lk = Tw + Wr$$

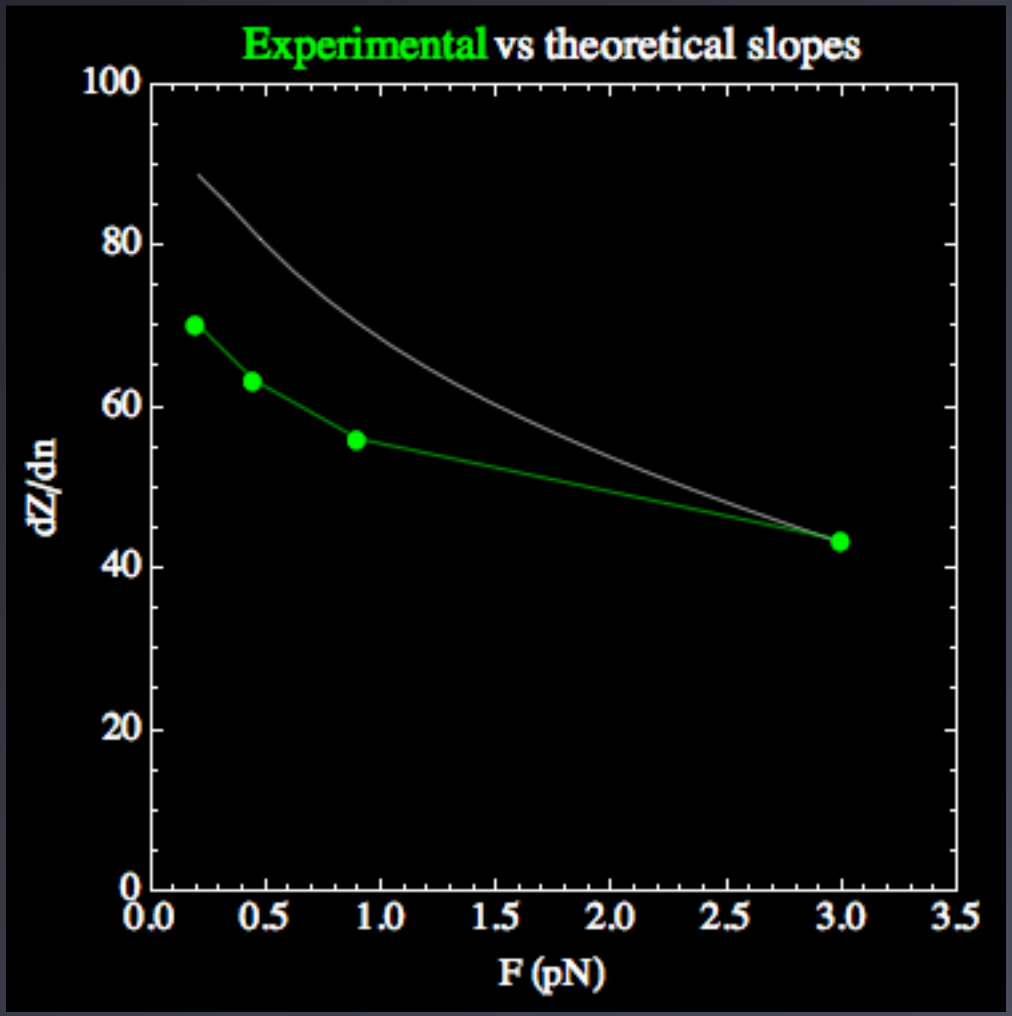
with Wr linear of z

$$\Rightarrow \frac{dZ}{dn} = \frac{4\pi R}{\sin 2\theta}\,\rho_{WLC}$$

$$\rho_{WLC} = \frac{Z(n=0)}{L}$$

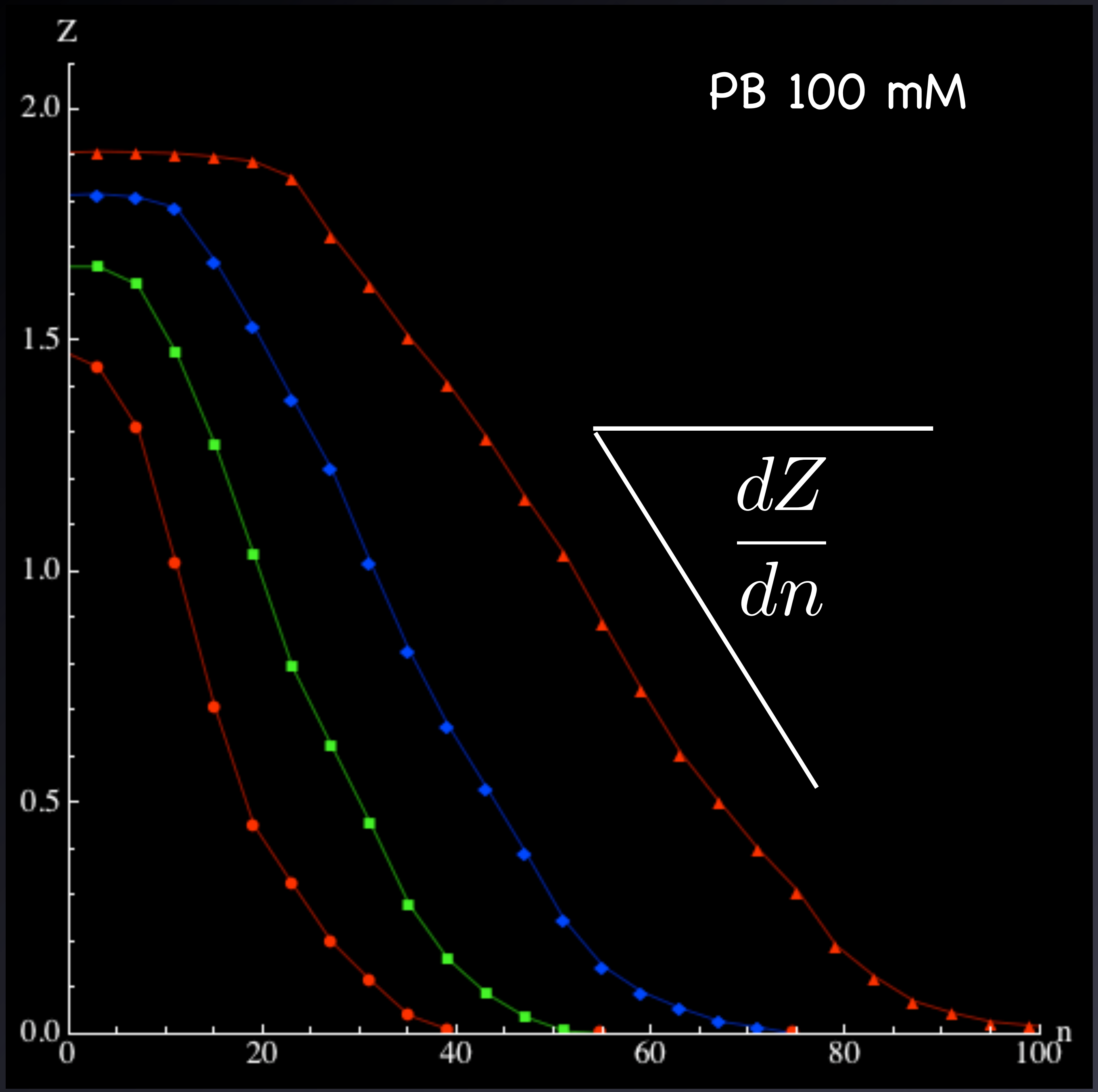
Results : comparison with experimental data

