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Monte Carlo simulations of single polymer force-extension relations

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Abstract. We present Monte Carlo simulations for studying the statistical mechanics of arbitrarily long single molecules under stretching. In many cases in which the thermodynamic limit is not satisfied, different statistical ensembles yield different macroscopic force-displacement curves. In this work we provide a description of the Monte Carlo simulations and discuss in details the assumptions adopted.

1. Introduction

In biological systems many important molecules are polymer chains. So far, different mechanical experiments on single molecules (e.g., stretching) provided a crucial elucidation about the molecoular behaviour of several biomolecular processes [1]. Single molecules tecniques may include mechanical and optical methods, such as laser optical tweezers (LOTs) [2], magnetic tweezers (MTs) [3] or atomic force microscope (AFM) [4]. The importance of understanding the force-extension relationship for macromolecules has attracted the attention of scientists, who produced several models and relationships to explain the experimental results. The earlier experiments on double-stranded DNA chains showed results in partial agreement with the freely jointed chain (FJC) model [5] but in very good agreement with the worm-like chain (WLC) model [6, 7].

The analytical developments of the FJC and WLC models work under the assumption of the finite, but large enough, contour length. This approximation is related to the concept of thermodynamic limit. In fact, the standard rules of equilibrium thermodynamics may not apply to experiments on individual, short-length polymer molecules. In such a case the results may depend on the boundary conditions imposed for stretching the polymer: a fixed end-to-end distance, pertinent to the Helmholtz ensemble, or a fixed force applied at one or both ends, rather representing the Gibbs ensemble. In this paper we consider the mechanical stretching response of extensible polymer chains of arbitrary length. To this aim we develop Metropolis Monte Carlo simulations performing the typical experiment in which the elasticity of single polymer is probed with an AFM tip (see Fig.1, left panel) and we quantitatively evaluate the stretching response differences between the Helmholtz and Gibbs ensembles (Fig.1, right panel).
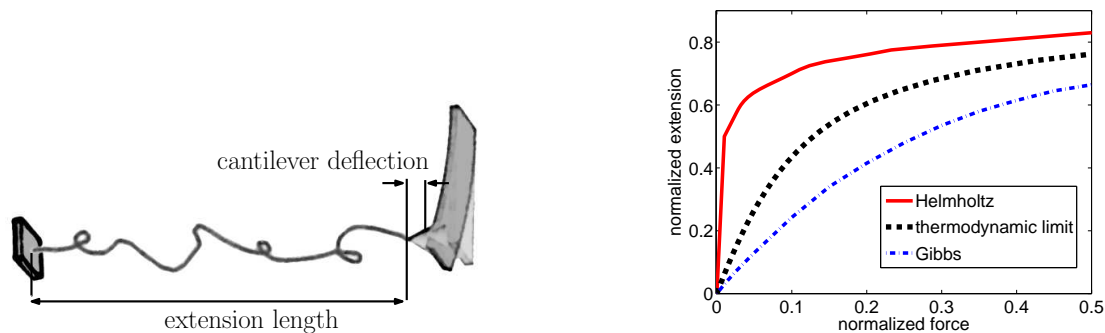
Figure 1. Left panel: a typical AFM experiment to measure the force-extension curve of a single molecule. Right panel: comparison between the normalized extensions in the Helmholtz and Gibbs ensembles for a WLC chain with $N = 10$ monomers.

2. Thermodynamics of polymer chains

Let us consider a chain of monomers in a long molecule, each monomer representing a group of atoms or molecules along the polymer backbone. The classical dynamics of monomers is described by the set of positions $\vec{r}_i$ ($i = 1, ..., N$) and momenta $\vec{p}_i$ ($i = 1, ..., N$). We assume that one terminal monomer is fixed at position $\vec{r}_0 \equiv (0, 0, 0)$ and that monomers interact through a harmonic potential. The dynamics of the system is described by the Hamiltonian

$$h_0(\vec{r}_1, .., \vec{r}_N, \vec{p}_1, .., \vec{p}_N) = \sum_{i=1}^{N} \frac{\vec{p}_i \cdot \vec{p}_i}{2m} + \frac{1}{2}k \sum_{i=0}^{N-1} (\|\vec{r}_{i+1} - \vec{r}_i\| - l)^2. \tag{1}$$

We consider this system to be in thermal equilibrium with a reservoir at temperature T and, therefore, its statistical properties are described by the canonical ensemble distribution $\rho(q, p) = \frac{1}{Z} e^{-\frac{h_0(q,p)}{k_B T}}$ where we have introduced the canonical variables $q = (\vec{r}_1, ..., \vec{r}_N)$ and $p = (\vec{p}_1, ..., \vec{p}_N)$, the Boltzmann constant k_B and the partition function Z.

