Elasticity and Electrostatics of plectonemic DNA

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joint work with:
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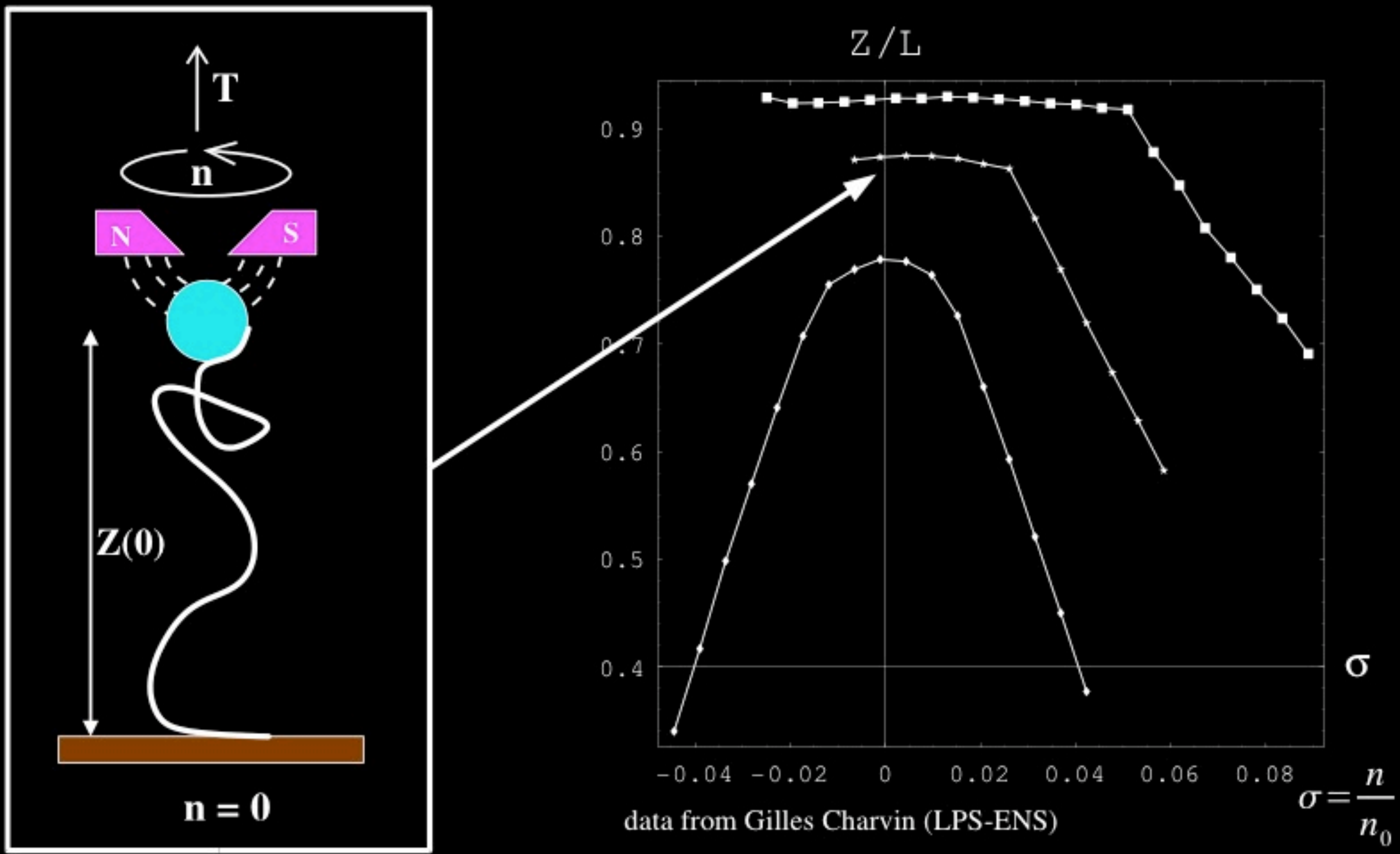
Basile Audoly

Why study DNA mechanical properties ?

mechanical properties influence biology of the cell

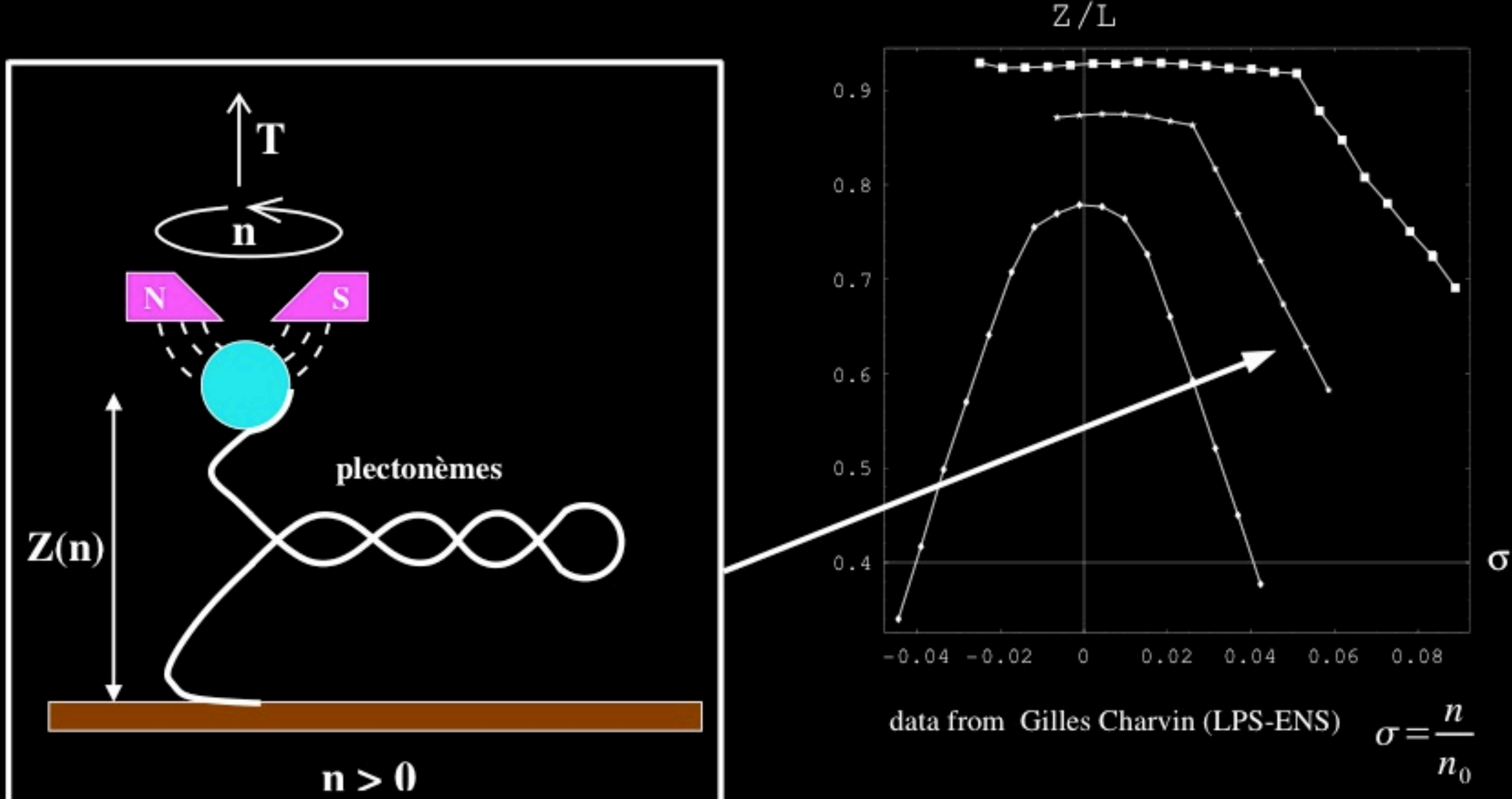
- 2 meters of DNA in a 10 micron wide nucleus
- ejection from viral capside
- transcription (RNApolymerase is torque dependent)
- protein binding is strain dependent, or induces strain on DNA
- chromatin compaction/decompaction (cell division)