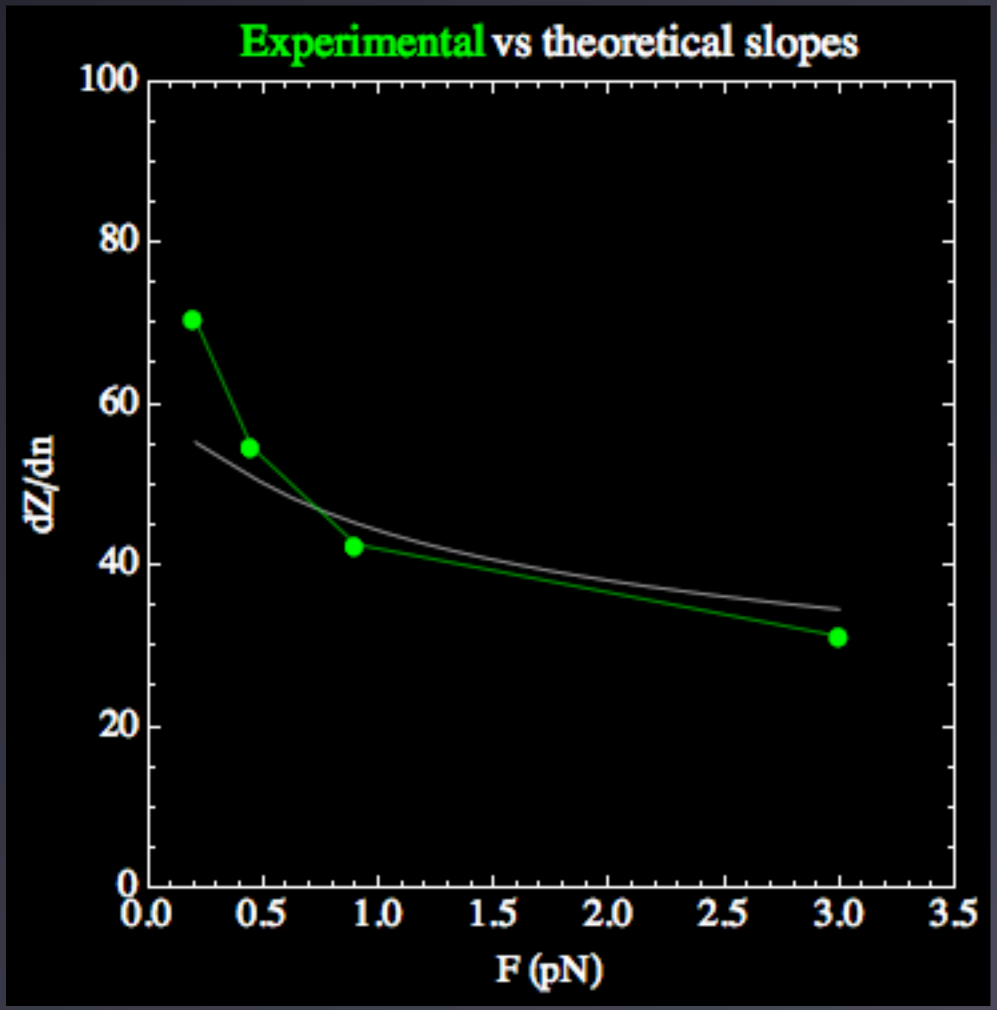




data from Gilles Charvin (ENS-Paris)

Results : comparison with experimental data

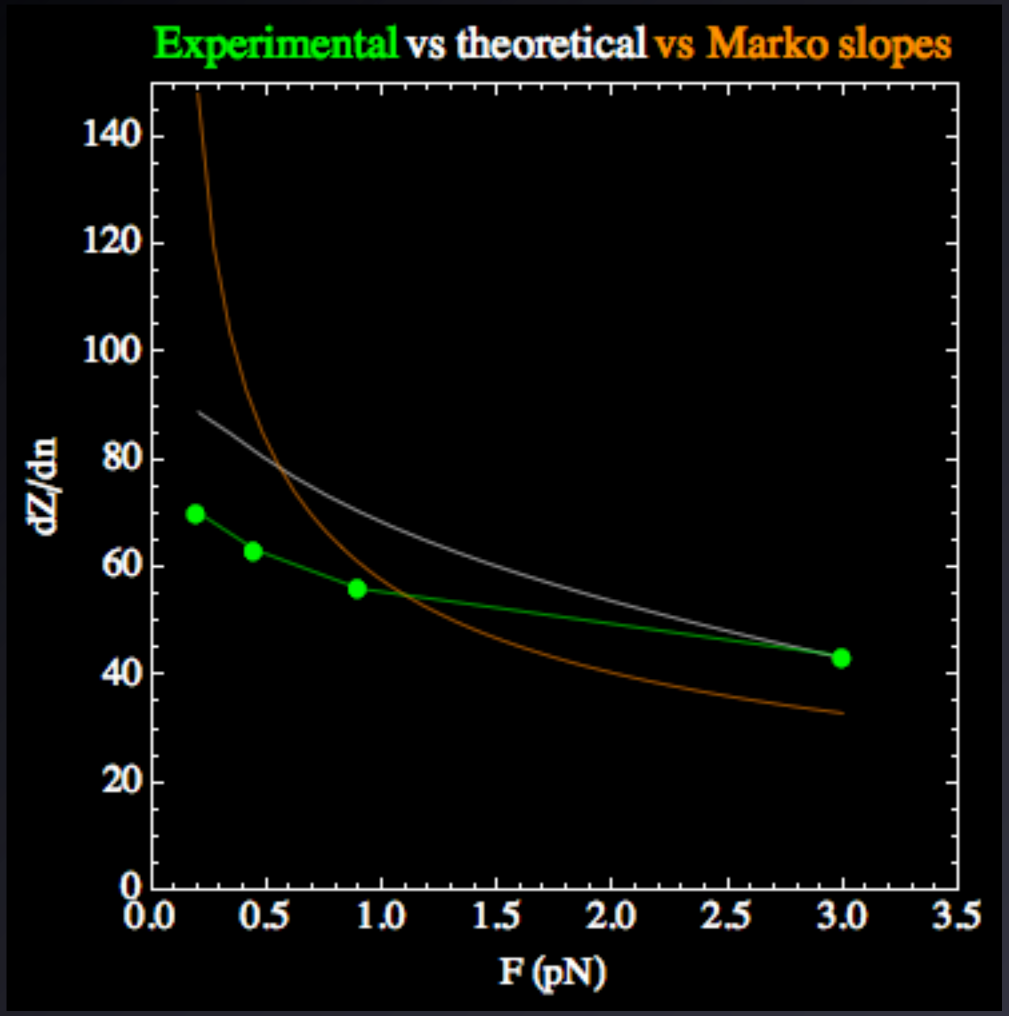




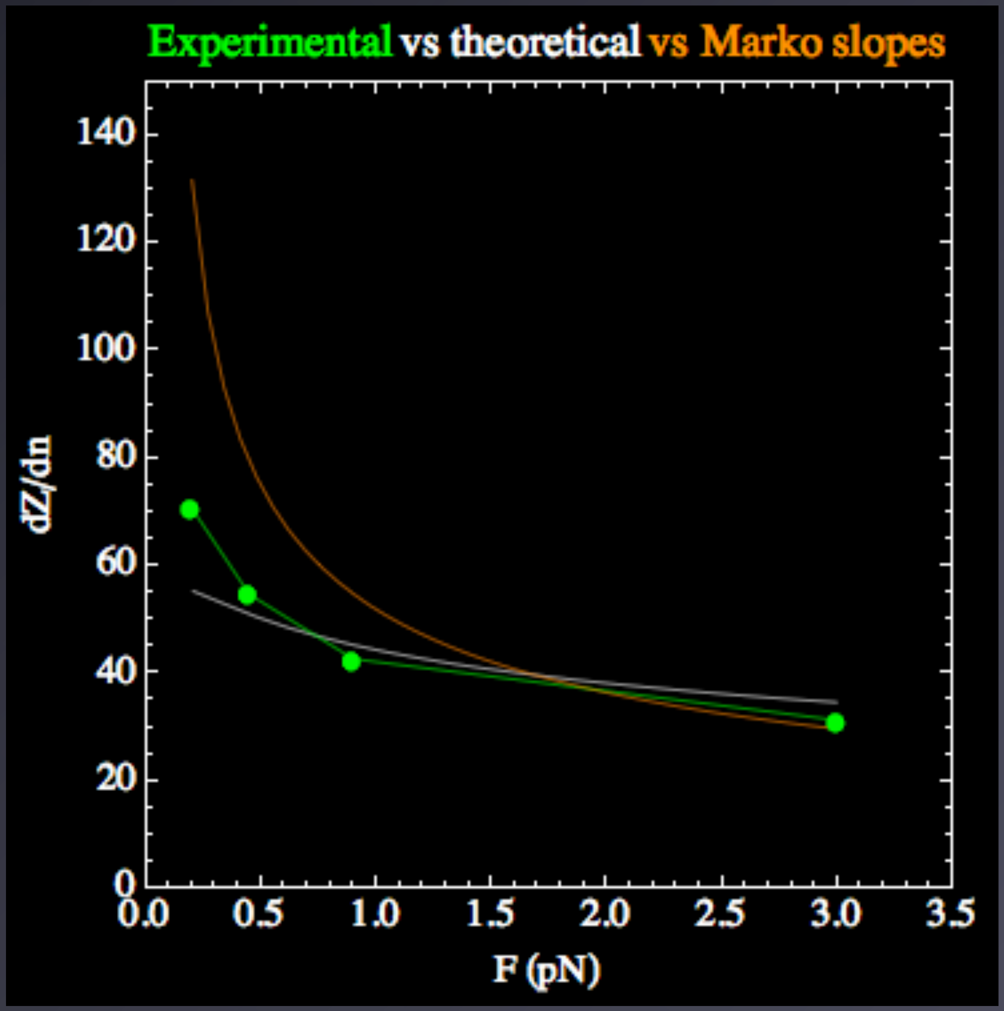
data from Gilles Charvin (ENS-Paris)

Results : comparison with Marko model

PB 10 mM



PB 100 mM



J. Marko, "Torque and dynamics of linking number ...", Phys. Rev. E. (2007)

Remarks

- Supercoiling radius R is always > 1nm (no DNA-DNA contact)

T (pN)	0.2	0.45	0.9	3
R (nm)	3.8	3.3	3.0	2.3

PB 100 mM

- Benchmark for DNA-DNA potentials:

  1. propose a potential $U(\theta,R)$
  2. compute theoretical slopes
  3. compare with experiments

