Mechanical properties of chains with bistable (two-state) units

Stefano Giordano

IEMN UMR CNRS 8520
Laboratoire International Associé LIA LICS/LEMAC
Université de Lille, Centrale Lille
Avenue Poincaré, BP 60069, 59652, Villeneuve d'Ascq, France

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Institut d'Electronique, de Microélectronique et de Nanotechnologie
UMR CNRS 8520

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Contents

- Introduction of the isometric or Helmholtz ensemble and the isotensional or Gibbs ensemble and their relation with real experiments.

- The equivalence of the ensembles in the thermodynamic limit (very long polymer chains): a theorem and some Monte-Carlo simulations.

- The force-extension overstretching regime: the understanding of the *plateau-like* response and the *saw-tooth* like response.

- The chain of bistable elements (domains) as a model to interpret the overstretching regimes observed.

- The spin variables method to study bistability and multistability in polymer systems.

- Generalizations to finite stiffness and Ising interaction (cooperativity)

- Perspective and conclusions

Statistical mechanics of (macromolecular) chains with bistable (two-state) units
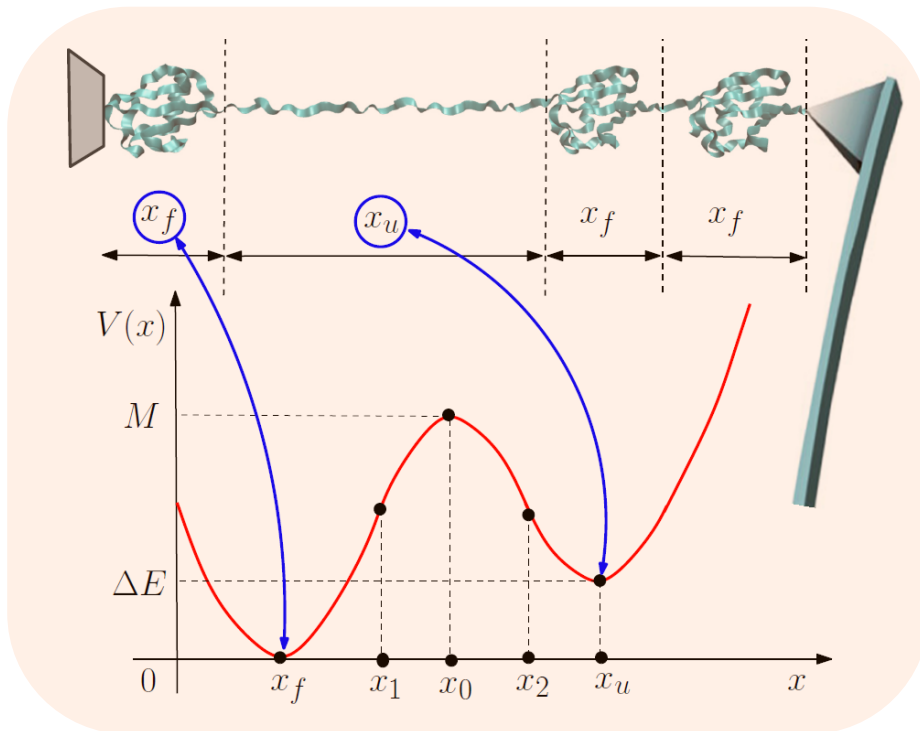
✓ **Elementary model for plasticity** (with hysteresis and/or martensitic transformations)

(*Ericksen, 1975; Müller and Villaggio, 1977; Fedelich and Zanzotto 1992; Puglisi and Truskinovsky, 2000…*)

✓ **Conformational transitions in** macromolecules observed by **force-spectroscopy** methodologies

(*Strick et al., 2003; Ritort, 2006…*)

Polymer chain statistical mechanics

Free polymer: the first monomer is clamped while the others are free to fluctuate
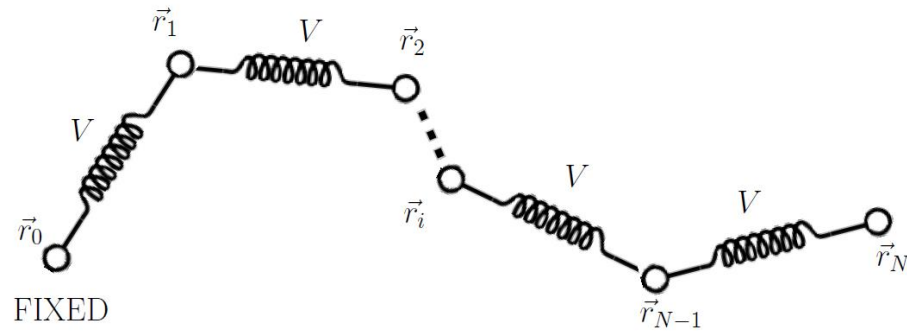
$$h_0(\vec{r}_1, \ldots, \vec{r}_N, \vec{p}_1, \ldots, \vec{p}_N) = \sum_{i=1}^{N} \frac{\vec{p}_i \cdot \vec{p}_i}{2m} + \mathcal{U}(\vec{r}_1, \ldots, \vec{r}_N)$$

Hamiltonian of the system with arbitrary interactions (FJC, WLC…)

$$\rho(q, p) = \frac{1}{Z} e^{-\frac{h_0(q,p)}{k_B T}}$$

Probability density in the phase space (Boltzmann/Gibbs distribution), where **Z** is the classicla partition function
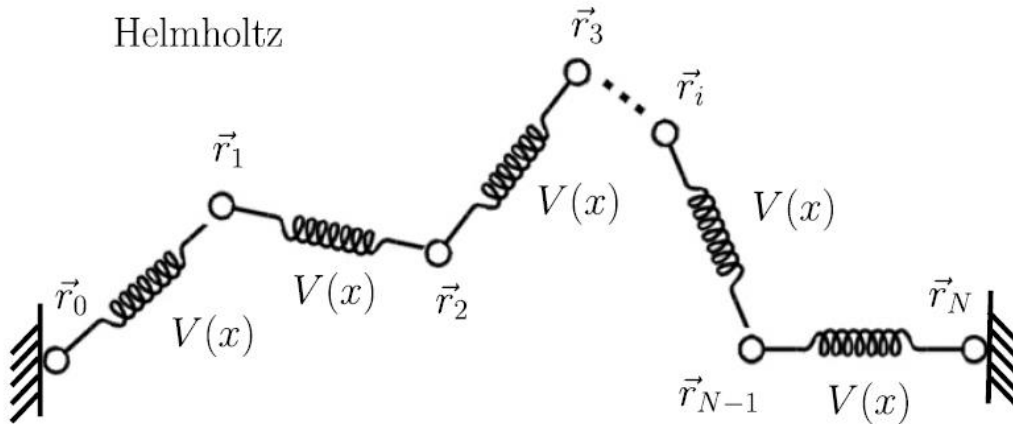
Isometric conditions (Helmholtz ensemble)

Stretching of the chain

Isotensional conditions (Gibbs ensemble)

Helmholtz ensemble: isometric conditions

$$h(\vec{r}_1, \ldots, \vec{r}_{N-1}, \vec{p}_1, \ldots, \vec{p}_{N-1}, \vec{r}) = h_0(\vec{r}_1, \ldots, \vec{r}_{N-1}, \vec{r}_N = \vec{r}, \vec{p}_1, \ldots, \vec{p}_{N-1}, \vec{p}_N = 0)$$

$$Z_{\vec{r}}(\vec{r}, T) = \iint_{\Gamma_{N-1}} e^{-\frac{h(q,p,\vec{r})}{k_B T}} \, dq \, dp,$$

$$\rho_{\vec{r}}(q, p\,; \vec{r}, T) = \frac{1}{Z_{\vec{r}}(\vec{r}, T)} e^{-\frac{h(q,p,\vec{r})}{k_B T}}$$

$$\langle \vec{f} \rangle = \langle \frac{\partial h}{\partial \vec{r}} \rangle$$

$$\boxed{\langle \vec{f}(\vec{r}, T) \rangle = -k_B T \frac{\partial}{\partial \vec{r}} \log Z_{\vec{r}} = \frac{\partial F(\vec{r}, T)}{\partial \vec{r}}}$$
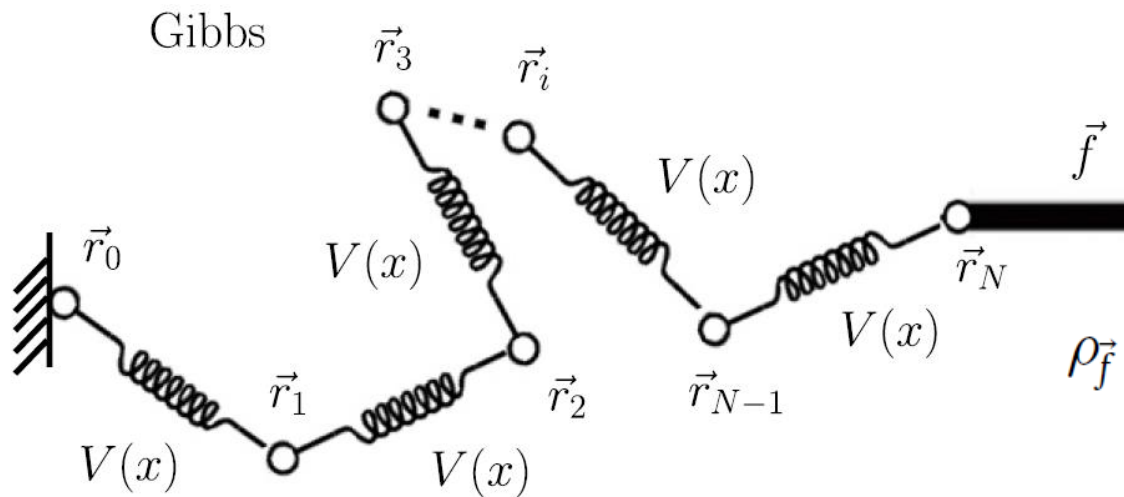
$$F(\vec{r}, T) = -k_B T \log Z_{\vec{r}}$$

Helmholtz free energy

JCP 137, 244907 (2012)
JCP 136, 154906 (2012)

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Gibbs ensemble: isotensional conditions

$$\widetilde{h}(\vec{r}_1, \ldots, \vec{r}_N, \vec{p}_1, \ldots, \vec{p}_N, \vec{f}) = h_0(\vec{r}_1, \ldots, \vec{r}_N, \vec{p}_1, \ldots, \vec{p}_N) - \vec{f} \cdot \vec{r}_N$$

$$Z_{\vec{f}}(\vec{f}, T) = \iint_{\Gamma_N} e^{-\frac{\widetilde{h}(q,p,\vec{f})}{k_B T}} \, dq dp,$$

$$\rho_{\vec{f}}(q, p; \vec{f}, T) = \frac{1}{Z_{\vec{f}}(\vec{f}, T)} e^{-\frac{\widetilde{h}(q,p,\vec{f})}{k_B T}}$$

$$\langle \vec{r} \rangle = -\langle \frac{\partial \widetilde{h}}{\partial \vec{f}} \rangle \Longrightarrow \boxed{\langle \vec{r}(\vec{f}, T) \rangle = k_B T \frac{\partial}{\partial \vec{f}} \log Z_{\vec{f}} = -\frac{\partial G(\vec{f}, T)}{\partial \vec{f}}}$$
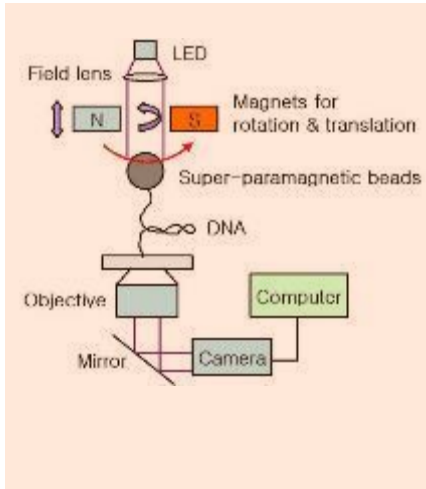
$$G(\vec{f}, T) = -k_B T \log Z_{\vec{f}}$$

Gibbs free energy
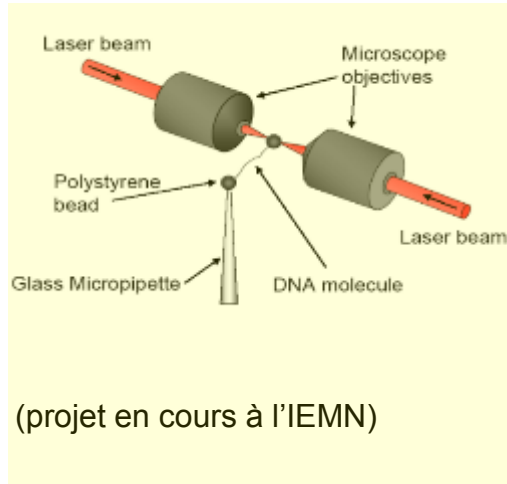
JCP 137, 244907 (2012)
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Force-spectroscopy methods (Neuman and Nagy, 2008)

Magnetic tweezers   **Optical tweezers**   **Atomic force microscope**   **MEMS**