Pulling and twisting DNA

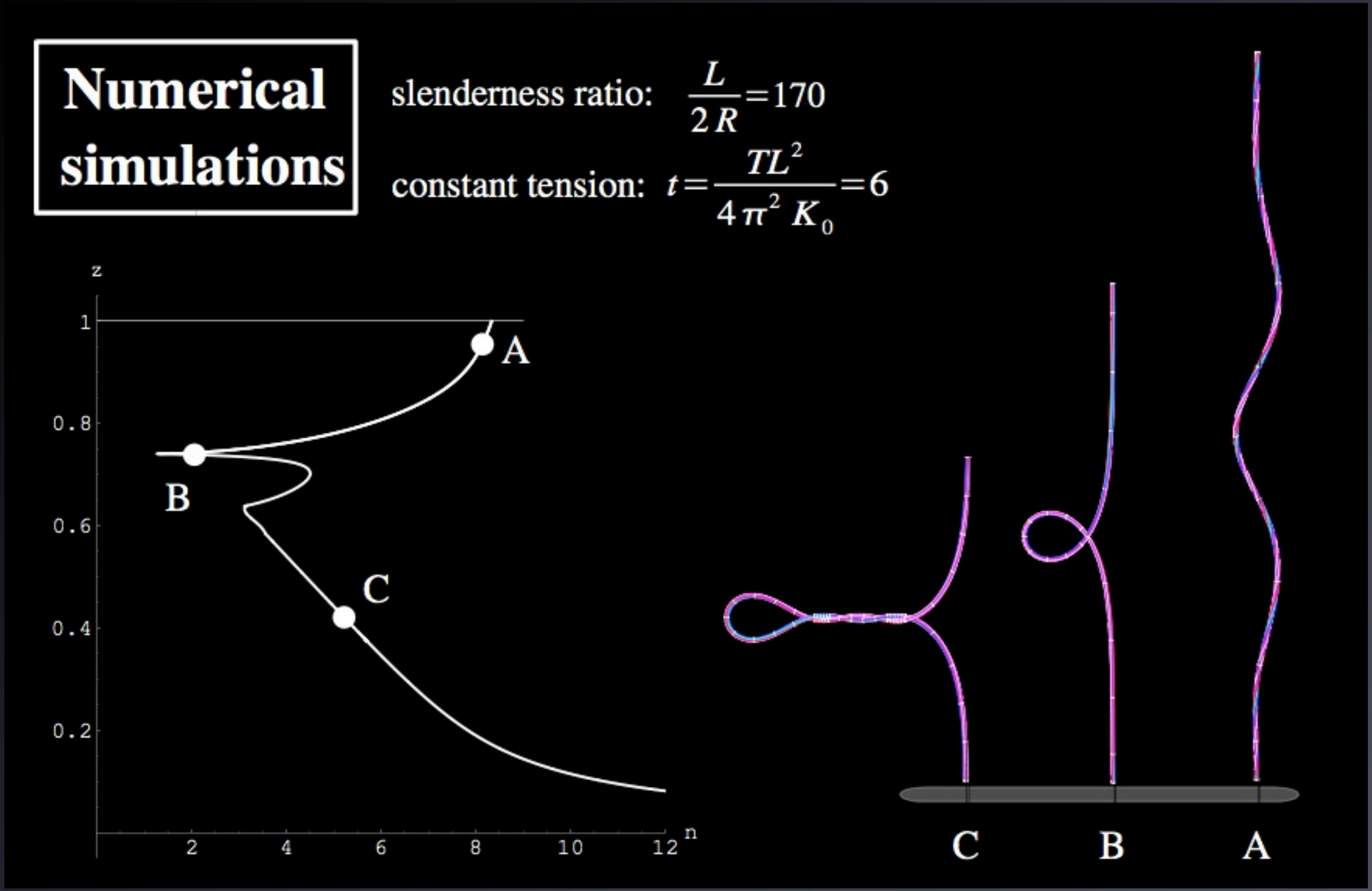


data from Gilles Charvin (LPS-ENS)

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)

Orders of magnitude

Buckling threshold for a clamped beam

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

$$\Rightarrow t = \frac{TL^2}{(2\pi)^2 K_0} = 1$$

DNA in tweezers experiments

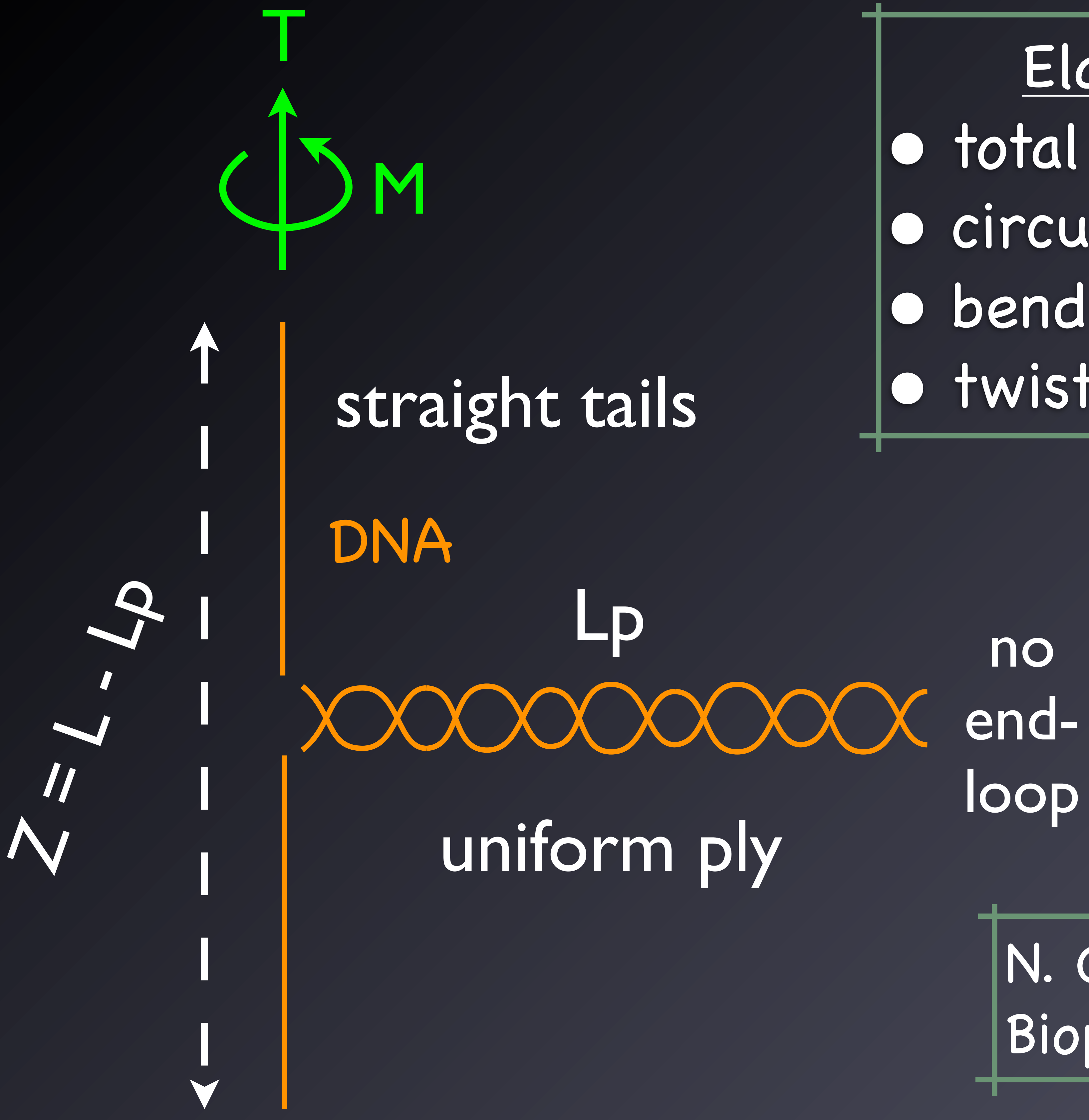
$$L \simeq 1\ \mu m$$ (few kbp)

$$K_0 \simeq 50\ nm\ k_B T$$

$$T \simeq 1\ p\mathrm{N}$$

$$\Rightarrow t \sim 10^4$$

Analytical model for plectonemic DNA



Elastic rod with :

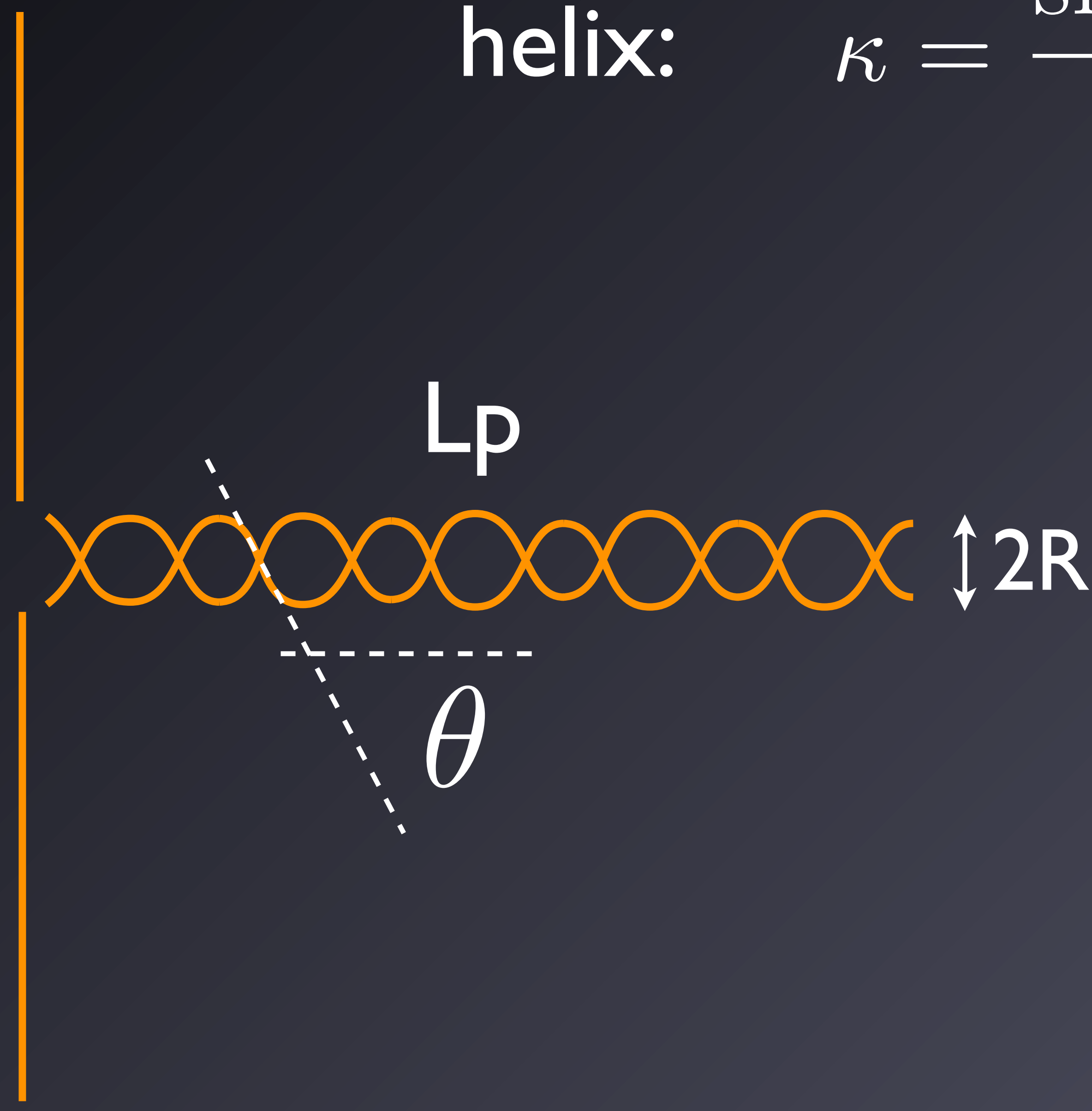
- total length L
- circular cross-section R_0
- bending rigidity K_0
- twist rigidity K_3

