Curvature of the energy landscape and folding of model proteins

Lorenzo N. Mazzoni & Lapo Casetti

Dipartimento di Fisica
& Centro per lo Studio delle Dinamiche Complesse
Università di Firenze, Italy

CSDC
CENTRO STUDI DINAMICHE COMPLESSE

Embio meeting Vienna

STUDIORUM UNIVERSITAS FLORENTINA

[Lorenzo N. Mazzoni, Lapo Casetti, arXiv:cond-mat/0603409]

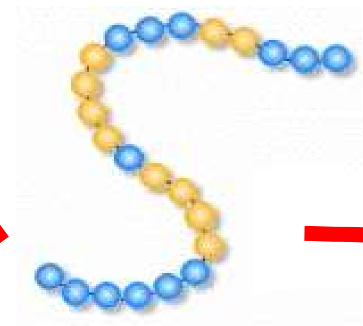
Topics

- Energy landscape
- Curvature
- Model
- Results
- Effective potential

aminoacid chain

protein

swollen



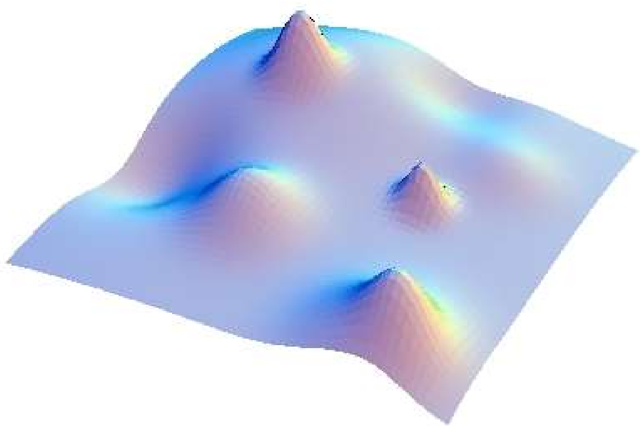
Compact structures

Compact structures

Native state

Which is the difference?

Energy landscape



$V(q_1,\ldots,q_N)$

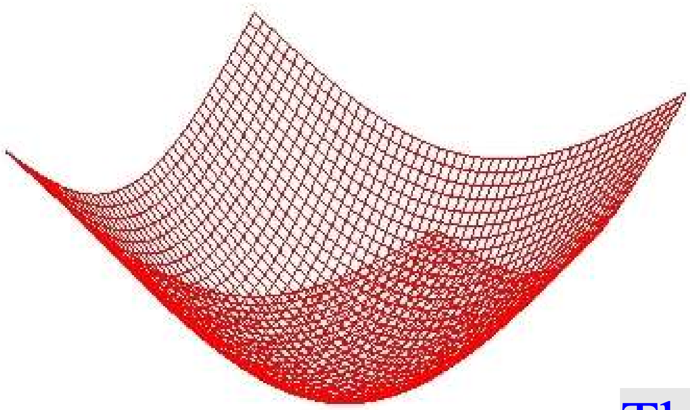
How to study the energy landscape?

Local properties

Global properties

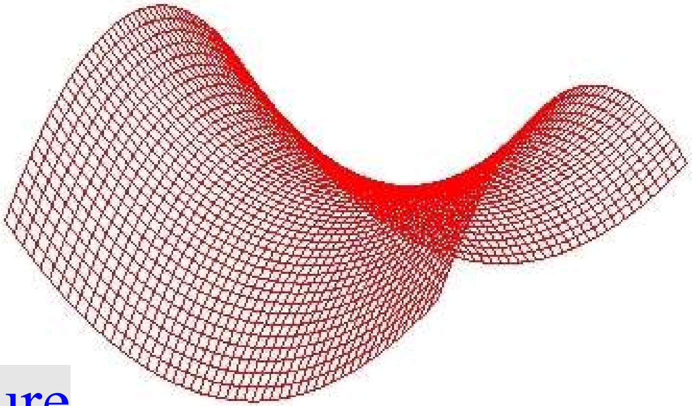
[L. Bongini et al., Phys. Rev. E **68**, 061111 (2003); **72**, 051929 (2005)]

Main regions of the energy landscape



minima

They have different curvature



saddles

↓

Could be interesting to calculate the curvature of the energy landscape

↓

We need a metric

Metric and curvature

local coordinates → to locate things

to measure lengths ← metric g

- *metric* → $ds^2 = g_{ij}(q)\,dq^i\,dq^j$
- *curvature tensor* → $R^i_{\ jkl} = \partial_k \Gamma^i_{\ jl} - \partial_j \Gamma^i_{\ kl} + \Gamma^r_{\ jl}\Gamma^i_{\ kr} - \Gamma^r_{\ kl}\Gamma^i_{\ jr}$
- *Ricci tensor* → $R_{ij} = R^k_{ikj}$
- *scalar measure of curvature* → $K_R(v) = R_{ij}\,v^i\,v^j$

Which metric?

- given by the immersion of V in $\mathbb{R}^{N+1}$
- other options...

Eisenhart metric

g_E

$$g_E = \begin{pmatrix} -2V(q) & 0 & \cdots & 0 & 1 \\ 0 & 1 & \cdots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \cdots & 1 & 0 \\ 1 & 0 & \cdots & 0 & 0 \end{pmatrix}$$