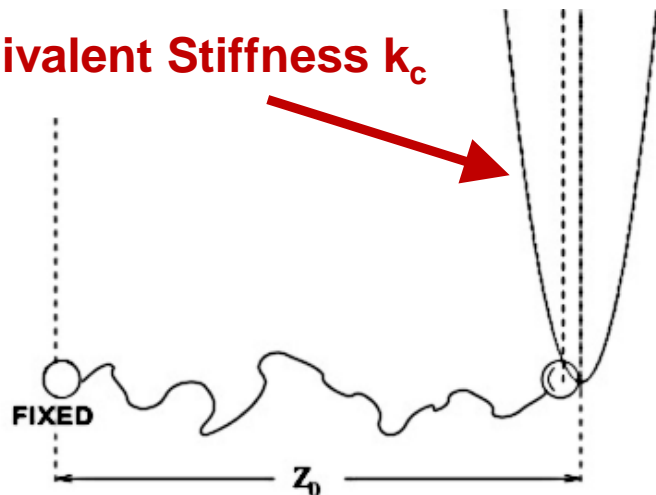(projet en cours à l'IEMN)
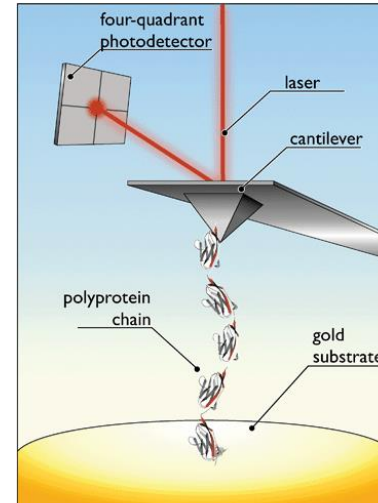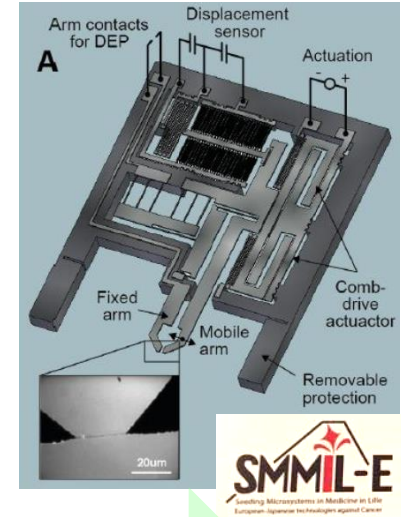
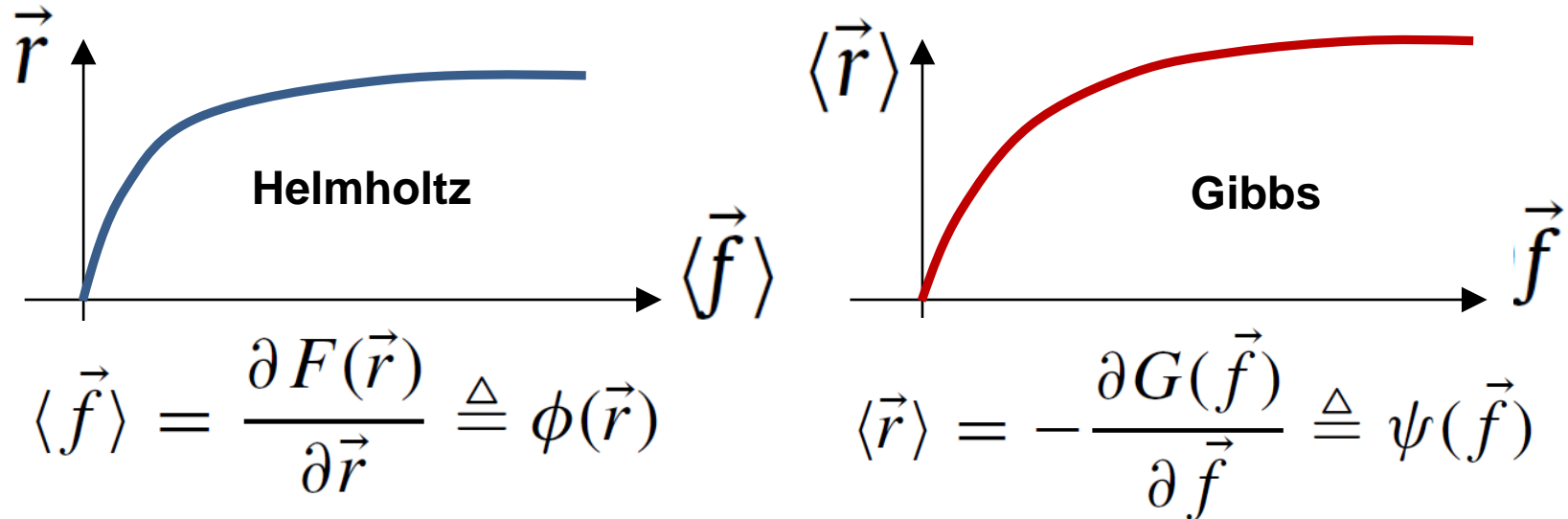**Devices with variable stiffness k_c (10^{-5} - 10^4 pN·nm^{-1})**

Equivalent Stiffness k_c

Soft cantilever → Gibbs ensemble

Hard cantilever → Helmholtz ensemble

Comparison between Helmholtz and Gibbs ensembles

Helmholtz

Gibbs

$$\langle \vec{f} \rangle = \frac{\partial F(\vec{r})}{\partial \vec{r}} \triangleq \phi(\vec{r}) \qquad \langle \vec{r} \rangle = -\frac{\partial G(\vec{f})}{\partial \vec{f}} \triangleq \psi(\vec{f})$$

Is it always true that $\phi = \psi^{-1}$ *or* $\psi = \phi^{-1}$?

If we compare the Helmholtz and Gibbs partition functions we have:

$$Z_{\vec{f}}(\vec{f}, T) = (2\pi m k_B T)^{\frac{3}{2}} \int_{\Re^3} Z_{\vec{r}}(\vec{r}, T) e^{\frac{\vec{f}\cdot\vec{r}}{k_B T}} \, d\vec{r}$$

(Laplace transform)

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Physica A 395, 2014, 154–170

Or, in terms of Gibbs and Helmholtz free energies:

$$e^{-\frac{G(\vec{f},T)}{k_B T}} = (2\pi m k_B T)^{\frac{3}{2}} \int_{\Re^3} e^{-\frac{F(\vec{r}',T)}{k_B T}} e^{\frac{\vec{f}\cdot\vec{r}'}{k_B T}} \, d\vec{r}'$$

Theorem (Physica A 395, 2014, 154–170)

For a polymer model described by a continuous pairing interaction between neighboring monomers (with convergent partition functions) we have $\phi=\psi^{-1}$ in the limit of N→∞ (equivalence between ensembles)
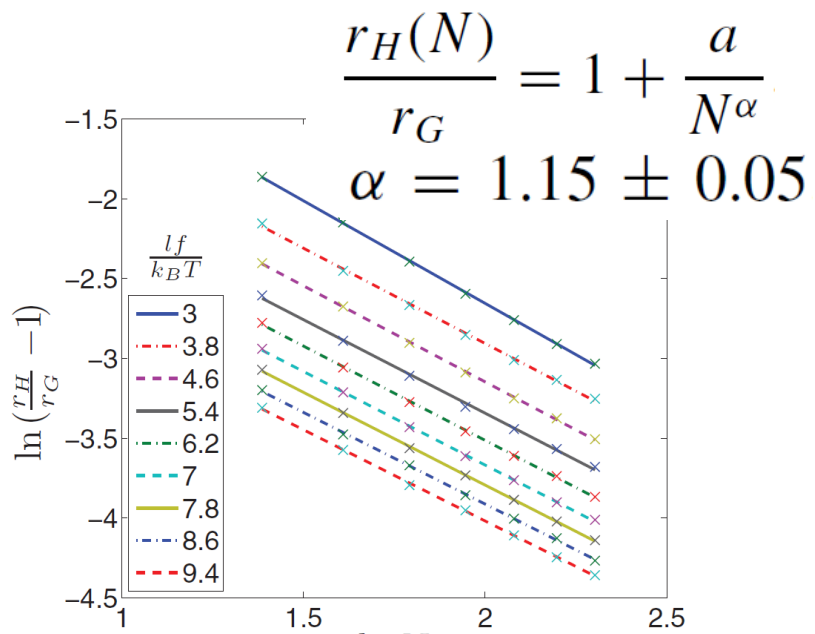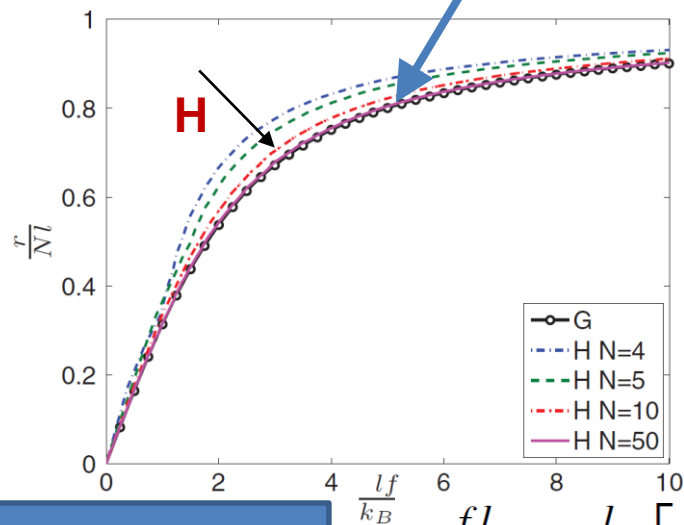
(It can be generalized to more general interactions: 3-body, WLC)

(Legendre transforms)

N→∞ $\Rightarrow$
$$\begin{cases} G(\phi(\vec{r})) = F(\vec{r}) - \phi(\vec{r}) \cdot \vec{r} \\ F(\psi(\vec{f})) = G(\vec{f}) + \vec{f} \cdot \psi(\vec{f}) \end{cases}$$
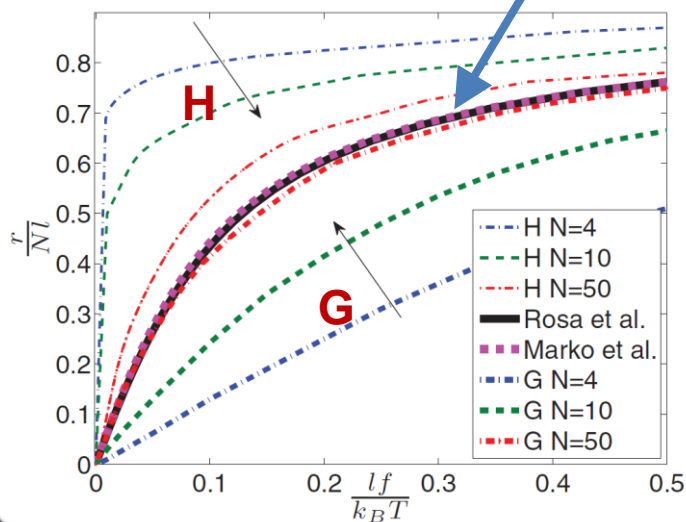
FJC

$$r = Nl\mathcal{L}\left(\frac{lf}{k_BT}\right) \text{ (G)}$$

$$\frac{r_H(N)}{r_G} = 1 + \frac{a}{N^\alpha}$$

$$\alpha = 1.15 \pm 0.05$$
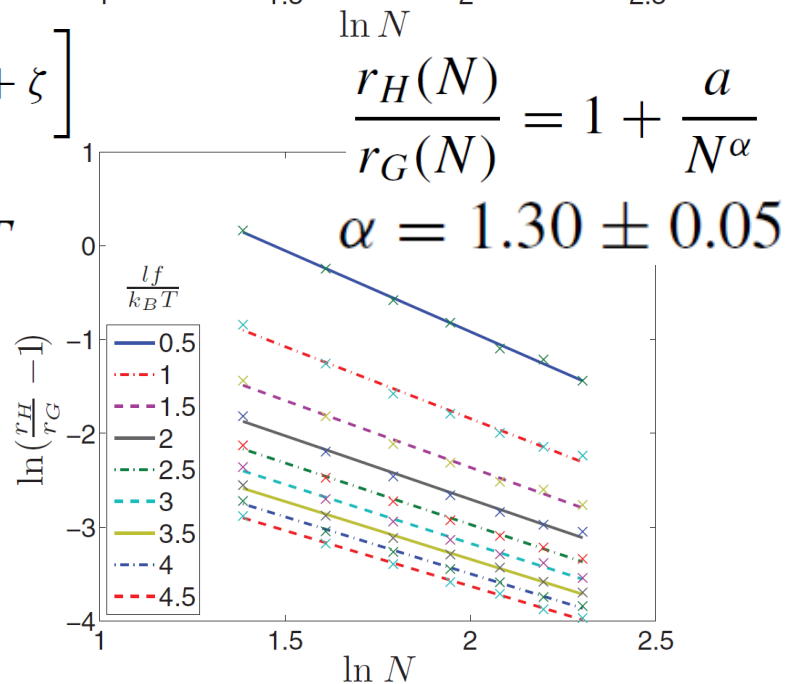
WLC

$$\frac{fl}{k_BT} = \frac{l}{L_p}\left[\frac{1}{4(1-\zeta)^2} - \frac{1}{4} + \zeta\right]$$

$$\kappa = 10k_BT$$

(bending)

$$\frac{r_H(N)}{r_G(N)} = 1 + \frac{a}{N^\alpha}$$

$$\alpha = 1.30 \pm 0.05$$

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Comments

- **We have proved the equivalence between Helmholtz and Gibbs ensembles in the thermodynamic limit for a chain with continuous pairing interactions (and more general schemes with 3-body potentials, WLC…);**

- **The convergence for high valus of N is described by a power law with specific exponents;**

- **The differences between the Helmholtz and Gibbs force-extension responses are however negligible for $N>50/100$ monomers (for FJC or WLC);**

- **Therefore, the differences are not relevant for long chains as DNA (during entropic and enthalpic stretchnig);**

