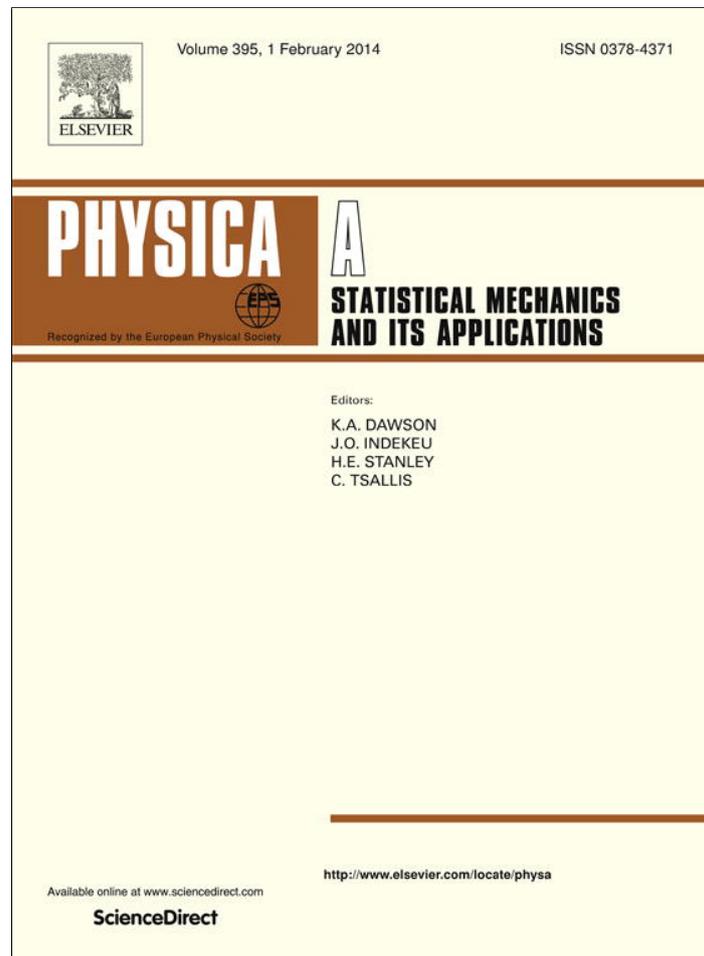


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On the equivalence of thermodynamics ensembles for flexible polymer chains



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HIGHLIGHTS

- The equivalence between Gibbs and Helmholtz ensembles for (not confined) polymer chains has been investigated.
- We rigorously proved the equivalence for a class of polymer models characterized by a continuous pairing interaction.
- We have introduced an original method based on the stationary phase technique.

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ABSTRACT

Although the problem of the ensembles equivalence for flexible polymers has aroused considerable interest, there is not an overall consensus on this topic. In this work, we present a theoretical investigation on the asymptotic equivalence of two ensembles for single flexible polymer chains (without confinement effects, i.e. fluctuating in the entire space): the first is the Gibbs (or isotensional) ensemble with one end-terminal of the chain tethered to a given point and the other subjected to an applied force; the other ensemble is the Helmholtz (or isometric) one characterized by both terminals tethered to fixed points. The equivalence property is rigorously proved for a class of potentials characterized by a continuous pairing interaction between neighboring monomers. To approach the problem we adopted an original analytical formalism based on the stationary phase technique and on the exact determination of the eigenvalues sign of the Hessian matrix of the phase function. To give some examples of application, the general result is successively applied to freely-jointed chains, to flexible polymers with extensible bonds and to chains with domains that exhibit conformational transitions between two stable states.

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1. Introduction

The problem of ensembles equivalence plays a central role in the assessment of the basic foundations of statistical mechanics. It consists in determining whether, in the thermodynamic limit (number of degrees of freedom approaching infinity), two statistical ensembles are equivalent, i.e. they lead to the same mathematical form of the constitutive equation describing the system under investigation (at equilibrium) [1–3]. Similarly, the equivalence can be also characterized by a Legendre transformation between the thermodynamic potentials (free energies) of the conjugated variables or by a Laplace–Stieltjes transformation between the partition functions of the conjugated ensembles [1].

