Hierarchical Subphase Transitions in Molecular First Order Nucleation Processes

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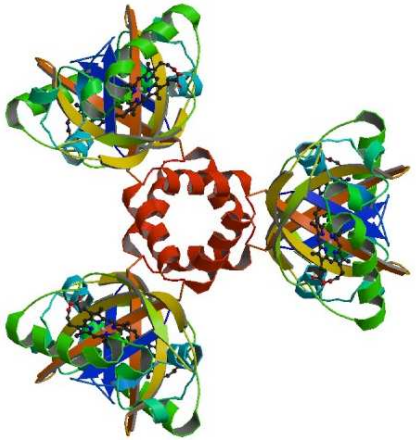


Workshop "Monte Carlo Algorithms in Statistical Physics", Melbourne, 26–28 July 2010

JÜLICH FORSCHUNGSZENTRUM

SOFT MATTER SYSTEMS RESEARCH GROUP

BONSAI — Bio-Organic Nucleation and Self-Assembly at Interfaces

0. Overview

1. Introduction

- Small systems • Temperature • Microcanonical analysis
- Multicanonical Monte Carlo method

2. Aggregation of Polymers

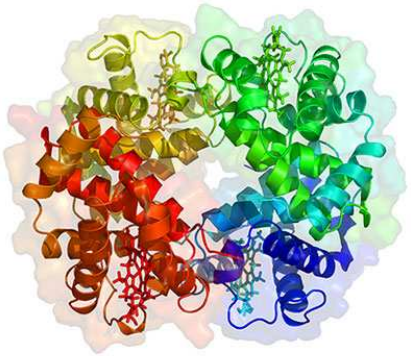
- Coarse-grained modeling of protein aggregation
- Canonical and microcanonical analysis • Hierarchy of subphases
- Homopolymer aggregation

3. Adsorption of Polymers at Substrates

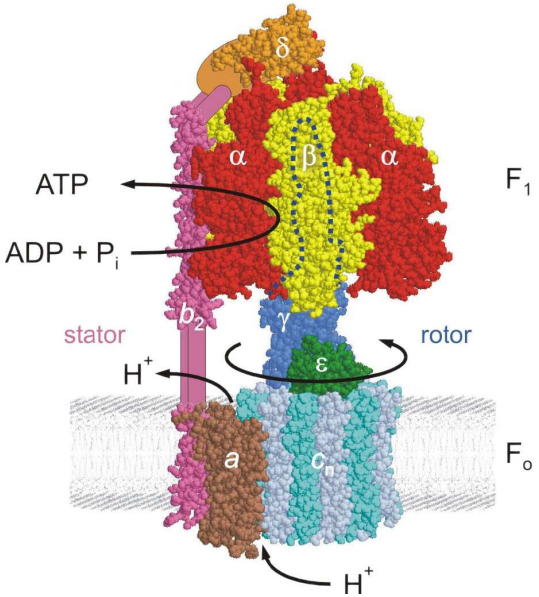
- Hybrid-system modeling • Flat substrates • Nanowires

Exemplified small molecular system: Proteins

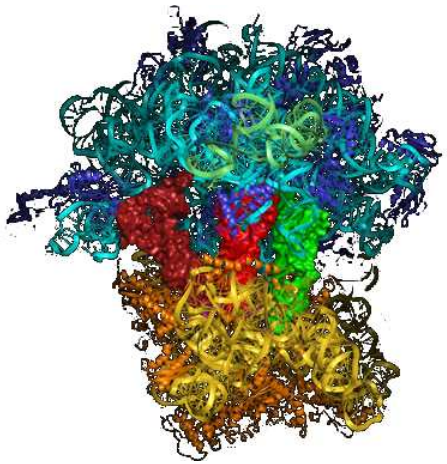
- Heterogeneous linear chains of 40...3000 amino acids
- Geometric structure $\Leftrightarrow$ Biological function
- Structure formation $\Leftrightarrow$ Structural phase transition?
- But: no thermodynamic limit, no scaling, no transition **points**
- Finite-size, surface, and disorder effects



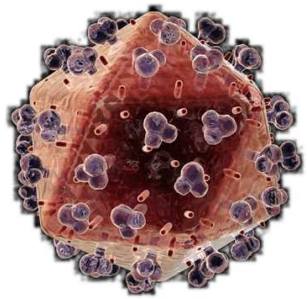
Hemoglobin
Oxygen transport in red blood cells, 4 units, 550 atoms



ATP synthase
Synthesis of ATP from ADP, 2 units, 40,000 atoms



Ribosome
Protein synthesis, 2 units, 200,000 atoms



Herpes
Icosahedral virus, 10^5–10^6 atoms

Definition of temperature

- microcanonical:

$$T^{\text{micro}}_{\text{system}}(E) = \left(\frac{\partial S^{\text{micro}}(E)}{\partial E} \right)^{-1}, \; S^{\text{micro}}(E) = k_B \ln g(E)$$

- canonical:

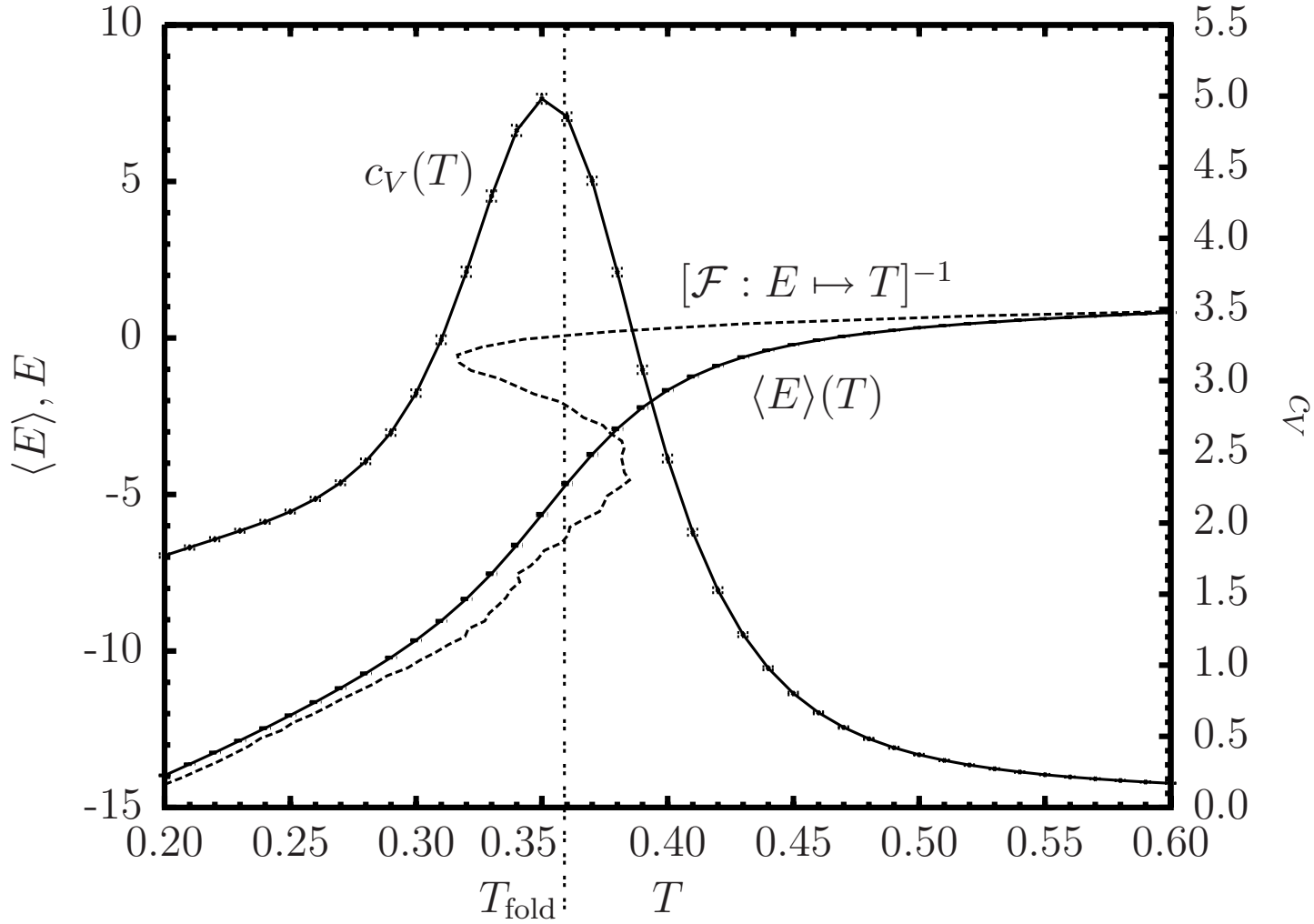
$$T_{\text{heatbath}} \equiv T^{\text{can}}_{\text{system}}(\langle E \rangle) = \left(\frac{\partial S^{\text{can}}(\langle E \rangle)}{\partial \langle E \rangle} \right)^{-1}_{N,V},$$

$$S^{\text{can}}(\langle E \rangle) = \frac{\langle E \rangle}{T^{\text{can}}_{\text{system}}(\langle E \rangle)} - k_B \ln Z(T^{\text{can}}_{\text{system}}(\langle E \rangle))$$

thermodynamic limit: $T^{\text{micro}}_{\text{system}} = T^{\text{can}}_{\text{system}}$

small systems: $T^{\text{micro}}_{\text{system}} \neq T^{\text{can}}_{\text{system}}$; deviation due to finite-size effects