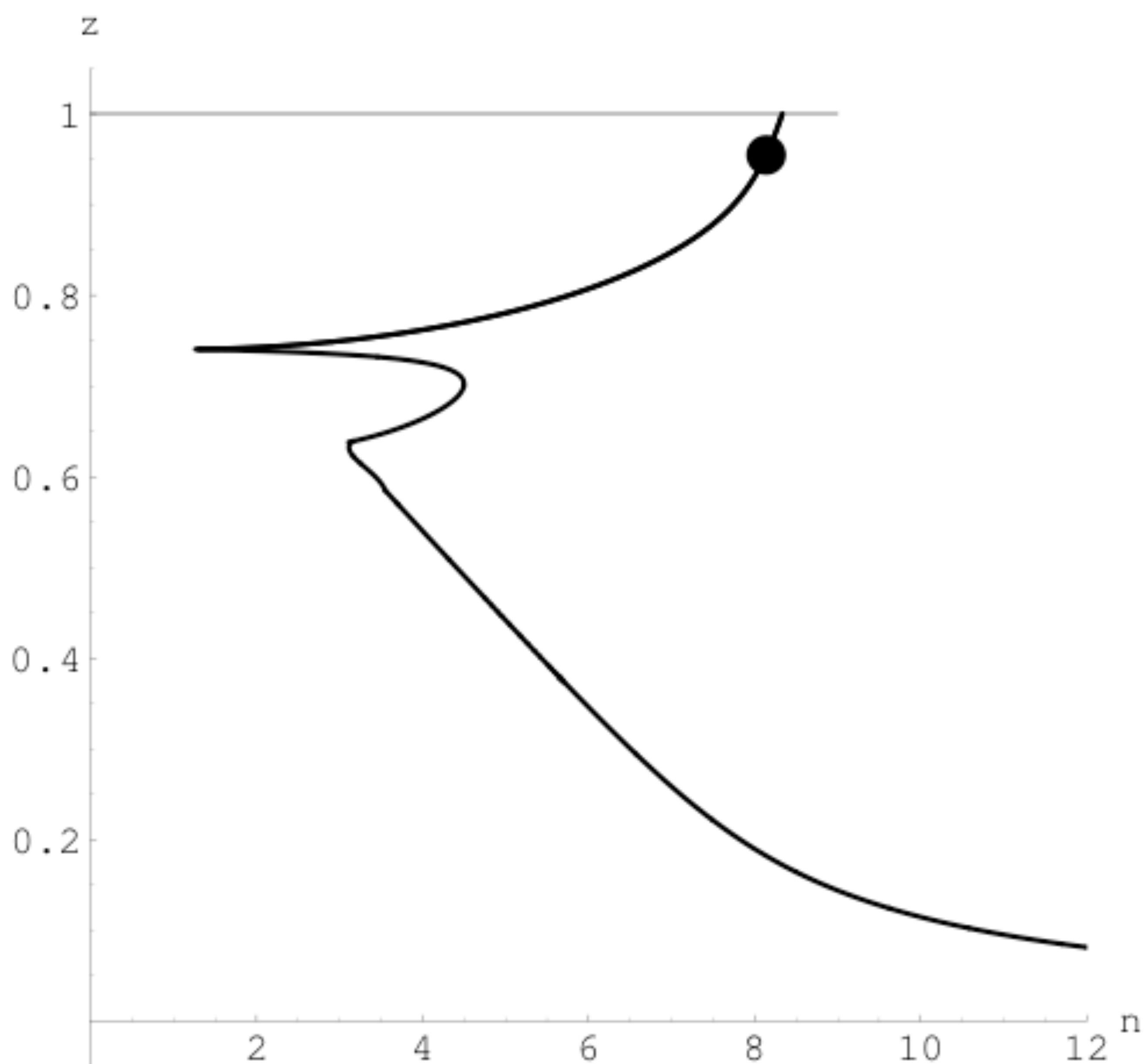
Conclusion

- Analytical model for plectonemic DNA
- Long-range DNA-DNA interaction potential
- Reproduces experimental curves (10-100 mM)
- Could serve as a benchmark for DNA-DNA potentials

- Thermal fluctuations

Numerical simulations
BVP
Path following

Results : how a twisted rod coils



$$\frac{L}{2R} = 170$$

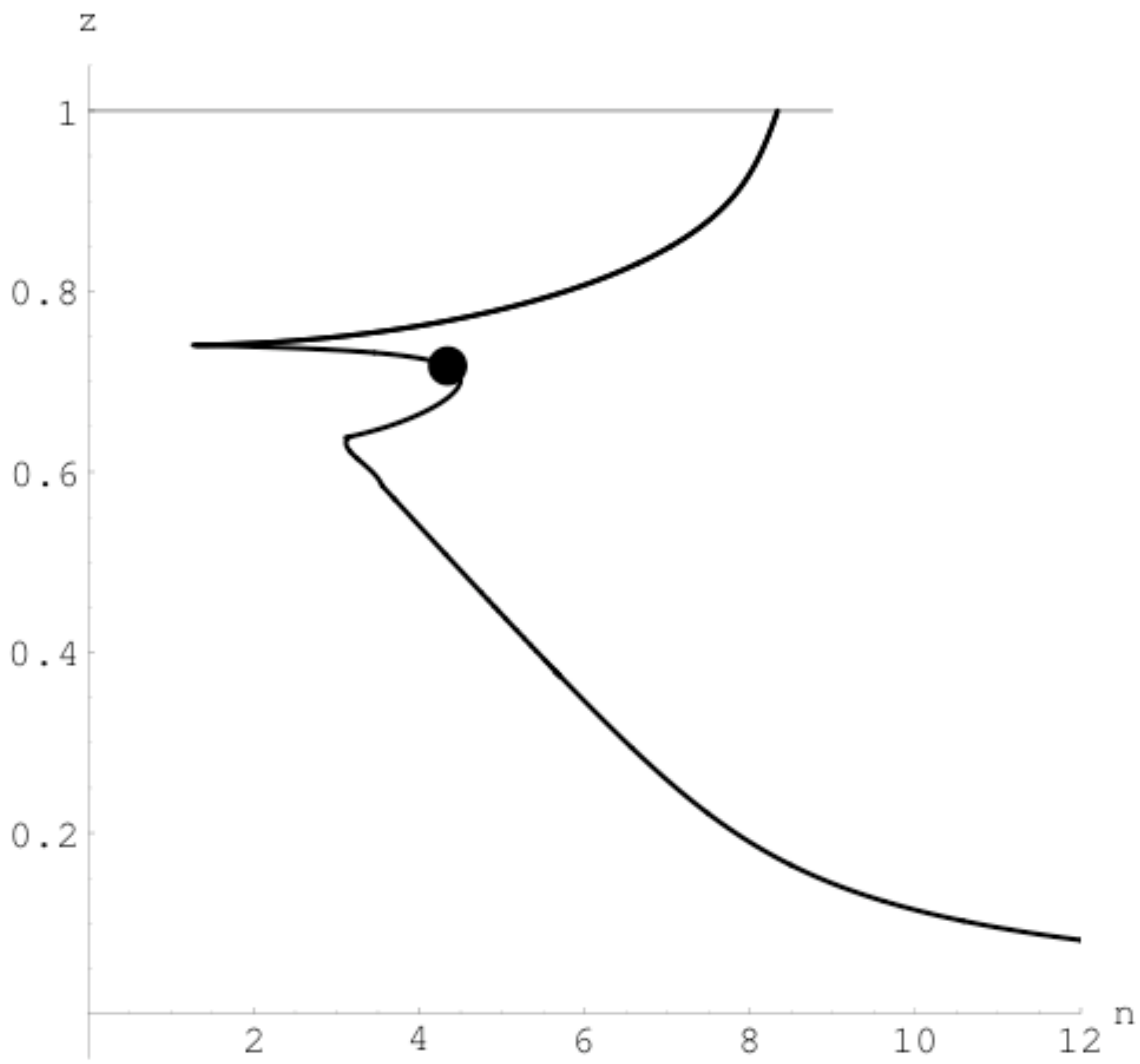
$$t = \frac{TL^2}{4\pi^2 K_0} = 6$$

0 contact(s)