- **Nevertheless, the analysis of different ensembles is useful for the understanding of experiments in the overstretching regime, where conformational transitions occur.**
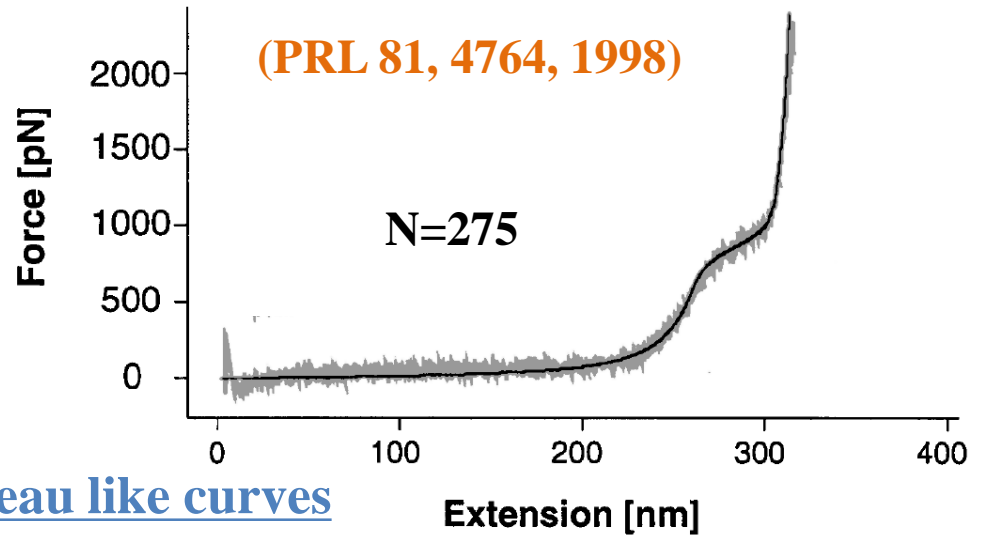
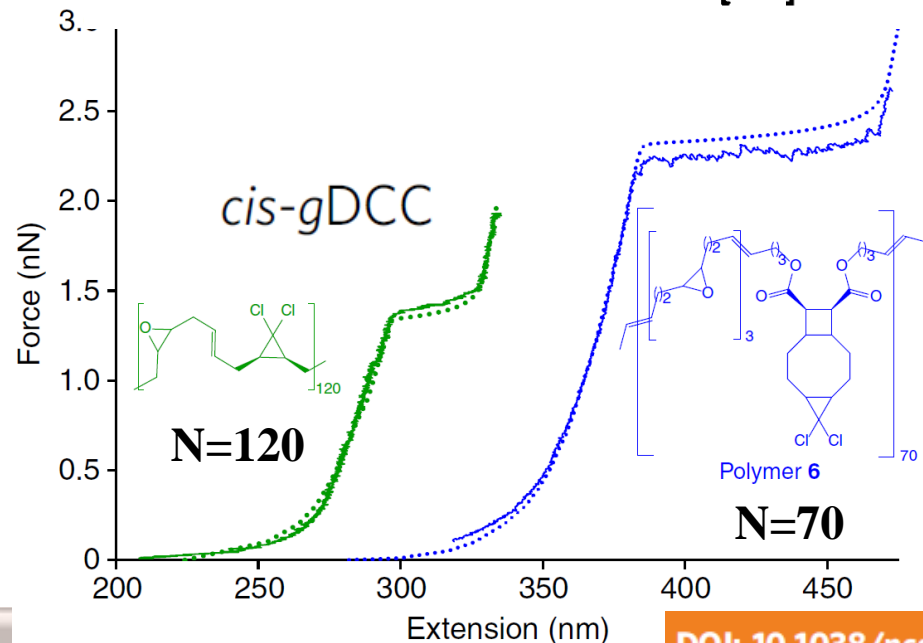# Overstretching experiments (COOPERATIVE RESPONSE)
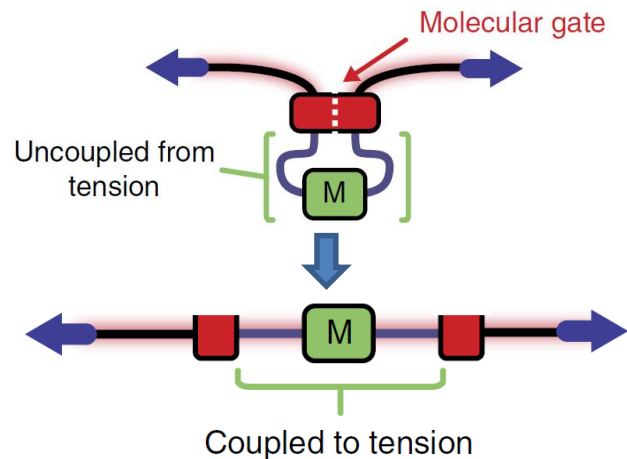
DNA (Nature 421, 423, 2003)
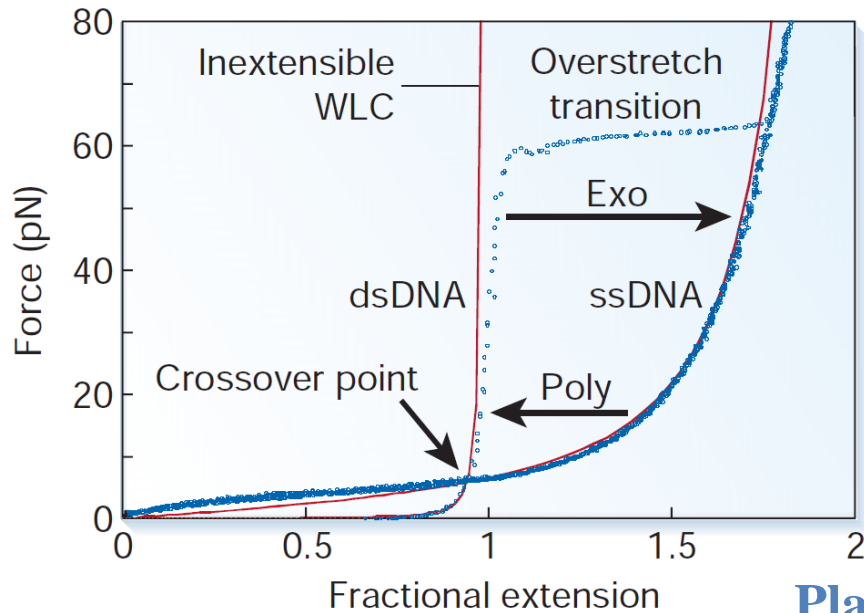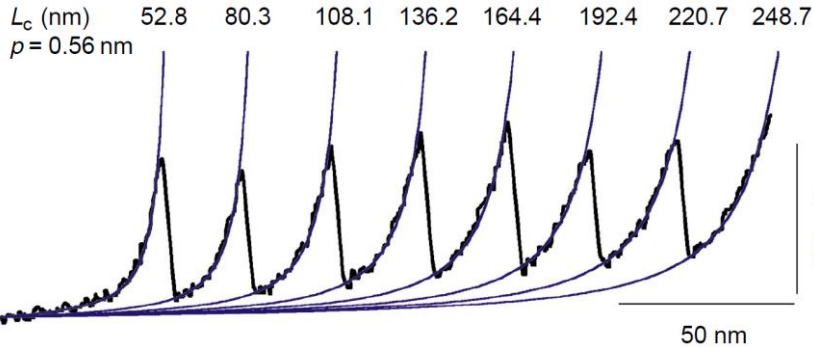

Dextran (polysaccharide)

(PRL 81, 4764, 1998)

N=275

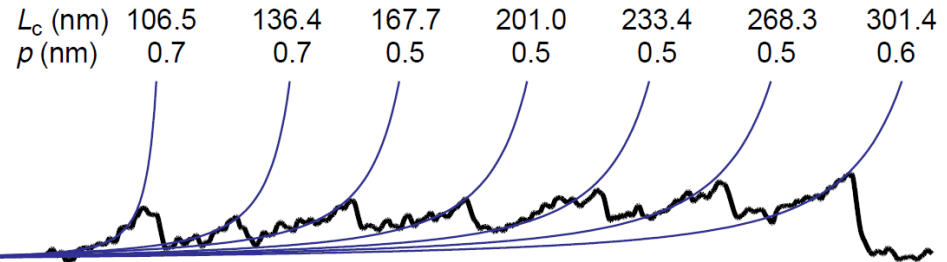### Plateau like curves

Overstretching experiments (NON-COOPERATIVE RESPONSE)

Human tenascin-C, N=7

L_c (nm) 52.8 80.3 108.1 136.2 164.4 192.4 220.7 248.7
p = 0.56 nm

100 pN

50 nm

Citoskeletal protein spectrin, N=6

L_c (nm)	106.5	136.4	167.7	201.0	233.4	268.3	301.4
p (nm)	0.7	0.7	0.5	0.5	0.5	0.5	0.6

Protein I27$_{12}$, N=12

200 pN

100 nm
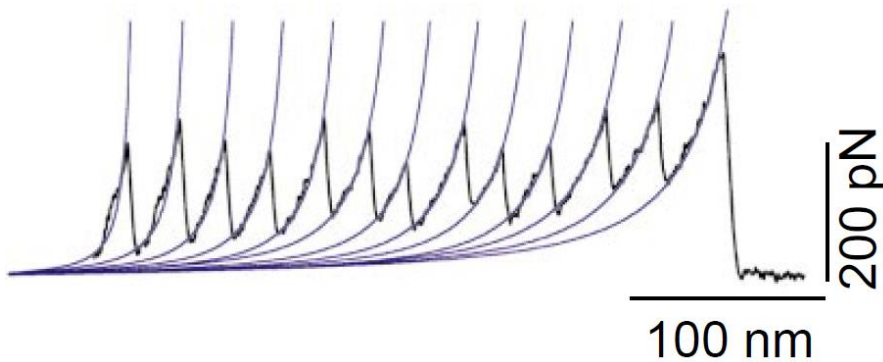
Sawtooth like curves

Titin, N=6 Ig domains

L_c (nm)	66.0	93.4	119.8	147.5	178.2	208.6	238.0
p (nm)	1.9	1.8	1.7	1.5	1.1	0.8	0.5

100 pN

50 nm

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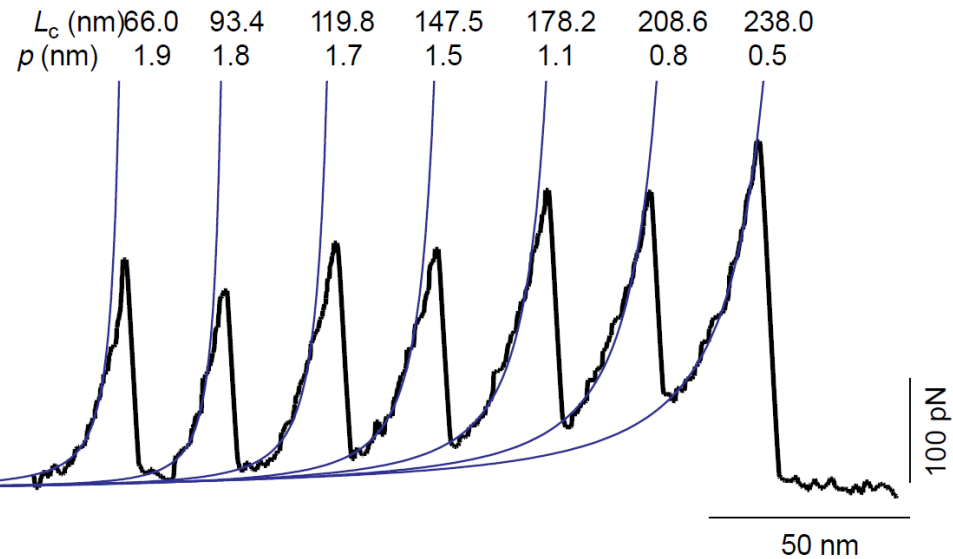
Chain with bistable elements
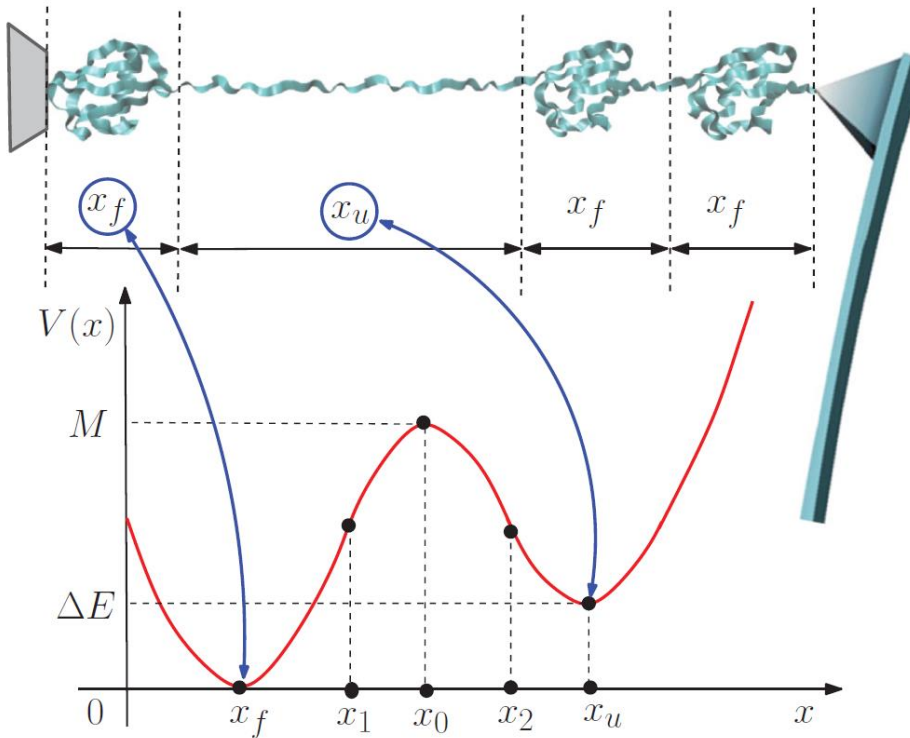
Potential energy function with an energy barrier M and two minima separated by an energy difference ΔE. Folded and unfolded domain lengths are x_f and x_u, respectively.

Pairing interaction potential:

$$V(x) = \begin{cases} \dfrac{1}{2}k(x - x_f)^2 & 0 < x < x_1 \\[2mm] -\dfrac{1}{2}k(x - x_0)^2 + M & x_1 < x < x_2 \\[2mm] \dfrac{1}{2}k(x - x_u)^2 + \Delta E & x > x_2. \end{cases}$$

Parameters:

$$\delta = x_u - x_f$$

$$x_0 = \frac{x_u + x_f}{2} + 2\frac{\Delta E}{k\delta},$$

$$M = \frac{k}{4}\left[\frac{\delta}{2} + 2\frac{\Delta E}{k\delta}\right]^2,$$

$$x_1 = x_f + \frac{\delta}{4} + \frac{\Delta E}{k\delta},$$

$$x_2 = x_u - \frac{\delta}{4} + \frac{\Delta E}{k\delta}.$$

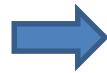# Gibbs ensemble for a chain with bistable elements

Analytical **expression** for the Gibbs partition function:

$$Z_{\vec{f}}(\vec{f}, T) = \left(\frac{2\pi m}{\beta}\right)^{3N/2} \left(\frac{2\pi}{\beta \|\vec{f}\|}\right)^N \times \left[\Pi\left(\beta k, \beta \|\vec{f}\|, x_f, 0, x_1\right) + e^{-\beta M} \Pi\left(-\beta k, \beta \|\vec{f}\|, x_0, x_1, x_2\right) \right.$$
$$\left. + e^{-\beta \Delta E} \Pi\left(\beta k, \beta \|\vec{f}\|, x_u, x_2, +\infty\right) \right]^N$$

where:
$$\Pi(\alpha, \gamma, x_0, a, b) = 2 \int_a^b x e^{-\frac{\alpha}{2}(x-x_0)^2} \sinh(\gamma x) dx$$

$$\langle \vec{r}(\vec{f}, T) \rangle = k_B T \frac{\partial}{\partial \vec{f}} \log Z_{\vec{f}} = -\frac{\partial G(\vec{f}, T)}{\partial \vec{f}}$$

- The force plateau appears for $f = \Delta E / \delta$, where $\delta = x_u - x_f$.