Example: Two-state protein folding

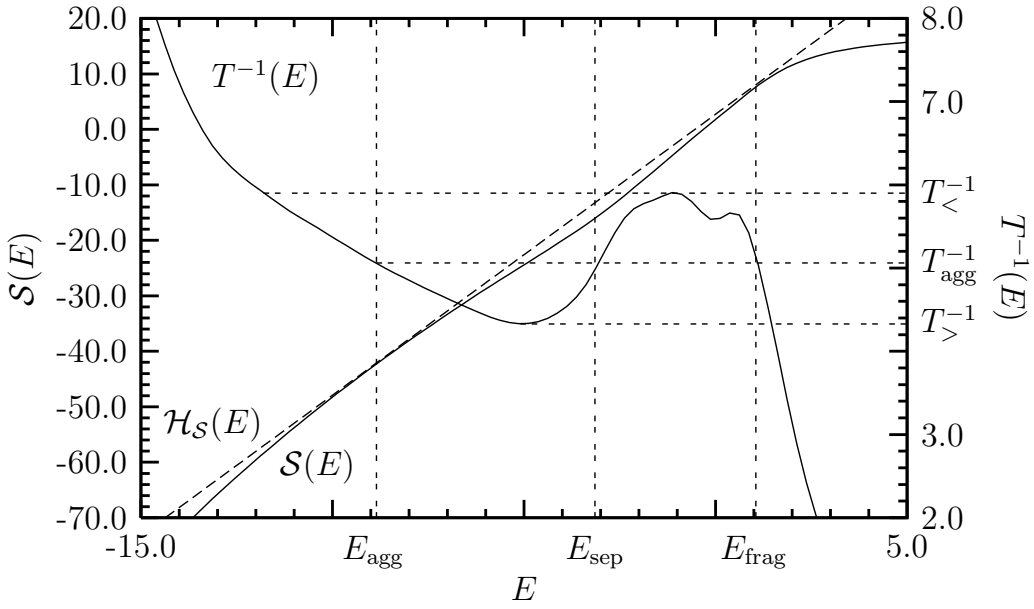


M.B., Phys. Proc. 3, 1387 (2010).

Microcanonical analysis

- Central quantity: density of states $g(E)$
- Microcanonical entropy: $S(E) = k_B \ln g(E)$
- Caloric temperature: $T(E) = [\partial S(E)/\partial E]^{-1}$

Example: Aggregation of two small (hetero)polymers:

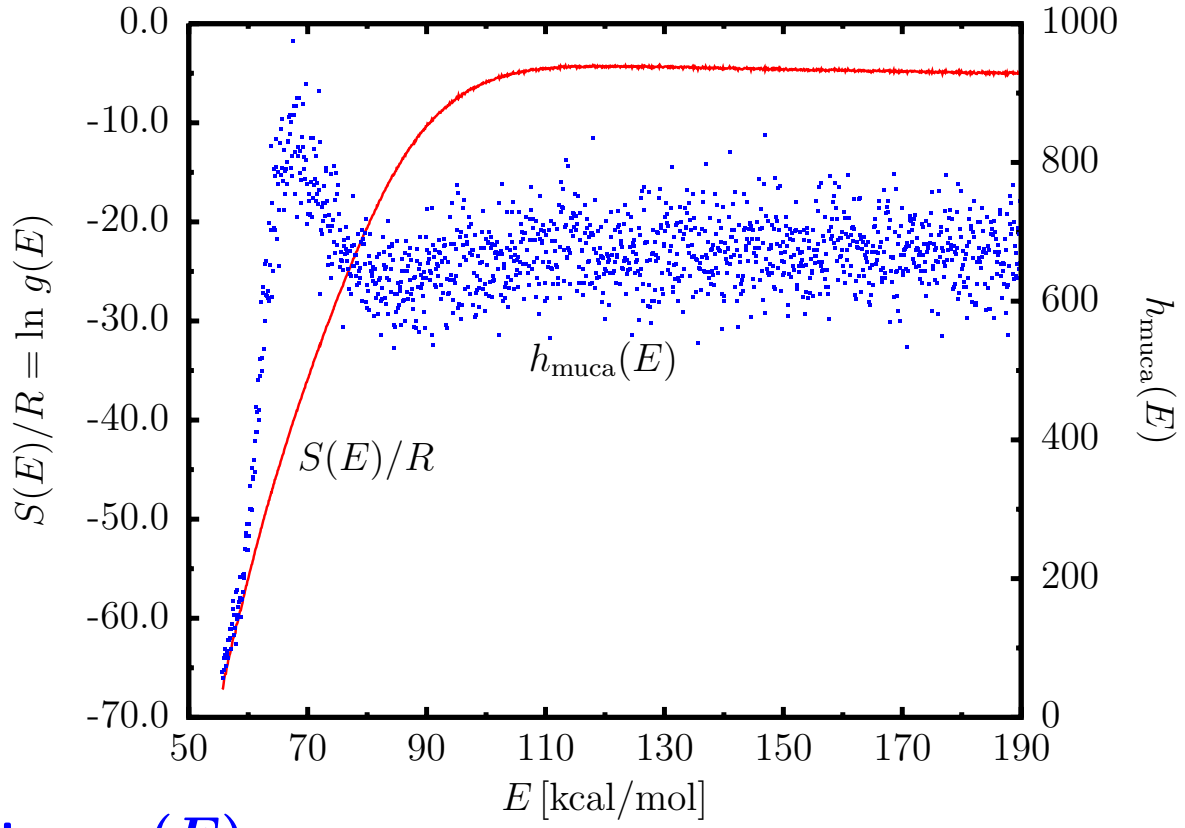


C. Junghans, M.B., W. Janke, PRL 97, 218103 (2006).

- Convex region: $E_{\rm agg} < E < E_{\rm frag}$
- Phase coexistence, latent heat $\Delta Q \neq 0$
- Gibbs construction $\mathcal{H}_S(E) = S(E_{\rm agg}) + E/T_{\rm agg}$
- Transition temperature $T_{\rm agg} = [\partial \mathcal{H}_S(E)/\partial E]^{-1}$
- Entropy reduction $\Delta S = \mathcal{H}_S(E_{\rm sep}) - S(E_{\rm sep})$

1. Introduction

Estimating the density of states by multicanonical sampling



Density of states: $g(E)$

$\Rightarrow$ **Microcanonical entropy:** $S(E) = k_B \ln g(E)$

$\Rightarrow$ **Canonical partition function:** $Z(T) = \int_{E_{\mathrm{min}}}^{\infty} dE\, g(E) e^{-E/k_B T}$

1. Introduction

Multicanonical computer simulation

Canonical partition sum $[\vec{X} = (\vec{x}_1, \vec{x}_2, \ldots, \vec{x}_N)]$:

$$Z = \int \mathcal{D}\mathrm{X} \exp\left[-S(E(\vec{X}))/k_B\right] W^{-1}(E(\vec{X}))$$

with $S(E) = E/T - k_B \log W(E)$ and **weights** $W(E) \sim 1/P_{\mathrm{can}}(E)$;

Sampling with transition probability

$$w(\vec{X} \to \vec{X}') = \min\left[e^{[S(E(\vec{X}))-S(E(\vec{X}'))]/k_B}, 1\right]$$

$\Longrightarrow$ Random walk in energy space

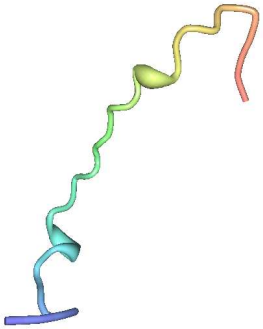
$\Longrightarrow$ "Flat Histogram": **Uniform density of energetic states**

Technical difficulty: Recursive estimation of the weights $W(E)$

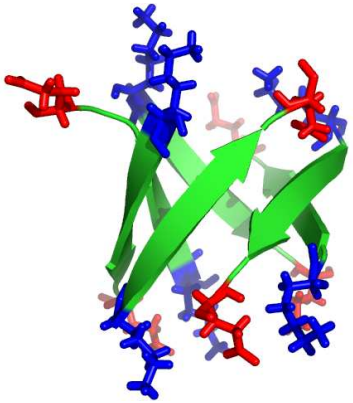
[B. A. Berg, T. Neuhaus, PLB 267, 249 (1991); PRL 68, 9 (1992)]

2. Aggregation of Polymers

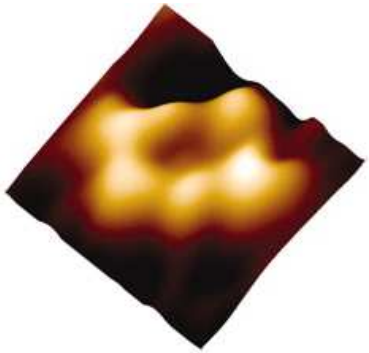
Toxicity of misfolded proteins: Alzheimer's Disease (amyloid hypothesis)