$$\frac{Z}{L} = 0.95$$

$$n = 8.1 \, turns$$

Results : how a twisted rod coils



$$\frac{L}{2R}=170$$

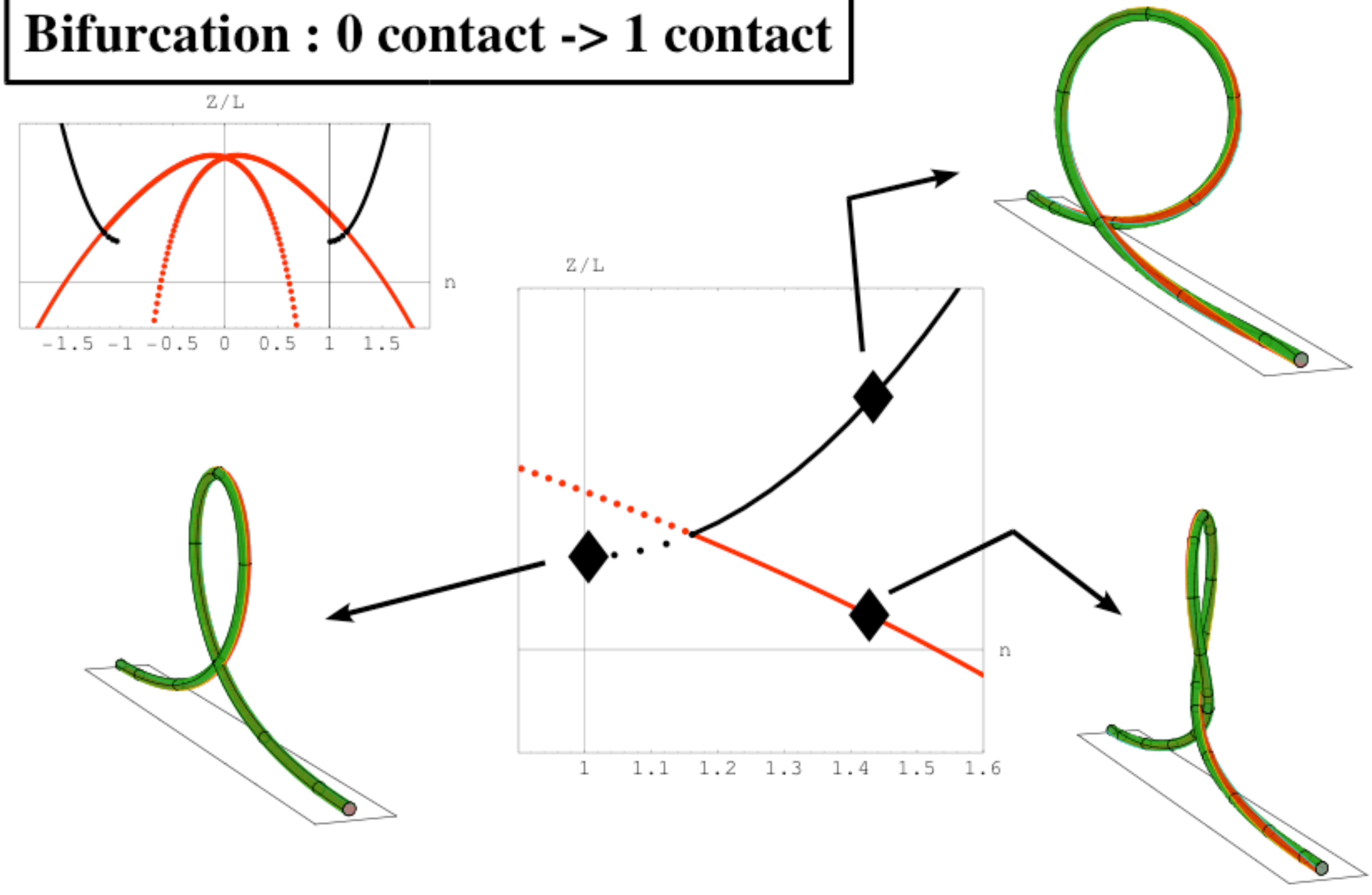
$$t=\frac{TL^2}{4\pi^2 K_0}=6$$

1 contact(s)

