



27th Annual CSP Workshops on “Recent Developments in Computer Simulation Studies in Condensed Matter Physics”, CSP 2014

Effect of bending stiffness on a homopolymer inside a spherical cage

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Abstract

In this work we investigate the effect of bending stiffness on a homopolymer inside a spherical confinement. In particular we are interested in the collapse transition and its dependence on the size of the confinement and the stiffness of the polymer. Using an advanced multicanonical Monte Carlo algorithm, we sample the phase space of a coarse-grained homopolymer model. We find that the confinement leads to a shift of the collapse transition temperature with a stiffness-dependent direction: flexible polymers become more unstable for a smaller confinement in contrast to semi-flexible polymers, where the transition temperature increases with decreasing size of the confinement.

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Peer-review under responsibility of The Organizing Committee of CSP 2014 conference

Keywords: Monte Carlo simulation, bead-stick polymer, collapse transition, spherical confinement

1. Introduction

There are a variety of studies which investigate the behaviour of proteins inside different kinds of constraints, some examples can be found in Klimov et al. (2002), Friedel et al. (2003), Takagi et al. (2003), Rathore et al. (2006) and Bilsel et al. (2012). This topic is of high interest, because closed environments are somehow the natural habitat of proteins. Understanding the influence is not only important to get an insight into their general behaviour. Also for applications like building biosensors or the design of drugs, it can be rewarding to understand the influence of the constraint, especially its influence on the stability of the protein. However, in this work we are not interested in the behaviour of any chemically realistic protein. Instead we investigate a model for a generic polymer in order to draw conclusion of the general influence of the confinement. In previous work on proteins, the introduction of confinement always led to a stabilization of the protein, which means that the transition temperature is shifted to higher temperatures for smaller sizes of the confinement. In Marenz et al. (2012) we have shown that this does not hold for a generic model for a flexible homopolymer. Here, we show that the direction of the shift depends on the stiffness of the polymer, by applying the same model and changing the bending stiffness such that we cover the full regime from flexible to stiff polymers.

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2. Model

We take a coarse grained approach to model the polymer. The so-called bead-stick polymer has been used before to study protein folding from a mesoscopic view, see Stillinger et al. (1993), Irbäck et al. (1997) and Bachmann et al. (2005). Here, we use it as a model for a homopolymer, which means that N identical monomers are aligned linearly, with \vec{r}_i being the position of monomer i . To model the backbone of a polymer, the distances between adjacent monomers are fixed and set to unity ($|\vec{r}_i - \vec{r}_{i+1}| = 1.0$). The short-range attraction and excluded-volume effects are modeled via a 12-6 Lennard-Jones potential between non-adjacent monomers. The stiffness is introduced by an additional cosine potential that depends on the angle between two bonds, which is well-known from the discretized worm-like chain model. The angle θ_i is defined as $\cos \theta_i = (\vec{r}_{i+1} - \vec{r}_i) \cdot (\vec{r}_{i+2} - \vec{r}_{i+1})$. The spherical cage is modeled as a geometric constraint with hard walls. In summary the Hamiltonian consists of three terms,

$$H \equiv E = E_{\text{LJ}} + E_{\text{bend}} + V_{\text{sphere}}. \quad (1)$$

The first term is the common Lennard-Jones potential defined as

$$E_{\text{LJ}} = 4 \sum_{i=1}^{N-2} \sum_{j=i+2}^N \left(\frac{1}{r_{ij}^{12}} - \frac{1}{r_{ij}^6} \right), \quad (2)$$

with a minimum at $r_{\min} = 2^{\frac{1}{6}}$ where $r_{ij} = |\vec{r}_i - \vec{r}_j|$ is the distance between two monomers. The second term in (1) is the bending energy

$$E_{\text{bend}} = \kappa \sum_{i=1}^{N-2} (1 - \cos \theta_i), \quad (3)$$

in which we can use the parameter κ to modify the bending stiffness of the polymer. The third term in (1) models the spherical constraint as a Θ -function which suppresses every state where at least one monomer is located outside a sphere of radius R ,

$$V_{\text{sphere}} = \begin{cases} 0 & \text{if all } |r_i| < R \\ \infty & \text{if any } |r_i| \geq R \end{cases}. \quad (4)$$

There is no additional potential induced by the sphere, as mentioned before it is just a geometrical restriction and the polymer can move freely inside it.