N. Clauvelin et al, Biophysical Journal (2009)

Energy formulation: elastic strain energy

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

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

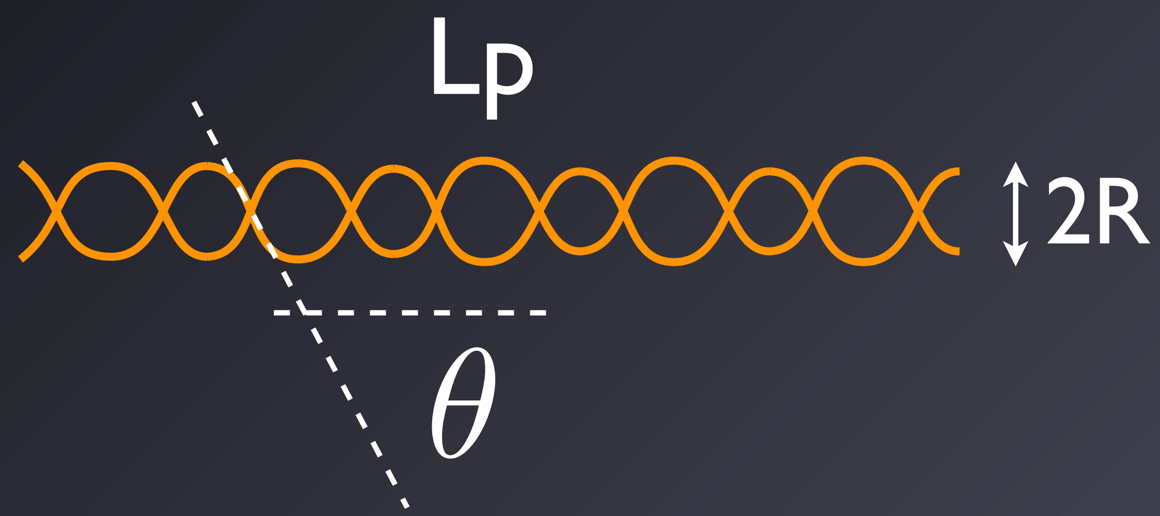


Energy formulation: elastic strain energy

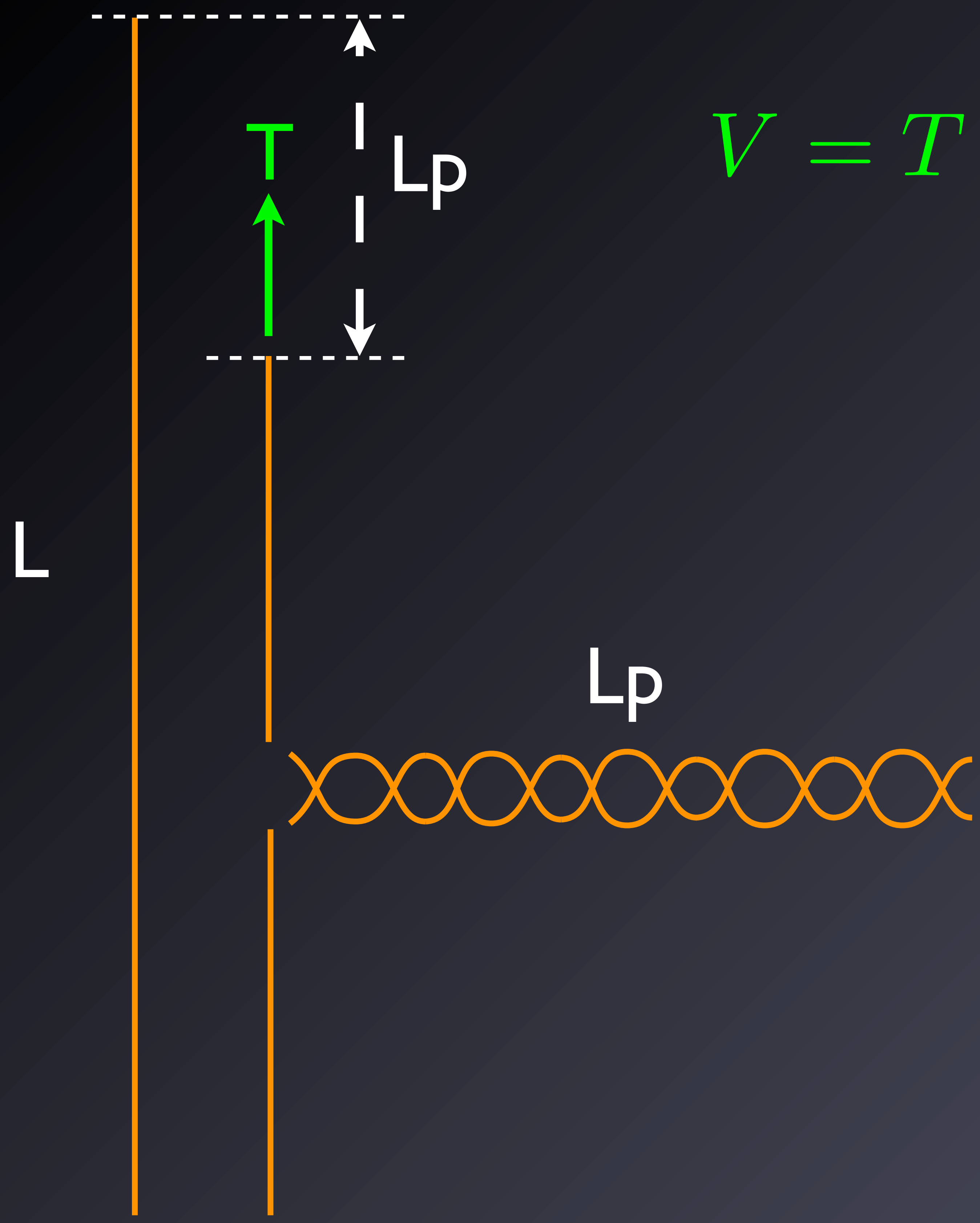
twisting: $V = \frac{1}{2} K_3 \tau^2 L$

twist τ is uniform along the rod

constitutive relation: $M = K_3 \tau$

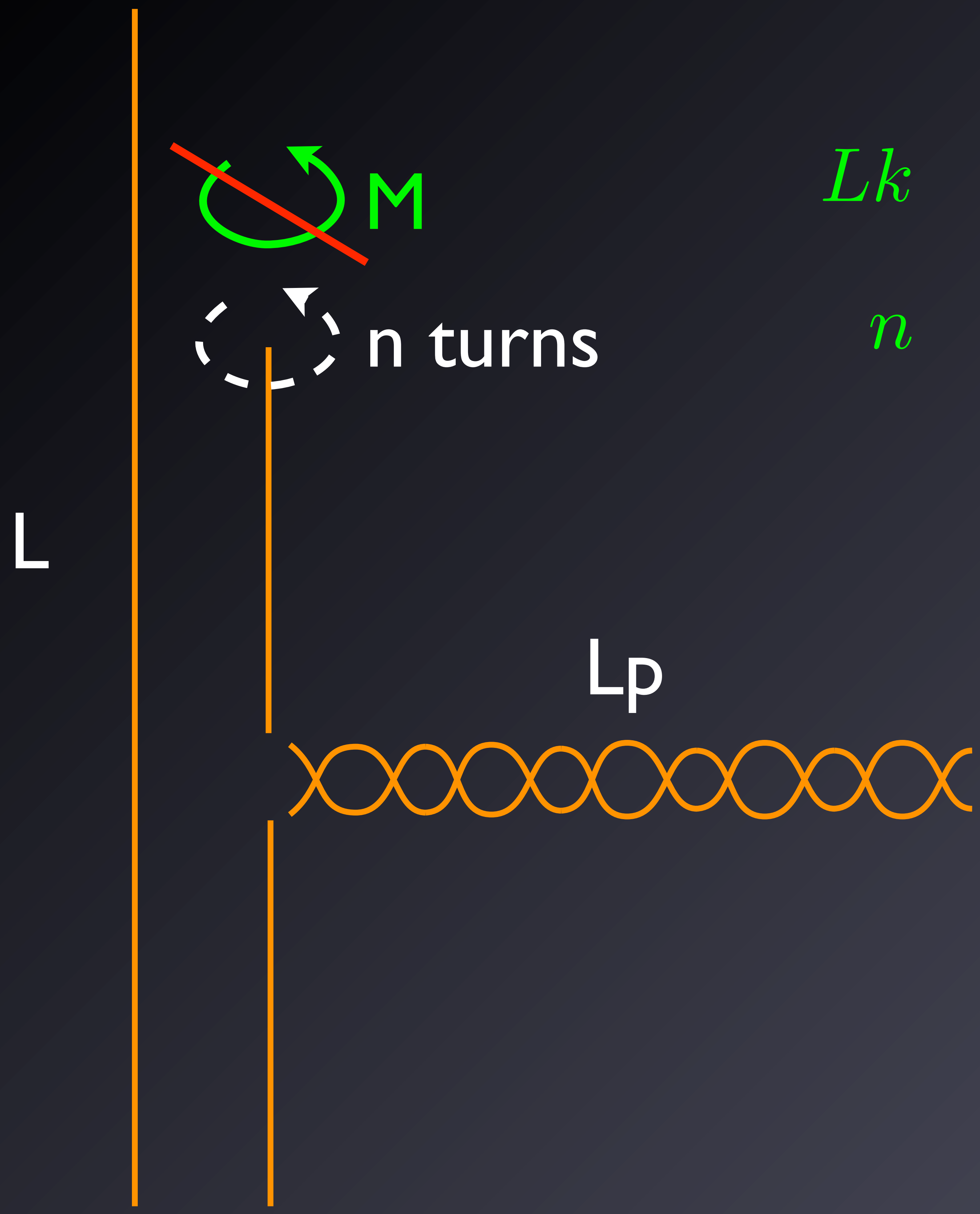


Energy formulation: work of external loads



$$V = T\ L_p$$

Energy formulation: link constraint



$$
\begin{aligned}
Lk &= Tw + Wr \\
n &= \frac{1}{2\pi}\left(\tau L + \frac{\sin 2\theta}{2R} L_p\right)
\end{aligned}
$$

Energy formulation: self-interaction

hard-wall (contact)
=> constraint:

$$V = \lambda \left(R - R_0\right)$$

long-range:
~ electrostatics

- S. Leikin
- D. Stigter
- Debye-Hückel
- G. Manning
- ...