$$\frac{Z}{L}=0.72$$

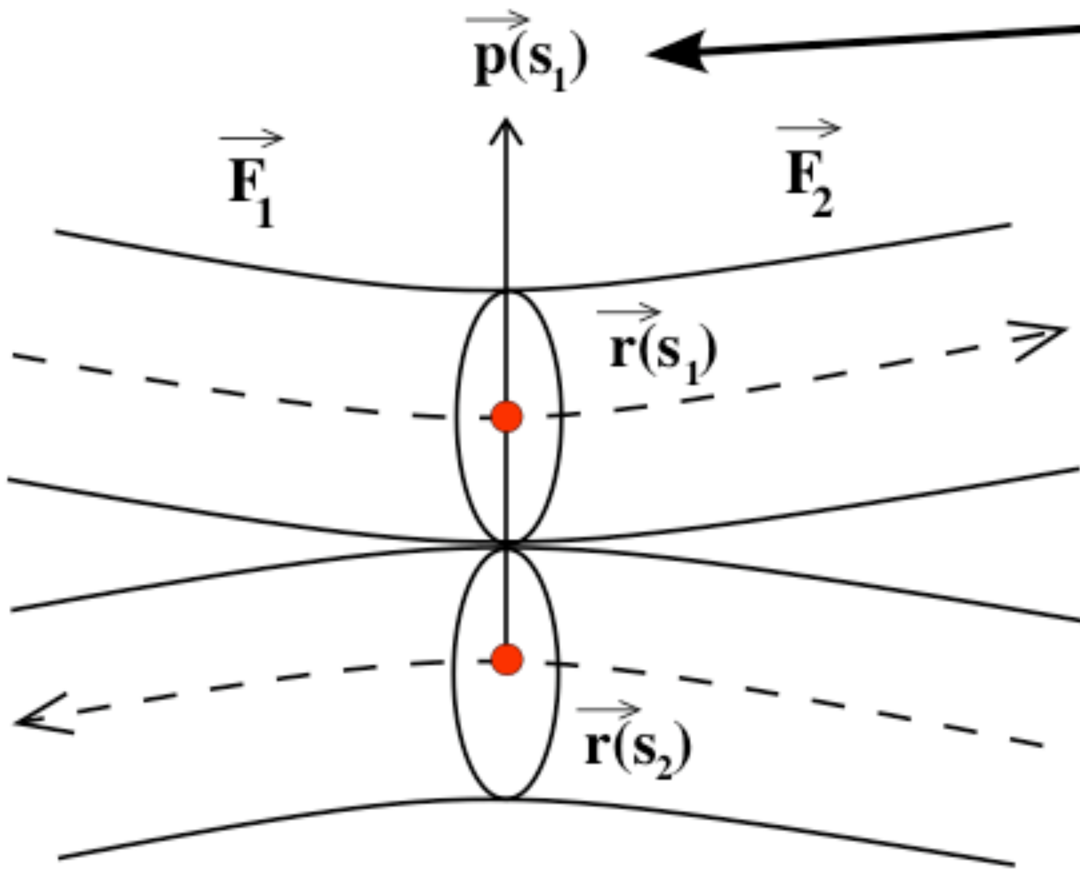
$n=4.3$ turns

Bifurcation : 0 contact -> 1 contact



Hard-wall contact, no friction

force from strand at s_2 acting on strand at s_1



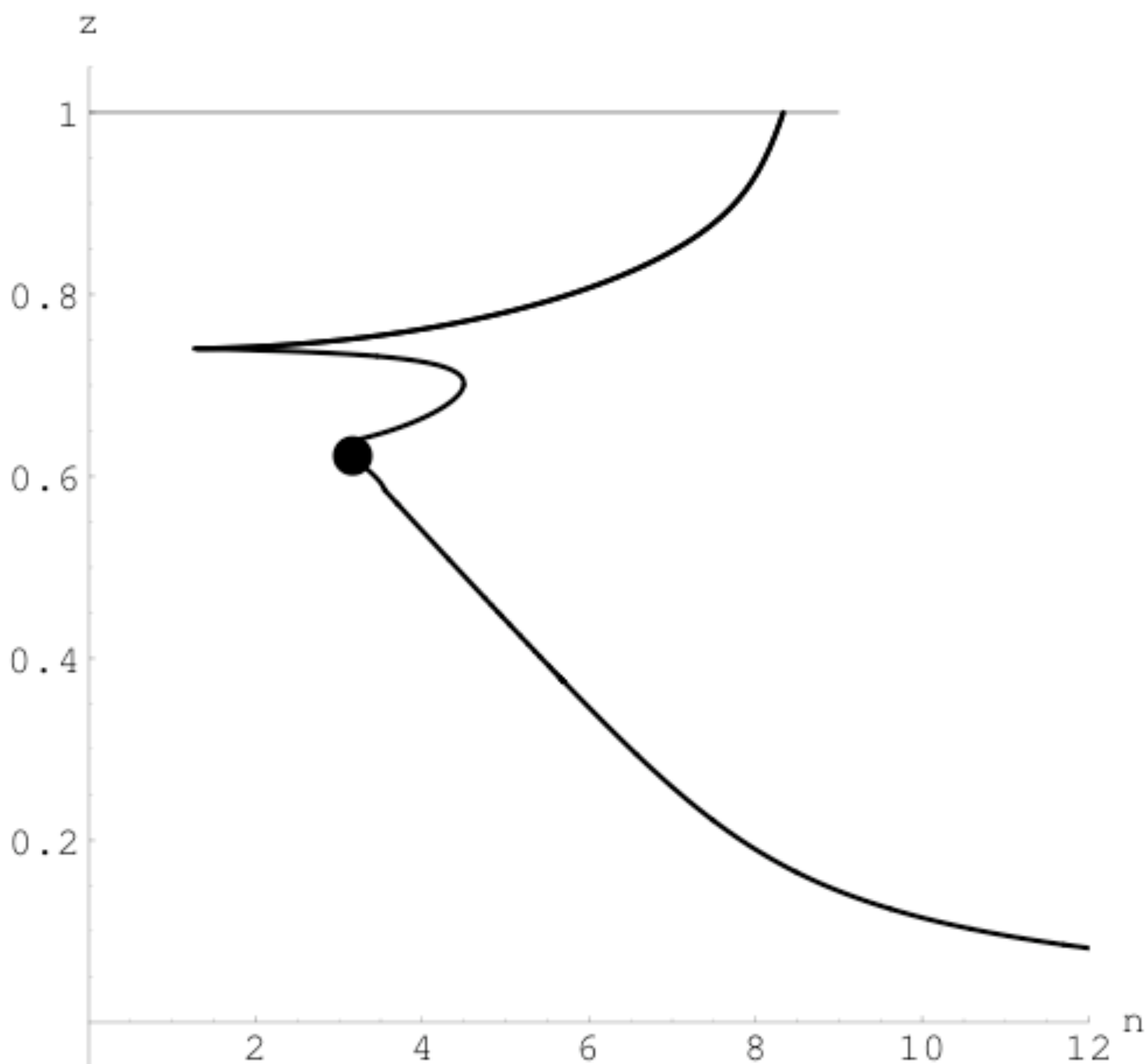
$$\vec{F}_1 = \vec{p} + \vec{F}_2$$

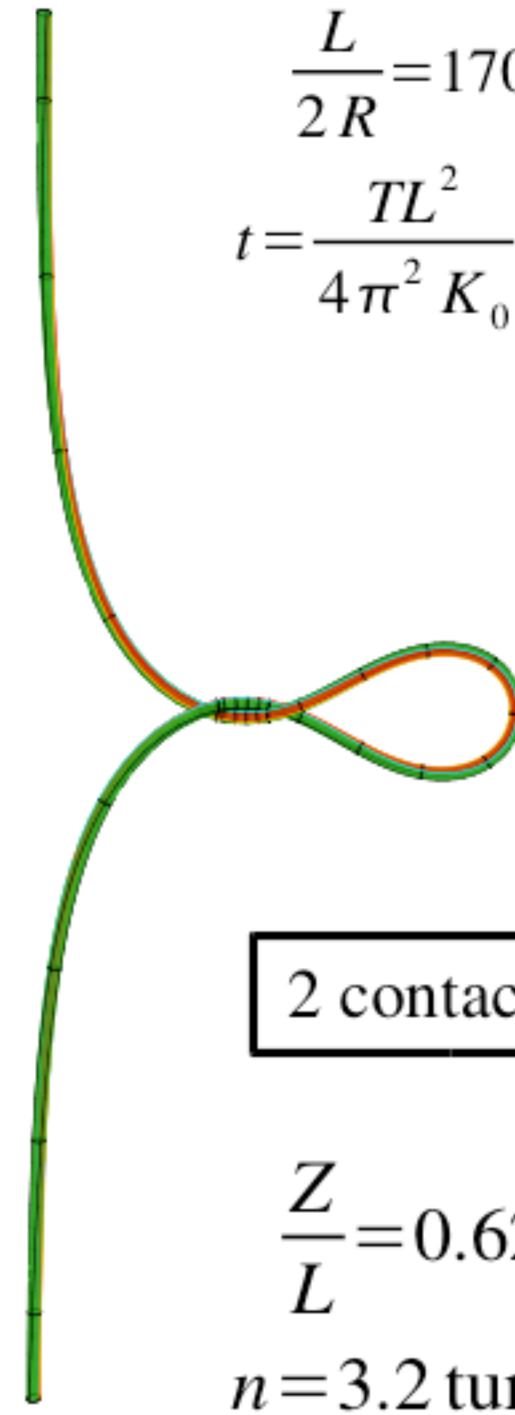
$$\vec{p} = p \frac{\vec{r}(s_1) - \vec{r}(s_2)}{|\vec{r}(s_1) - \vec{r}(s_2)|}$$

touching conditions :

$$\begin{cases} |\vec{r}(s_1) - \vec{r}(s_2)| = \text{thickness} \\ (\vec{r}(s_1) - \vec{r}(s_2)) \perp \vec{d}_3(s_1) \\ (\vec{r}(s_1) - \vec{r}(s_2)) \perp \vec{d}_3(s_2) \end{cases}$$