physical

geodesics of (M, g_E) ⟷ dynamical trajectories of the system

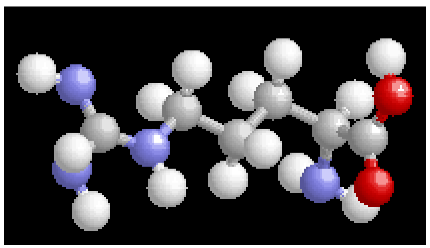
$$R_{0i0j} = \partial_i \partial_j V$$

$$K_R(v) = \Delta V$$

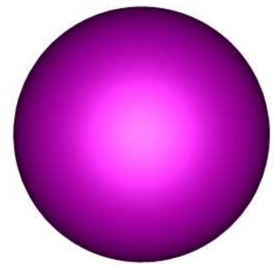
simple

Coarse grained models

Minimal models → coarse grained description

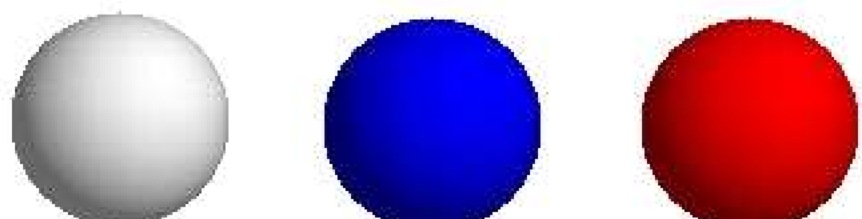


→



Thirumalai model → only three kinds of beads

(Klimov & Thirumalai, 1996)



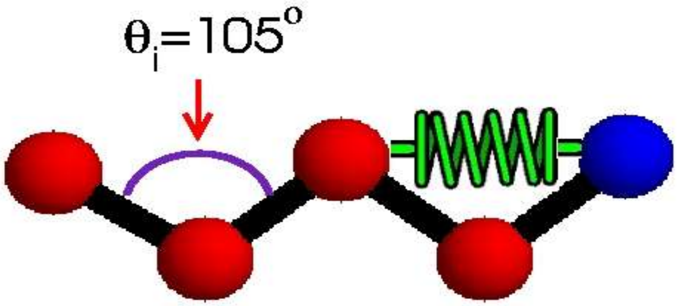
Potential energy

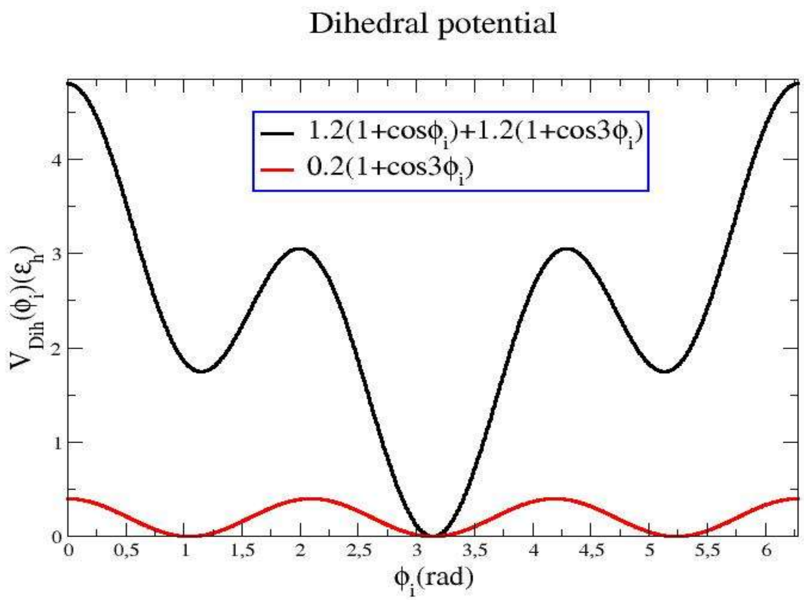
Potential energy

$$V(q_1,\ldots,q_N) = V_{Pep} + V_{Ang} + V_{Dih} + V_{NB}$$

$$V_{Pep} = \sum_{i=1}^{N-1} k_r (d_i - a)^2$$

$$V_{Ang} = \sum_{i=1}^{N-2} k_\theta (\theta_i - \theta_0)^2$$

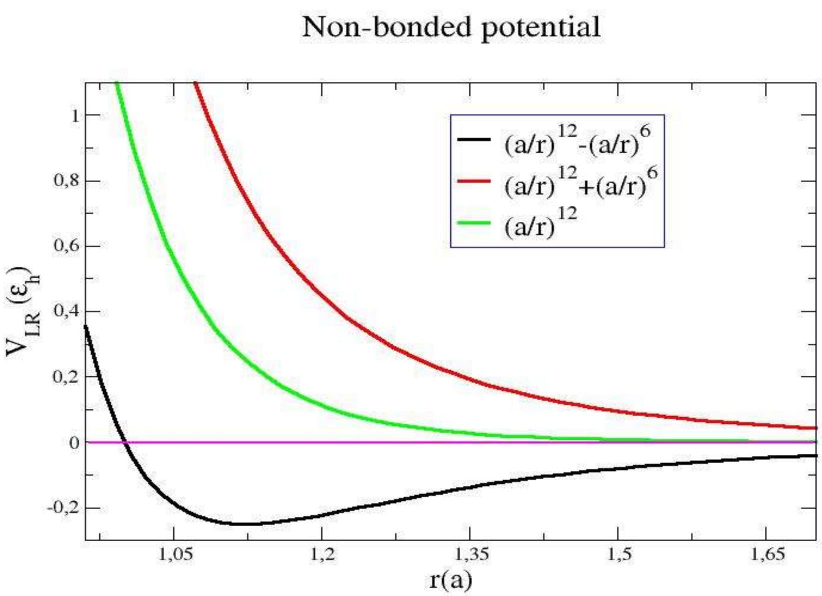




Dihedral potential

$$V_{Dih} = \sum_{i=1}^{N-3} [A_i(1+\cos(\phi_i)) + B_i(1+3\cos(\phi_i))]$$

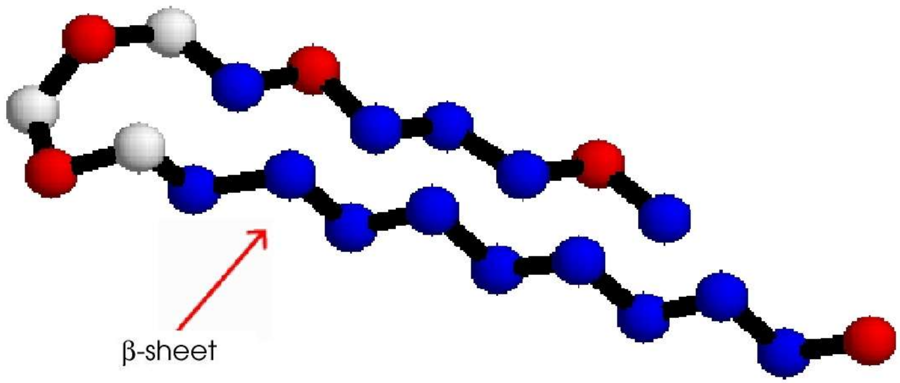
(non planar structures)