2.1. Polymer chain with fixed end-to-end distance

By setting a given end-to-end distance, positions $\vec{r}_0$ and $\vec{r}_N$ are fixed and we can use the following reduced Hamiltonian

$$h(\vec{r}_1, .., \vec{r}_{N-1}, \vec{p}_1, .., \vec{p}_{N-1}, \vec{r}) = h_0(\vec{r}_1, .., \vec{r}_{N-1}, \vec{r}_N = \vec{r}, \vec{p}_1, .., \vec{p}_{N-1}, \vec{p}_N = 0). \tag{2}$$

In this case the microscopic variables are defined as $q = (\vec{r}_1, .., \vec{r}_{N-1})$ and $p = (\vec{p}_1, .., \vec{p}_{N-1})$, in terms of which the system partition function is written

$$Z_{\vec{r}}(\vec{r}, T) = \iint_{\Gamma_{N-1}} e^{-\frac{h(q, p, \vec{r})}{k_B T}} dq dp, \tag{3}$$

where $\Gamma_{N-1} = \Re^{6(N-1)}$. The net force exerted on the monomer at position $\vec{r}$ by the remaining monomers is by definition $-\frac{\partial h}{\partial \vec{r}}$. Such a force can be used to define the mechanical constitutive equation of the chain. In fact, the force exerted on the system (from the outside) in order to keep fixed the last monomer is $\vec{f} = \langle \frac{\partial h}{\partial \vec{r}} \rangle$, thus providing the statistical nonlinear generalization of Hooke's law for the chain

$$\vec{f}(\vec{r}, T) = -k_B T \frac{\partial}{\partial \vec{r}} \log Z_{\vec{r}} = \frac{\partial F(\vec{r}, T)}{\partial \vec{r}}, \tag{4}$$

where $F(\vec{r}, T) = -k_B T \log Z_{\vec{r}}$ is the Helmholtz free energy.

2.2. Polymer chain under constant load
We next assume that a given force $\vec{f}$ is applied to the terminal monomer at $\vec{r}_N$, while the end-to-end distance is free to fluctuate. This external force is described by an additional potential energy term given by $-\vec{f} \cdot \vec{r}_N$ since $-\frac{\partial}{\partial \vec{r}_N}(-\vec{f} \cdot \vec{r}_N) = \vec{f}$. Therefore, the system is described by the following augmented Hamiltonian

$$\widetilde{h}(\vec{r}_1, ..., \vec{r}_N, \vec{p}_1, ..., \vec{p}_N, \vec{f}) = h_0(\vec{r}_1, ..., \vec{r}_N, \vec{p}_1, ..., \vec{p}_N) - \vec{f} \cdot \vec{r}_N, \tag{5}$$

where $q = (\vec{r}_1, ..., \vec{r}_N)$ and $p = (\vec{p}_1, ..., \vec{p}_N)$ are the microscopic variables and $\vec{f}$ acts as a macroscopic variable. The ensemble partition function is now given by

$$Z_{\vec{f}}(\vec{f}, T) = \iint_{\Gamma_N} e^{-\frac{\widetilde{h}(q,p,\vec{f})}{k_B T}} dq \, dp, \tag{6}$$

where $\Gamma_N = \Re^{6N}$. We observe that $\frac{\partial \widetilde{h}}{\partial \vec{f}} = -\vec{r}_N$ and we calculate the mean position of the last monomer of the chain through the average value $\vec{r} = \langle \vec{r}_N \rangle$ or, more explicitly, $\vec{r} = -\langle \frac{\partial \widetilde{h}}{\partial \vec{f}} \rangle$. This constitutive equation can also be expressed in terms of the partition function $Z_{\vec{f}}$. In fact, by differentiating Eq.(6) with respect to $\vec{f}$, we get

$$\vec{r}(\vec{f}, T) = k_B T \frac{\partial}{\partial \vec{f}} \log Z_{\vec{f}} = -\frac{\partial G(\vec{f}, T)}{\partial \vec{f}}, \tag{7}$$

where $G(\vec{f}, T) = -k_B T \log Z_{\vec{f}}$ is the Gibbs free energy. It is possible to prove that the Helmholtz and Gibbs ensembles provide the same constitutive equation for large systems ($N \to \infty$) [8].