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As an example, we can mention the microcanonical and canonical ensembles, representing the two most important statistical descriptions of many-particle systems. As initially observed by Gibbs, their definitions, in general, do not guarantee the equivalence in the thermodynamic limit [4]. Therefore, many theoretical studies have been conducted in order to understand how the equivalence property depends on the system considered, i.e. on the type of interaction acting among the particles [5–7]. It has been recently shown that the ensemble inequivalence can be observed in several systems with long-range interactions [8–10]. In particular, this behavior has been studied for generalized Ising Hamiltonians [8,9] and for nonlinear spherical spin glass models [10].

The issue of the equivalence of statistical ensembles is notably important for one-dimensional systems. In particular, this concept plays a crucial role in the theory of single polymer chains [11–14]. In this case, the deviation of the behavior corresponding to different statistical ensembles is indeed easily observable at both theoretical and experimental level (for chains with a finite number N of domains). In other words, short chains exhibit different physical responses (i.e. constitutive equations) when subjected to different boundary conditions (i.e. statistical ensembles). A large spectrum of single molecule manipulation techniques such as atomic force microscopy, optical and magnetic tweezers, have been recently developed and they allow to study these deviations for arbitrarily long molecules, such as DNA or proteins [15–18]. For the case of single polymer chains under stretching (without confinement effects, i.e. free to fluctuate in the whole space), two ensembles are typically considered [1]: the first one is the Gibbs (or isotensional) ensemble characterized by a deterministic force applied to the free end of the chain (being the other end clamped at the origin of the axes); the second one is the Helmholtz (or isometric) ensemble obtained with both the ends of the polymer tethered at two different points of the space. We remark that these two ensembles correspond to a couple of different canonical distributions, obtained with distinct boundary conditions. In this sense, we are dealing with the equivalence characterization between two dual versions of the canonical ensemble. On the one hand, when the thermodynamic limit is not satisfied (small number of monomers), these two situations are not equivalent, leading to different force–displacement curves [19,20]. This fact has been proven for different polymer models in the literature [21–23]. On the other hand, whenever N approaches infinity, it is important to elucidate if the equivalence of ensembles occurs or not.

Earlier investigations concerning the ensembles equivalence for flexible polymers have been performed adopting both theoretical approaches [21,24–31,19,32,33] and computational methodologies [30,34–37]. Typically the problem is studied by comparing force–extension relations [24,30,37], or by considering conjugated partition functions and the corresponding thermodynamic potentials [31,38]. As anticipated, despite several investigations, there is not an overall consensus on this topic. There are some authors that find agreement between averages determined by different ensembles in the thermodynamic limit, [21,25,22,28,31,30,19,33] while others emphasize non-equivalence [24,26,35–37,32] even in the thermodynamic limit. One of the source of the controversy is the following. The force–extension laws for the two ensembles map different quantities: $\langle \vec{f} \rangle$ and \vec{r} for the Helmholtz ensemble and $\langle \vec{r} \rangle$ and \vec{f} for the Gibbs one. Some authors [24,26,37] have introduced different average values. In particular, they considered the force–extension responses $\langle |\vec{f}| \rangle$ versus $|\vec{r}|$ for the Helmholtz case and the curve $\langle |\vec{r}| \rangle$ versus $|\vec{f}|$ for the Gibbs one. These assumptions involved some apparent inequivalences related to the transformation of random variables introduced to determine the average value of the modulus of the vectors \vec{r} and \vec{f} (in general $\langle |\vec{w}| \rangle \neq \langle |\vec{w}| \rangle$ if \vec{w} is a random vector) [19,32,33]. The reader can find a complete discussion about the origin of the contrasts concerning this problem in Ref. [31].