Non bonded potential

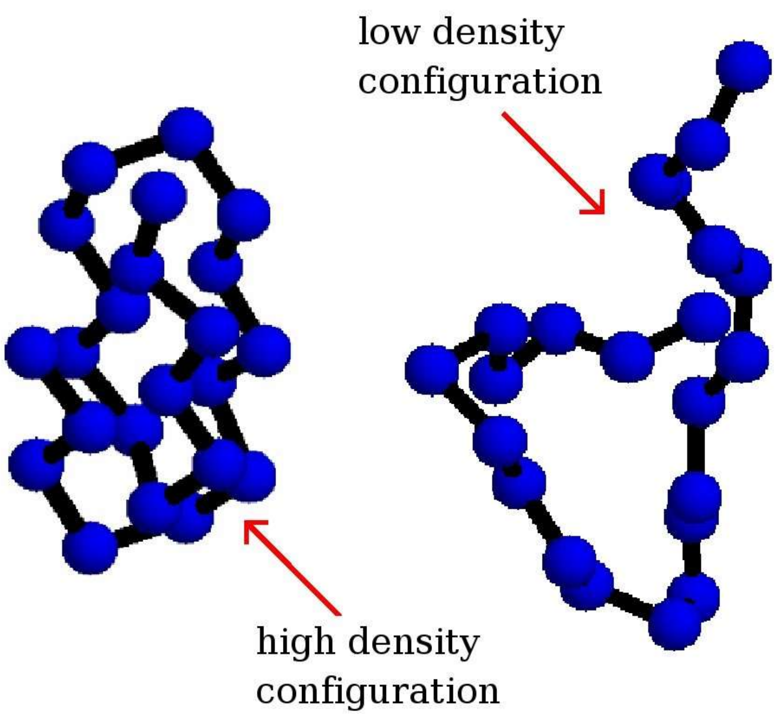
$$V_{NB} = \sum_{i=1}^{N-3} \sum_{j=i+3}^{N} V_{ij}(r)$$

(hydrophobic interaction)



Good folder

- folding transition
- only one compact structure
- protein like behaviour

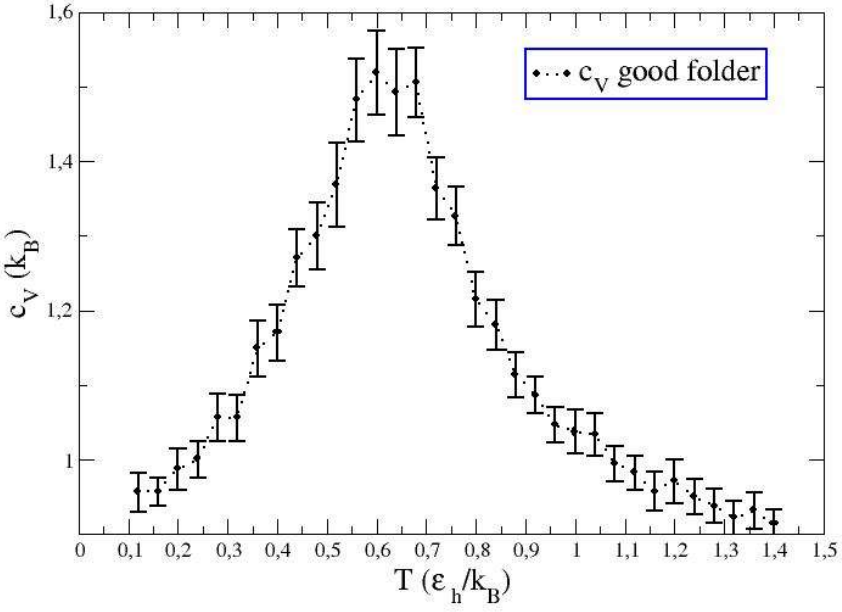


bad folder

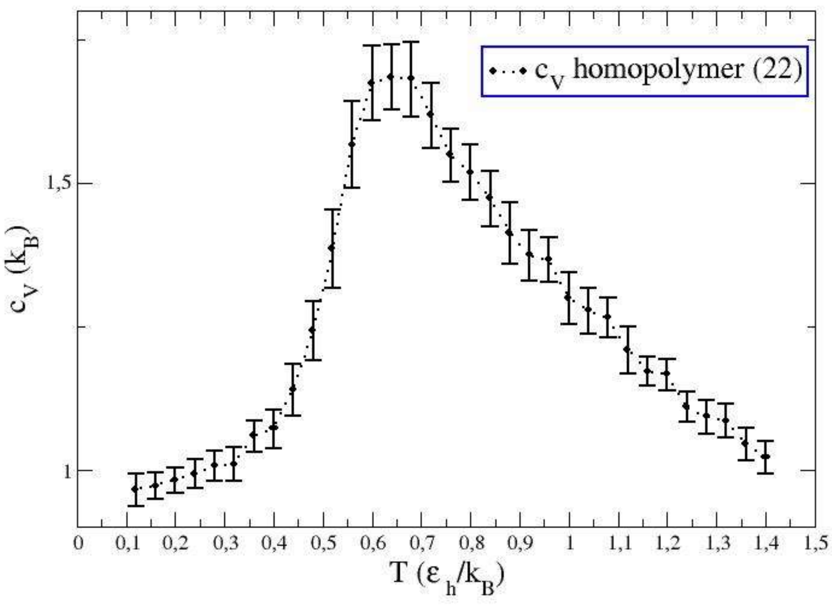
- Θ transition
- many compact structures