Folding of peptide $A\beta_{1-42}$

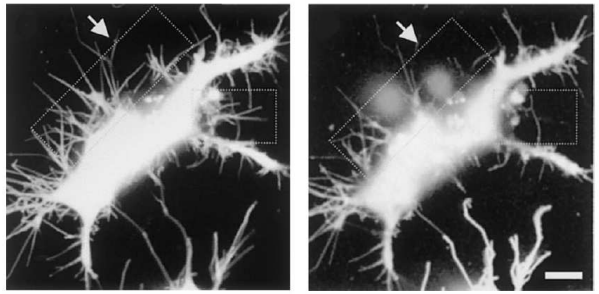


Local unfolding, aggregation



Fusion into neural cell membrane, pore formation

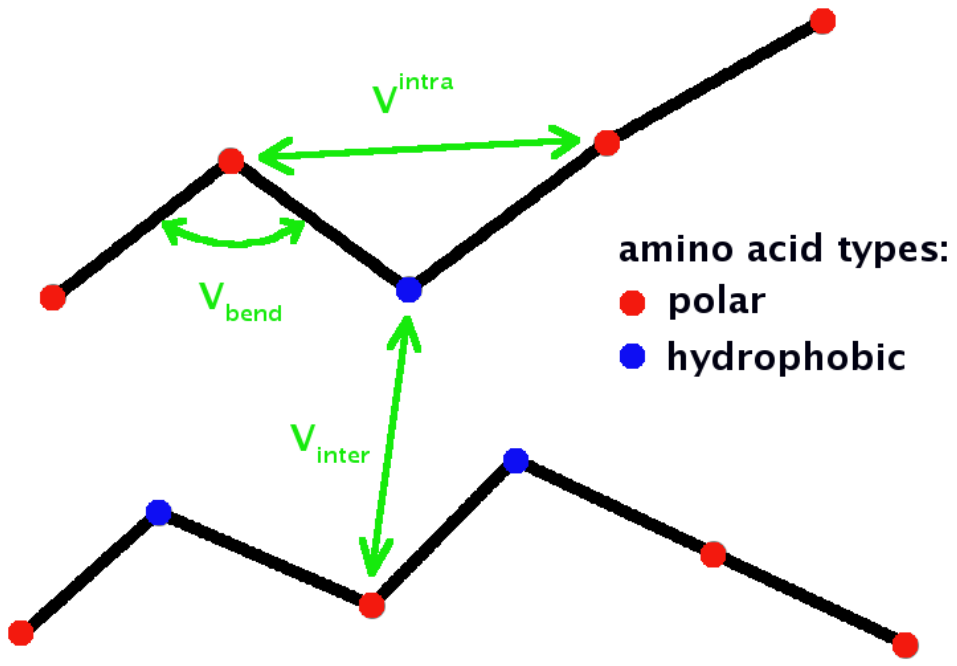
Degeneration of neurons by Ca^{2+} ions



[H. Lin et al., FASEB J. 15, 2433 (2001); A. Quist et al., PNAS 102, 10427 (2005); H. A. Lashuel and P. T. Lansbury jr., Quart. Rev. Biophys. 39, 167 (2006); S. Tomaselli et al., ChemBioChem 7, 257 (2006); S. Mitternacht and A. Irbäck, Proteins 71, 207 (2008)]

Coarse-grained model for the aggregation of proteins

- Heteropolymer chains of a sequence of amino acids (disorder!)
- Simple hydrophobic-polar protein aggregation model:



V_{intra}: interaction between non-bonded amino acids of the same chain

V_{inter}: interaction between amino acids of different chains

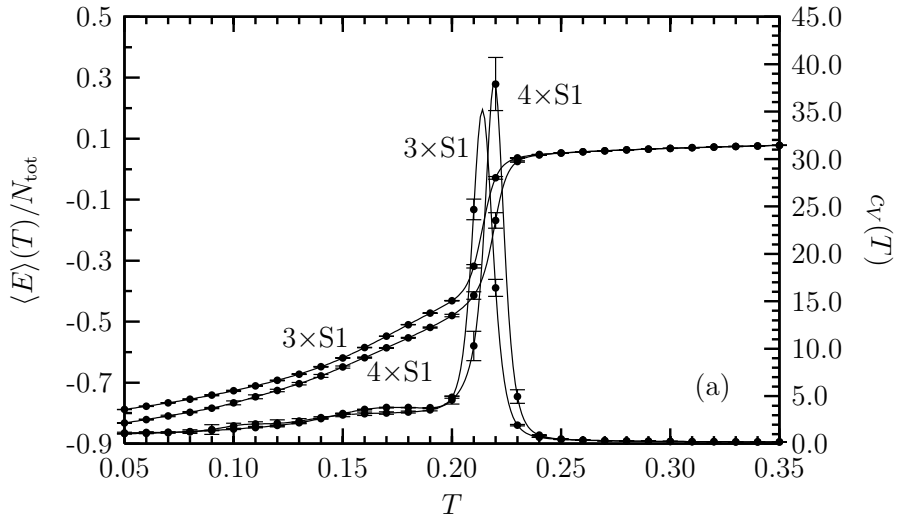
V_{bend}: bending energy

Bond length is constant (stiff bonds)

2. Aggregation of Polymers

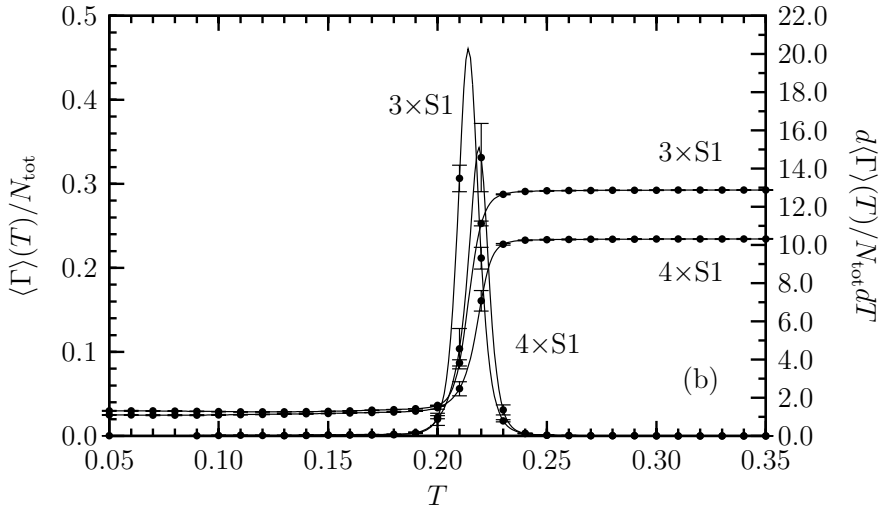
Canonical analysis for systems of 3 and 4 chains (13 monomers each)