The investigations above dealt with the case of a polymer chain tethered at both ends with different types of boundary conditions (isometric or isotensional). In all cases no confinement effects have been considered. Another class of problems concerns a flexible polymer chain with one end tethered on a flat substrate surface and the other end free to fluctuate. In this system a piston of fixed geometry tries to confine the chain between the substrate and the piston itself, controlling the desorption and the escape transition [39–41]. The piston behavior can be defined to introduce the h -ensemble, where the distance between piston and substrate is directly controlled, and the f -ensemble, where the compression force applied to the cylinder is the independent parameter. In this system, which falls beyond the scope of the present paper, the confinement effects are of crucial importance. It has been proved that the escape transition of a polymer in these conditions exhibits an unusual non-equivalence between the defined statistical ensembles [39–41]. These results have been theoretically proved and confirmed by molecular dynamic simulations. Such an investigation is very important since it proves the possibility to have a real inequivalence between different versions of the canonical distribution in statistical mechanics. Nevertheless, we remark that these findings cannot be compared with the results of the present paper because of the completely different assumptions on the geometry defining the statistical ensembles considered. In fact, as previously declared, in this paper we do not take into consideration any form of confinement of the polymer chain.

In this paper, the equivalence of the Helmholtz and the Gibbs ensembles in the thermodynamic limit is rigorously proved for a specific class of polymer chains defined by the following assumptions that will be always considered throughout all the paper:

- we suppose to study a non-branched single chain without confinements, i.e. freely fluctuating in the whole space;
- the only constraints consist in the punctual boundary conditions defining the Helmholtz and the Gibbs ensembles;
- we consider all polymer models characterized by an arbitrary pairing interaction between adjacent monomers, described by a continuous energy function $V(x)$;
- we always suppose that the integrals defining both Helmholtz and Gibbs partition functions are convergent everywhere.

The third hypothesis leads to a Gibbs partition function which can be exactly written as a power of N (always convergent for the fourth assumption). As a matter of fact, this form is particularly convenient because allows us to draw a thorough analytical comparison of the two ensembles. In particular, the equivalence between the Gibbs and the Helmholtz ensembles is proved by performing a direct asymptotic comparison ($N \rightarrow \infty$) of the two corresponding force–extension relations. Such an analysis is conducted by elaborating the integrals through the vector version of the stationary phase technique [42,43]. The possibility to apply this method has been rigorously proved by investigating the sign of the eigenvalues of the Hessian matrix of the characteristic phase function. After having developed a general proof, valid for the entire class of potentials considered, the ensembles equivalence is further discussed for three particular systems, which are important for many applications: a freely jointed chain [11], a flexible polymer with extensible bonds [19] and a chain with domains that exhibit conformational transitions between two stable states [20]. Despite their simplicity, these models adequately describe different physical properties of many real polymer structures [11,12,19,20,44,45].

It is important to recall that a general criterion for the equivalence of thermodynamic ensembles exists and it is valid for a large class of physical systems: it affirms that the convexity of the Helmholtz free energy is sufficient to assure the equivalence between the ensembles (see Section 2.4 for details) [5–9]. However, this general criterion is of difficult applicability to polymer systems when the function $V(x)$ is sufficiently complicated, e.g. describing conformational transitions with multi-basin energy landscapes. On the other hand, our proof of the equivalence specifically developed for polymer systems can be easily applied to these complex interactions, furnishing a simpler result of large direct applicability.

The paper is organized as follows. In Section 2 we briefly describe the properties of the Helmholtz and Gibbs ensembles and we introduce an exact relationship between the corresponding partition functions. We also discuss the link between their free energies and the equivalence criterion based on the convexity of the Helmholtz free energy. In Section 3 we define the class of polymer models with pairing interactions and we present the three specific examples above mentioned. Moreover, in Section 4 we accurately prove the equivalence of the Gibbs and Helmholtz statistical ensembles for the class of polymers above introduced. Finally, in Section 5 we discuss the equivalence for the three specific examples.