Thermodynamics

protein-like



homopolymer



Geometrical quantities

Curvature fluctuations

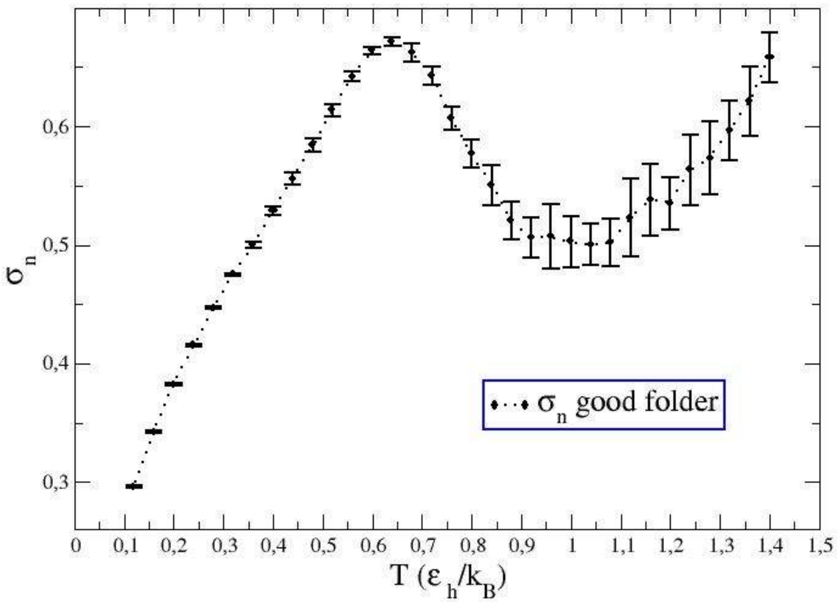
$$\sigma_K = \left[\frac{1}{N} \left(\langle K_R^2 \rangle - \langle K_R \rangle^2 \right) \right]^{\frac{1}{2}}$$

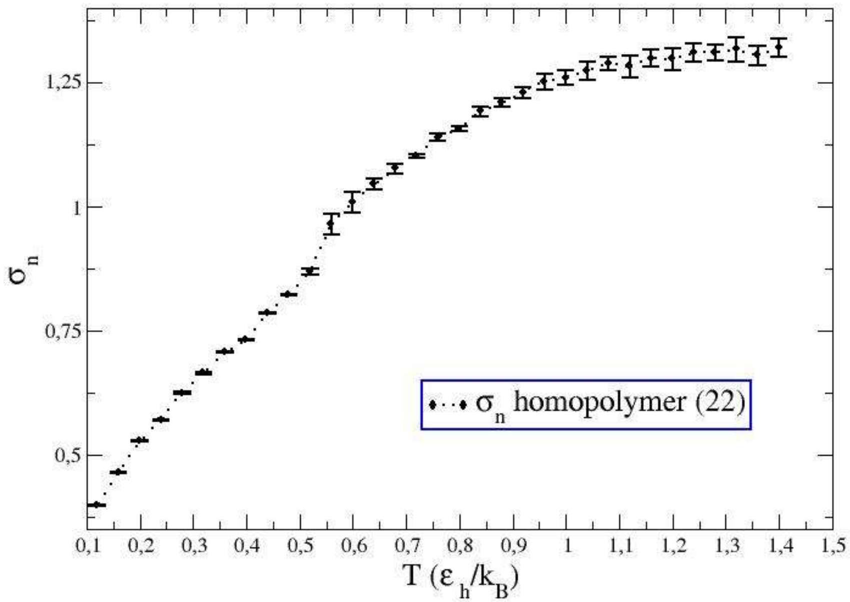
Normalized curvature fluctuations

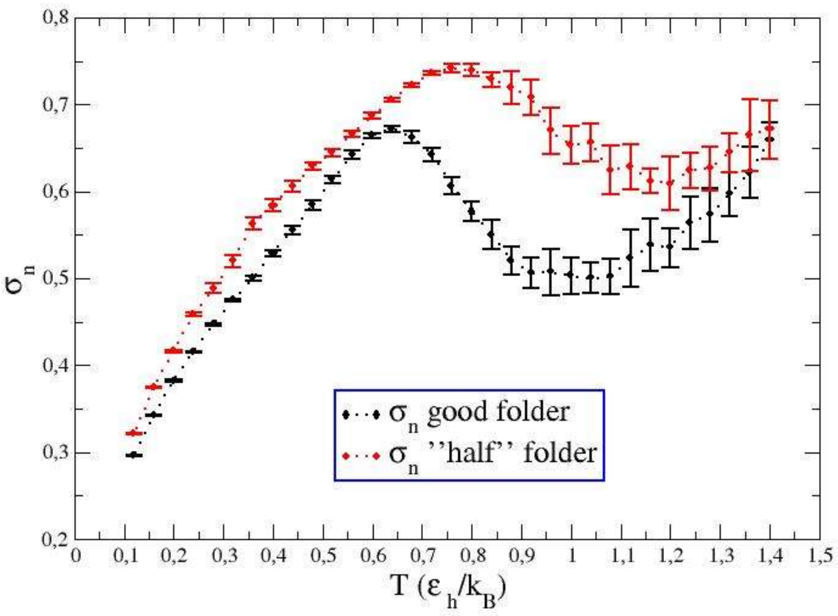
$$\sigma_n = \frac{\sigma_K}{\langle K_R \rangle}$$