Results : how a twisted rod coils





$$\frac{L}{2R} = 170$$

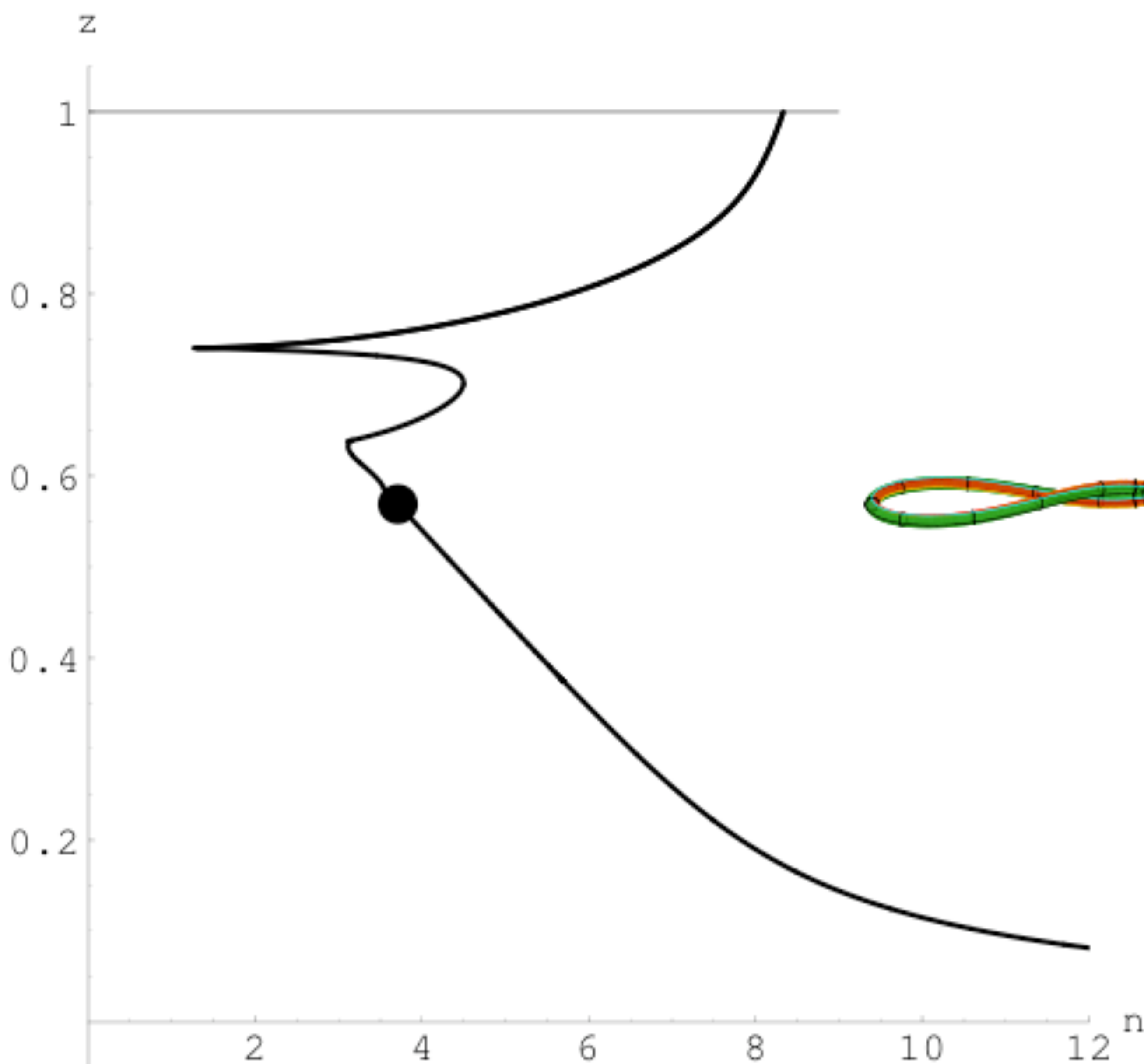
$$t = \frac{TL^2}{4\pi^2 K_0} = 6$$

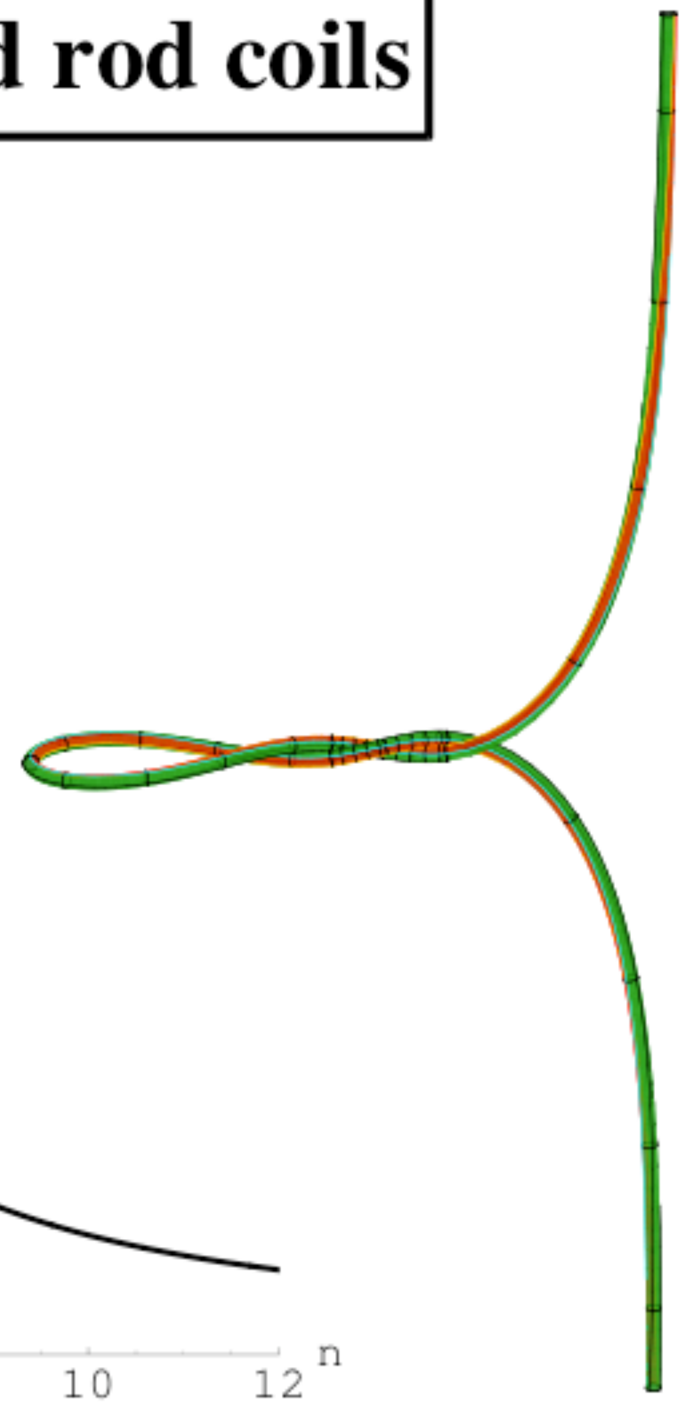
2 contact(s)

$$\frac{Z}{L} = 0.62$$

$n = 3.2$ turns

Results : how a twisted rod coils





$$\frac{L}{2R} = 170$$

$$t = \frac{TL^2}{4\pi^2 K_0} = 6$$

3 contact(s)