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

Energy formulation: equilibrium

$$V(\theta, R, \tau, L_p) = \frac{1}{2} K_0 \frac{\sin^4\theta}{R^2} L_p + \frac{1}{2} K_3 \tau^2 L + T\ L_p + L_p\ U(\theta, R)$$

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

$$\text{constraint} \Rightarrow L_p = \dots$$

$$\Rightarrow V = V(\theta, R, \tau)$$

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

Energy formulation: stability

For some T values,
there are two solutions to: $\left(\frac{\partial V}{\partial \theta}, \frac{\partial V}{\partial R}, \frac{\partial V}{\partial \tau}\right) = 0$

=> we compute the Hessian matrix :

$$H = \begin{bmatrix} \partial_{\theta\theta}V & \partial_{\theta R}V & \partial_{\theta\tau}V \\ \partial_{R\theta}V & \partial_{RR}V & \partial_{R\tau}V \\ \partial_{\tau\theta}V & \partial_{\tau R}V & \partial_{\tau\tau}V \end{bmatrix}$$

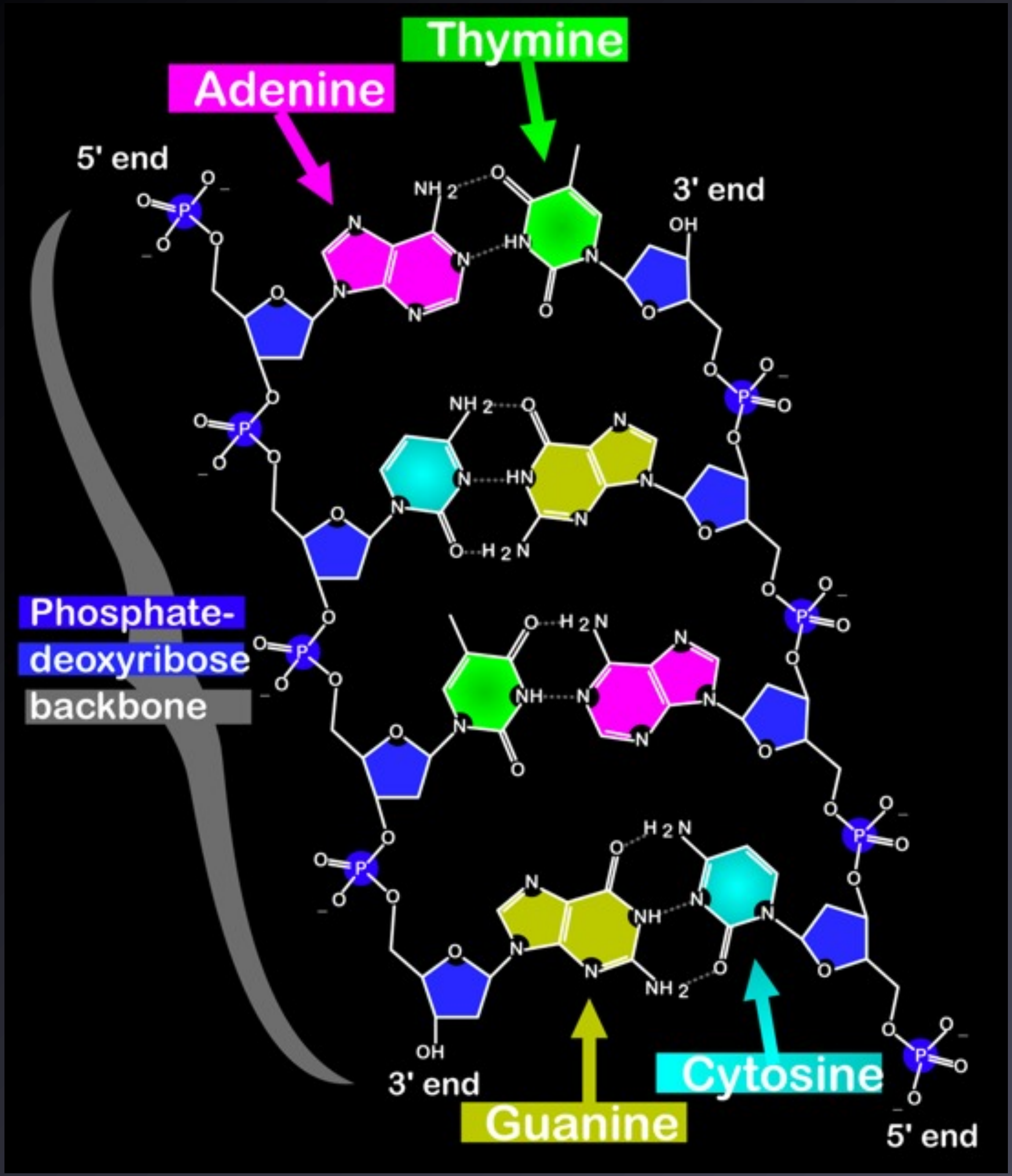
and we focus on the stable solution.

Energy formulation: equilibrium

$$
\begin{aligned}
\frac{\partial V}{\partial \theta} &= 2K_0 \frac{\cos\theta\, \sin^3\theta}{R^2} + \frac{\partial U}{\partial \theta} - \frac{2}{\tan 2\theta}\left(\frac{K_0}{2}\frac{\sin^4\theta}{R^2} + T + U(R,\,\theta)\right) = 0 \\
\frac{\partial V}{\partial R} &= T - \frac{K_0}{2\,R^2}\sin^4\theta + R\frac{\partial U}{\partial R} + U(R,\,\theta) = 0 \\
\frac{\partial V}{\partial \tau} &= K_3\tau - \frac{2\,R}{\sin 2\theta}\left(\frac{K_0}{2}\frac{\sin^4\theta}{R^2} + T + U(R,\,\theta)\right) = 0
\end{aligned}
$$