2. Helmholtz and Gibbs ensembles

Let us consider a chain of monomers in a polymer molecule. The classical dynamics of monomers is described by the set of positions \vec{r}_i ($i = 1, \dots, N$) and momenta \vec{p}_i ($i = 1, \dots, N$). We assume that one terminal monomer is fixed at position $\vec{r}_0 \equiv (0, 0, 0)$ and that monomers interact through a potential $\mathcal{U} = \mathcal{U}(\vec{r}_1, \dots, \vec{r}_N)$. This implies that our scheme will be able to describe all types of polymer models, implemented by imposing the potential \mathcal{U} . The dynamics of the system is described by the Hamiltonian

$$h_0(\vec{r}_1, \dots, \vec{r}_N, \vec{p}_1, \dots, \vec{p}_N) = \sum_{i=1}^N \frac{\vec{p}_i \cdot \vec{p}_i}{2m} + \mathcal{U}(\vec{r}_1, \dots, \vec{r}_N), \quad (1)$$

where m is the mass of the monomers. 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

$$\rho(q, p) = \frac{1}{Z} e^{-\frac{h_0(q, p)}{k_B T}}, \quad (2)$$

where we have introduced the canonical variables $q = (\vec{r}_1, \dots, \vec{r}_N)$ and $p = (\vec{p}_1, \dots, \vec{p}_N)$, the Boltzmann constant k_B , and the partition function Z . The aim of this section is to obtain the thermodynamics of the system when the end terminal monomer is either clamped at a fixed position $\vec{r}_N = \vec{r}$, or it is subjected to a constant traction force \vec{f} (see Fig. 1). These two boundary conditions correspond to the Helmholtz and Gibbs statistical ensembles, respectively.

2.1. Isometric conditions

By setting a given (vector) end-to-end distance, positions \vec{r}_0 and \vec{r}_N are fixed (see Fig. 1 top) and we can use the following reduced Hamiltonian

$$h(\vec{r}_1, \dots, \vec{r}_{N-1}, \vec{p}_1, \dots, \vec{p}_{N-1}, \vec{r}) = h_0(\vec{r}_1, \dots, \vec{r}_{N-1}, \vec{r}_N = \vec{r}, \vec{p}_1, \dots, \vec{p}_{N-1}, \vec{p}_N = 0). \quad (3)$$

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

$$Z_{\vec{r}}(\vec{r}, T) = \int \int_{\Gamma_{N-1}} e^{-\frac{h(q, p, \vec{r})}{k_B T}} dq dp, \quad (4)$$

where $\Gamma_{N-1} = \mathfrak{R}^{6(N-1)}$. The equilibrium distribution is therefore

$$\rho_{\vec{r}}(q, p; \vec{r}, T) = \frac{1}{Z_{\vec{r}}(\vec{r}, T)} e^{-\frac{h(q, p, \vec{r})}{k_B T}}. \quad (5)$$

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 (hereafter referred as the “force–extension curve”) of the chain. In fact,

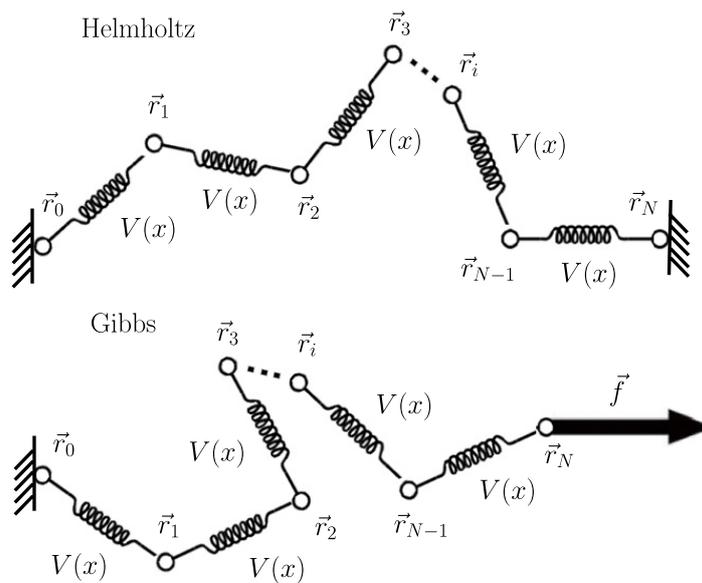


Fig. 1. Schemes of the mechanical boundary conditions leading to the Helmholtz (top) and Gibbs (bottom) statistical ensembles.