Mean energy



Specific heat

Order parameter of aggregation

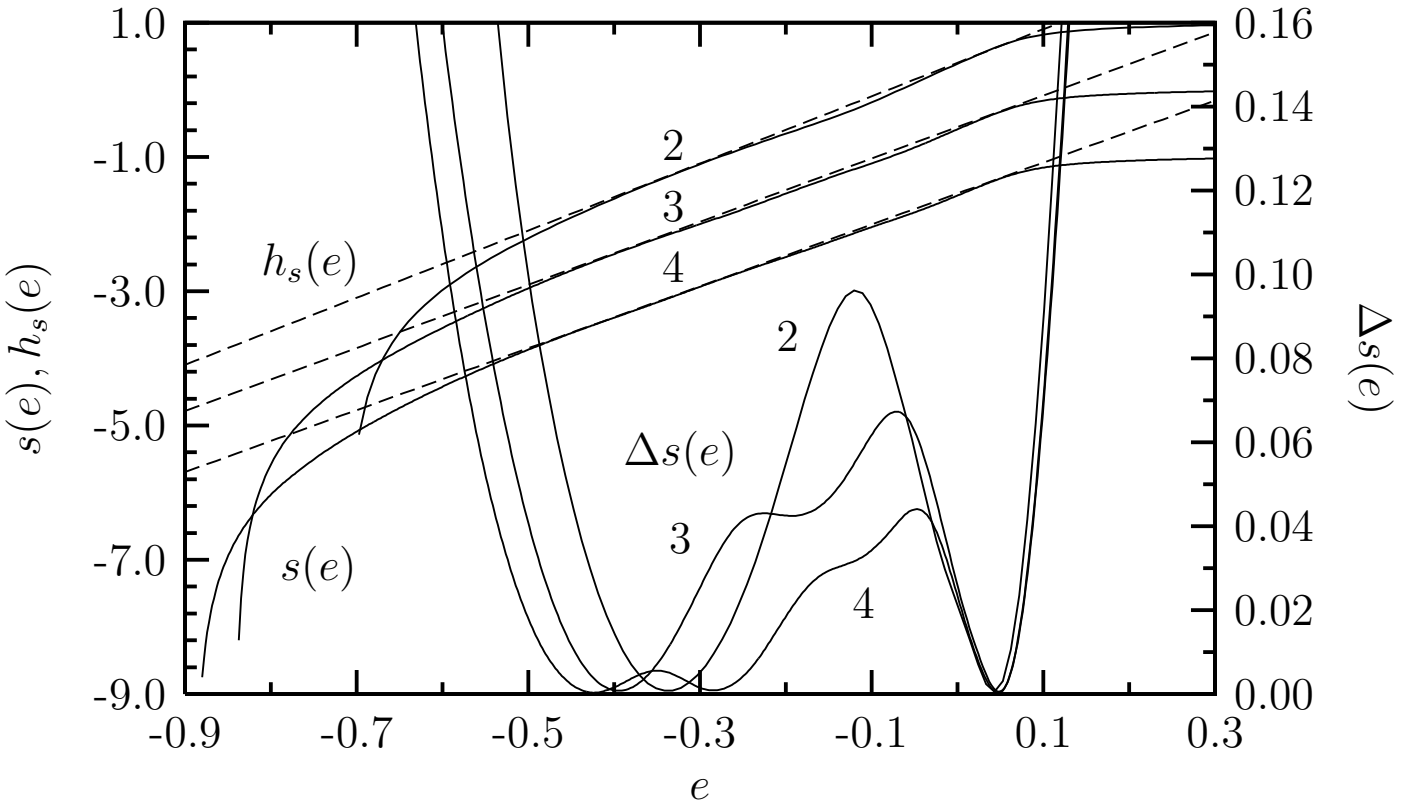


Fluctuations

C. Junghans, M.B., W. Janke, JCP 128, 218103 (2008).

2. Aggregation of Polymers

Microcanonical analysis (2 to 4 chains)

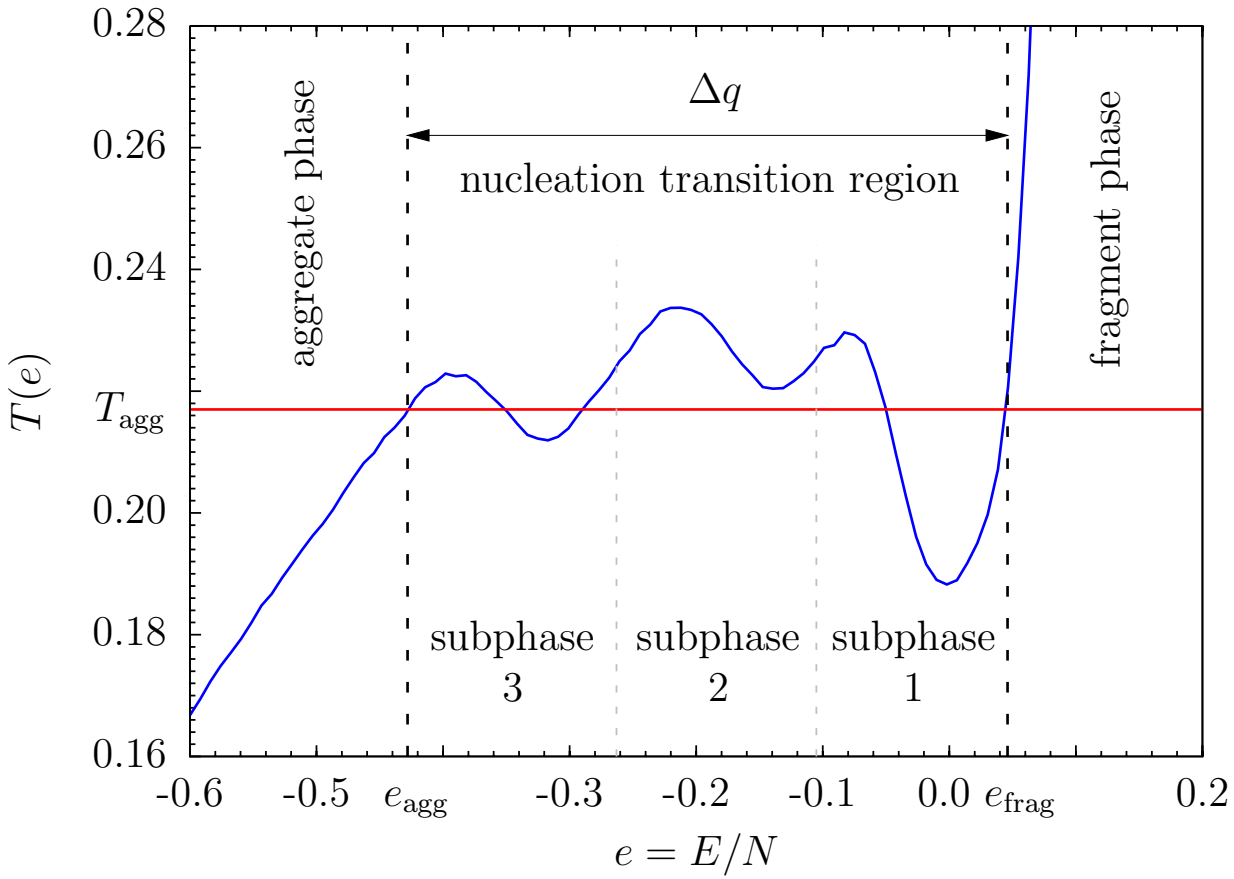


- Δs decreases with system size ($\longrightarrow$ finite-size effect)
- Δq (latent heat) does not vanish ($\longrightarrow$ first-order transition)
- "Oscillations" of Δs for 3 & 4 chains indicate subphase transitions

C. Junghans, M.B., W. Janke, PRL 97, 218103 (2006); JCP 128, 218103 (2008).

2. Aggregation of Polymers

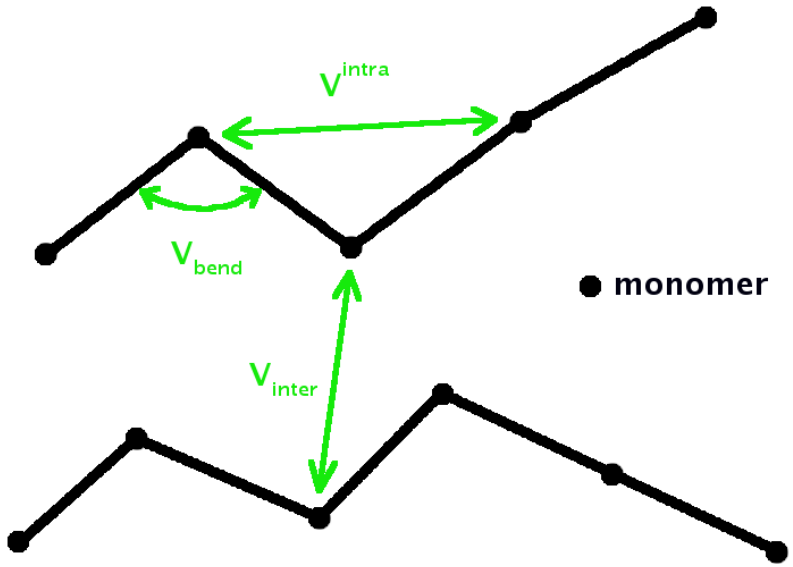
Hierarchy of subphase transitions (4 chains)



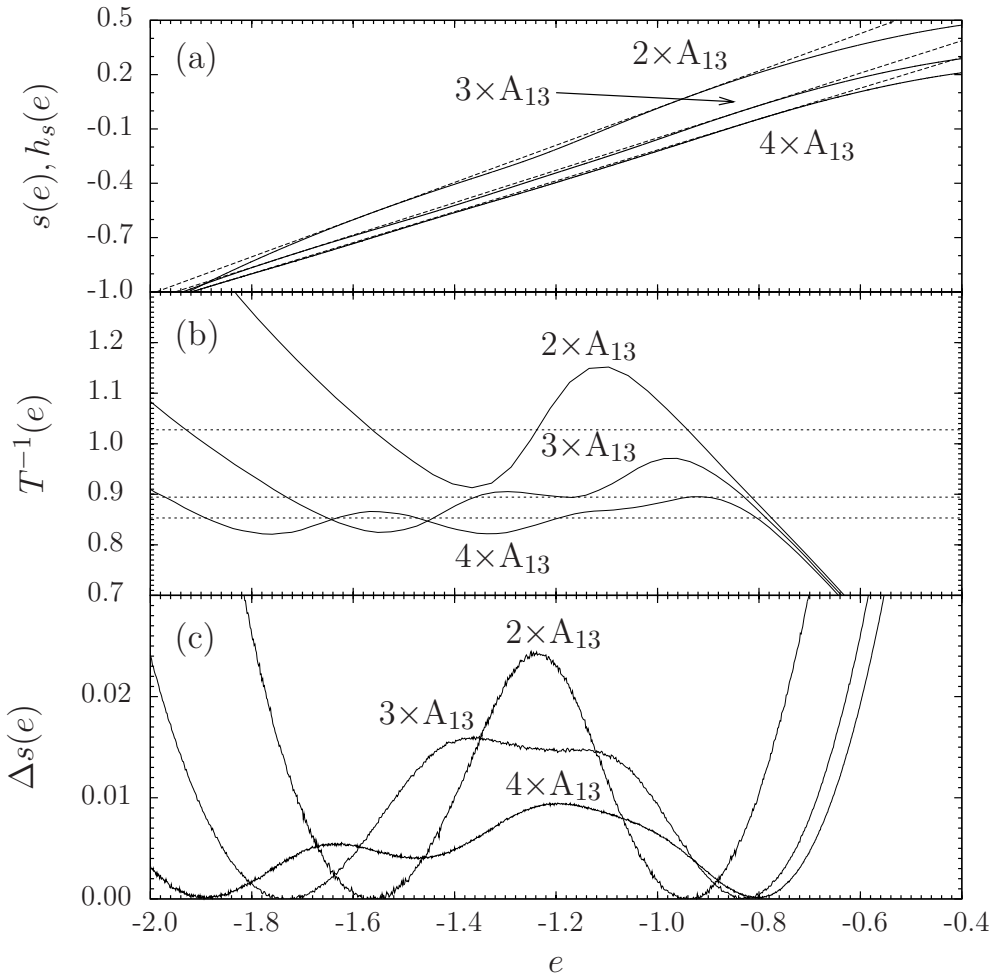
C. Junghans, W. Janke, M.B., preprint (2010).