- Unfortunaltly, the analytical approach cannot be used with the Helmholtz ensemble→Montecarlo
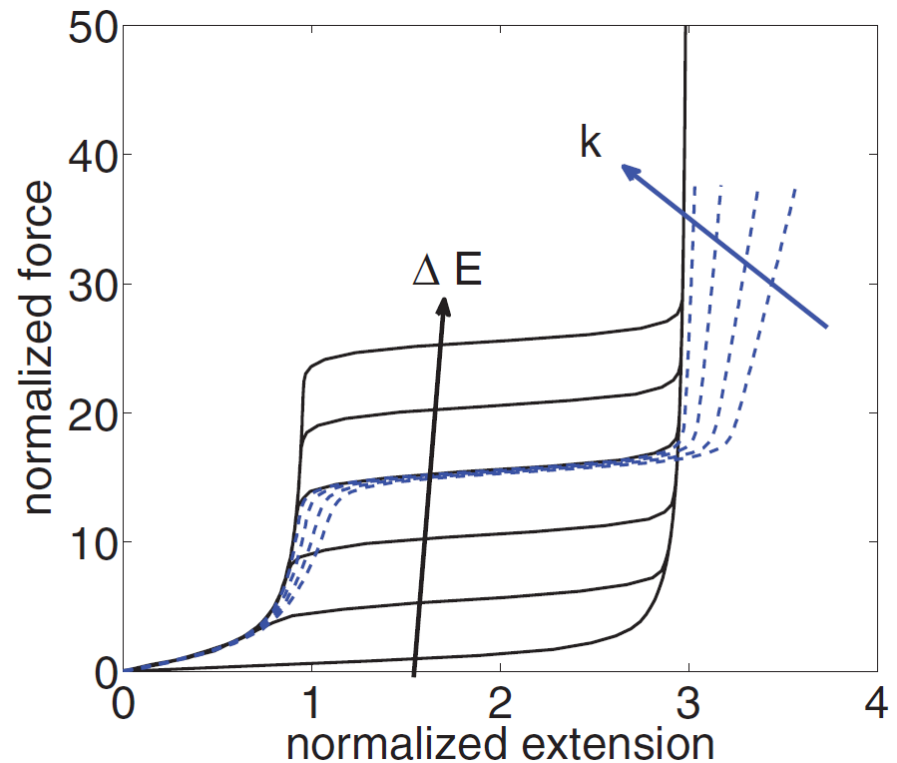
Ensemble comparisons with bistable elements
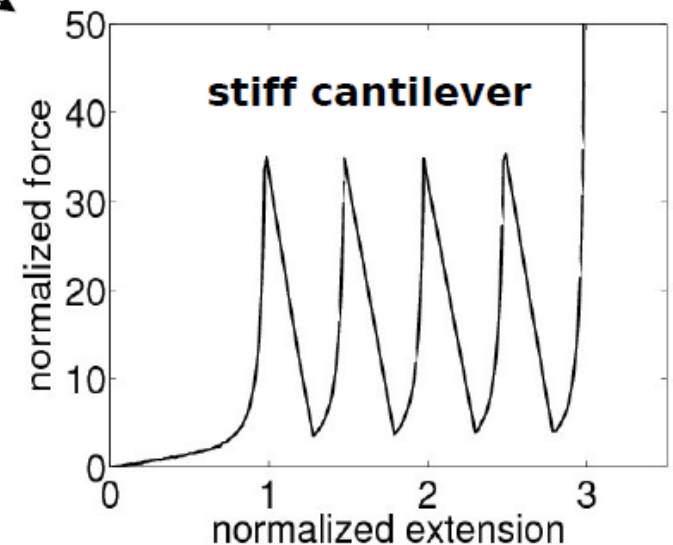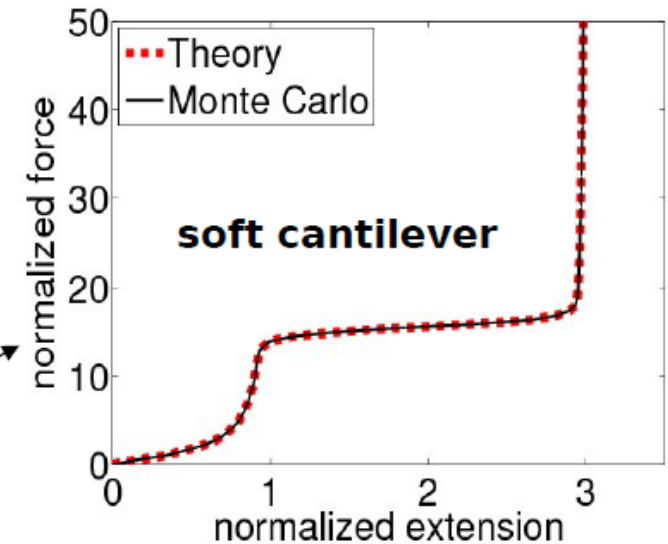
cantilever stiffness $\to 0$ (Gibbs ensemble)

conformational change occur simultaneously for all the domains at a given threshold force (cooperativity)

different results for the same polymer chain

cantilever stiffness $\to \infty$ (Helmholtz ensemble)

conformational change not simultaneously

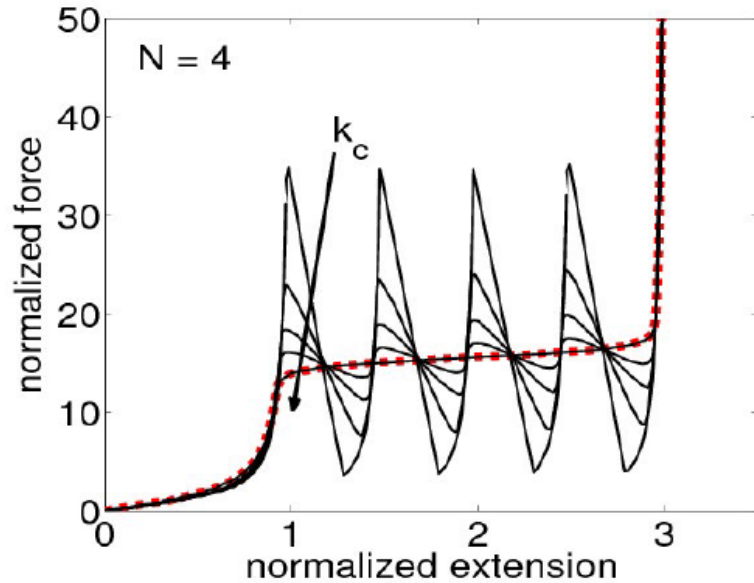**typical 'sawtooth' pattern: conformational transformation of the domain geometry**

but in practice, real experiments always fall inbetween these two ideal extremes!

$N=4$

Overstretching regime, intermediate cases:
not Gibbs nor Helmholtz

same polymers length
the transition from
the 'sawtooth' response
to the 'plateau'
is recovered for
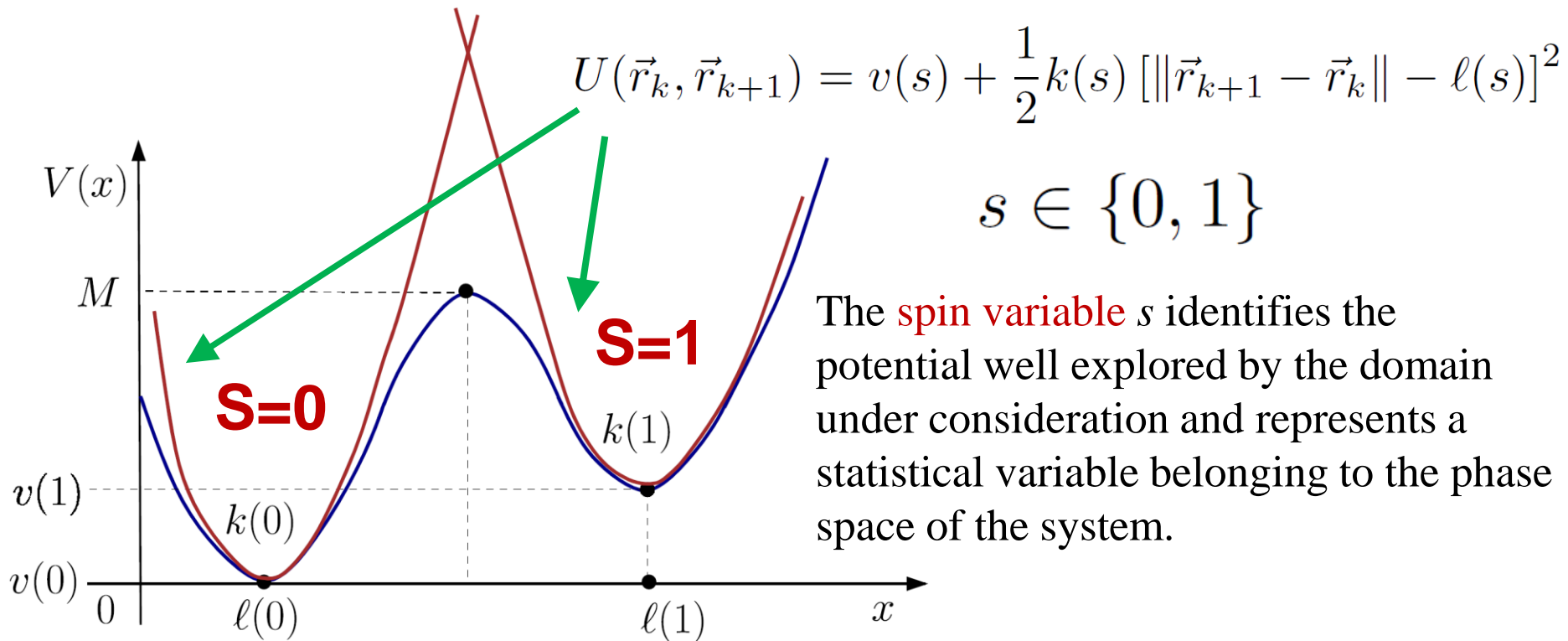**decreasing values** of the
cantilever stiffness k_c

the typical 'sawtooth'
pattern (titin) and the
'plateau' or kink (dextran),
have a **common origin** in
the **size-dependence** of the
polymer response to the
external force

$$k_c = 2\ k_B T/(\text{nm})^2$$

N = 4, 30, 300
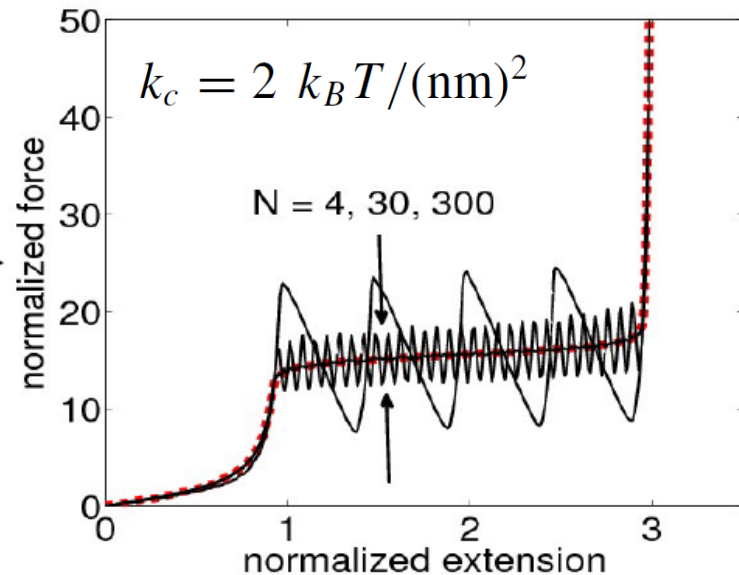
Spin variables approach for multistable systems

We introduce a quadratic curve approximating each potential well of the multi-basin energy landscape of a unit of the chain.

$$U(\vec{r}_k, \vec{r}_{k+1}) = v(s) + \frac{1}{2}k(s)\left[\|\vec{r}_{k+1} - \vec{r}_k\| - \ell(s)\right]^2$$

$$s \in \{0, 1\}$$

S=0

S=1

The spin variable s identifies the potential well explored by the domain under consideration and represents a statistical variable belonging to the phase space of the system.

$$H = \sum_{i=1}^{N} \frac{\vec{p}_i \cdot \vec{p}_i}{2m} + \sum_{i=1}^{N} v(s_i) + \sum_{i=1}^{N} \frac{1}{2}k(s_i)\left[\|\vec{r}_{k+1} - \vec{r}_k\| - \ell(s_i)\right]^2 - \vec{f} \cdot \vec{r}_N$$

Hamiltonian in the Gibbs ensembles

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Calculation of the partition function in the Gibbs ensemble

$$Z_G = \sum_{s_1 \in \{0,1\}} \cdots \sum_{s_N \in \{0,1\}} \int_{\Re^{3N}} \int_{\Re^{3N}} e^{-\frac{H(\vec{p},\vec{q},\vec{s})}{k_B T}} d\vec{p} \, d\vec{q}$$
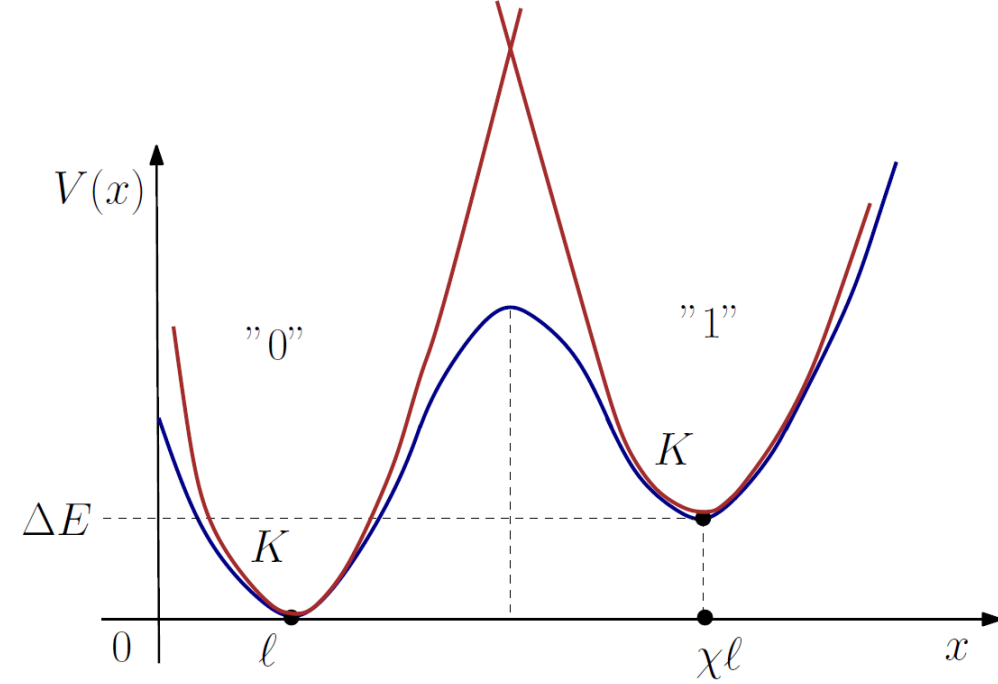
or, equivalently, by considering the complete expression for the Hamiltonian:

$$Z_G = const. \times \left\{ \sum_{s \in \{0,1\}} \int_{\Re^3} \exp\left[-\frac{v(s)}{k_B T} - \frac{k(s)}{2k_B T} \left[\|\vec{\xi}\| - \ell(s) \right]^2 + \frac{\vec{f} \cdot \vec{\xi}}{k_B T} \right] d\vec{\xi} \right\}^N$$