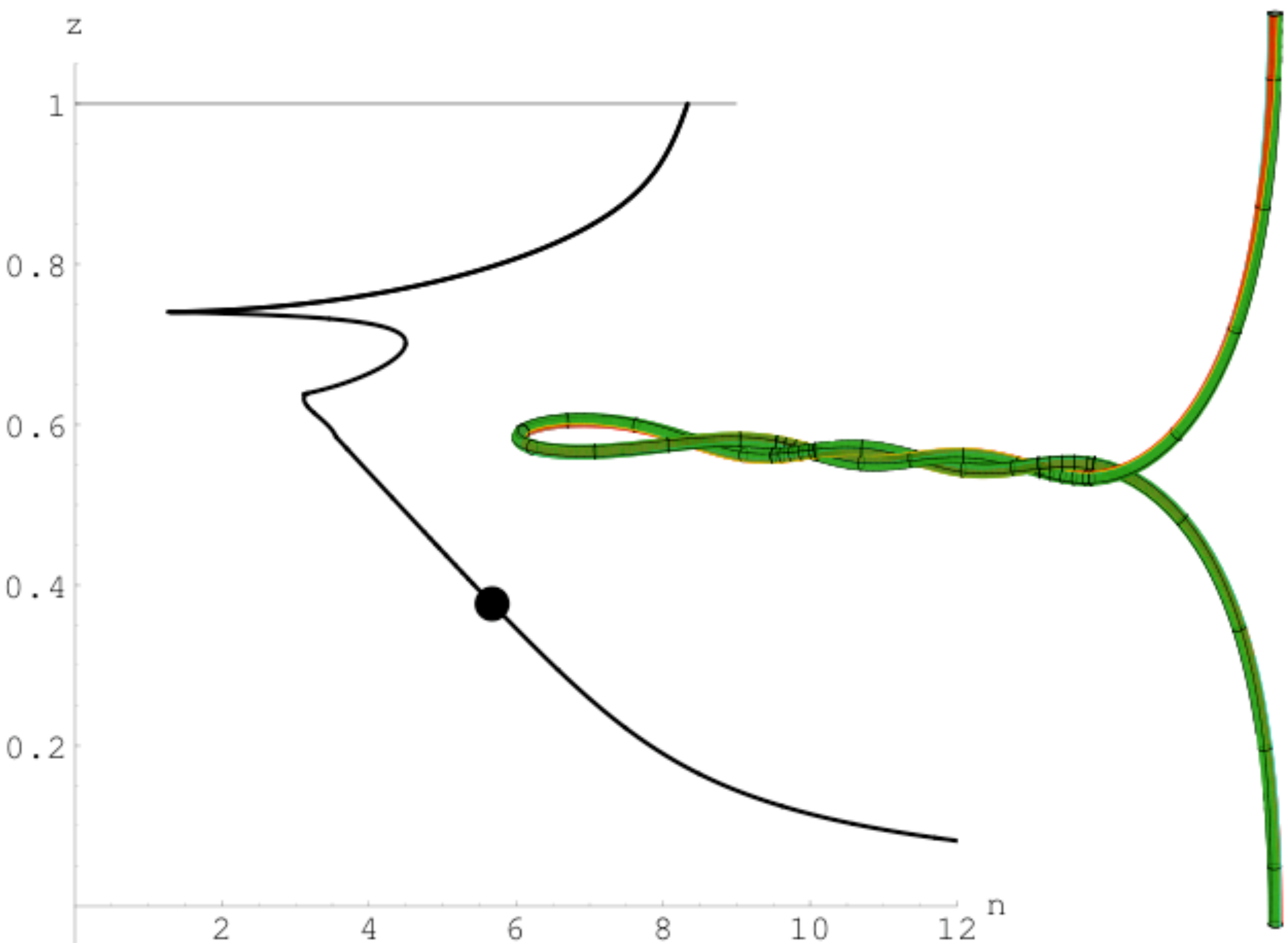
$$\frac{Z}{L} = 0.57$$

$n = 3.7$ turns

Results : how a twisted rod coils

$$\frac{L}{2R} = 170$$

$$t = \frac{TL^2}{4\pi^2 K_0} = 6$$

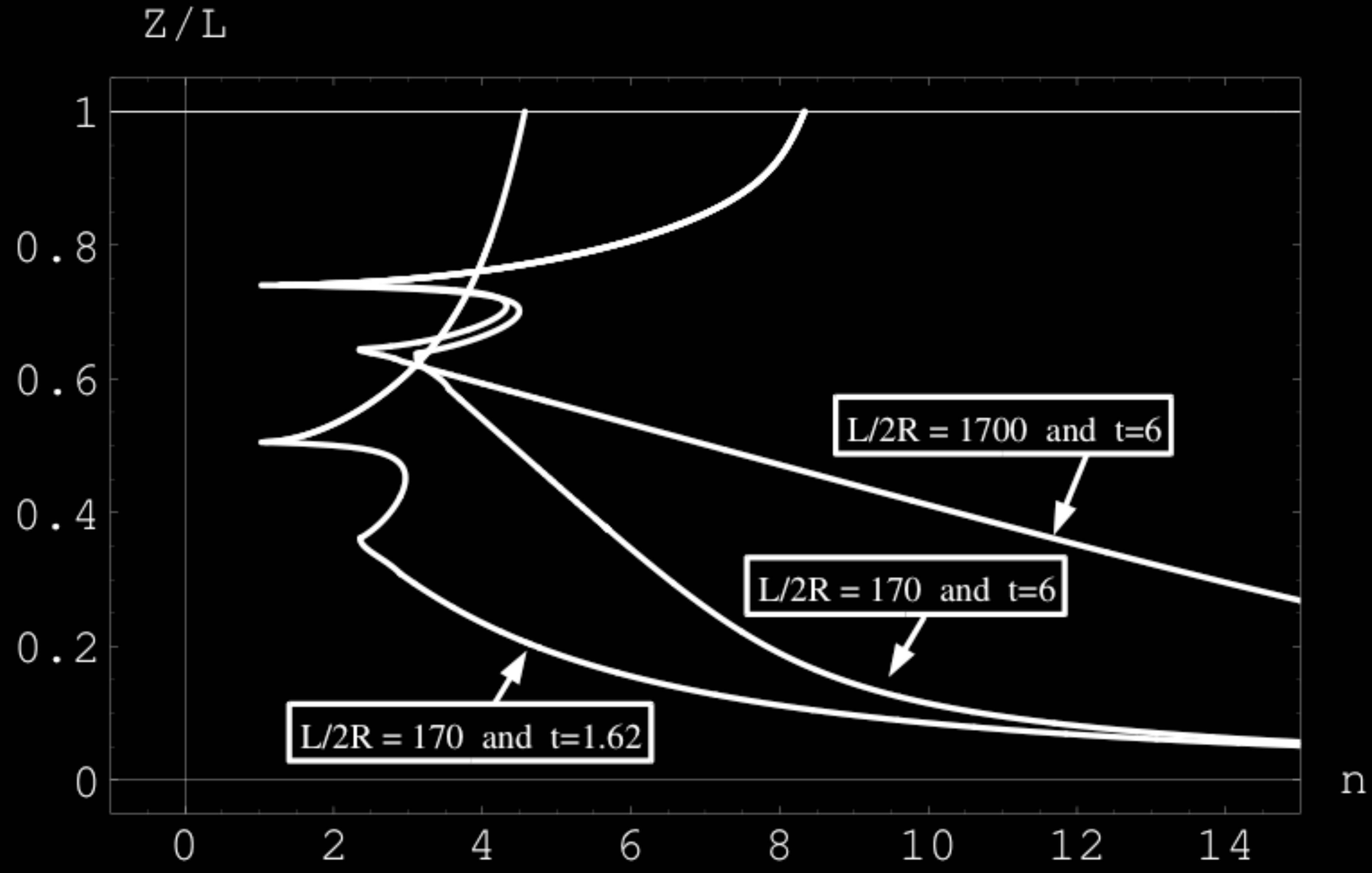


1L1 contact(s)