the force exerted on the system (from the outside) in order to keep fixed the last monomer is $\langle \vec{f} \rangle = \langle \frac{\partial \tilde{h}}{\partial \vec{r}} \rangle$, thus providing the statistical nonlinear generalization of the Hooke's law for the chain

$$\langle \vec{f}(\vec{r}, T) \rangle = -k_B T \frac{\partial}{\partial \vec{r}} \log Z_{\vec{r}} = \frac{\partial F(\vec{r}, T)}{\partial \vec{r}}, \quad (6)$$

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

2.2. Isotensional condition

We next assume that a given deterministic force \vec{f} is applied to the terminal monomer at \vec{r}_N , while the end-to-end distance is free to fluctuate (see Fig. 1 bottom). 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

$$\tilde{h}(\vec{r}_1, \dots, \vec{r}_N, \vec{p}_1, \dots, \vec{p}_N, \vec{f}) = h_0(\vec{r}_1, \dots, \vec{r}_N, \vec{p}_1, \dots, \vec{p}_N) - \vec{f} \cdot \vec{r}_N, \quad (7)$$

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

$$Z_{\vec{f}}(\vec{f}, T) = \iint_{\Gamma_N} e^{-\frac{\tilde{h}(q,p,\vec{f})}{k_B T}} dq dp, \quad (8)$$

where $\Gamma_N = \mathfrak{N}^{6N}$ and the corresponding statistical distribution is

$$\rho_{\vec{f}}(q, p; \vec{f}, T) = \frac{1}{Z_{\vec{f}}(\vec{f}, T)} e^{-\frac{\tilde{h}(q,p,\vec{f})}{k_B T}}. \quad (9)$$

We observe that $\frac{\partial \tilde{h}}{\partial \vec{f}} = -\vec{r}_N$ and we calculate the mean position of the last monomer of the chain through the average value $\langle \vec{r} \rangle = \langle \vec{r}_N \rangle$ or, more explicitly, $\langle \vec{r} \rangle = -\langle \frac{\partial \tilde{h}}{\partial \vec{f}} \rangle$. This constitutive equation can also be expressed in terms of the partition function $Z_{\vec{f}}$. In fact, by differentiating Eq. (8) with respect to \vec{f} , we get

$$\langle \vec{r}(\vec{f}, T) \rangle = k_B T \frac{\partial}{\partial \vec{f}} \log Z_{\vec{f}} = -\frac{\partial G(\vec{f}, T)}{\partial \vec{f}}, \quad (10)$$

where $G(\vec{f}, T) = -k_B T \log Z_{\vec{f}}$ is the Gibbs free energy.

2.3. Relation between partition functions

By taking into consideration Eqs. (4) and (8), an exact relationship between $Z_{\vec{f}}$ and $Z_{\vec{r}}$ can be easily obtained

$$Z_{\vec{f}}(\vec{f}, T) = (2\pi m k_B T)^{\frac{3}{2}} \int_{\mathfrak{N}^3} Z_{\vec{r}}(\vec{r}, T) e^{\frac{\vec{f} \cdot \vec{r}}{k_B T}} d\vec{r}, \quad (11)$$

showing that the Gibbs partition function is the three-dimensional (bilateral or two-sided) Laplace transform of the Helmholtz partition function (except for a non relevant multiplicative constant).