To distinguish the different pseudo-phases we use the thermal derivative of different observables, such as the energy $\langle E \rangle$, the squared radius of gyration $\langle R_g^2 \rangle$, and the mean angle $\frac{1}{N} \langle \sum_i \theta_i \rangle$. Since in this work we are mainly interested in the location of the collapse transition, we concentrate on the maximum of the thermal derivative of the squared radius of gyration $\frac{d}{dT} \langle R_g^2 \rangle$ with $R_g^2 = \frac{\sum_{i=1}^N (\vec{r}_i - \vec{r}_{\text{cm}})^2}{N} = \frac{\sum_{i=1}^N \sum_{j=1}^N (\vec{r}_i - \vec{r}_j)^2}{2N^2}$ and $\vec{r}_{\text{cm}} = \frac{\sum_{i=1}^N \vec{r}_i}{N}$.

3. Simulation method

To simulate this model we used a modified version of the multicanonical Monte Carlo algorithm, see Berg and Neuhaus (1991, 1992) and Janke (2012). The multicanonical algorithm overcomes the problem of supercritical slowing down at first-order phase transition, shown in Janke (1992, 2012), by constructing a weight function such that in the resulting simulation the probability for every energy is equally distributed over the desired energy range. Therefore the simulation spends an equal amount of time at every energy and acts as a random walker in the energy landscape so it can sample also the very suppressed regions of the phase space reasonably well. We apply two modifications to this algorithm. The first modification is that we make the update ranges of the Monte Carlo moves energy dependent, such that the acceptance probability is roughly 2/3 at every energy bin. The details of this procedure are described in Schnabel et al. (2011). Although this simulation technique copes with the most intrinsic problem of the Monte Carlo method, the convergence procedure may need some time especially if one wants to simulate very low temperatures,

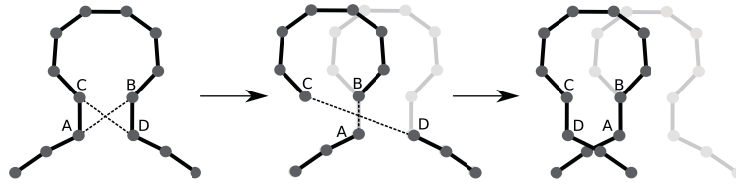


Figure 1. Schematic description of the double-bridge move for polymers where the distance of adjacent monomers is fixed. First we choose two random bonds (here \overline{AC} and \overline{BD} , delete these bonds and reconnect the polymer via new bonds (here \overline{AB} and \overline{CD}). Now the middle part of the polymer (B to C) is moved so that B has now the old coordinates of C. Finally the end of the polymer, beginning with D, is shifted so that afterwards the new bond \overline{CD} has the same direction and length as the old bond \overline{CA} . This move improves the dynamics of the simulation and still satisfies the fixed bond-length constraint and the detailed balance condition.

which corresponds to very low energy values. To overcome this problem we used a parallel implementation, as described by Zierenberg et al. (2012). This technique enables us to use modern HPC hardware and reduces drastically the wall-clock time needed for the convergence procedure.

Due to the fixed distance of adjacent monomers we can only use a restricted set of Monte Carlo moves. We use a spherical move, a crank-shaft move and a sort of double-bridging move. The first one rotates one bond of the polymer with a random angle and afterwards shifts every monomer from this end of the polymer by a constant vector, such that the fixed distance between adjacent monomers is conserved. The second one moves only a single monomer by rotating it around the axis spanned by its two adjacent monomers by a random angle. The “double-bridge” move exchanges two bonds of the polymer with each other in such a way that the fixed bond length is not violated, a schematic description is shown in Fig. 1.