Once U(R,θ) is given,
3 equations for
3 unknowns (θ, R, M) $(M = K_3\tau)$

DNA electrostatics

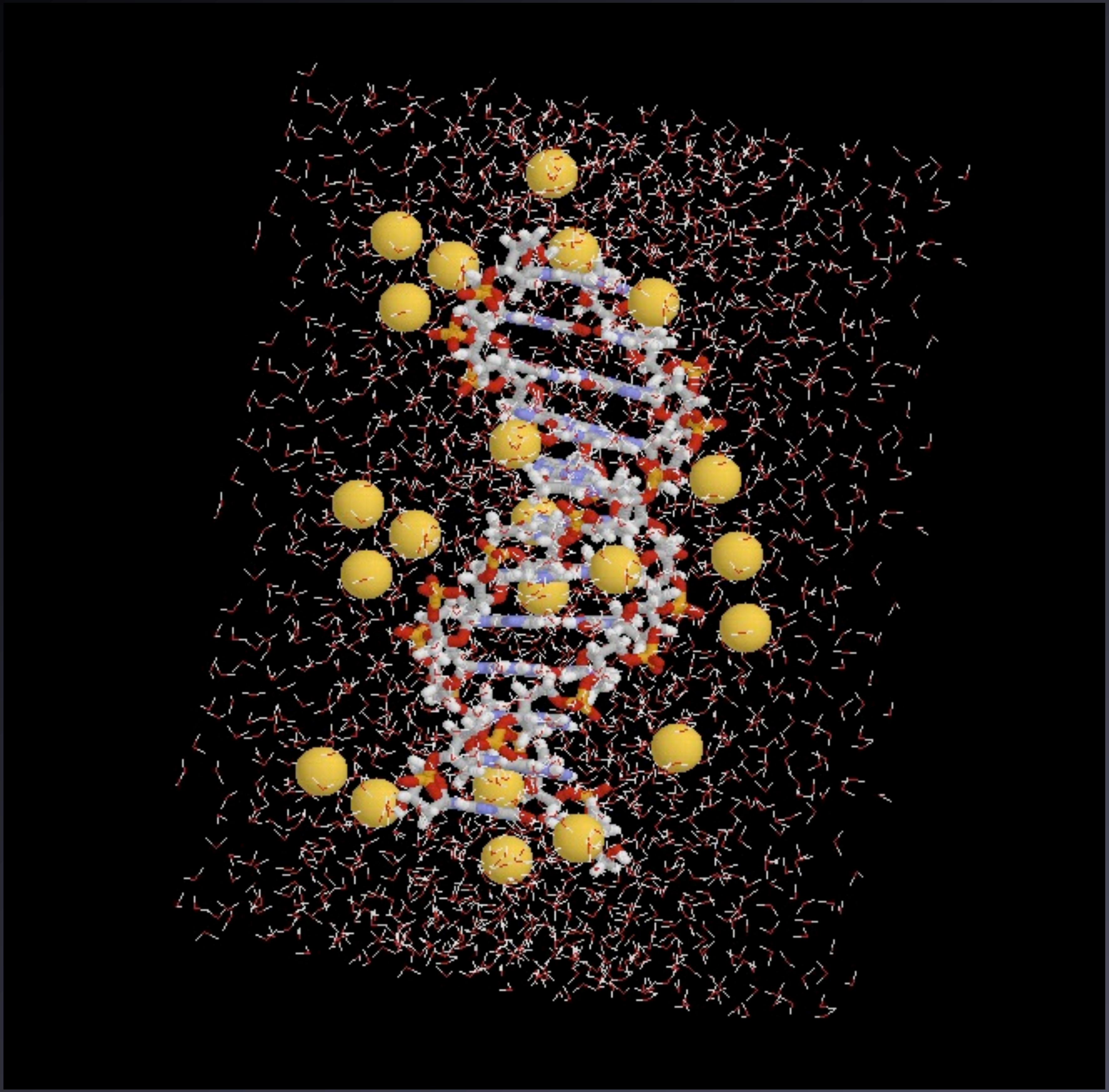


Wikipedia

2 e^- per base-pair

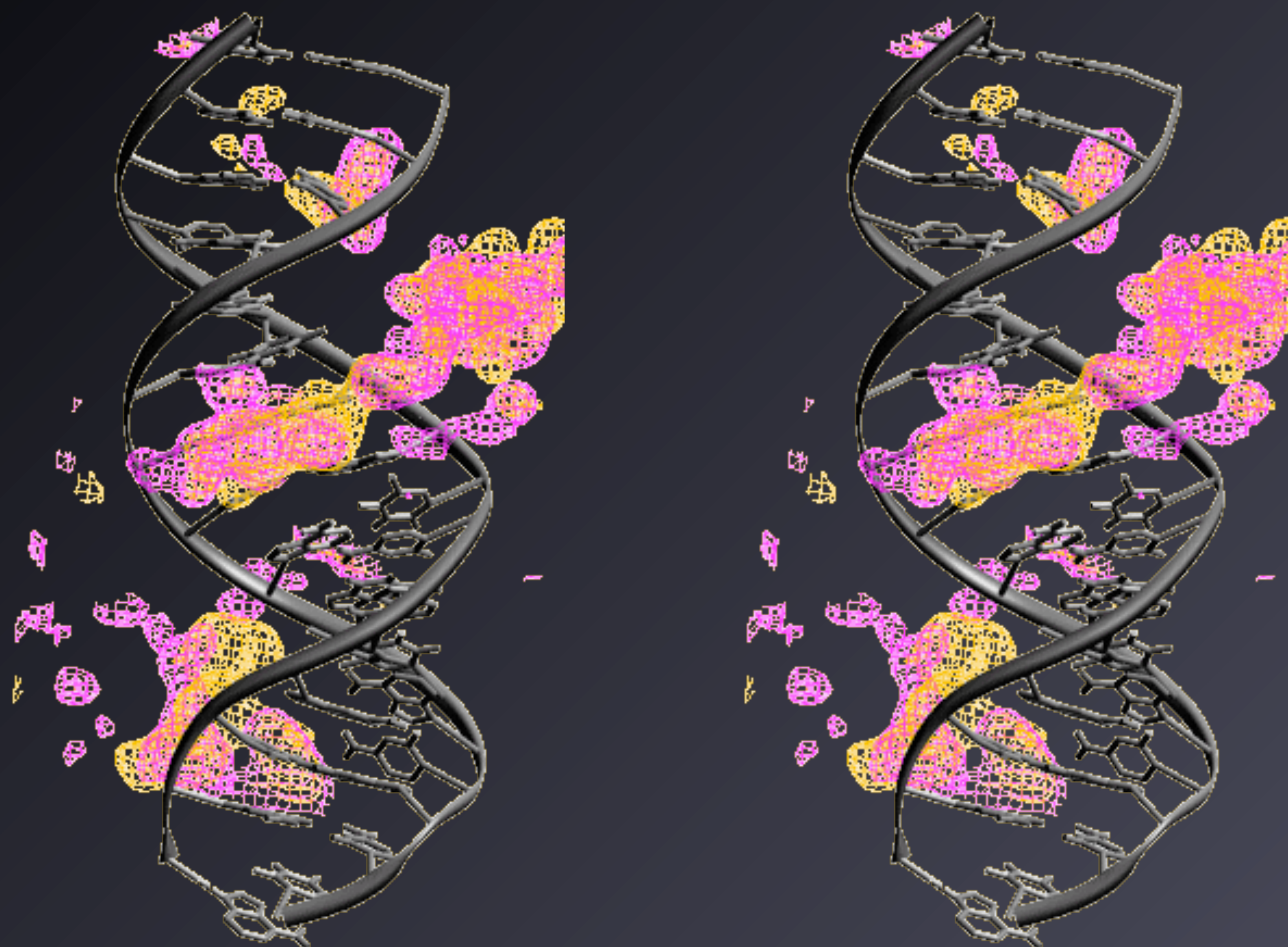
<=> 1 e^- / 0.17 nm

DNA electrostatics



Alexander
MacKerell
www.psc.edu

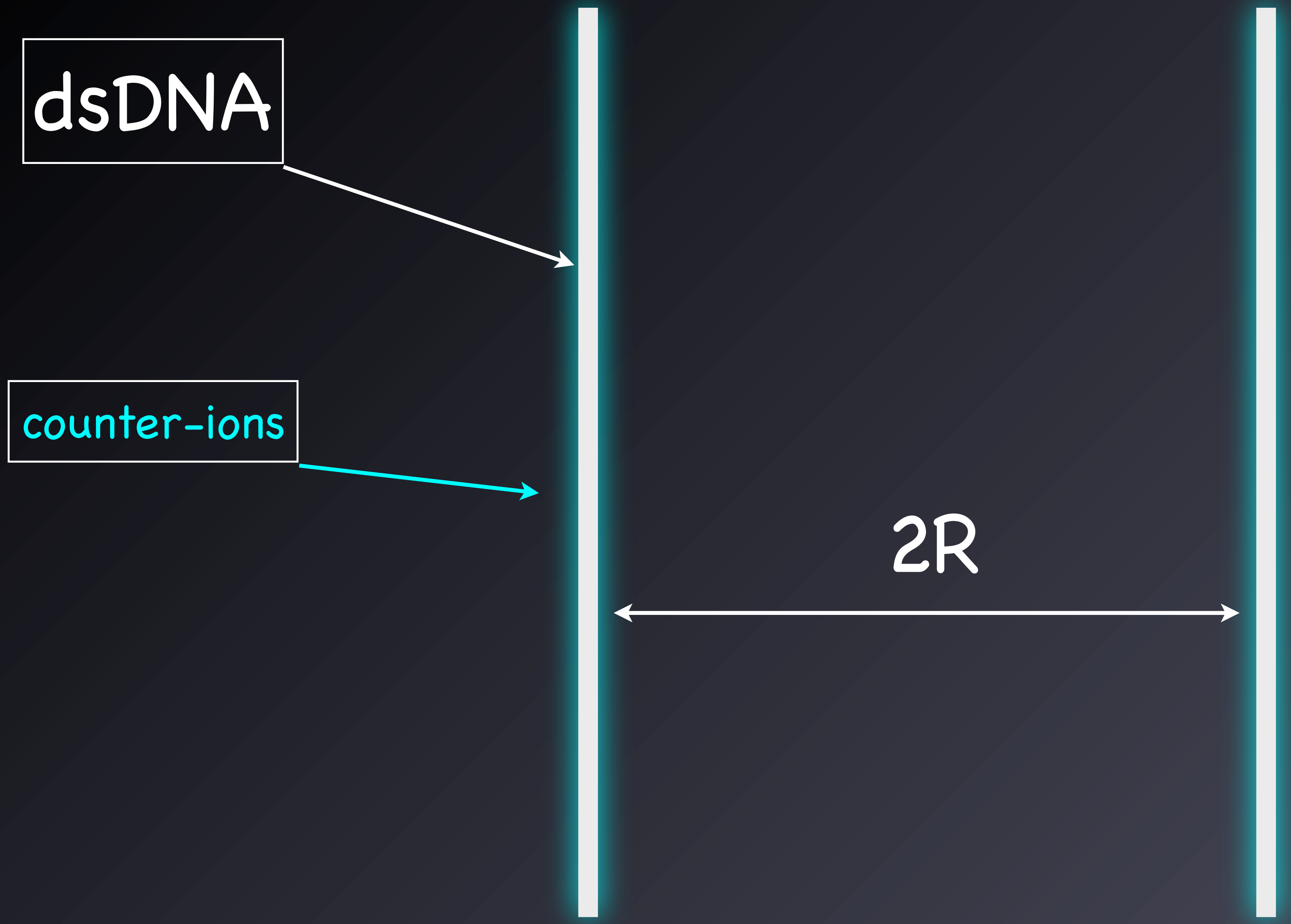
DNA electrostatics



Alexandre Bonvin

www.nmr.chem.uu.nl

DNA electrostatics : Poisson-Boltzmann



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

$L_B = \frac{e^2}{4\pi\epsilon_0\epsilon_r kT}$