For the following purposes, it is useful to invert the previous integral relation. In Eq. (11) we let $\vec{f} = -k_B T \vec{s}$, where \vec{s} is the vector Laplace variable

$$Z_{\vec{f}}(-k_B T \vec{s}, T) = (2\pi m k_B T)^{\frac{3}{2}} \int_{\mathfrak{R}^3} Z_{\vec{r}}(\vec{r}, T) e^{-\vec{s} \cdot \vec{r}} d\vec{r}. \quad (12)$$

Now, we can remember that the definition of the one-dimensional Laplace transform of $f(t)$,

$$F(s) = \int_{-\infty}^{+\infty} f(t) e^{-st} dt, \quad (13)$$

leads to the inverse relation

$$F(s) = \frac{1}{2\pi i} \int_{\gamma - i\infty}^{\gamma + i\infty} F(s) e^{st} ds, \quad (14)$$

where the integration from $\gamma - i\infty$ to $\gamma + i\infty$ corresponds to the standard Bromwich contour on the complex plane and $\gamma \in \mathfrak{R}$ belongs to the range of convergence. For two-sided Laplace transforms we have a strip-shaped convergence domain $\alpha < \Re(s) < \beta$ and, therefore, we must select $\gamma \in (\alpha, \beta)$ [46]. In our case we assumed that $Z_{\vec{f}}(\vec{f}, T)$ is defined $\forall \vec{f} \in \mathfrak{R}^3$ and that $Z_{\vec{r}}(\vec{r}, T)$ is defined $\forall \vec{r} \in \mathfrak{R}^3$. In particular, Eq. (12) is valid for all $\Re(\vec{s}) \in \mathfrak{R}^3$. Therefore, to invert Eq. (12) we use three times Eq. (14), where we can always fix $\gamma = 0$ since $\Re(\vec{s}) = 0$ belongs to the convergence domain. This approach can also be found in Ref. [47], where the same conclusions have been drawn. Anyway, we easily obtain

$$Z_{\vec{r}}(\vec{r}, T) = \frac{1}{(2\pi i)^3} \frac{1}{(2\pi m k_B T)^{3/2}} \int_{-i\infty}^{+i\infty} \int_{-i\infty}^{+i\infty} \int_{-i\infty}^{+i\infty} Z_{\vec{f}}(-k_B T \vec{s}, T) e^{\vec{s} \cdot \vec{r}} d\vec{s}. \quad (15)$$

We use the substitution $\vec{s} = -i\vec{\eta}/(k_B T)$ and we eventually find the final result

$$Z_{\vec{r}}(\vec{r}, T) = \frac{1}{[(2\pi k_B T)^3 m]^{3/2}} \int_{\mathfrak{R}^3} Z_{\vec{f}}(i\vec{\eta}, T) e^{-i \frac{\vec{\eta} \cdot \vec{r}}{k_B T}} d\vec{\eta}, \quad (16)$$

which states that, in order to derive the Helmholtz partition function, one must use the analytic continuation of the Gibbs partition function over the imaginary argument. A complete discussion about Eqs. (11) and (16) can be found in a recent paper [19]. The relationship between the two partition functions plays a crucial role for proving the equivalence in the thermodynamic limit, as described below.

2.4. Free energies and their relationship

We take into consideration the Helmholtz free energy $F(\vec{r}, T)$ for the isometric ensemble and the Gibbs free energy $G(\vec{f}, T)$ for the isotensional one. They are related to the corresponding partition functions through the standard expressions

$$Z_{\vec{r}}(\vec{r}, T) = e^{-\frac{F(\vec{r}, T)}{k_B T}}, \quad (17)$$

$$Z_{\vec{f}}(\vec{f}, T) = e^{-\frac{G(\vec{f}, T)}{k_B T}}. \quad (18)$$

By inserting Eqs. (17) and (18) in Eq. (11) we obtain

$$e^{-\frac{G(\vec{f}, T)}{k_B T}} = (2\pi m k_B T)^{\frac{3}{2}} \int_{\mathfrak{R}^3} e^{-\frac{F(\vec{r}', T)}{k_B T}} e^{\frac{\vec{f} \cdot \vec{r}'}{k_B T}} d\vec{r}', \quad (19)$$