Homopolymer aggregation

- Chains of identical monomers

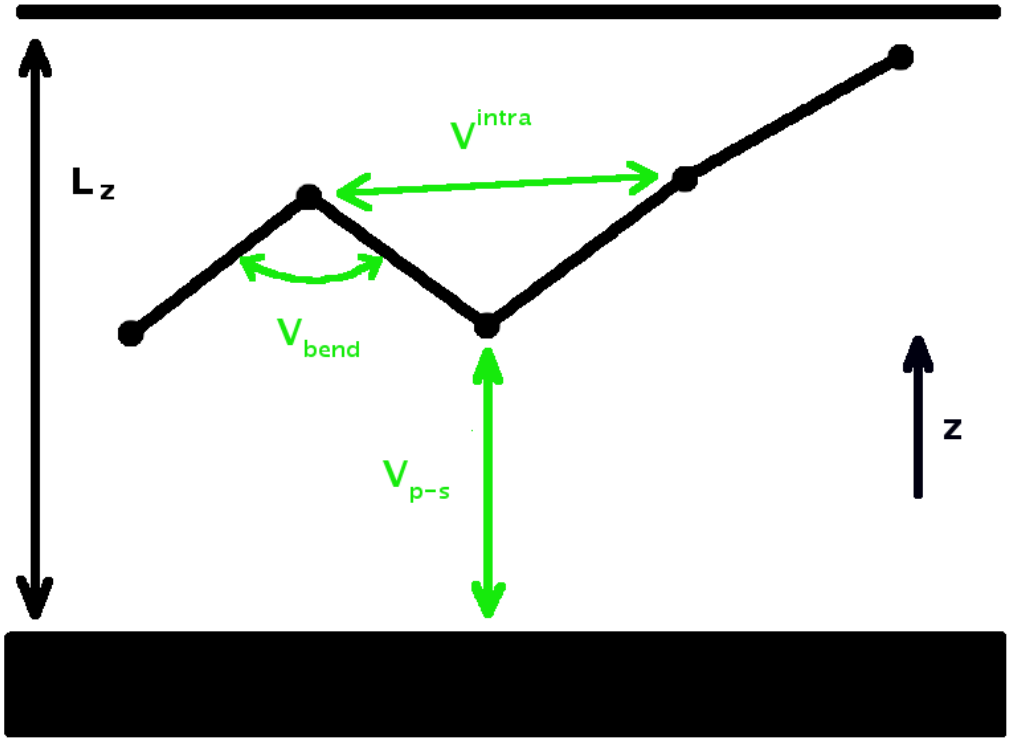


- Fluctuations about Maxwell line
- Oscillations $\Leftrightarrow$ Hierarchies



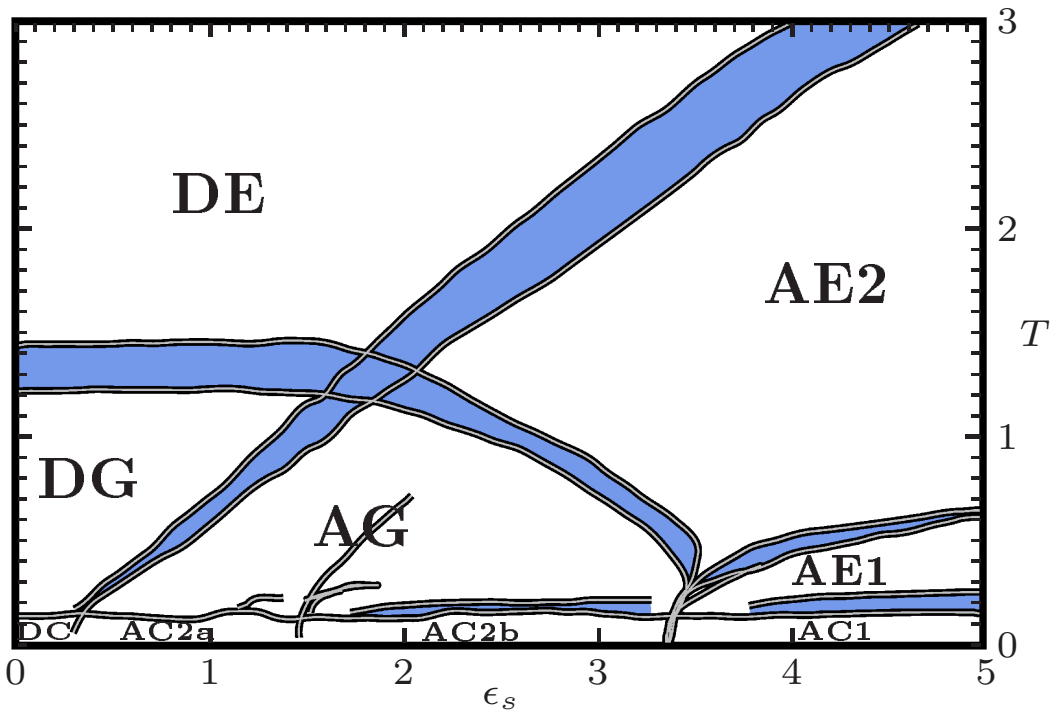
C. Junghans, M.B., W. Janke, EPL 87, 40002 (2009).

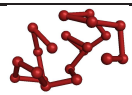
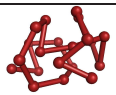
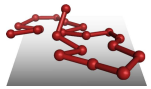
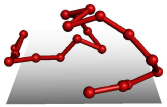
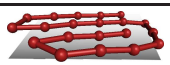
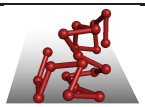
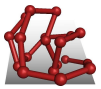
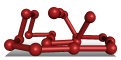
Flexible polymer interacting with continuous substrate



$$E = 4 \sum_{i=1}^{N-2} \sum_{j=i+2}^{N} \left(r_{ij}^{-12} - r_{ij}^{-6} \right) + \frac{1}{4} \sum_{i=1}^{N-2} \left[1 - \cos\left(\vartheta_i\right) \right] + \epsilon_s \sum_{i=1}^{N} \left(\frac{2}{15} z_i^{-9} - z_i^{-3} \right)$$

(Pseudo-)Phase diagram of adsorption (20mer)