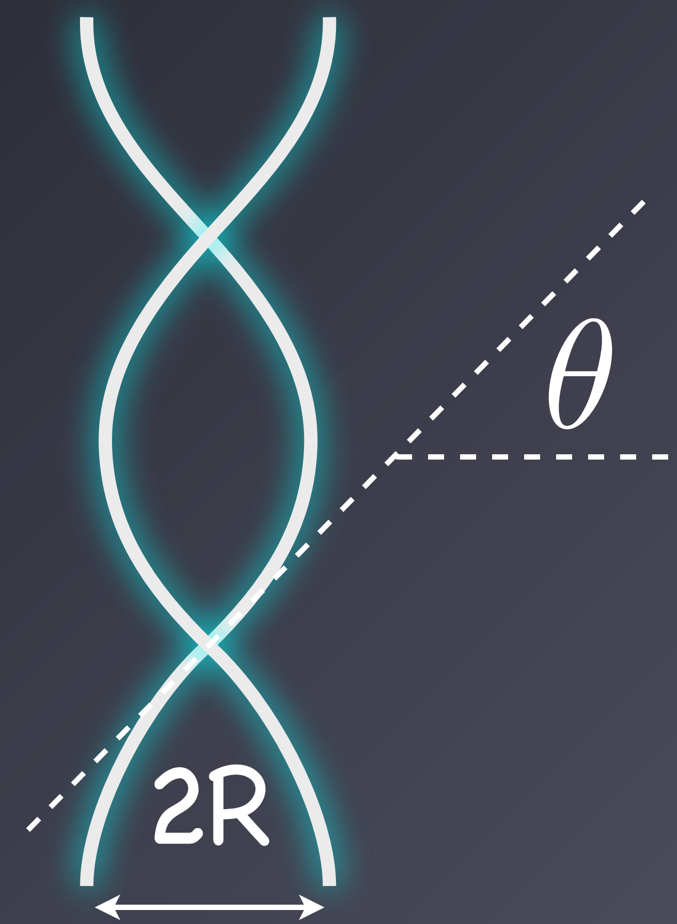
DNA electrostatics : Poisson-Boltzmann

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

κ : Debye

$$L_B = \frac{e^2}{4\pi\epsilon_0\epsilon_r kT}$$

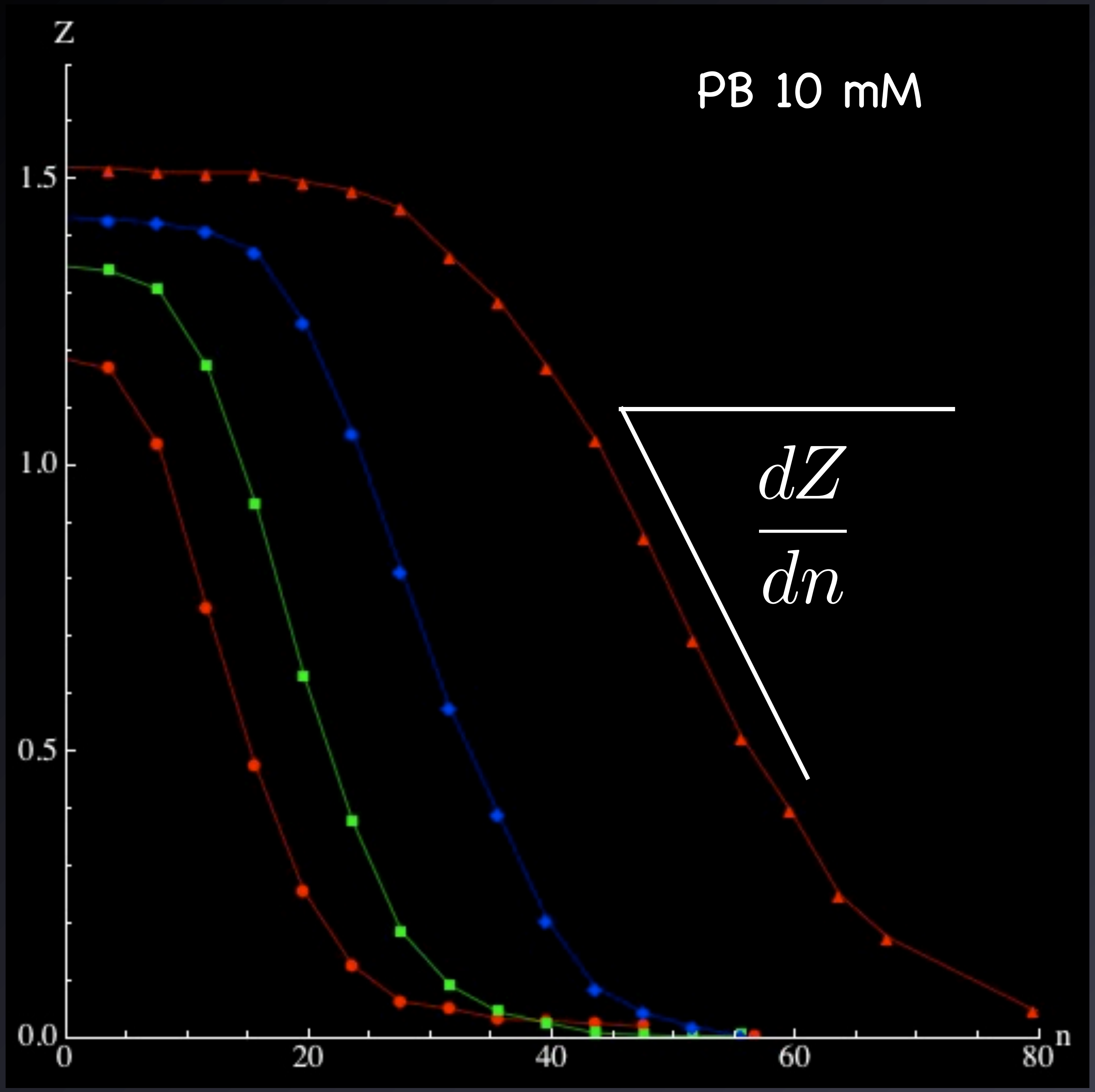
$\phi(\theta) = 1$



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

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

Results : comparison with experimental data



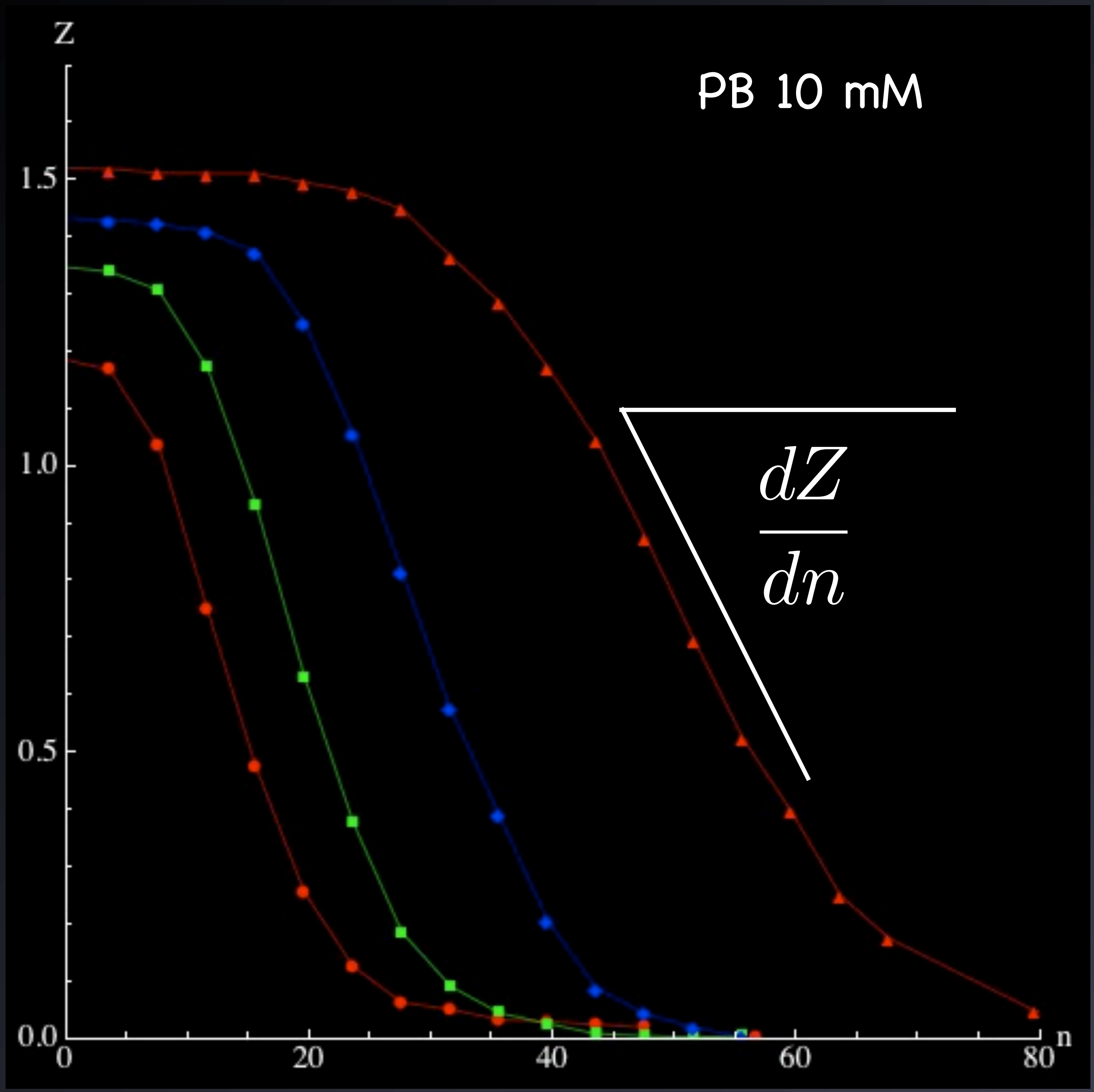
data from Gilles Charvin (ENS-Paris)

$$n = Lk = Tw + Wr$$

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)