Because of the isotropy of the spring-like interactions, we have:

$$\vec{f} = (0, 0, f), \quad d\vec{\xi} = \xi^2 \sin\vartheta \, d\xi \, d\varphi \, d\vartheta$$

$$\|\vec{\xi}\| = \xi, \quad \vec{f} \cdot \vec{\xi} = f\xi \cos\vartheta$$

$$Z_G = const. \times \left\{ \sum_{s \in \{0,1\}} e^{-\frac{v(s)}{k_B T}} \int_0^\infty \exp\left[-\frac{k(s)}{2k_B T} [\xi - \ell(s)]^2 \right] \frac{\sinh\left(\frac{f\xi}{k_B T}\right)}{\frac{f\xi}{k_B T}} \xi^2 d\xi \right\}^N$$

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We define χ as the ratio between the unfolded and folded length of each domain and we consider each spring characterized by the stiffness K. Moreover, the energy difference between the stable states is ΔE.

$$s = 0 \Rightarrow v(0) = 0, \ \ell(0) = \ell, \ k(0) = K$$

$$s = 1 \Rightarrow v(1) = \Delta E, \ \ell(1) = \chi\ell, \ k(1) = K$$

$$Z_G = const. \times \left\{ \int_0^\infty \exp\left[-\frac{K}{2k_BT} [\xi - \ell]^2 \right] \frac{\sinh\left(\frac{f\xi}{k_BT}\right)}{\frac{f\xi}{k_BT}} \xi^2 d\xi \right.$$

$$\left. + e^{-\frac{\Delta E}{k_BT}} \int_0^\infty \exp\left[-\frac{K}{2k_BT} [\xi - \chi\ell]^2 \right] \frac{\sinh\left(\frac{f\xi}{k_BT}\right)}{\frac{f\xi}{k_BT}} \xi^2 d\xi \right\}^N$$

Bistable freely jointed chain under Gibbs conditions

In order to define a bistable freely jointed chain we assume that K→∞
(it means that the domain lenght is ℓ or $\chi\ell$) and by using the Delta representation

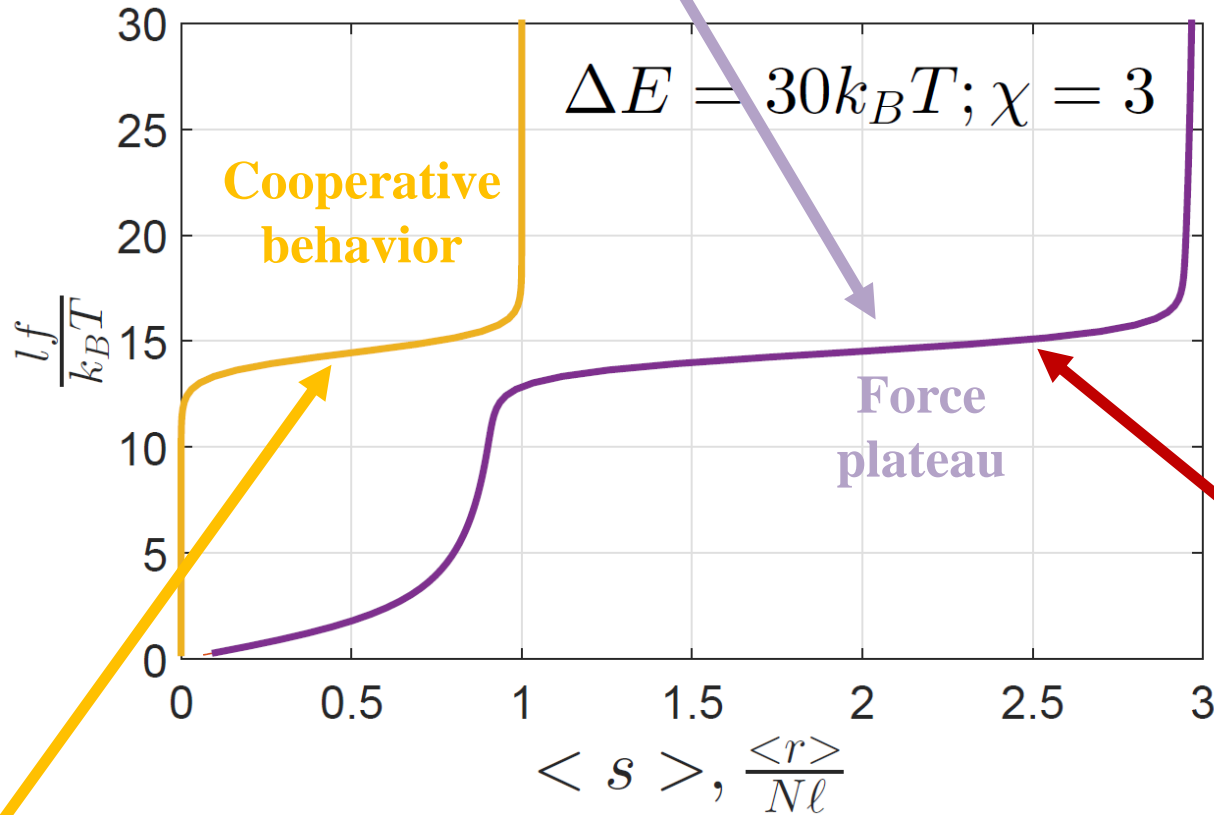$$\sqrt{\frac{\alpha}{\pi}}e^{-\alpha x^2} \underset{\alpha\to\infty}{\to} \delta(x)$$

we obtain:

$$Z_G = const. \times \left\{ \frac{\sinh y}{y} + \chi e^{-\frac{\Delta E}{k_B T}} \frac{\sinh \chi y}{y} \right\}^N \quad \textbf{(BFJC)}$$

which is a direct generalization of classical freely jointed chain partition function

$$Z_G = const. \times \left\{ \frac{\sinh y}{y} \right\}^N \quad \textbf{(FJC)}$$

$$y = \frac{\ell f}{k_B T}$$

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$$\langle r \rangle = k_B T \frac{\partial \log Z_G}{\partial f} = N\ell \frac{\mathcal{L}(y) + \chi^2 e^{-\frac{\Delta E}{k_B T}} \mathcal{L}(\chi y) \frac{\sinh \chi y}{\sinh y}}{1 + \chi e^{-\frac{\Delta E}{k_B T}} \frac{\sinh \chi y}{\sinh y}}$$

$\Delta E = 30 k_B T; \chi = 3$

Cooperative behavior

Force plateau

Langevin function:
$$\mathcal{L}(y) = \coth y - \frac{1}{y}$$

$$f^* = \frac{\Delta E}{(\chi - 1)\ell}$$

$$\langle s \rangle = \frac{1}{N} \left\langle \sum_{i=1}^{N} s_i \right\rangle = -k_B T \frac{\partial \log Z_G}{N \partial \Delta E} = \frac{\chi e^{-\frac{\Delta E}{k_B T}} \frac{\sinh \chi y}{\sinh y}}{1 + \chi e^{-\frac{\Delta E}{k_B T}} \frac{\sinh \chi y}{\sinh y}}$$

If we look at the obtained results:

$$\langle r \rangle = N\ell \frac{\mathcal{L}(y) + \chi^2 e^{-\frac{\Delta E}{k_B T}} \mathcal{L}(\chi y) \frac{\sinh \chi y}{\sinh y}}{1 + \chi e^{-\frac{\Delta E}{k_B T}} \frac{\sinh \chi y}{\sinh y}}$$

$$\langle s \rangle = \frac{\chi e^{-\frac{\Delta E}{k_B T}} \frac{\sinh \chi y}{\sinh y}}{1 + \chi e^{-\frac{\Delta E}{k_B T}} \frac{\sinh \chi y}{\sinh y}}$$

we can write:

$$\langle r \rangle = N \left[(1 - \langle s \rangle) \ell \mathcal{L}(y) + \langle s \rangle \chi \ell \mathcal{L}(\chi y) \right]$$

which is a linear combination of *NℓL(y)* and *NχℓL(χy)* (two freely jointed chain models), weighted by the average value of the spin variable.

Bistable freely jointed chain under Helmholtz conditions

The three-dimensional Laplace transform between the Gibbs and Helmholtz partition functions can be written in scalar form for radially symmetric functions:

$$Z_H(r) = \int_{-\infty}^{+\infty} Z_G(i\eta) \frac{\eta}{r} \sin \frac{\eta r}{k_B T} d\eta$$

(BFJC)

$$Z_H(r) = \int_{-\infty}^{+\infty} \left\{ \frac{\sin y}{y} + \chi\phi \frac{\sin \chi y}{y} \right\}^N \frac{y}{r} \sin \frac{ry}{\ell} dy$$

which is a direct generalization of the classical Rayleigh-Polya integral describing the freely jointed chain partition function:

$$Z_H(r) = \int_{-\infty}^{+\infty} \left\{ \frac{\sin y}{y} \right\}^N \frac{y}{r} \sin \frac{ry}{\ell} dy \quad \textbf{(FJC)}$$

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Soft Matter 13, 6877-6893 (2017)

Calculation of the partition function in the Helmholtz ensemble

The analysis of the integral through the complex variables method allows the exact calculation in the following form:

$$Z_H(r) = \frac{\pi}{r2^{(N-1)}(N-2)!} \sum_{k=0}^{N} \sum_{p=0}^{N-k} \sum_{q=0}^{k} \binom{N}{k} \binom{N-k}{p} \binom{k}{q} (-1)^{p+q} \alpha^k (-\Lambda)^{N-2} \mathbf{1}(\Lambda)$$

where:

Soft Matter 13, 6877-6893 (2017)

$$\alpha = \chi e^{-\frac{\Delta E}{k_B T}} \qquad \text{and} \qquad \Lambda = k - N + 2p - \chi k + 2\chi q - \frac{r}{\ell}$$