protein-like

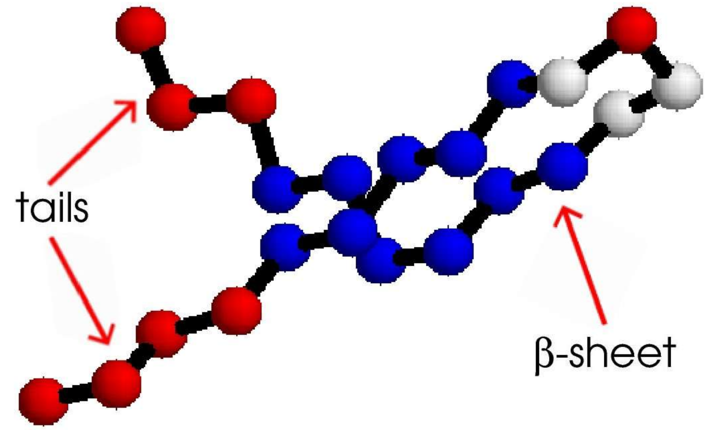
homopolymer







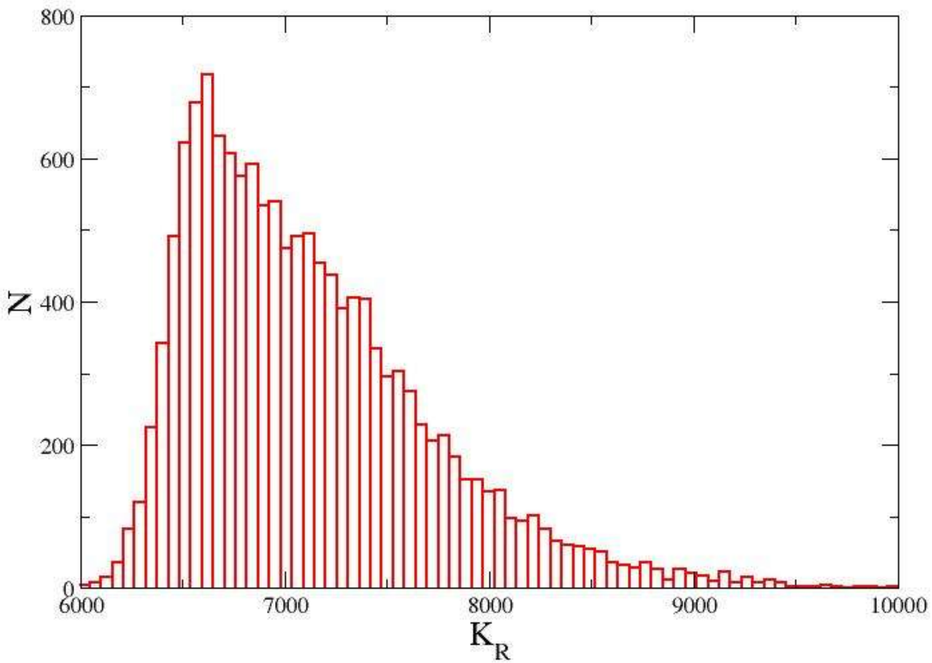
"half" folder



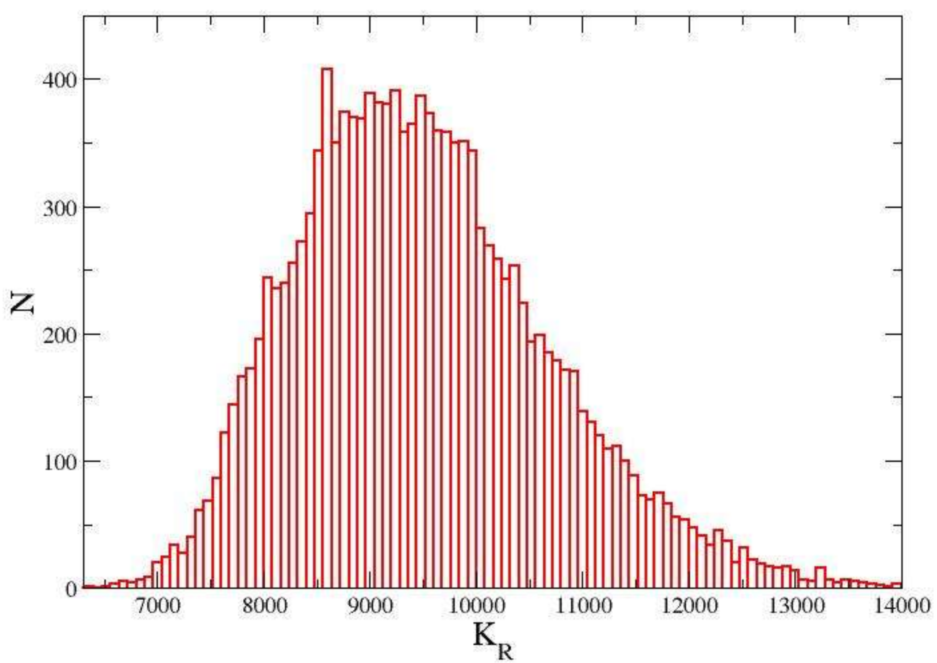
σ_n identifies "good folders" without knowing the native configuration