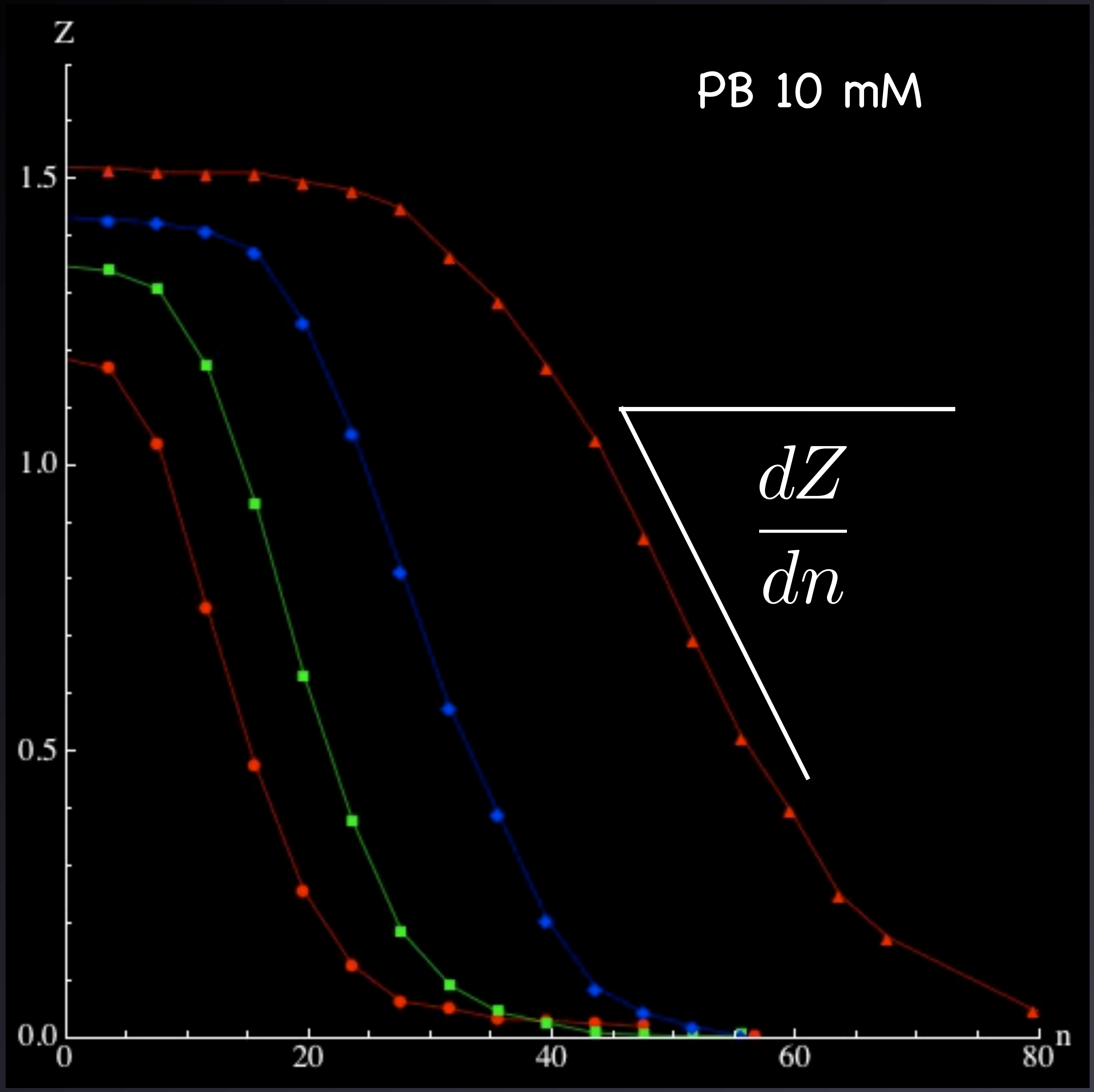
$$n = Lk = Tw + Wr$$

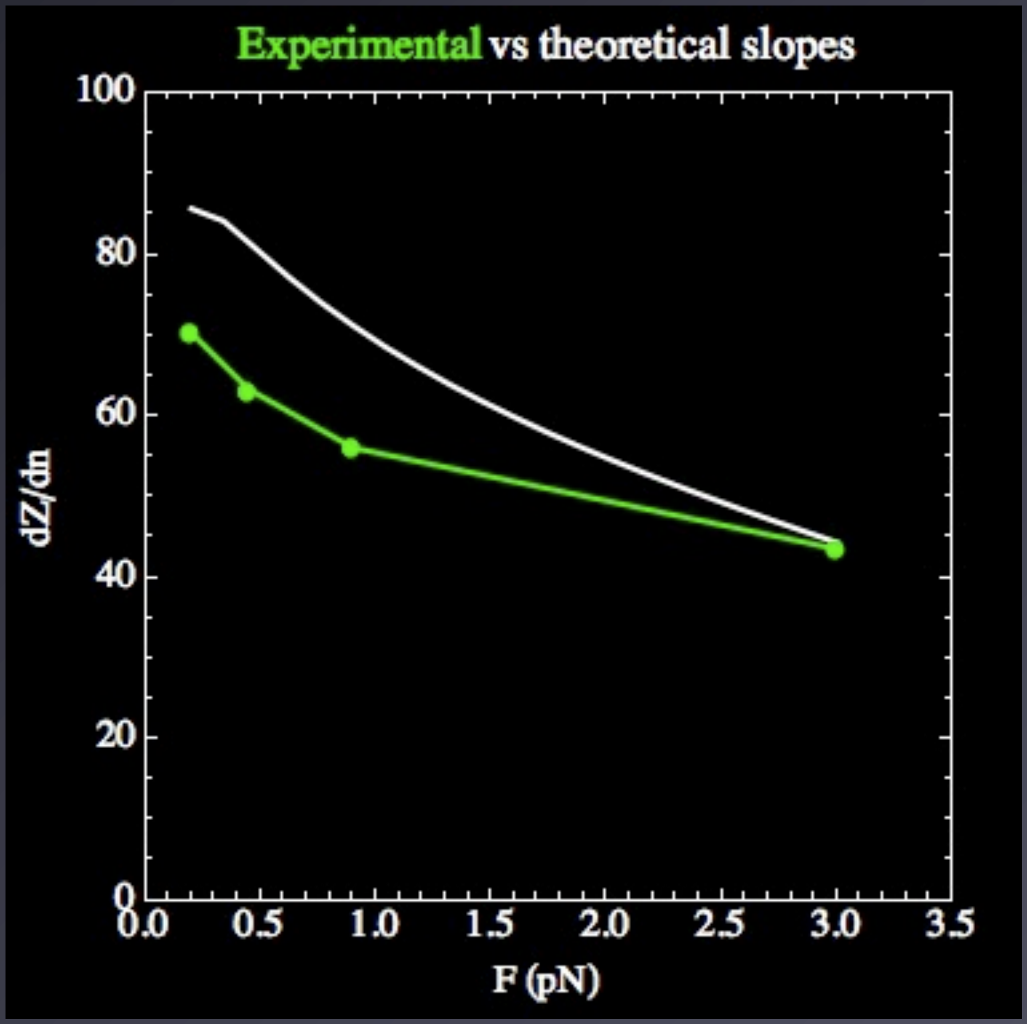
with Wr linear of z

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

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

Results : comparison with experimental data