pseudophase	typical configuration
DE	
DG	
DC	
AE1	
AE2	
AC1	
AG	
AC2a	
AC2b	

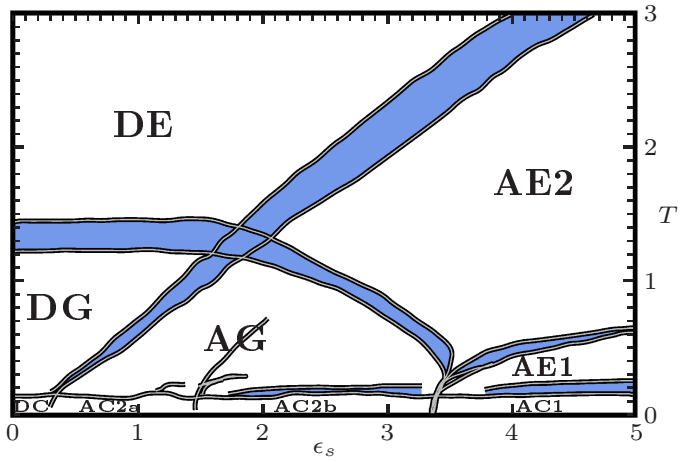
AE/DE: adsorbed/desorbed expanded

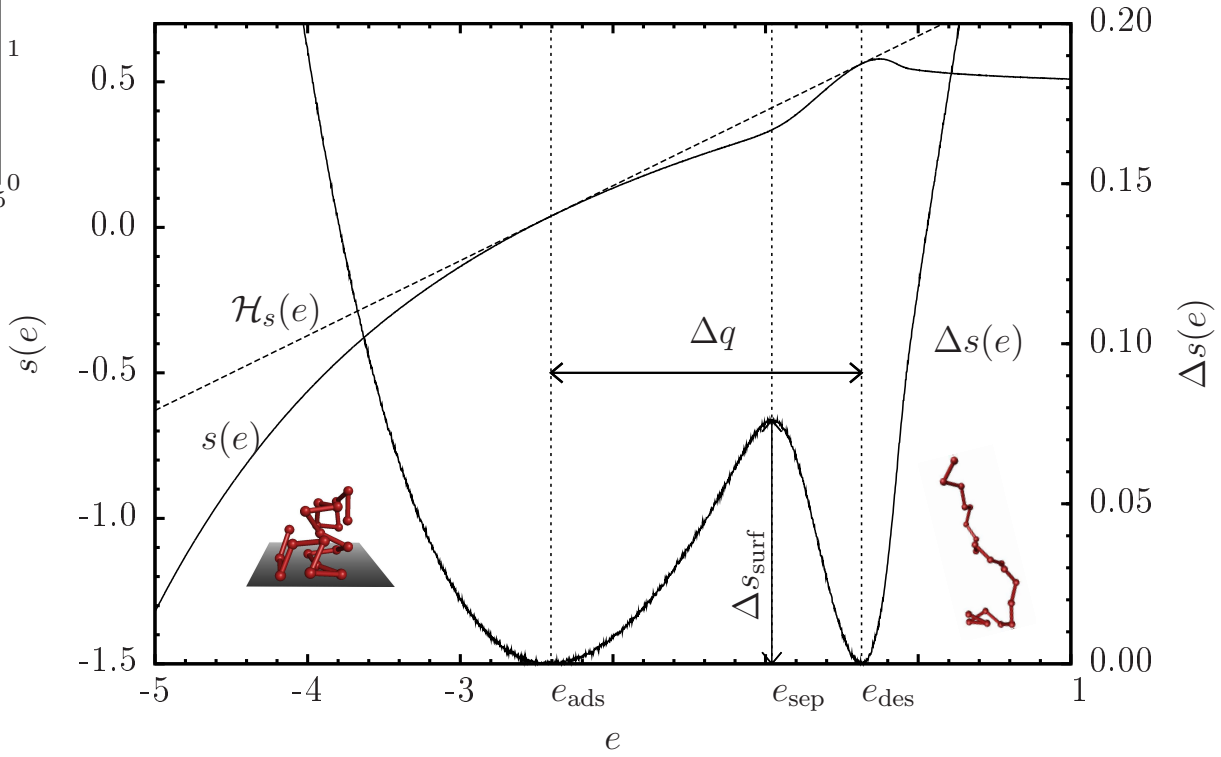
AG/DG: adsorbed/desorbed globular

AC/DC: adsorbed/desorbed compact

M. Möddel, M.B., W. Janke, JPCB 113, 3314 (2009).

Adsorption transition AE2⇔DE (20mer, $\varepsilon_s = 5$)