K_R distribution

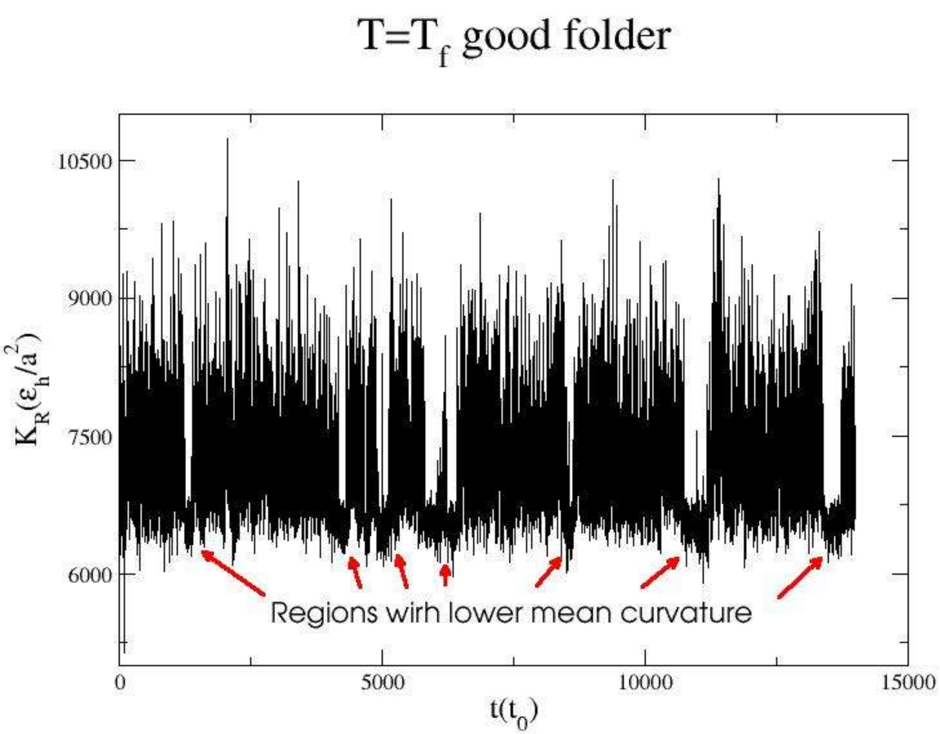
T=T_f (good folder)

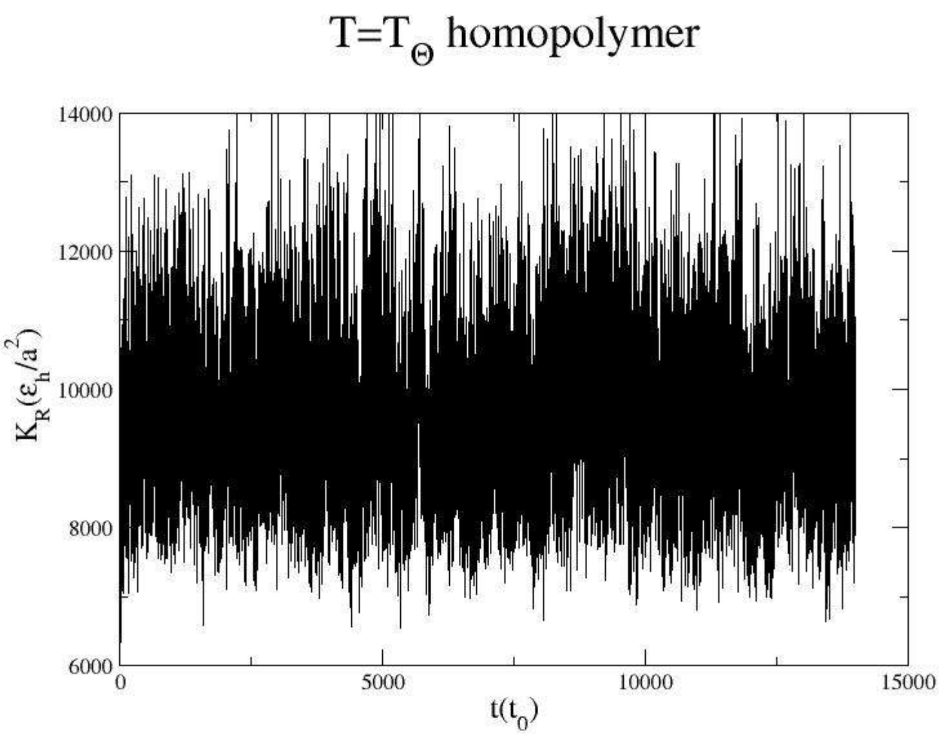


T=T_Θ (homopolymer)