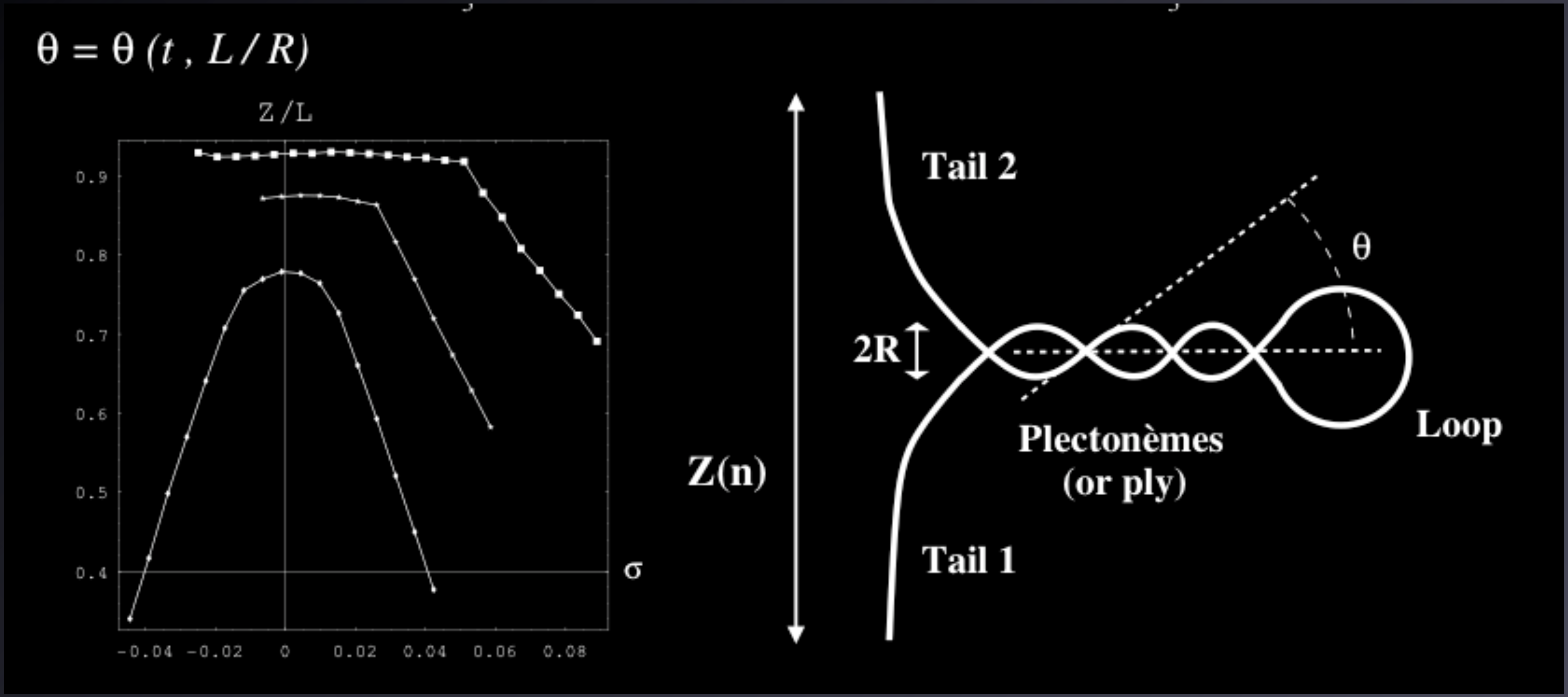
$$\frac{Z}{L} = 0.38$$

$n = 5.7$ turns

Slope of linear part : fonction of *t* and *L/R*



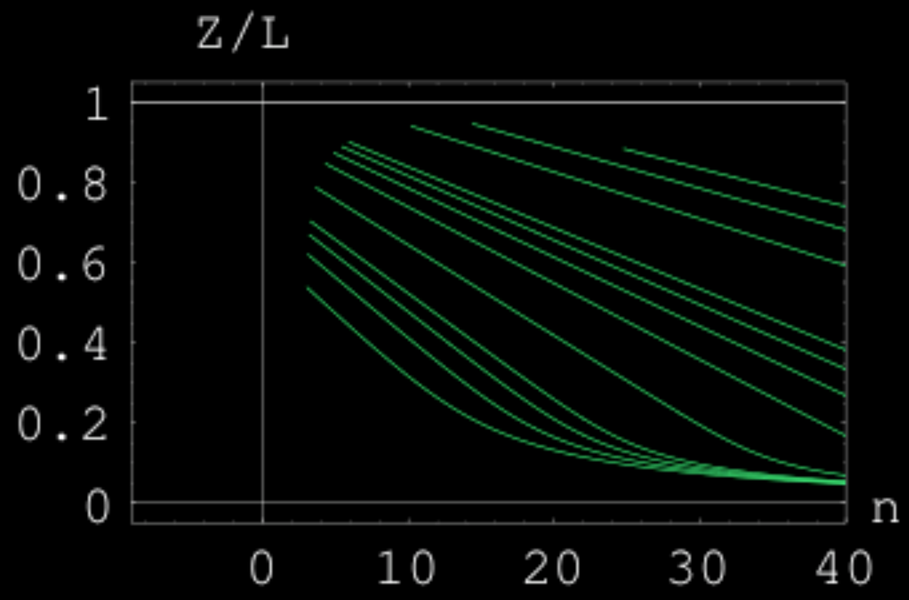
Plectonemes geometry

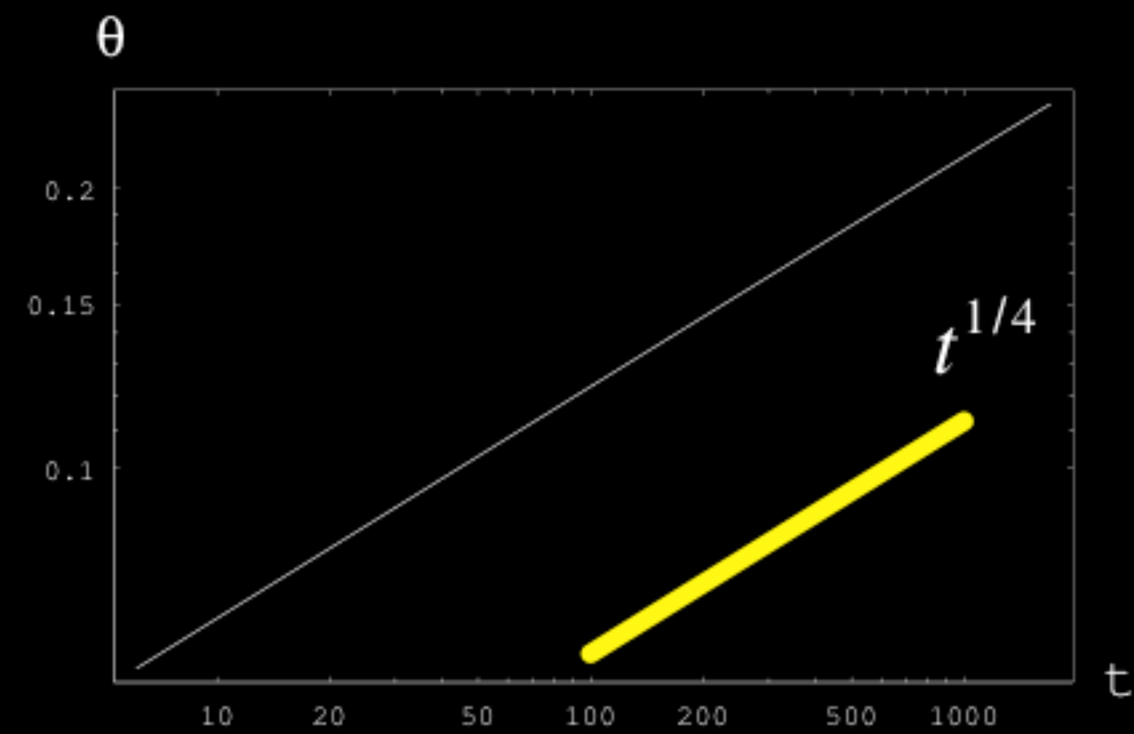


Helical angle θ : fonction of *t* and *L/R*

we vary *t* while keeping L / R fixed

$$\frac{L}{2R} = 1700$$



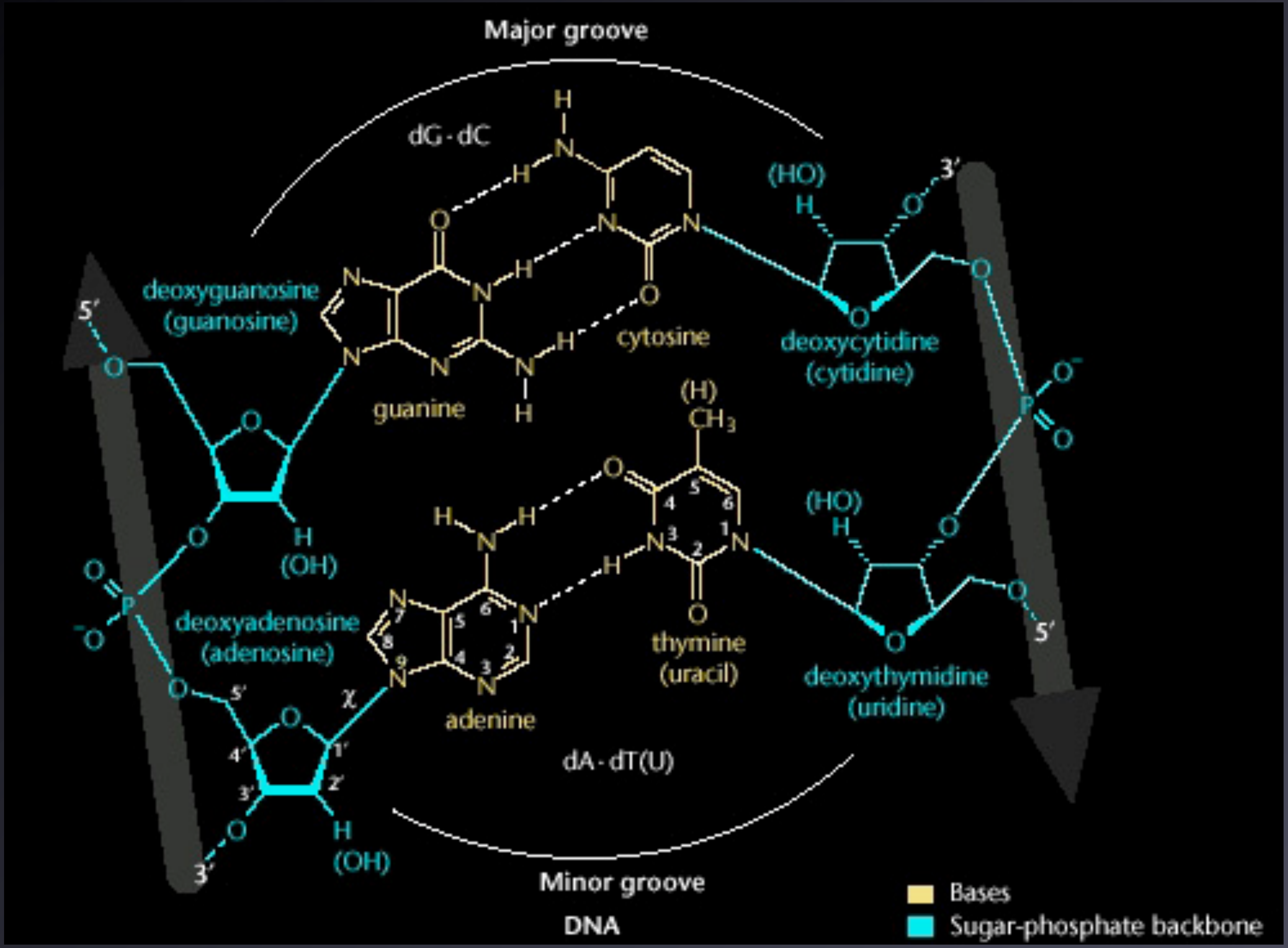


$$t = \frac{T L^2}{(2\pi)^2 K_0}$$

polynomial interpolation : $\frac{R^2 T}{K_0} = \varphi(\theta) = 1.66\ \theta^4$

S. Neukirch, "Extracting DNA ...", Phys. Rev. Lett. **93** (2004)

DNA electrostatics

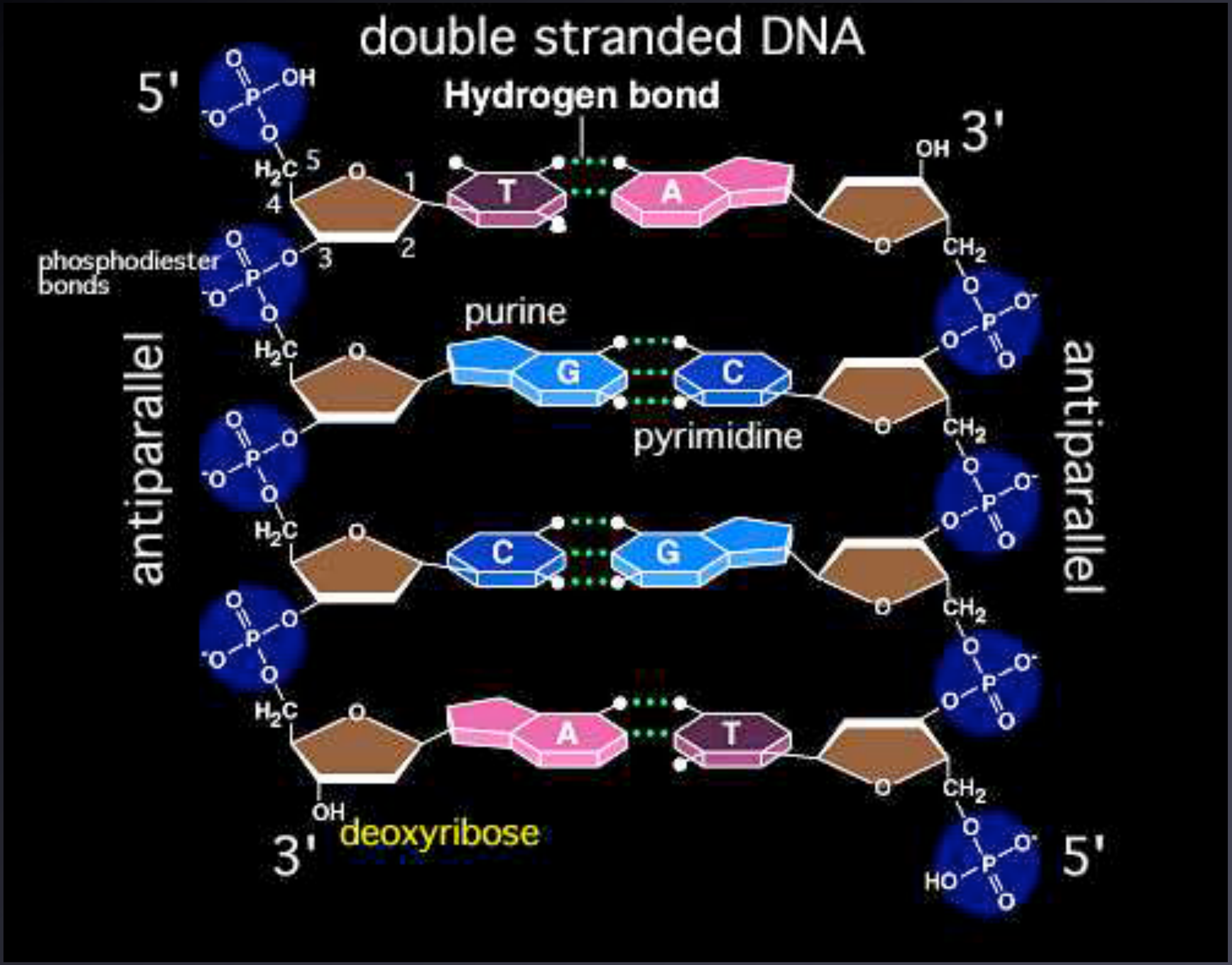


www.boc.uu.se
Upsala University

2 e^- per base-pair

<=> 1 e^- / 0.17 nm

DNA electrostatics



brooklyn.cuny.edu
Brooklyn college

2 e^- per base-pair

<=> 1 e^- / 0.17 nm