3. Flexible polymer with elastic bonds
We firstly consider a model in which each bond is represented by a harmonic spring with finite extension, while no potential is acting on bending or torsional degrees of freedom. Each spring is defined by the potential energy $V(x) = (1/2)k(x - l)^2$ for $x \in (l - \Delta, l + \Sigma)$ where k is the spring constant, l is the equilibrium bond length and x is the actual extension of the bond. We start with the Gibbs ensemble considering the augmented Hamiltonian in Eq.(5). In this case the determination of the spherically-symmetric partition function $Z_f(f, T)$ can be made in closed form (Ref. [8]) and directly provides the (scalar) constitutive equation $r(f) = k_B T \partial \log Z_f(f, T)/\partial f$. Similarly, using the proper partition function for the Helmholtz ensemble $Z_r(r, T)$, we obtain the scalar constitutive equation $f(r) = -k_B T \partial \log Z_r(r, T)/\partial r$ representing the elastic behaviour in the Helmholtz ensemble which depends on the number of monomers N (Ref. [8]). We expect a family of curves approaching the Gibbs solution for large N (thermodynamic limit).

4. Monte Carlo simulations
The Monte Carlo approach simulates the stretching of the polymer under a force provided by a cantilever mimiking the loading by an atomic force microscope. The device is characterized by its own effective elastic constant k_c, which is coupled in series to the chain of k domain springs. In the limit of a soft device, $k_c/k \to 0$, the statistics of the coupled system reduces to the Gibbs ensemble for the isolated molecule fluctuating under a constant force. On the other hand, for a very stiff device, $k_c/k \to \infty$, one recovers the Helmholtz ensemble for the isolated molecule held at a fixed extension by the fluctuating force [9]. In details, we adopted $k_c/k = 10^{-3}$ (soft cantilever) and $k_c/k = 10^2$ (stiff cantilever).
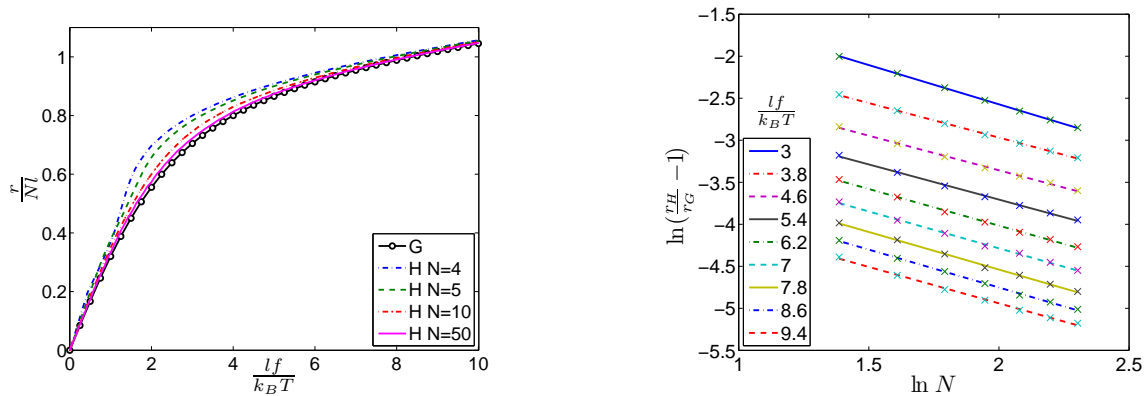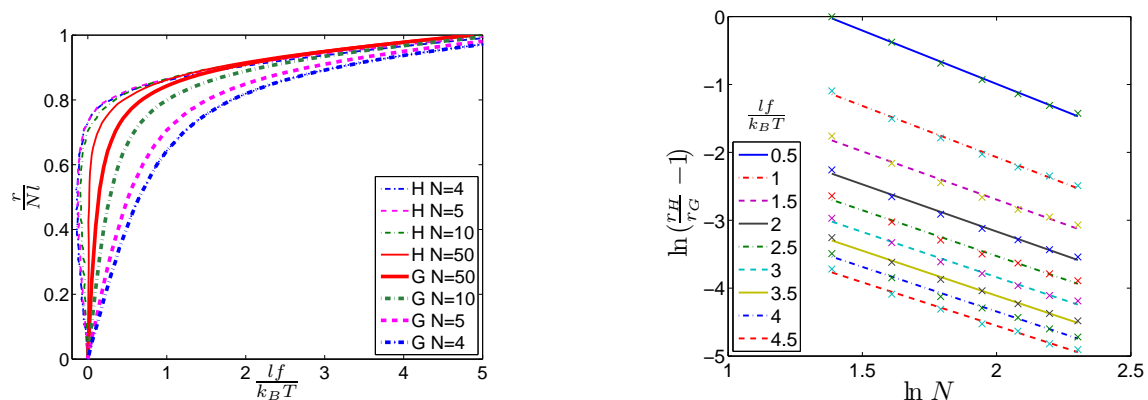
Figure 2. Left panel: constitutive relation provided by Monte Carlo simulations for a FJC model with elastic bonds between the monomers, both under Helmholtz (H) and Gibbs (G) boundary conditions. Right panel: comparison between the elongations r_H and r_G for the FJC model with elastic bonds between the monomers.