asymmetric distribution



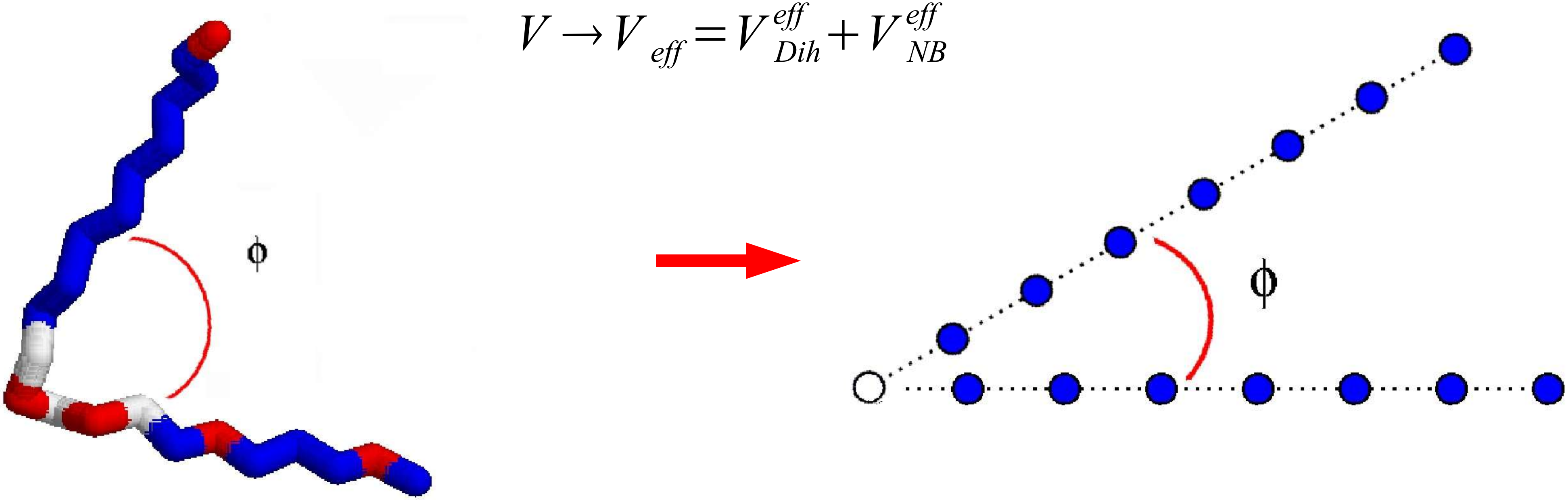


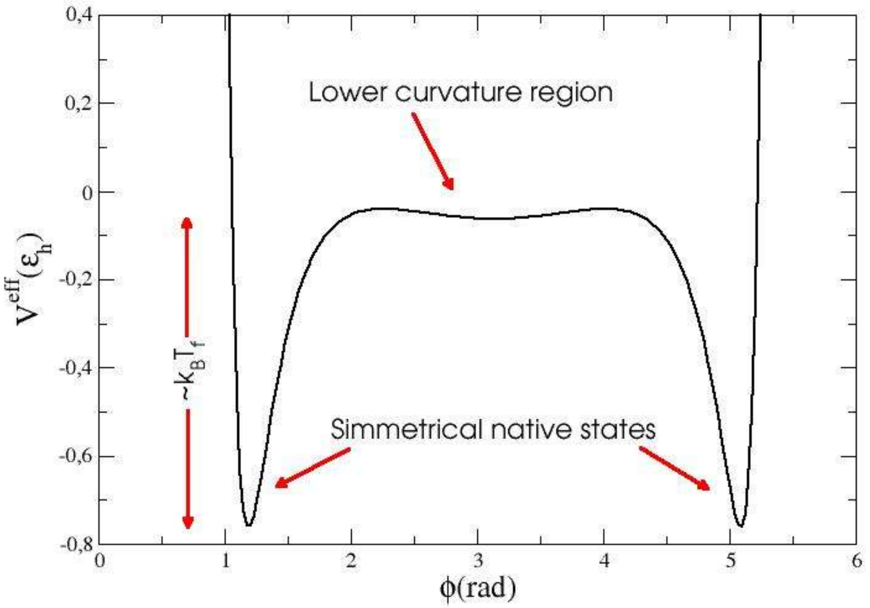
Near T_f the system visits regions of the energy landscape with smaller $\langle K_R \rangle$