4. Results

4.1. Unconstrained behaviour

We first give a rough overview of the complete phase diagram of a semi-flexible bead-stick polymer without any geometrical constraint. A detailed description will be given elsewhere, where we also compare with the case of a bead-spring polymer, see Seaton et al. (2013). In the flexible case ($\kappa = 0.00$) it is well known that there are three basically different pseudo-phases, see Fig. 2. At high temperatures the polymer is a random coil and entropy dominated (gas-

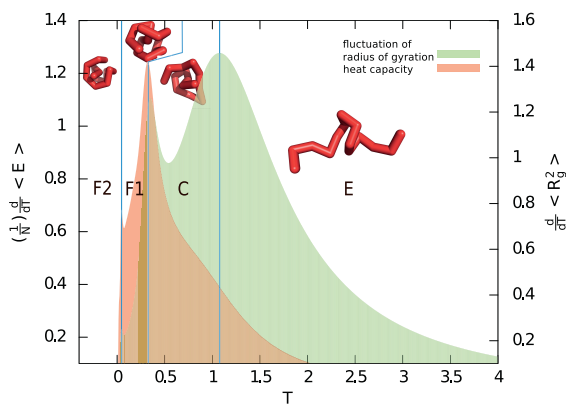


Figure 2. Specific heat (red) and thermal fluctuation of the radius of gyration (green) for a flexible homopolymer with $\kappa = 0.00$ consisting of 14 monomers. The peaks indicate pseudo-phase transitions, which are labeled as follows: F1/F2 - frozen/solid phase, C - collapsed phase, E - extended phase.

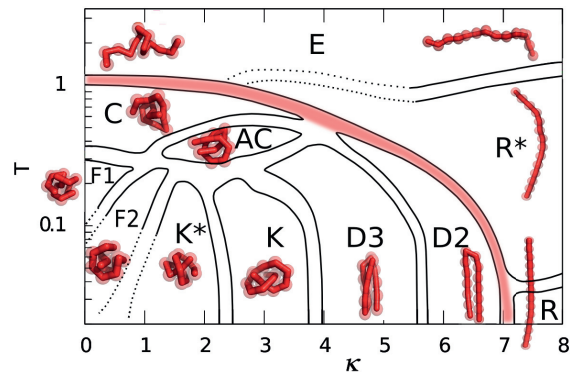


Figure 3. Overview of the phase diagram of a 14mer in the stiffness-temperature plane. The phases are labeled as follows: E - extended phase, C - collapsed phase, AC - aligned collapsed, F1/F2 - frozen, K/K* - knot-like, DN - bended N-1 times, R/R* - rod-like. Note that the temperature is given on a logarithmic scale.