The initial state of the chain is defined by a set of randomly chosen positions for the monomers. The displacement extent $\delta \vec{r}_i$ of the positions vectors governs the magnitude of the trial move and the overall efficiency of the configurational space sampling. However, while a larger $\delta \vec{r}_i$ could speed up the search for the minimum, a too large $\delta \vec{r}_i$ leads to a high rejection frequency. Therefore, we analysed several runs in order to optimize its value. We avoided the dynamical adjustment of this parameter since this approach can violate the detailed balance [10].

In Fig.2 (left panel) we report our Monte Carlo results for the FJC model with elastic bonds in both statistical mechanics ensembles. In particular, we selected the value $k = 10 \ k_B T/(\text{nm})^2$ at $T = 293$ K. While we observe a single curve for the Gibbs ensemble we get different elastic response curves for the Helmholtz ensemble with polymer length $N = 4, 5, 10$ and 50. It is interesting to note that the Helmholtz curves approach the Gibbs one for large N, as expected for the convergence to the thermodynamic limit. In order to better characterize the convergence toward the thermodynamic limit, we investigate the ratio between the elongation $r_H(N) = r/(Nl)$ calculated in the Helmholtz ensemble and the elongation $r_G = r/(Nl)$ for the Gibbs ensemble. Fig.2 (right panel) proves that Monte Carlo simulations are nicely fitted by the power law $r_H(N)/r_G = 1 + a/N^\alpha$ where a and α are fitting parameters. Each curve provides the same scaling exponent $\alpha = 0.80 \pm 0.05$. Therefore, we argue that the convergence to the thermodynamic limit of the FJC model is quantitatively controlled by a unique scaling exponent.

5. Semiflexible polymer with elastic bonds
We now extend our model to a semiflexible chain which incorporates elastic bonds into a discrete version of the WLC. The augmented Hamiltonian for the Gibbs ensemble is given by Eq.(2) with the additional term $\frac{1}{2}\kappa \sum_{i=1}^{N-1} \left(\vec{t}_{i+1} - \vec{t}_i \right)^2$ where κ is the bending modulus and $\vec{t}_i$ is the unit vector collinear with the i-th bond. The corresponding reduced Hamiltonian for the Helmholtz ensemble is given by Eq.(5) with the same additional term. In Fig.3 (left panel) we report the Monte Carlo results for the WLC model with elastic bonds. We adopted the value $\kappa = 10 \ k_B T$ for the bending modulus. This value is comparable to that of polymer chains of biological interest (for example for DNA $\kappa = 15 \ k_B T$[11]). We consider again the data in Fig.3 (left panel) and the ratio $r_H(N)/r_G(N)$ (Fig.3, right panel) at a given fixed value of the normalized force. As before Monte Carlo simulations are nicely fitted by the power law $r_H(N)/r_G(N) = 1 + a/N^\alpha$

Figure 3. Left panel: constitutive relation provided by Monte Carlo simulations for the WLC model with elastic bonds between the monomers, both under Helmholtz (H) and Gibbs (G) boundary conditions. Right panel: comparison between the elongations r_H and r_G for the WLC model with elastic bonds between the monomers.

where $\alpha = 1.40 \pm 0.05$. Again, the convergence to the thermodynamic limit is controlled by a unique scaling exponent.

6. Conclusions

In this work we investigated how the force-extension curve of a model polymer chain is affected by the loading protocol which can typically be fixed-ends or fixed-force. We showed how such macroscopic boundary conditions can be formulated within the Helmholtz and the Gibbs ensembles of the statistical mechanics. We adopted flexible and semiflexible polymer models, with extensible bonds. In all cases here investigated (FJC and WLC with extensible bonds) we found that the convergence to the thermodynamic limit is well described by suitable power laws with well defined scaling exponents.

Acknowledgments

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