and we can determine the average values of force and spin

$$\langle f \rangle = -k_B T \frac{\partial \log Z_H}{\partial r}$$

$$\langle s \rangle = \frac{1}{N} \left\langle \sum_{i=1}^{N} s_i \right\rangle = -k_B T \frac{\partial \log Z_H}{N \partial \Delta E}$$
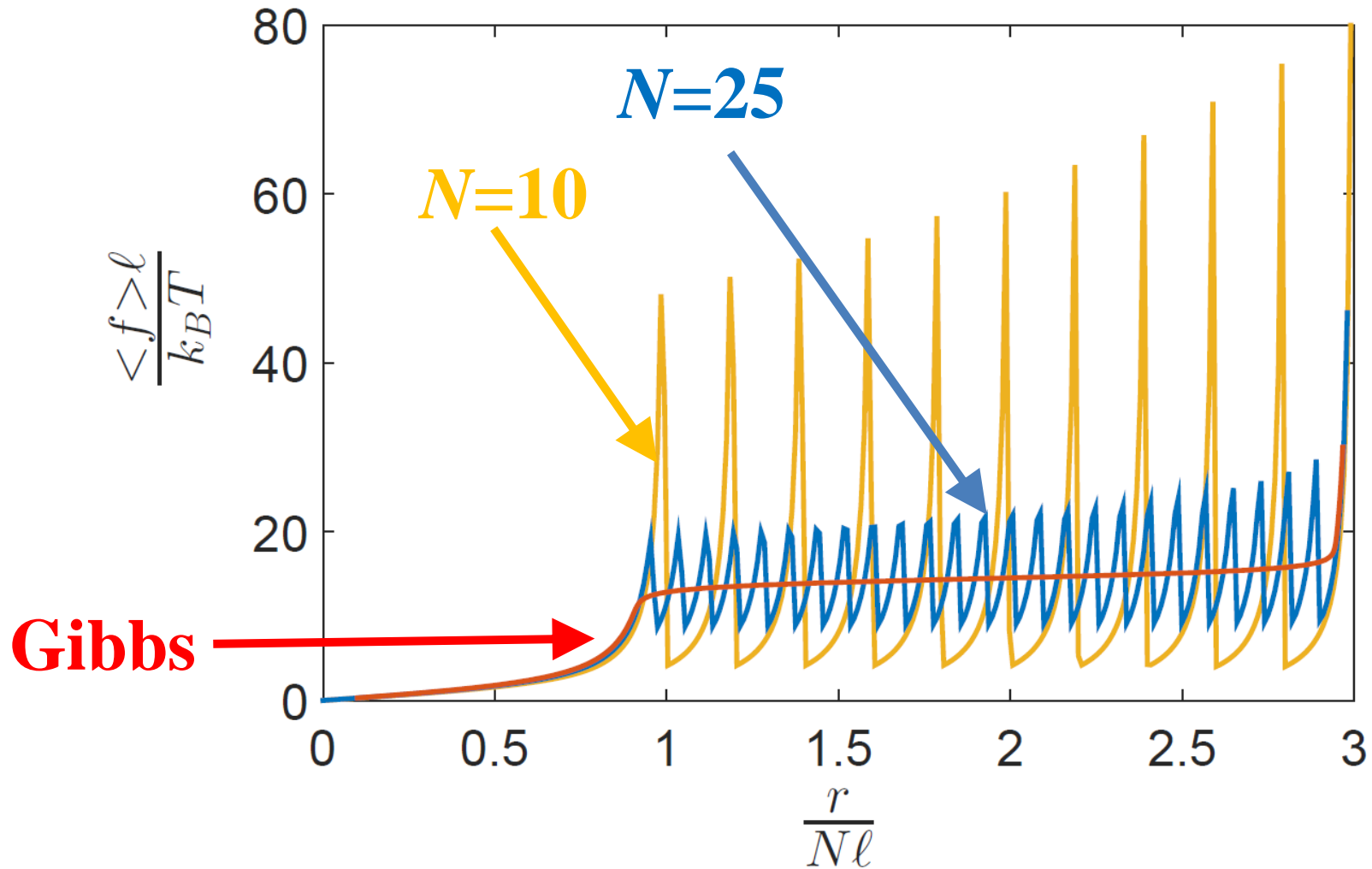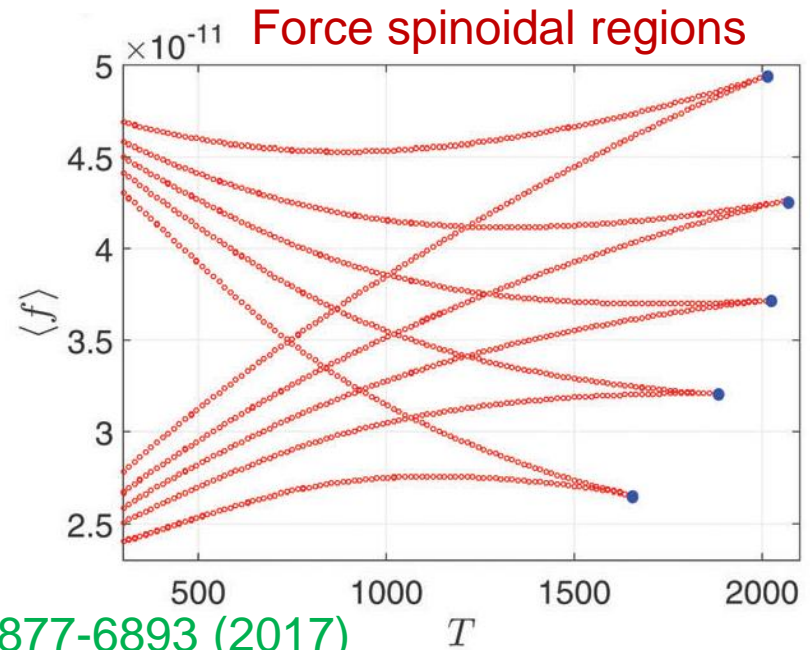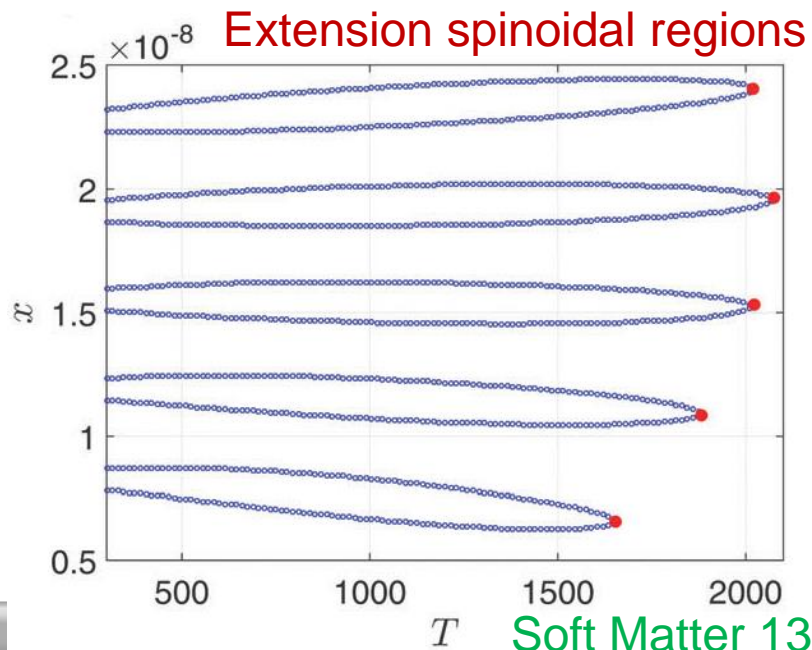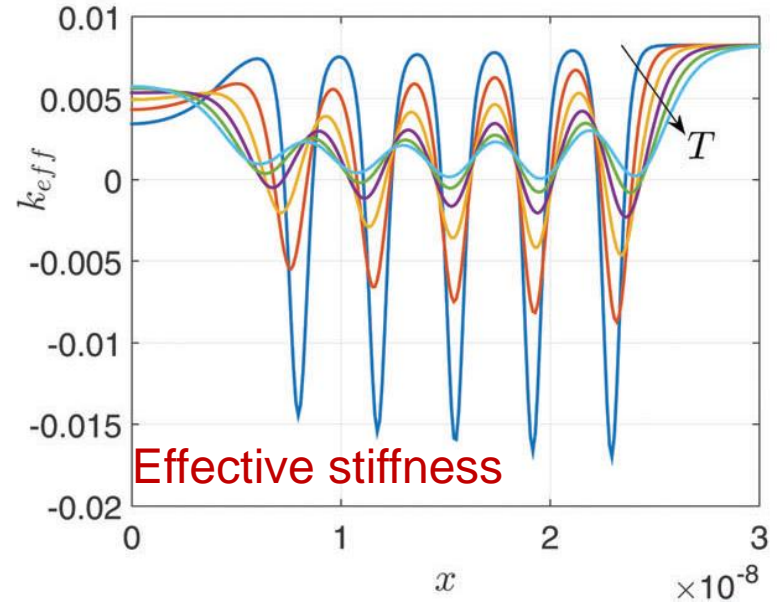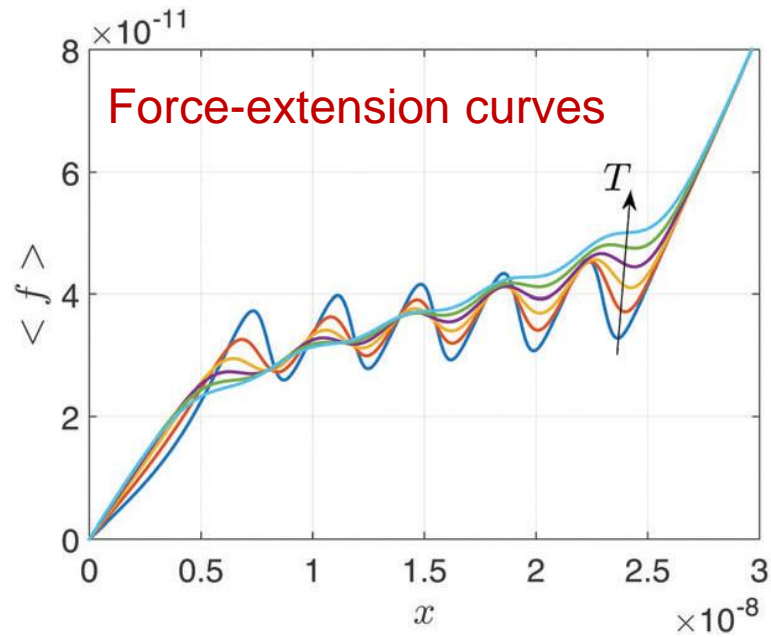
f (Gibbs)

$$\langle f \rangle = -k_B T \frac{\partial \log Z_H}{\partial r}$$
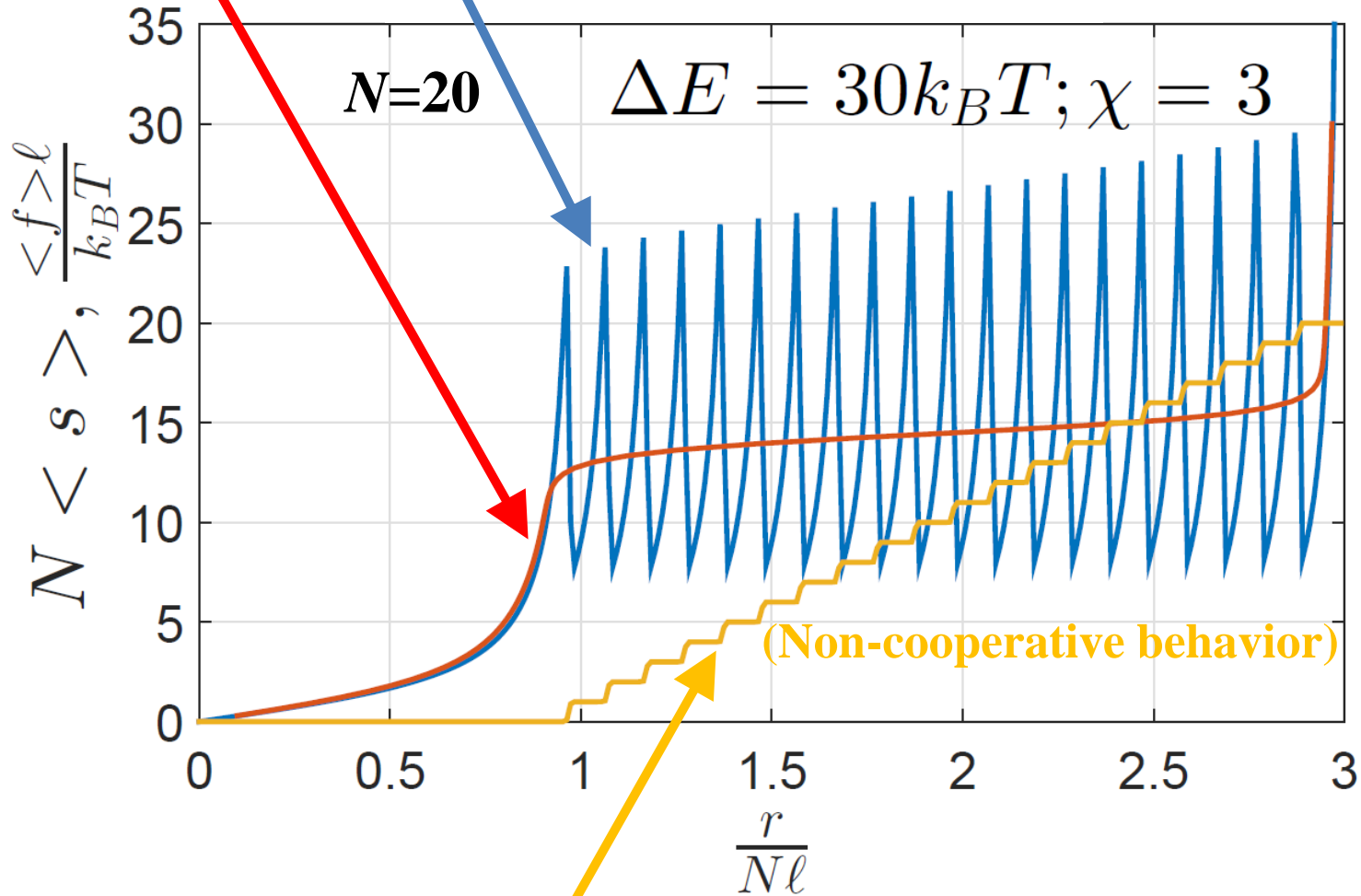
N=20

$$\Delta E = 30 k_B T; \chi = 3$$

(Non-cooperative behavior)

$$\frac{r}{N\ell}$$

$$N \langle s \rangle = \left\langle \sum_{i=1}^{N} s_i \right\rangle = -k_B T \frac{\partial \log Z_H}{\partial \Delta E}$$

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Equivalence of the ensembles in the thermodynamic limits

$N=25$

$N=10$

$\frac{<f>\ell}{k_B T}$

Gibbs

$\frac{r}{N\ell}$

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Critical behavior

Force-extension curves

Effective stiffness

Extension spinoidal regions

Force spinoidal regions

Two-state freely jointed chains with extensible units

a) Gibbs ensemble

z

applied f

measured $< z >$

- folded domain
- unfolded domain

x

y

b) Helmholtz ensemble

z

imposed z

measured $< f >$

x

y

Dimensionless extensibility

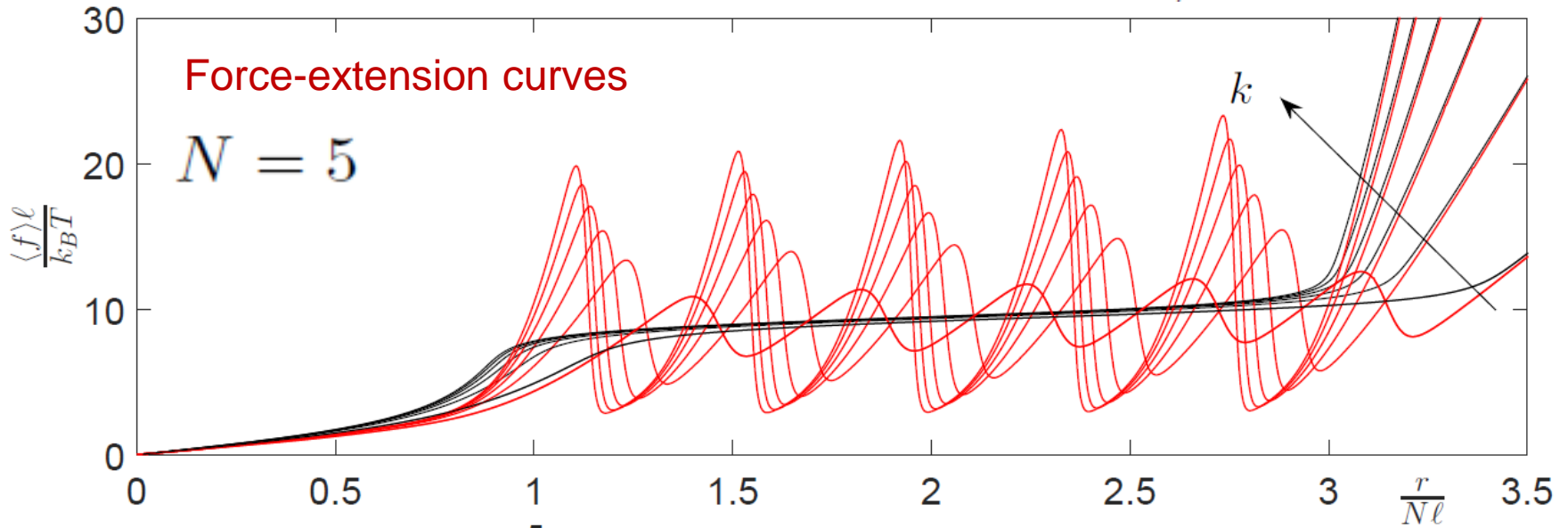$$\alpha = \frac{K_B T}{k \ell^2}$$

Dimensionless force

$$y = \frac{\ell f}{k_B T}$$

$$Z_G(f) = \left(\frac{\sinh y}{y} + \phi \chi \frac{\sinh \chi y}{y} \right)^N \exp \left(\frac{N \alpha y^2}{2} \right)$$

$$Z_H(r) = -\frac{1}{2r} \sum_{k=0}^{N} \sum_{p=0}^{N-k} \sum_{q=0}^{k} \binom{N}{k} \binom{N-k}{p} \binom{k}{q} (-1)^{p+q}$$

$$\times (\chi \phi)^k \left[\sqrt{\pi} \left(\frac{N\alpha}{2} \right)^{\frac{N-2}{2}} e^{-\frac{\Lambda^2}{2N\alpha}} H_{-N+1} \left(\frac{\Lambda}{\sqrt{2N\alpha}} \right) \right.$$

$$\left. + \mathbf{1}(\Lambda) \sum_{h=0}^{\left[\frac{N}{2}-1 \right]} \frac{(-1)^{N-1} \pi \left(\frac{\Lambda}{2} \right)^{N-2}}{h!(N-2-2h)!} \left(\frac{N\alpha}{2\Lambda^2} \right)^h \right],$$