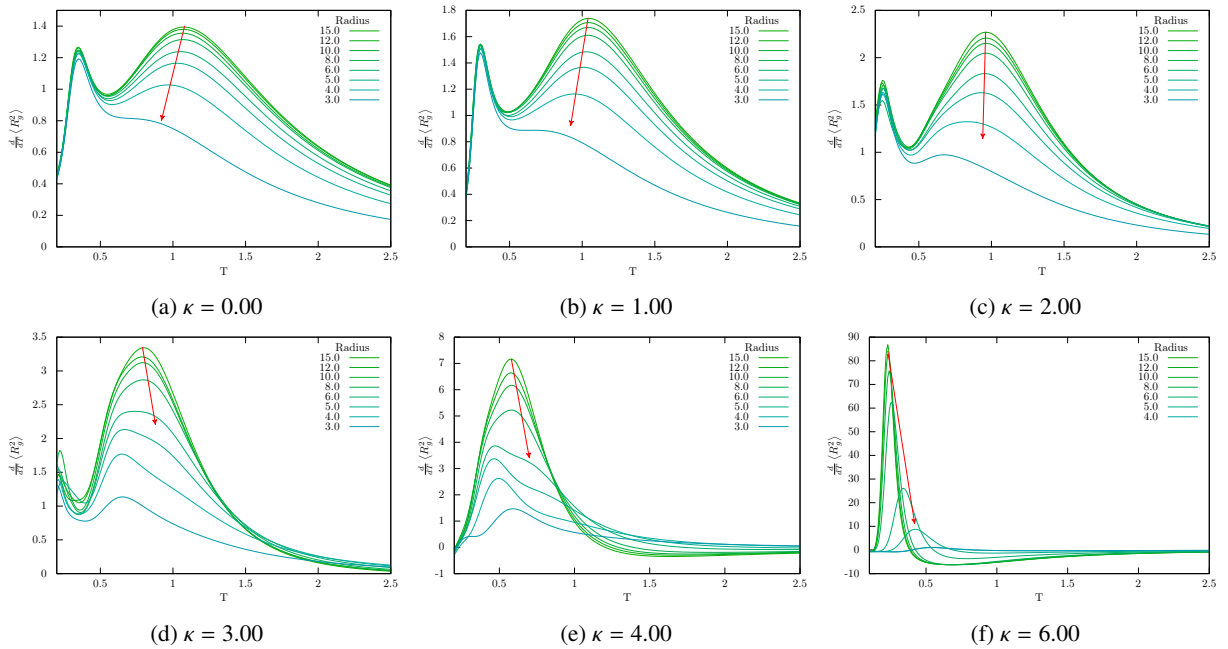


Figure 4. All graphs show $\frac{d}{dT} \langle R_g^2 \rangle$ plotted versus the temperature of a homopolymer consisting of 14 monomers for different values of κ . The peak corresponding to the collapse transition is indicated by a red arrow.

like), we denote this phase as E (extended). At lower temperatures, below the collapse transition, the polymer is in a more dense but also disordered liquid-like state C (collapsed). The third phase F (frozen) is comparable to a solid state, which is completely energy dominated and the intermolecular distances between the monomers are minimized. Due to the mismatch of the minima of the Lennard-Jones potential and the fixed bond length, the polymer cannot enter crystal-like shapes as seen for similar models where the bonds are allowed to change their lengths as shown in Schnabel et al. (2009a, 2009b).

Turning on bending stiffness, we see a very rich phase diagram, shown in Fig. 3. In this work, we focus on the collapse transition which distinguishes the extended from the collapsed or bended states (the red line in the phase diagram). In contrast to most other pseudo-phase transitions, the collapse transition persists over a large range of κ and its existence is also quite insensitive to the length of the polymer.

4.2. Spherical confinement

The plots in Fig. 4 give an overview of the influence of the confinement on the collapse transition and how it depends on bending stiffness. One can see that the position and the height of the peak of $\frac{d}{dT} \langle R_g^2 \rangle$ shifts with changing radius of the confining sphere. The height becomes smaller with smaller radius until it vanishes at a certain size of the sphere. This is due to the fact that the sphere compresses the polymer, such that the conformations of the extended and collapsed phase become more similar. This implies that the difference in $\langle R_g^2 \rangle$ becomes smaller and thus the transition is less and less pronounced. At certain values for κ (2.00, 3.00 and 4.00) a second peak in $\frac{d}{dT} \langle R_g^2 \rangle$ emerges if the radius is small enough. This peak indicates another pseudo-phase transition which is not influenced in the same way as the collapse transition by the confining sphere. For large radii the peak of $\frac{d}{dT} \langle R_g^2 \rangle$ coming from the collapse transition overlaps this other pseudo-phase transition completely, but it is nonetheless existent and can be observed with different estimators, where the collapse transition is less pronounced. The amplitude of the shift of the collapse transition depends on the bending stiffness of the polymer. For small κ the transition temperature shifts to lower values. This effect becomes smaller as we increase κ until the transition point stays stable ($\kappa \approx 2.00 - 3.00$). If we further increase κ the transition temperature starts to shift to higher temperatures.

5. Conclusions

We have shown that for a very generic model of a homopolymer the introduction of a confining sphere can lead to a stabilizing or destabilizing effect, depending on the bending stiffness of the polymer. This is not in contrast to former work on chemically realistic protein models, due to the fact that proteins are relatively stiff polymers. In our case, this is the regime where the transition shifts to higher temperatures.

Acknowledgments

This project is funded by the European Union and the Free State of Saxony through the “Sächsische AufbauBank” and by the DFG (German Science Foundation) through SFB/TRR 102 (project B04), Grant No. JA 483/24-3, and the Graduate School GSC 185 “BuildMoNa”. We also thank the NIC Forschungszentrum Jülich for time on their supercomputer JUROPA under Grant No. hlz21.

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