An effective potential

We "freeze" degrees of freedom whose energy scales are larger than $k_B T_f$

$$V \rightarrow V_{eff} = V^{eff}_{Dih} + V^{eff}_{NB}$$





ϕ main degree of freedom

presence of a flat region

symmetry breaking

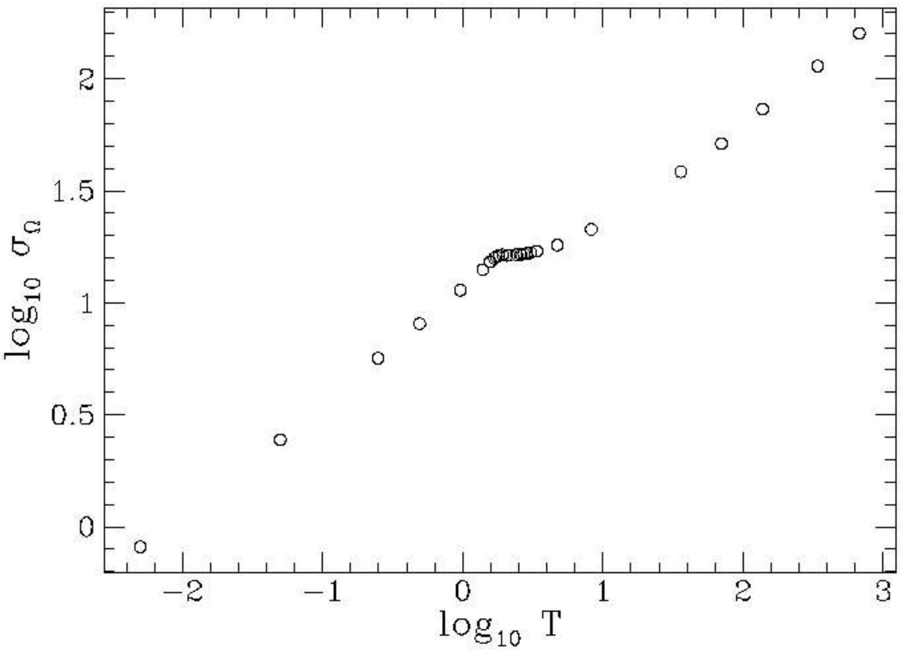
Protein-like behaviour

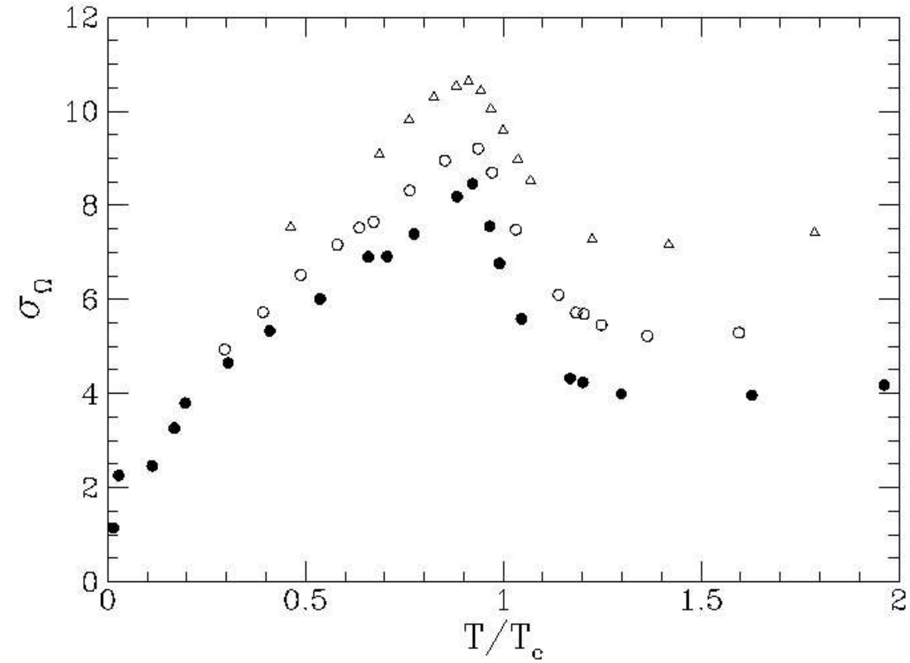
Conclusions

- Curvature fluctuation as geometrical marker of the folding
- Relevant degree of freedom for the good folder

☆Could be interesting to calculate σ_n using other models

[L. Casetti, M. Pettini, E. G. D. Cohen,
Phys. Rep. **337,** 237 (2000)]





BKT transition

↓

homopolymer

Symmetry breaking transition

↓

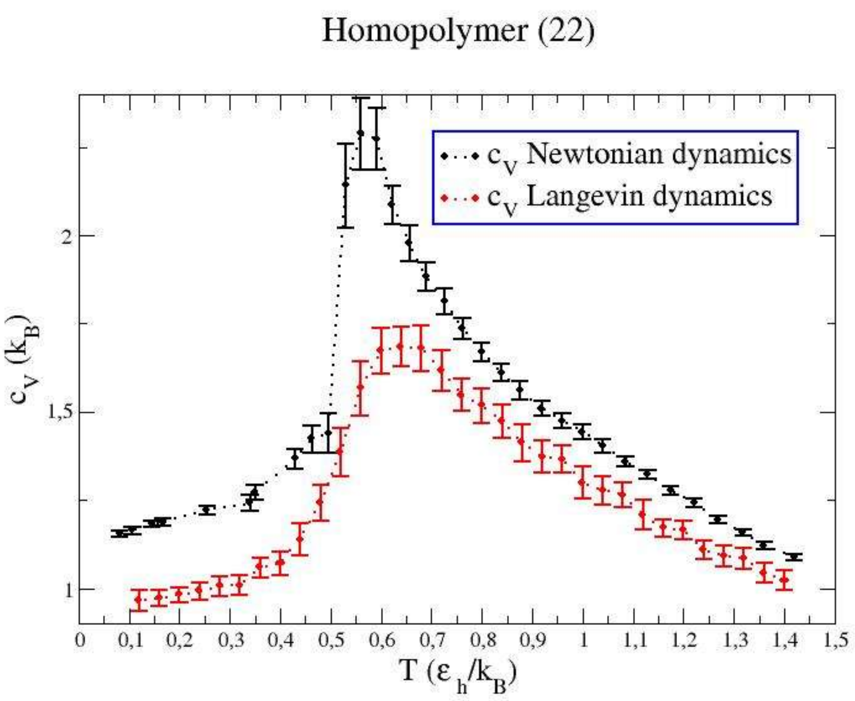
good folder

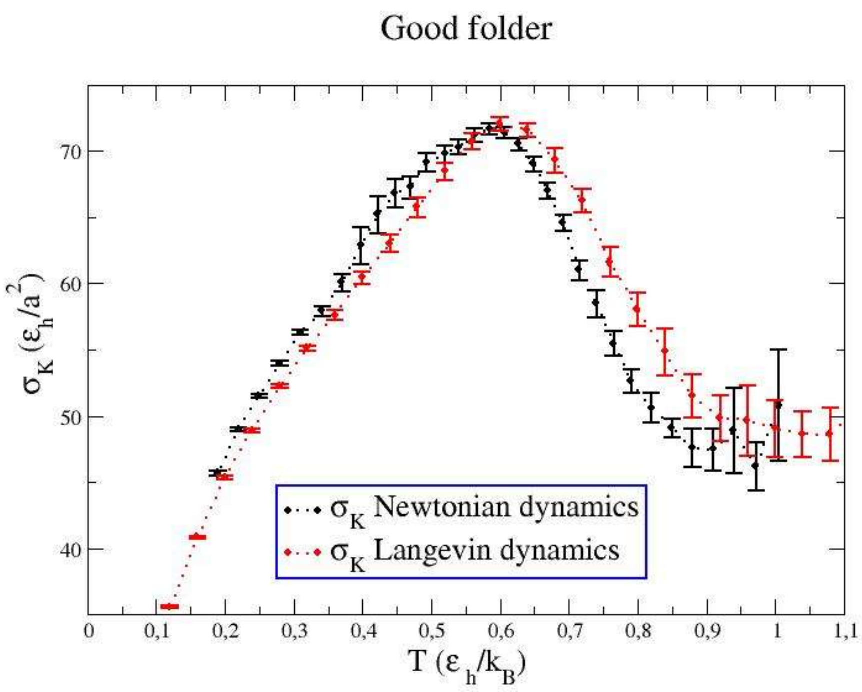
Newtonian dynamics

$$m\ddot{x}_i = -\nabla_{x_i} V$$

Langevin dynamics

$$m\ddot{x}_i = -\nabla_{x_i} V - \zeta \dot{x}_i + \Gamma$$





Same behaviour

$$\frac{D}{ds}\dot{\gamma} = \frac{d^2}{ds^2} q^i + \Gamma^i_{jk} \frac{dq^j}{ds} \frac{dq^k}{ds} = 0$$

geodesics

$$(M \times \mathbb{R}^2, g_E)$$

manifold

$$\pi : M \times \mathbb{R}^2 \rightarrow M \times \mathbb{R}$$

projection

Arc-lengths positive definite + $ds^2 = c^2 dt^2$

Trajectories of the system

geodesics equations → Newton equations