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$$\Lambda = k - N + 2p - \chi k + 2\chi q - \frac{r}{\ell}$$

$k = 0.4\, j\, \mathrm{N/m},\ \forall j = 1, ..., 6$

Force-extension curves

$N = 5$

k

Average number of unfolded units

k

(JCP submitted)

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$\ell = 0.5 \times 10^{-9}\mathrm{m},\ T = 300\mathrm{K},\ \chi = 3,\ \Delta E = 20 k_B T = 8.28 \times 10^{-20}\mathrm{J}$
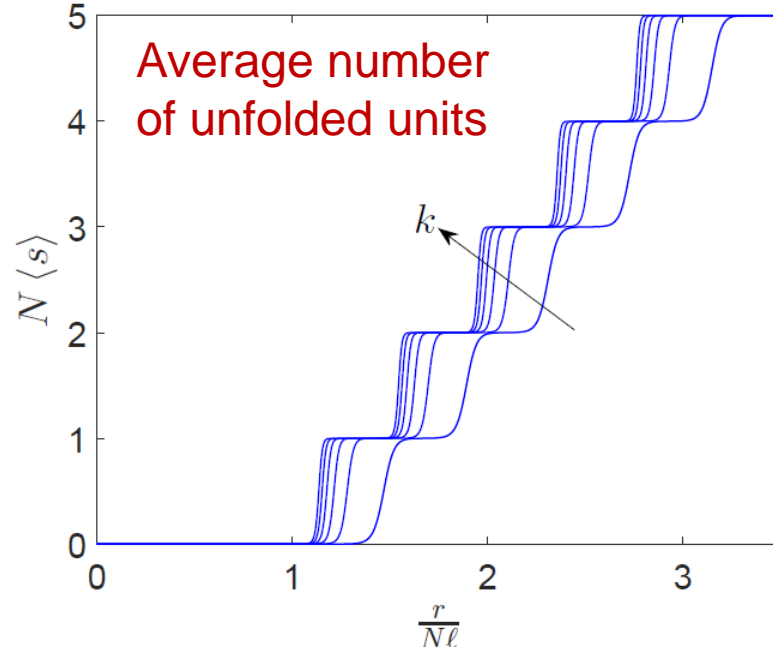
The interactions among the units

Ising potential energy $(s_i=-1,+1; \lambda>0$ ou $\lambda<0)$:

$$U_{tot} = -\lambda \sum_{i=1}^{N-1} s_i\, s_{i+1} - \vec{f} \cdot \vec{r}_N + \sum_{i=1}^{N} \left\{ v(s_i) + \frac{1}{2} k(s_i) \Big[\|\vec{r}_i - \vec{r}_{i-1}\| - \ell(s_i) \Big]^2 \right\}$$

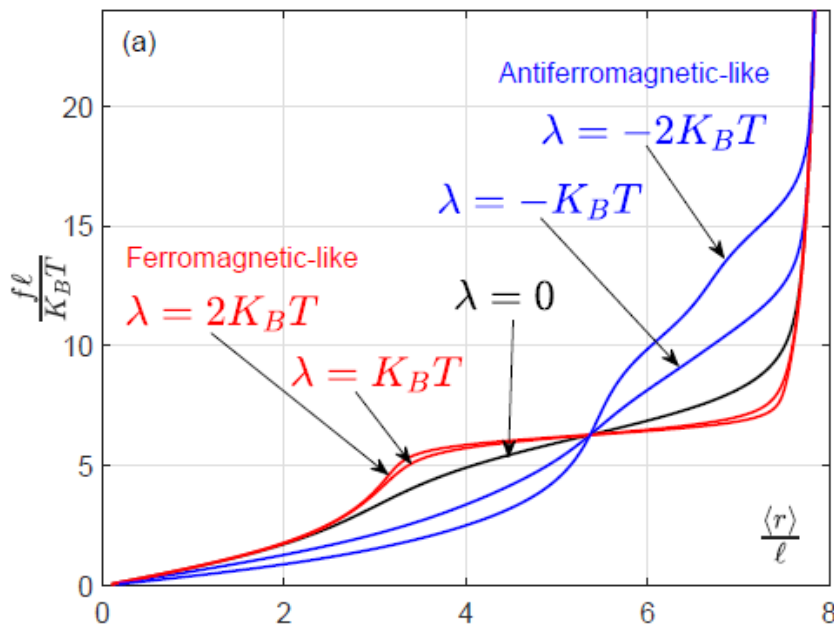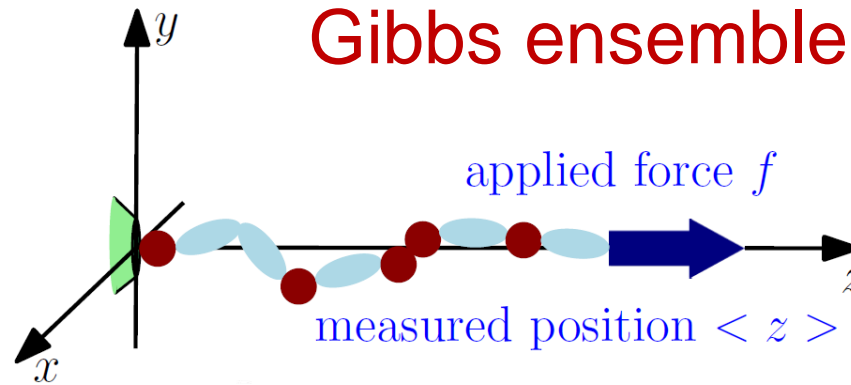(coupling betweeen elasticity and units folded-unfolded states)

● Folded unit
● Unfolded unit
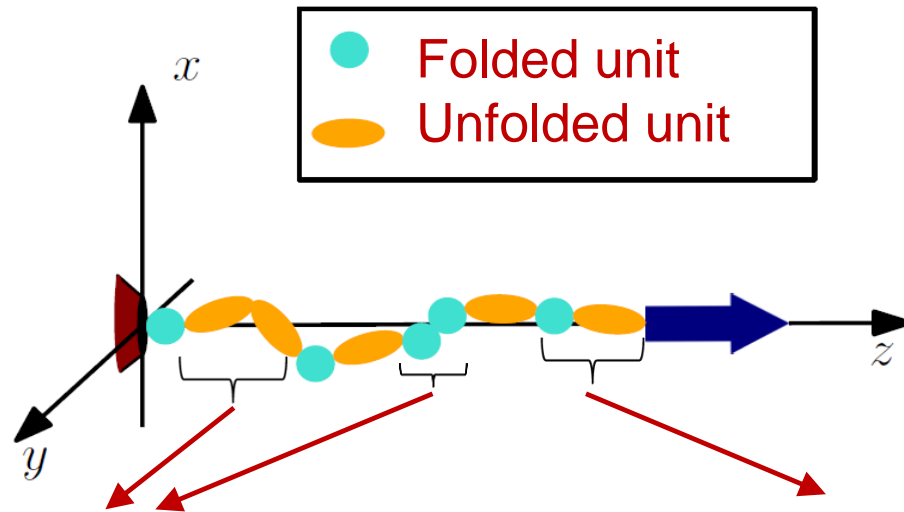
Positive interaction $(\lambda>0)$,
analogy with *ferromagnetism*
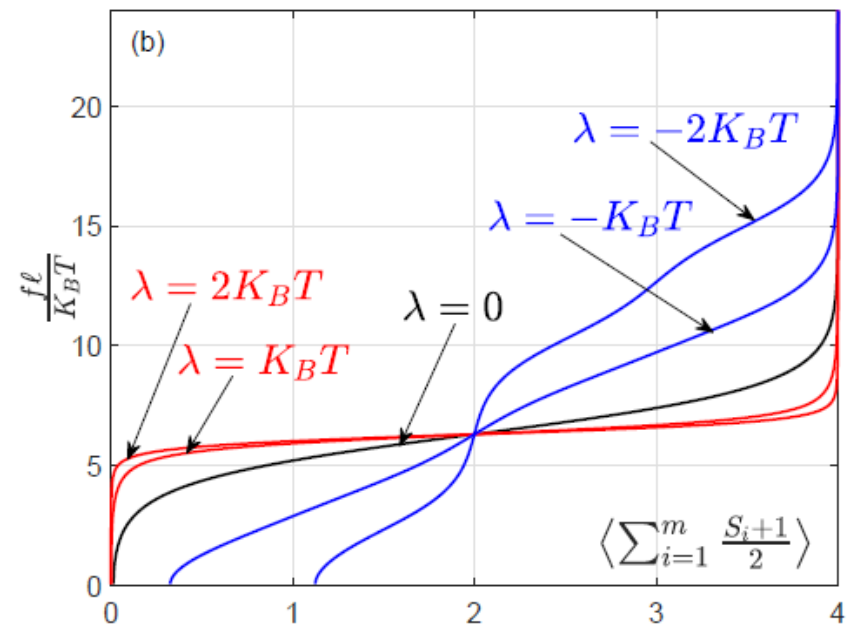
Negative interaction $(\lambda<0)$
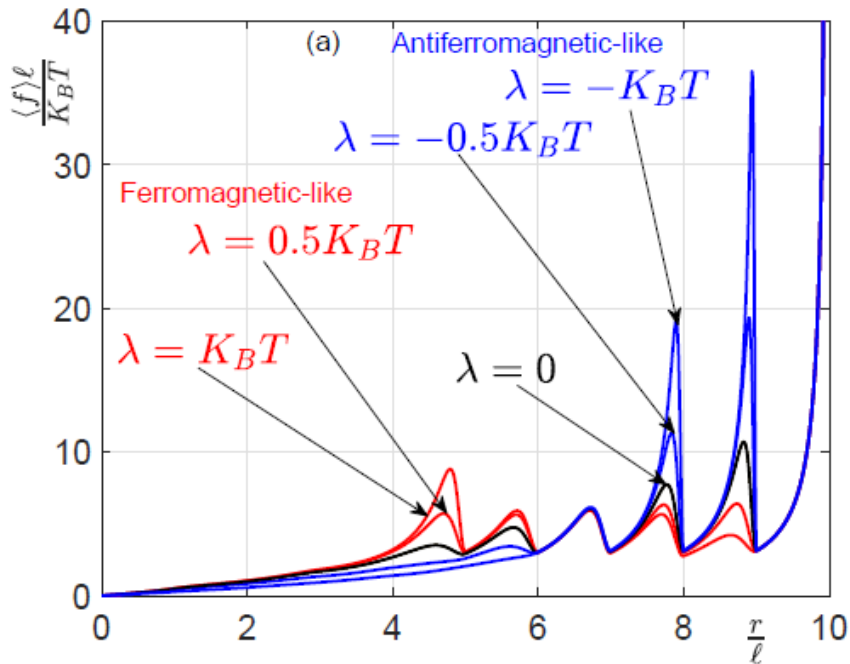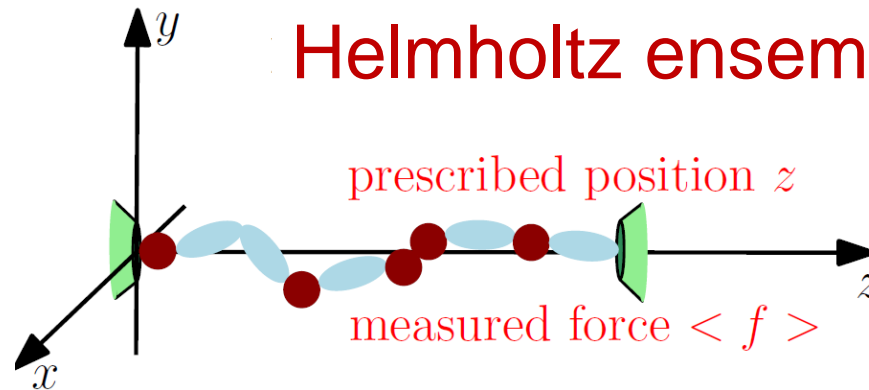analogy with *antiferromagnetism*

(PRE submitted)

Gibbs ensemble

applied force f

measured position $< z >$

Force-extension curves

Average number of unfolded units

Helmholtz ensemble

prescribed position z

measured force $< f >$

Force-extension curves

Average number of unfolded units

(PRE submitted)

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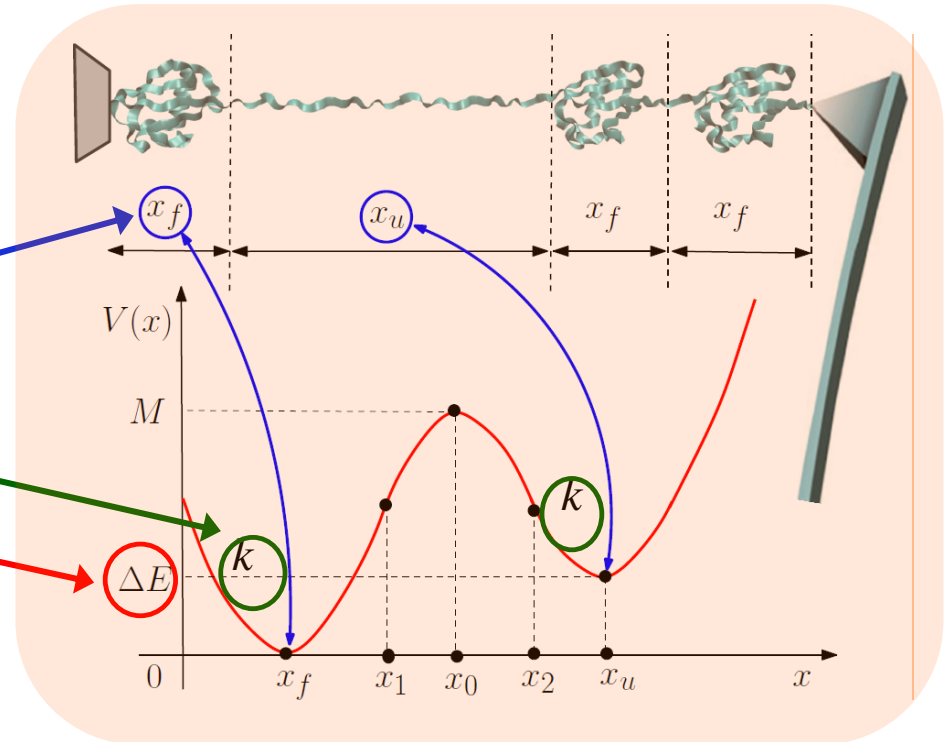UMR CNRS 8520
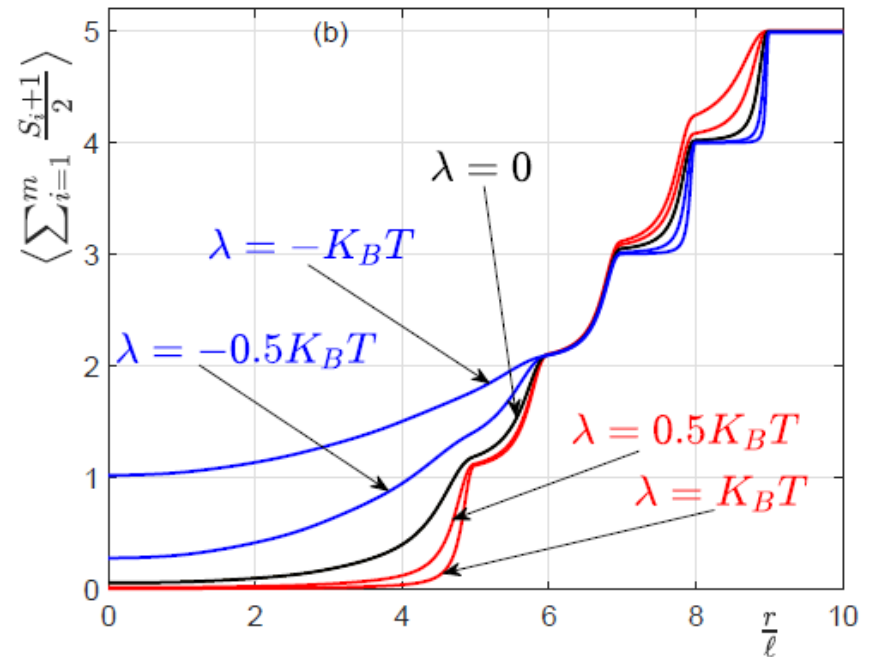
Perspective: heterogeneity of the chain