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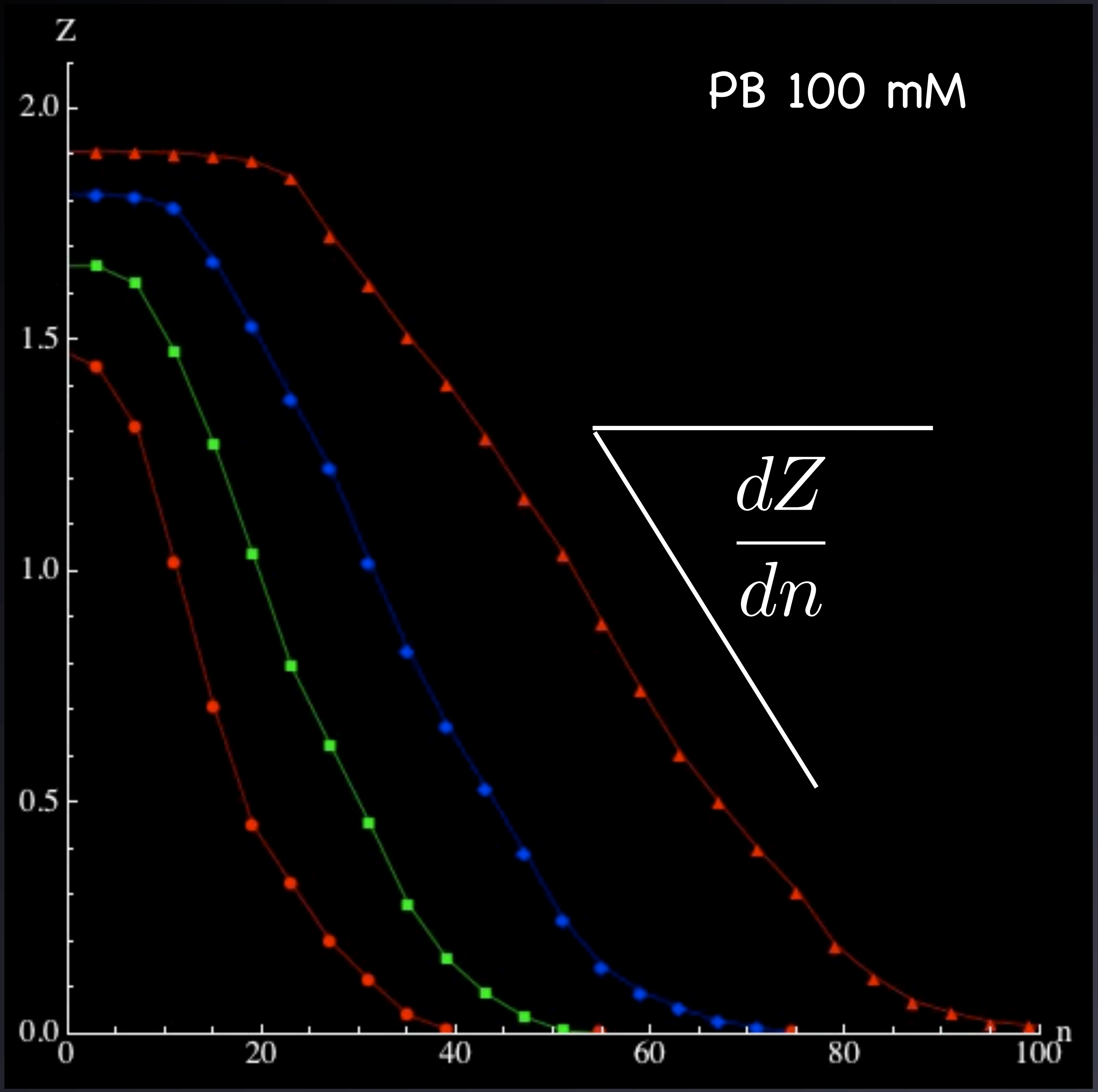
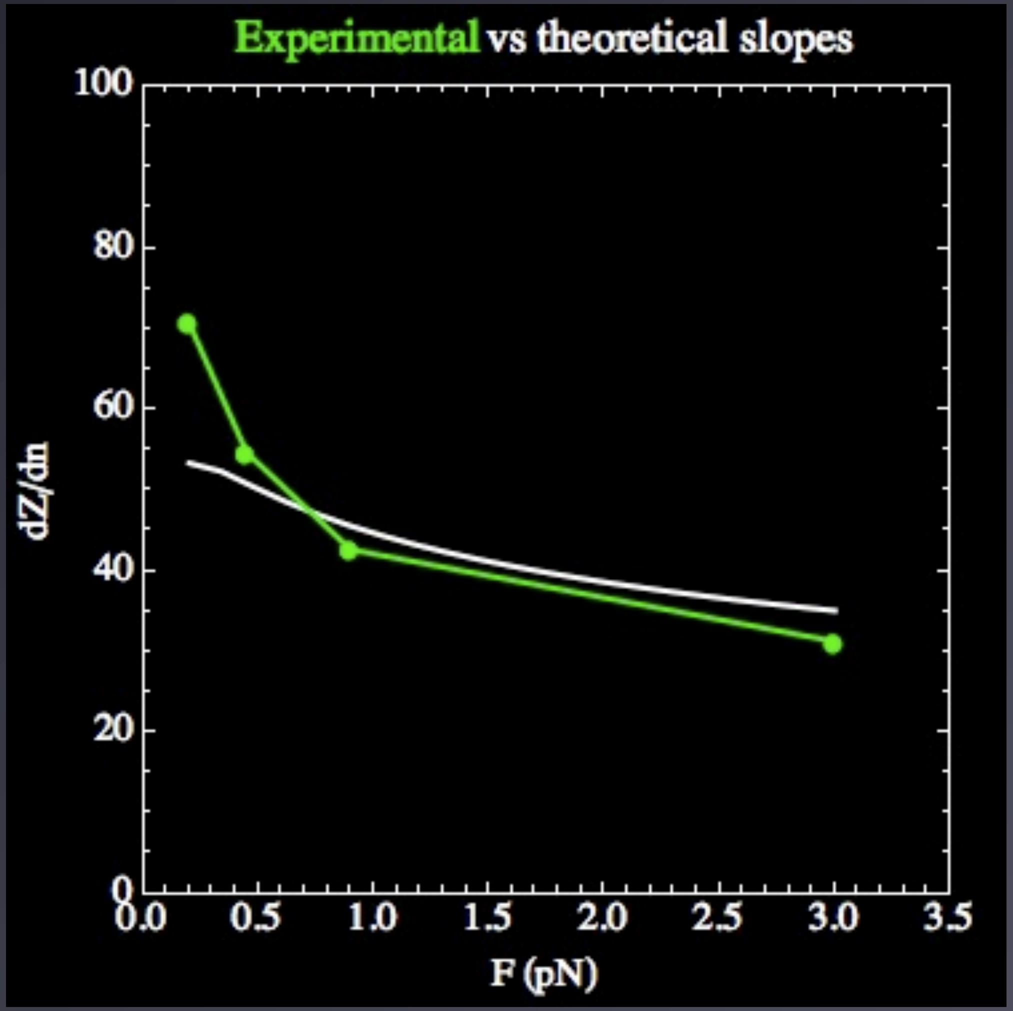
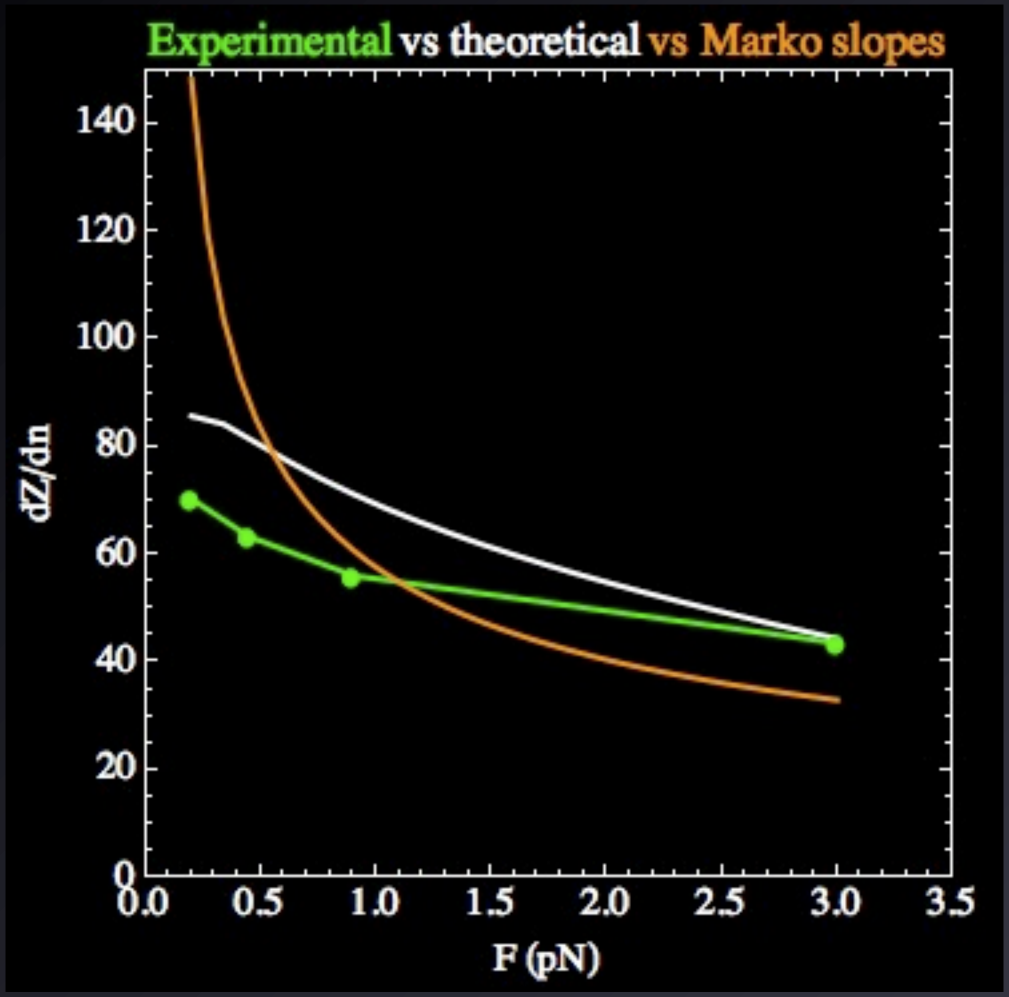




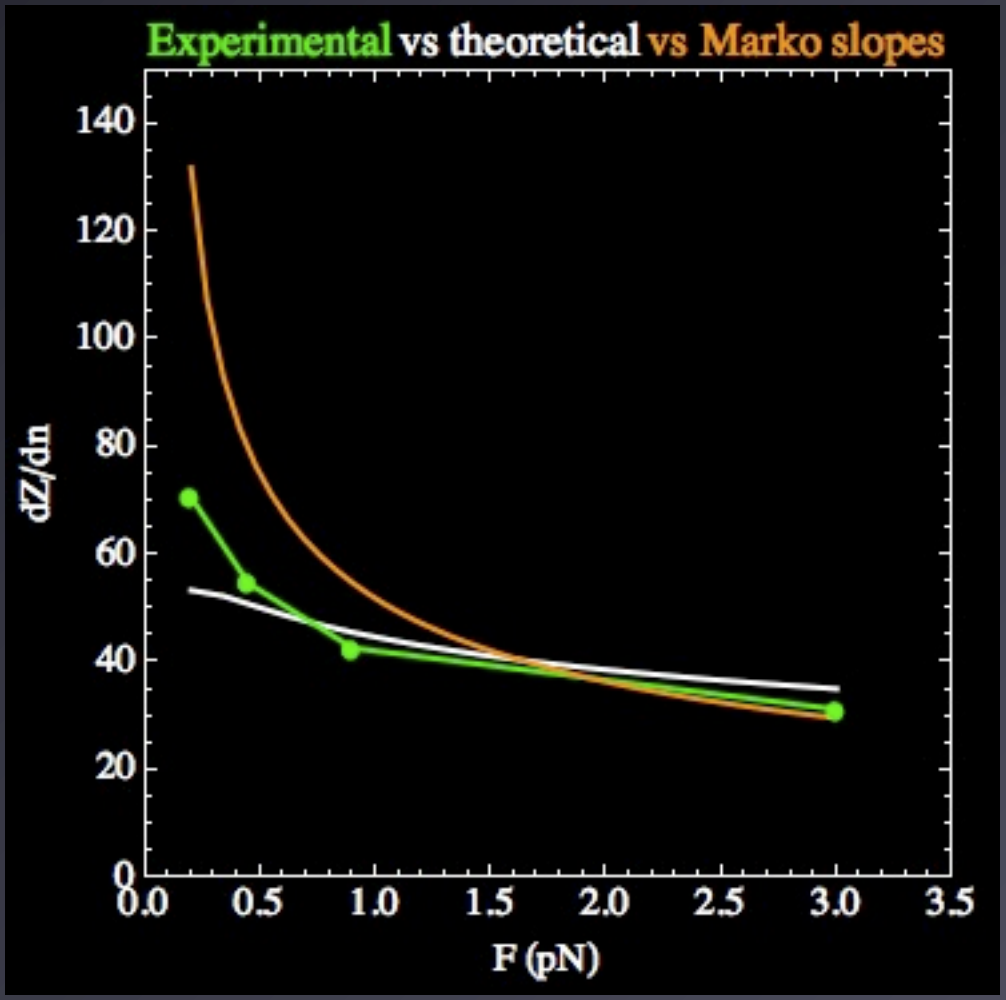
data from Gilles Charvin (ENS-Paris)

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