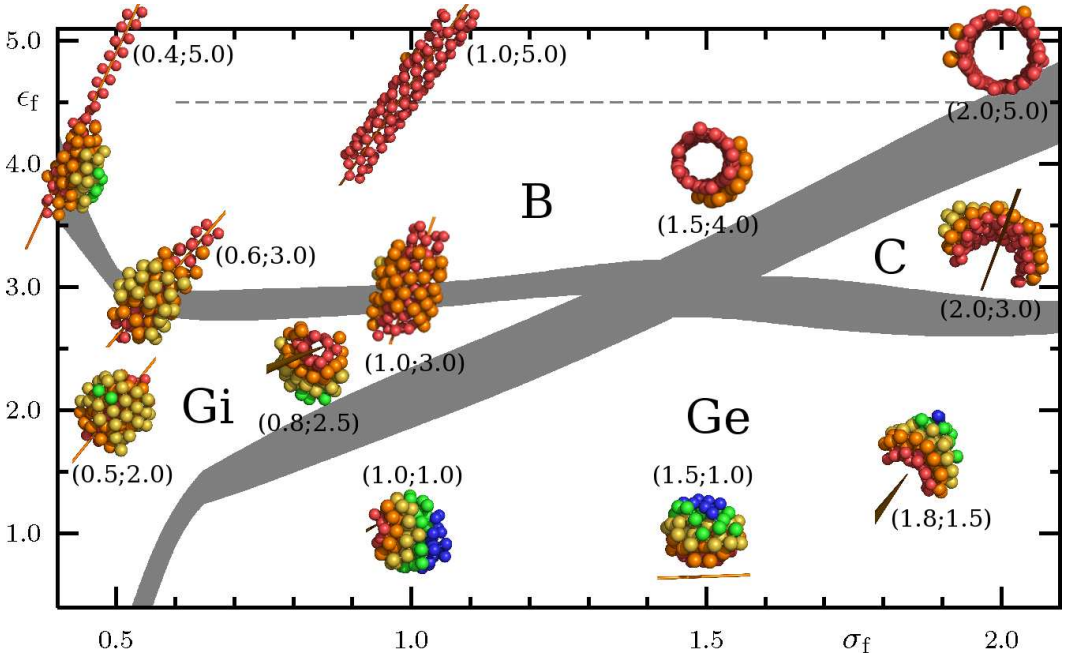




M. Möddel, W. Janke, M.B.,
PhysChemChemPhys, in print (2010).

3. Polymer Adsorption at Substrates

Polymer adsorption on a nanowire

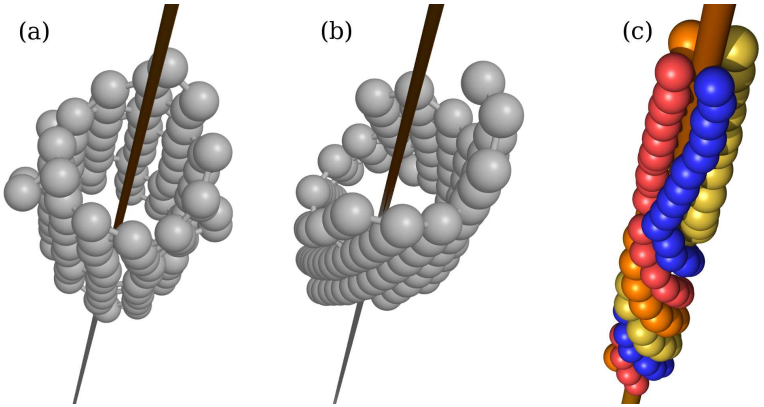


Structural phase diagram

parametrized by vdW radius and adsorption strength

Monolayer structures in phase B

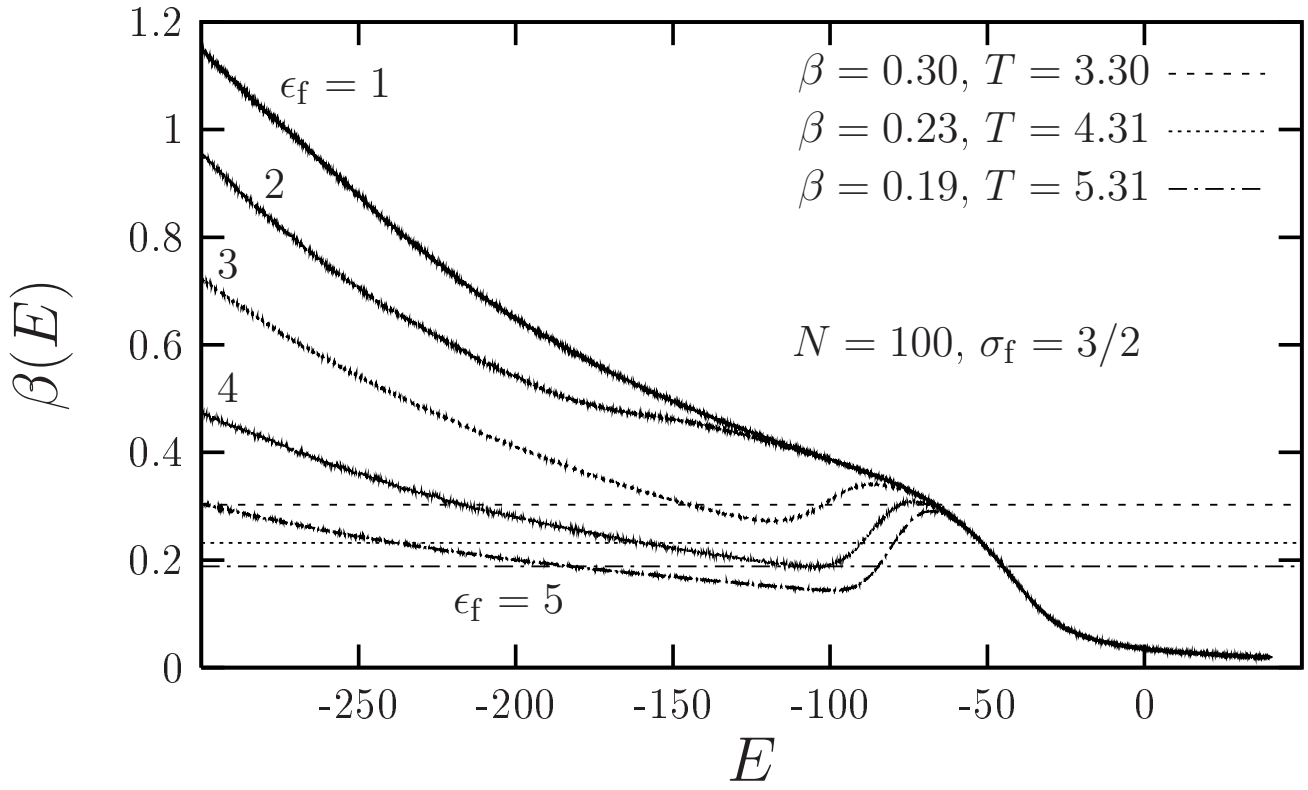
similarities to carbon nanotubes



T. Vogel, M.B., PRL 104, 198302 (2010).

3. Polymer Adsorption at Substrates

Microcanonical thermodynamics of polymer–wire adsorption



First-order character increases with increasing wire attraction strength ε_f

T. Vogel, M.B., preprint (2010).

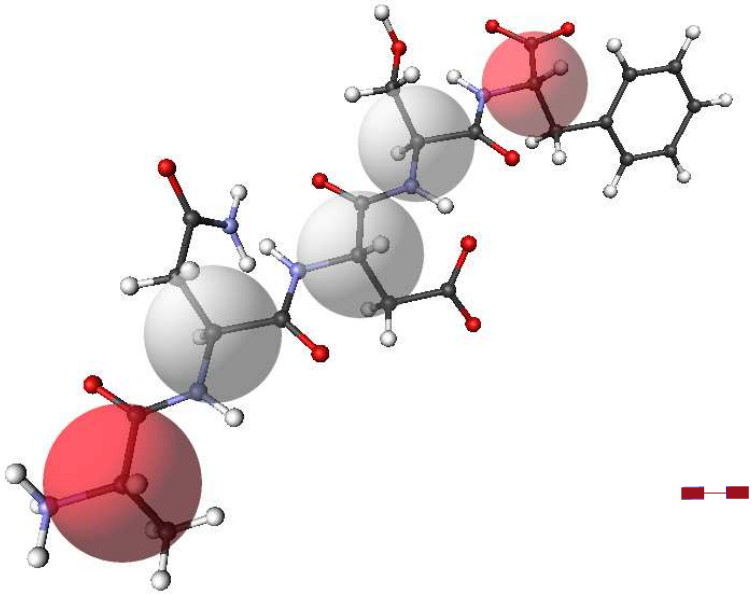
Summary and Conclusions

- **Goal:** Understanding mechanisms of [molecular] nucleation processes
- **Tool:** Microcanonical analysis
- **Approach:** Coarse-grained models for aggregation and adsorption transitions of homopolymers and heteropolymers
- **Result:** Hierarchy of structural subphase transitions; 1^{st} and 2^{nd} order like behavior $\Rightarrow$ finite-size & surface effects
- **Conclusion:** Microcanonical analysis enables quantitative analysis of general features that apply to all nucleation processes

Collaborators: C. Junghans, M. Möddel, T. Vogel, W. Janke

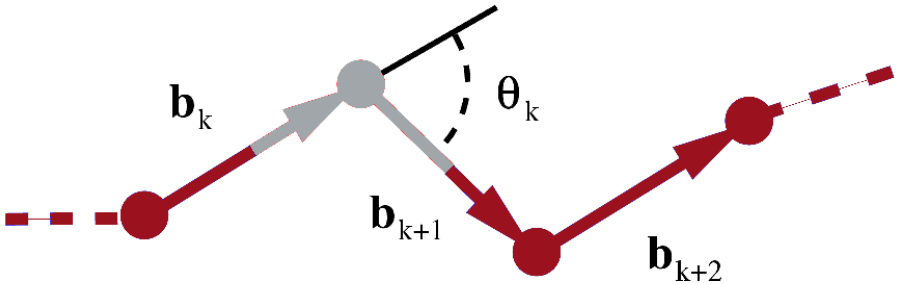
2. Aggregation of Polymers

(i) Hydrophobic-polar (HP) "united atom" C^{α} models:



hydrophobic (H)

hydrophilic, polar (P)



$$E_{\mathrm{HP}} = \frac{1}{4}\sum_{k=1}^{N-2}(1-\cos\theta_k) + 4\sum_{i=1}^{N-2}\sum_{j=i+2}^{N}\left(\frac{1}{r_{ij}^{12}} - \frac{C(\sigma_i,\sigma_j)}{r_{ij}^{6}}\right)$$

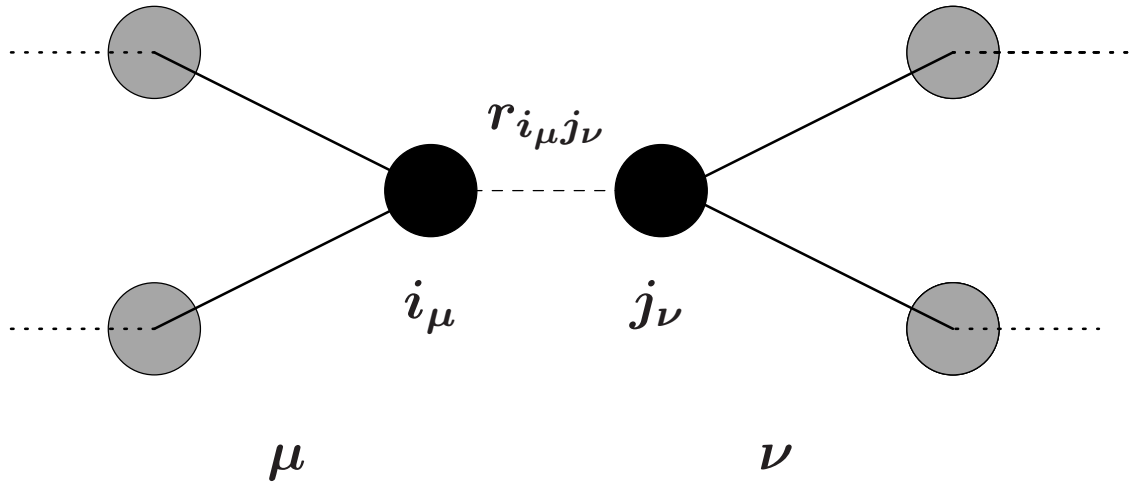
$C(H,H) > C(P,P) > 0$ (attractive), $C(H,P) < 0$ (repulsive)

[lattice: K. F. Lau, K. A. Dill, Macromolecules 22, 3986 (1989); off-lattice: F. Stillinger, T. Head-Gordon, C. L. Hirshfeld, Phys. Rev. E 48, 1469 (1993)]

2. Aggregation of Polymers

(ii) Self-assembly of molecules: Aggregation model

$$E = \sum_{\mu} E_{\mathrm{HP}}^{(\mu)} + 4 \sum_{\mu<\nu} \sum_{i_\mu, j_\nu} \left[r_{i_\mu j_\nu}^{-12} - C(\sigma_{i_\mu}, \sigma_{j_\nu}) r_{i_\mu j_\nu}^{-6} \right]$$



Periodic boundary conditions: Box with edge lengths L

2. Aggregation of Polymers

Aggregation transition: "Order parameter"

$$\Gamma^2 = \frac{1}{2M^2} \sum_{\mu,\nu=1}^{M} \left(\vec{r}_\mu^{\,\mathrm{COM}} - \vec{r}_\nu^{\,\mathrm{COM}} \right)^2_{\mathrm{per}}$$

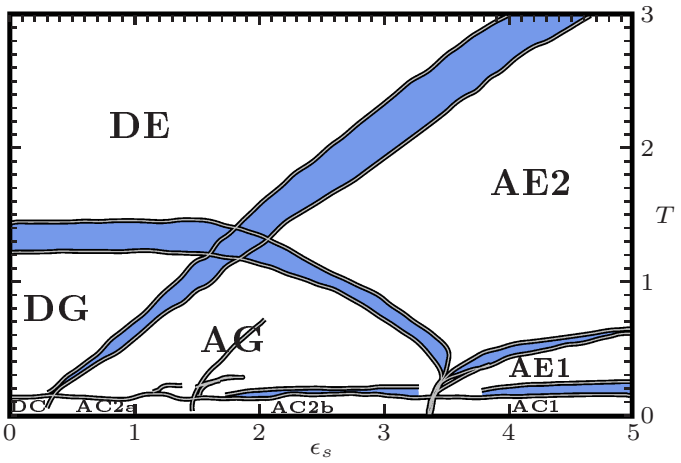
- Center of mass: $\vec{r}_\mu^{\,\mathrm{COM}} = \sum_{i=1}^{N} \vec{r}_{\mu_i}/N$
- Definition similar to gyration radius $r_{\mathrm{gyr}}^2 = \sum_{i,j}^{N} (\vec{r}_i - \vec{r}_j)^2/(2N^2)$
- Statistical average: $\langle \Gamma \rangle = Z^{-1} \prod_{\mu=1}^{M} \left[\int \mathcal{D}X_\mu \right] \Gamma \exp(-E/k_B T)$
- Fluctuations