Heterogeneous units with respects to:
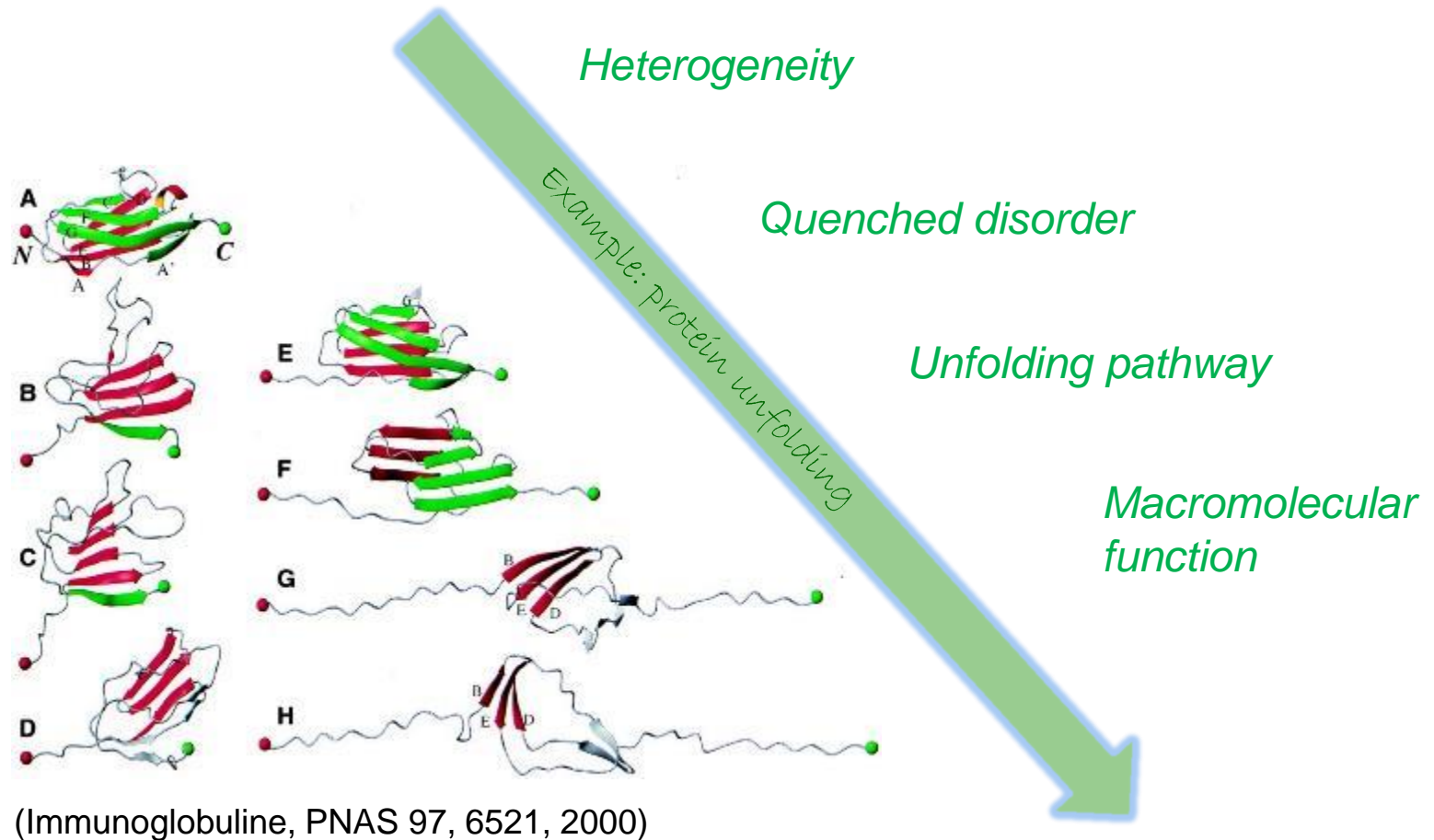
- Unit length
- Unit stiffness
- Energy jump

(*topologic* et *energetic* heterogeneity)

Without heterogeneity
- ✓ Same unfolding probability for the units;
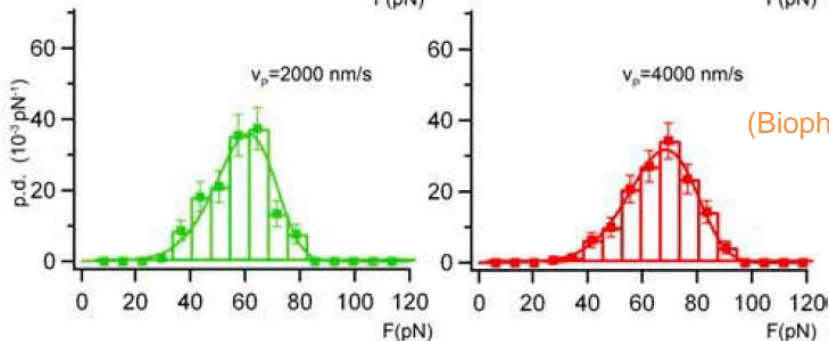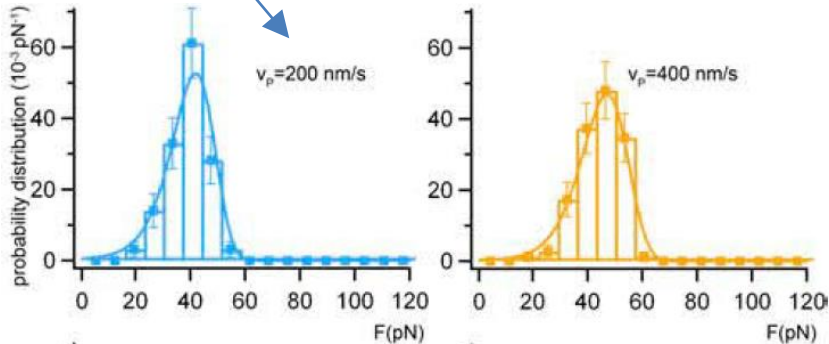- ✓ We cannot have an unfolding pathway.

Perspective: heterogeneity of the chain
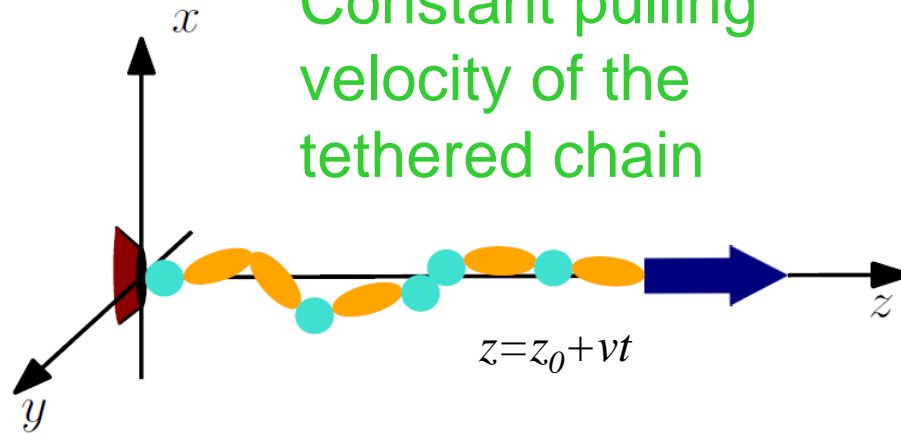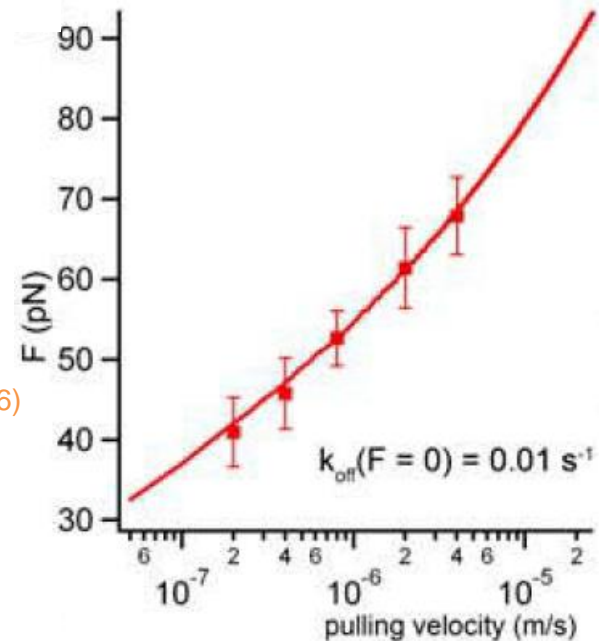

Heterogeneity

Quenched disorder

Unfolding pathway

Macromolecular function

Example: protein unfolding

(Immunoglobuline, PNAS 97, 6521, 2000)

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Perspective: unfolding dynamics

Constant pulling velocity of the tethered chain

Force peaks histograms

$$z=z_0+vt$$

v_p=200 nm/s

v_p=400 nm/s

v_p=2000 nm/s

v_p=4000 nm/s

probability distribution (10^{-3} pN^{-1})

p.d. (10^{-3} pN^{-1})

F(pN)

F(pN)

(Biophys. J. 90, L33, 2006)

F (pN)

k_{off}(F = 0) = 0.01 s^{-1}

pulling velocity (m/s)

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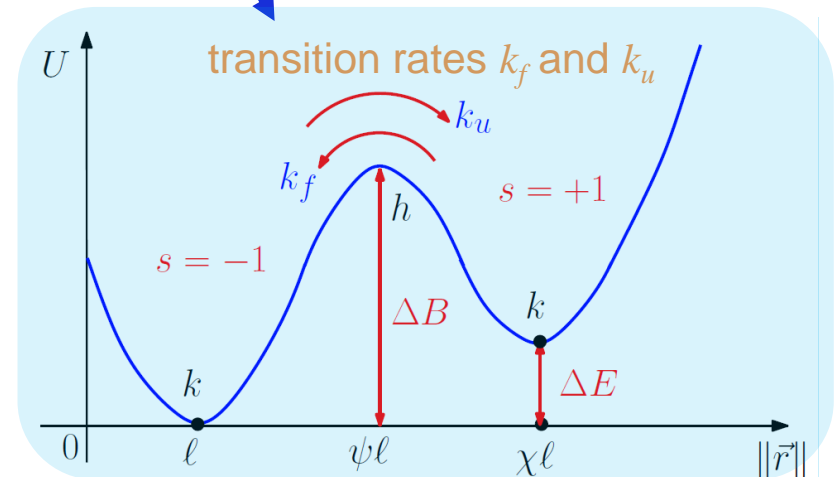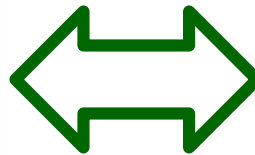Institut d'Electronique, de Microélectronique et de Nanotechnologie
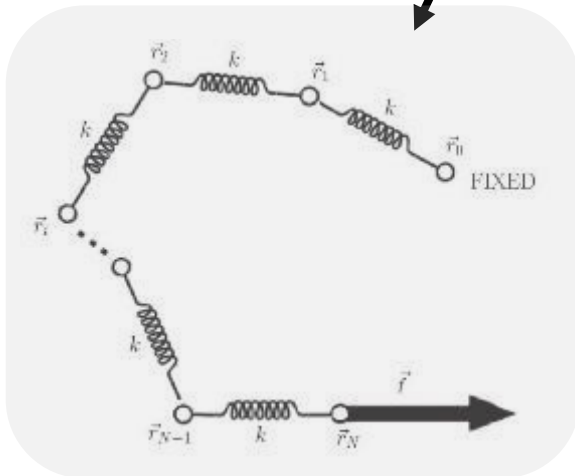
Perspective: unfolding dynamics

Exploiting the spin variable approach to

decupling the characteristic times

mechanical   **induced by energy barriers**

Conclusion

- The rescaling (multiscale) methods for the nanomechanics of macromolecules strongly depend on the applied boundary conditions (imposed force or prescribed extension);

- This is important for the thermodynamic of small systems, which are far from the thermodynamic limit (small number of unit in the chains);

- The spin variable approach allows the analysis of the system within both the Gibbs and Helmholtz ensembles, giving results in qualitative agreement with experiments;

- Moreover, it can be adopted to develop several generalization concerning finite stiffness and Ising interactions (already implemented) or heterogeneity and dynamics (work on progress);

- Interactions and heterogeneity will help the understanding of cooperativity and folding pathways in complex macromolecules (such as proteins).

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THANK YOU FOR YOUR ATTENTION !

Main publications:

JCP 137, 244907 (2012)
JCP 136, 154906 (2012)
PRE 87, 032705 (2013)
Phys. A: Stat. Mech. Appl. 395, 154 (2014)
PRL 113, 255501 (2014)
EPJE 38, 44 (2015)
Eur. J. Mech. - A/Sol. 60, 145 (2016)
Annalen der Physik 528, 381 (2016)
Microsystems & Nanoengineering 2, 16062 (2016)
Soft Matter 13, 6877-6893 (2017)
Continuum Mechanics and Thermodynamics 30, 459 (2018)

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