which is an exact relation between F and G , always satisfied (i.e. valid for any N). In order to prove that the Helmholtz and Gibbs ensembles provide the same constitutive equation for large systems ($N \rightarrow \infty$), we need to verify that Eq. (6) coincides with the inverse function of Eq. (10). Alternatively, we can say that this statement is proved provided that the Helmholtz and the Gibbs energy functions are related, for large N , by a Legendre transformation $G = F - \vec{f} \cdot \vec{r}$, as widely discussed elsewhere [1].

We try to understand how Eq. (19) may yield a Legendre transformation between F and G . By expanding $F(\vec{r}, T)$ up to the second order in \vec{r} we obtain

$$F|_{\vec{r}'} \simeq F|_{\vec{r}} + \frac{\partial F}{\partial \vec{r}} (\vec{r}' - \vec{r}) + \frac{1}{2} (\vec{r}' - \vec{r}) \cdot \frac{\partial^2 F}{\partial \vec{r}^2} (\vec{r}' - \vec{r}), \quad (20)$$

where $\frac{\partial^2 F}{\partial \vec{r}^2}$ represents the Hessian matrix of F . In the previous series expansion we did not consider the third order term and higher since, for large N , their effects are negligible with respect to the leading terms (first and second order). This is

a typical approximation adopted and justified within the Laplace method useful for obtaining the asymptotic behavior of integrals (e.g. used for proving the standard Stirling approximation for the factorial function, largely used in several statistical mechanics evaluations) [48]. By substituting Eq. (20) in Eq. (19) we eventually obtain

$$G = F - \vec{f} \cdot \vec{r} - k_B T \ln \Gamma, \quad (21)$$

where

$$\Gamma = (2\pi m k_B T)^{\frac{3}{2}} \int_{\mathbb{R}^3} e^{-\frac{1}{2k_B T} (\vec{r}' - \vec{r}) \frac{\partial^2 F}{\partial \vec{r}^2} (\vec{r}' - \vec{r})} d\vec{r}'. \quad (22)$$

The quantities G , F , Γ and $\vec{f} \cdot \vec{r}$ assume an extensive character (i.e. they are proportional to N) and, therefore, the logarithmic term in Eq. (21) becomes negligible for large systems. Of course, it is true if the Hessian of F is positive definite in order to have the convergence of the integral in Γ . Thus, for $N \rightarrow \infty$, the Legendre transformation is fulfilled if the free energy F is convex everywhere. Finally, a convex everywhere function F yields always equivalence.