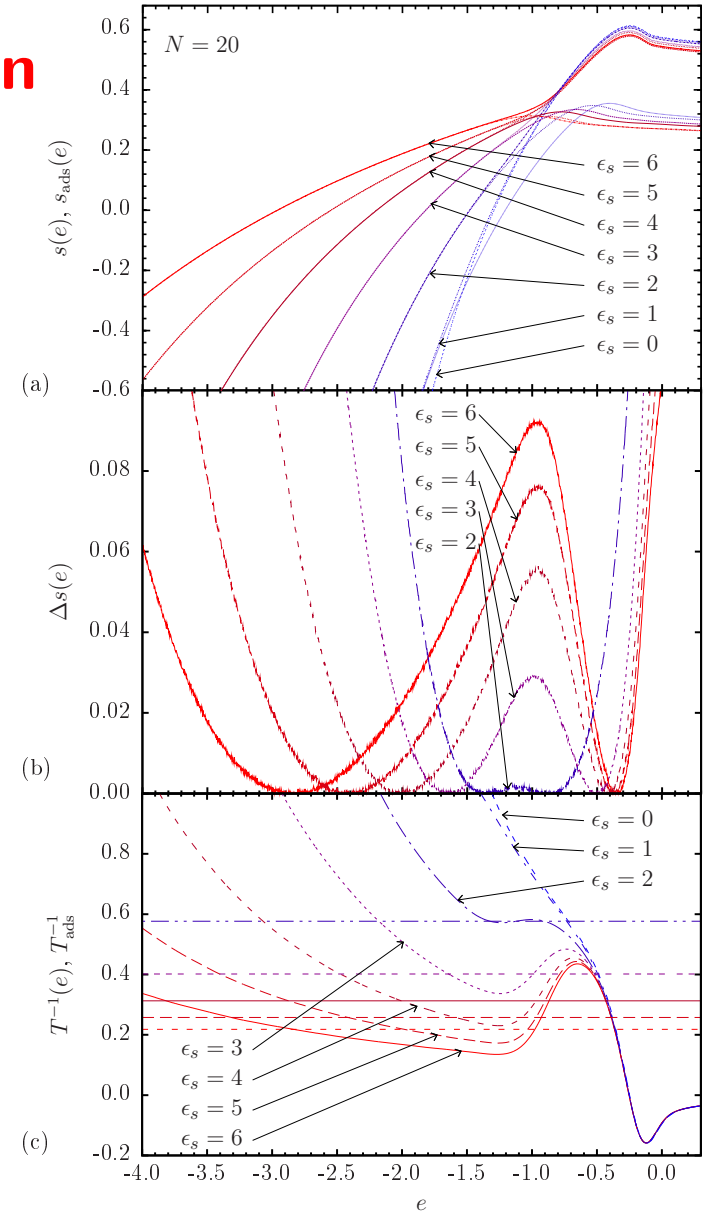
$$\frac{d\langle \Gamma \rangle}{dT} = \frac{1}{k_B T^2} \left(\langle E\,\Gamma \rangle - \langle E \rangle \langle \Gamma \rangle \right)$$

should signalize aggregation transitions, if any!

Dependence on adsorption strength ε_s (20mer)

- Δs increases with ε
- Δq increases with ε





entropy

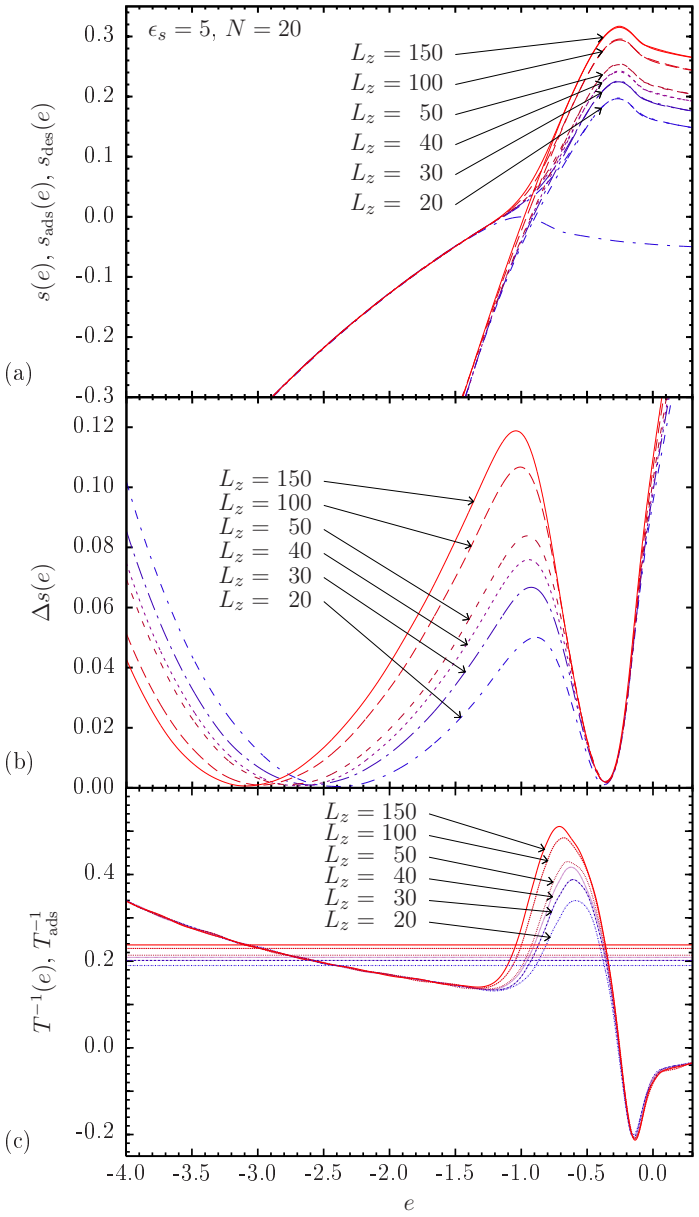
entropy reduction

inverse temperature

Dependence on box size ($N = 20$, $\varepsilon_s = 5$)

- Δs increases with L_z
- Δq increases with L_z

$\Rightarrow$ Translational entropy vs. conformational entropy



entropy

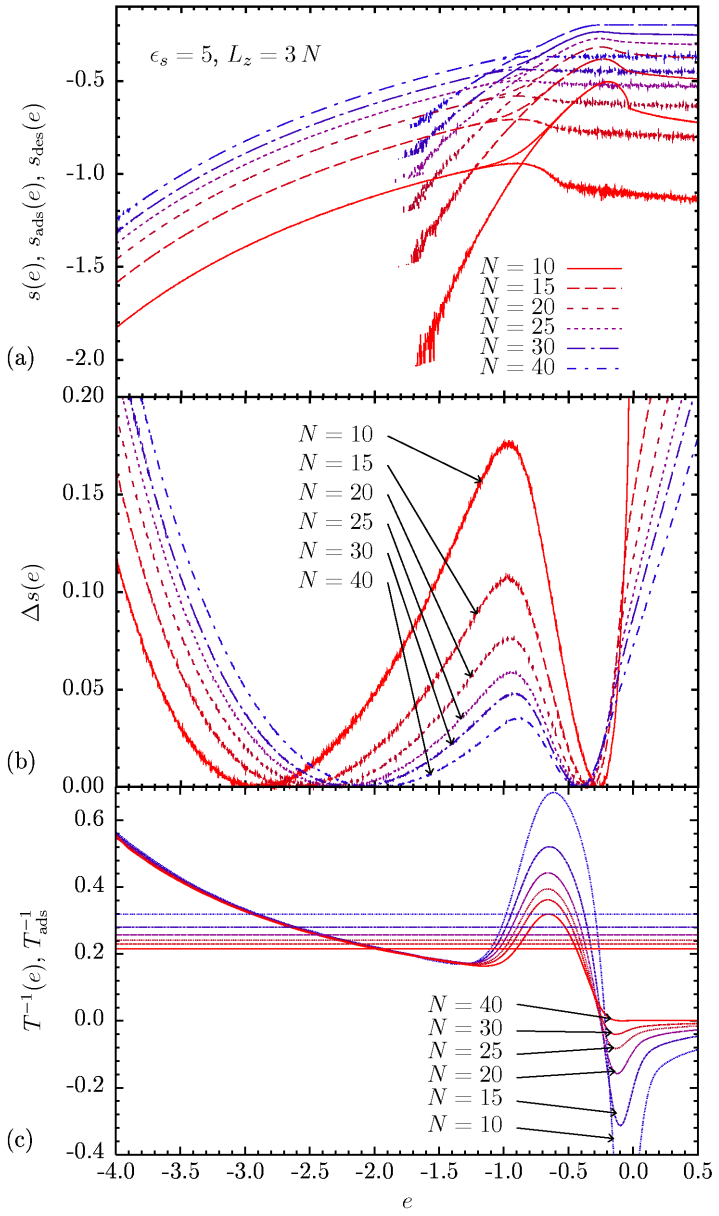
entropy reduction

inverse temperature

Dependence on chain length N ($\varepsilon_s = 5$)

- Δs decreases with N
- Δq decreases with N

$N \to \infty$: Second-order phase transition with first-order signature for finite chains



entropy

entropy reduction

inverse temperature

M. Möddel, W. Janke, M.B., PhysChemChemPhys, in print (2010).