This is a universal result largely utilized in general statistical mechanics since it can be applied to arbitrary systems and not only to polymer structures [1]. Moreover, it is not only valid to characterize the equivalence between Helmholtz and Gibbs ensembles (which are two particular cases of canonical ensemble with different boundary conditions), but also the equivalence between microcanonical and canonical ensembles (see, e.g. Refs. [8,6]). This criterion is therefore of indubitable theoretical importance. However, although it has been largely used to infer the equivalence of Helmholtz and Gibbs ensembles of polymer systems, it has regrettably conducted to some controversies briefly discussed in the introduction [1,19,32,33]. In addition, while the convexity verification for F may be elementary for simple polymer structures (see the first two examples in the next section), it can be rather complicated for polymers described by more elaborated Hamiltonians. As an example we can mention the interactions among monomers described by a potential energy exhibiting more than one minimum point, corresponding to different macroscopic states (see the third case in the next section). Incidentally, we remark that there is a great interest in the polymer community in analyzing complex chemical structures characterized by multiple-basin energy landscapes and multi-state conformational transitions [49–52]. As a matter of fact, these structures are very important to understand the behavior of biomolecules (proteins and nucleic acids) which often undergo folding and unfolding processes in order to execute their functions (e.g. binding or releasing ligands or signals transduction). For these reasons we search for a more specific alternative equivalence criterion that is simpler from the mathematical point of view and more related to the quantities really measurable in standard single molecule manipulation techniques. We therefore analyze the equivalence by directly examining the force–extension response in the two ensembles, for an increasing number of monomers. To do this we do not need to use the free energies and, consequently, we ground our method on the comparison between Eqs. (6) and (10). We remark that this approach is original since no equivalence analyses have been developed in the literature by directly examining the coincidence of the constitutive equations for large systems. This procedure is thoroughly described in Section 4. The mathematical methods based on the Laplace transforms have been largely used in the literature for studying the equivalence through the free energies approach [1,5–9,22,47,19]. Here we use the same techniques, but directly applied to the force–extension relationships. We are finally able to prove the following result. We consider a polymer chain with a pairing interaction between monomers described by the potential energy $V(x)$ (being x the distance between two adjacent monomers). If we suppose (i) to avoid any form of confinement, (ii) to consider the Helmholtz and the Gibbs boundary conditions, (iii) to use a potential function $V(x)$ continuous, and (iv) to assume partition functions $Z_{\vec{r}}(\vec{r}, T)$ and $Z_{\vec{f}}(\vec{f}, T)$ convergent everywhere, then the ensembles are certainly statistically equivalent. Of course, this is a particular case of the more general result based on the convexity of the Helmholtz free energy F ; the new statement is indeed valid for a more restricted class of physical systems. Nevertheless, for the polymer community this result should be important since it is more easily applicable than the convexity of F , also for the case where $V(x)$ exhibits more than one minimum point. Moreover, the technique applied to obtain this result is also useful to approach the following problem. While the Gibbs partition function can be analytically studied without difficulties in many cases, the Helmholtz partition function can never be written in closed form. The scheme here presented can be also adopted to obtain the approximated form of the Helmholtz partition function for N large. This point is thoroughly developed in Ref. [22].

3. A class of polymer models

Let us take into consideration the class of polymer models described by a pairing interaction between neighboring monomers

$$\mathcal{U}(\vec{r}_1, \dots, \vec{r}_N) = \sum_{i=1}^N V(\|\vec{r}_i - \vec{r}_{i-1}\|), \quad (23)$$

where $V(x)$ represents the potential acting between each couple of adjacent monomers. This class of models is able to take into consideration any linear or nonlinear form of the contraction/extension of the chemical bond between monomers. On the contrary, it is not able to describe angular interactions between adjacent bonds, which are sometimes useful to model the bending response of the chain. As an example, we cannot take into consideration the so called worm like chain model

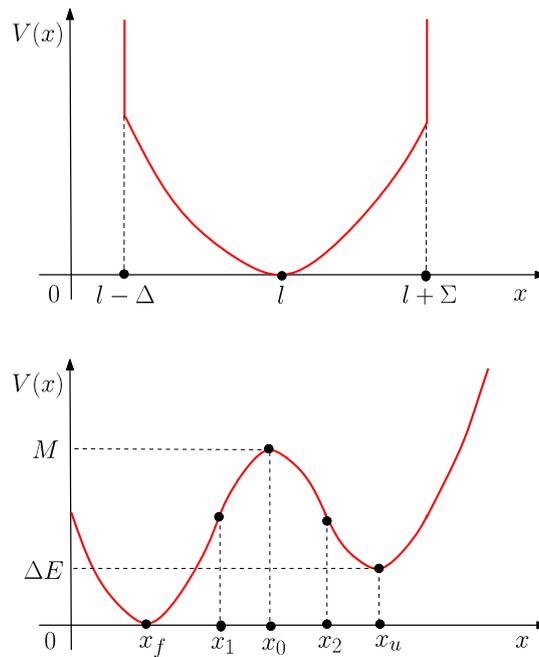


Fig. 2. Plots of two examples of pairing interaction potentials. Top panel: EBS (extensible bonds chain) model; bottom panel: TSC (two-state chain) model.

(and its several modifications) [11,12]. By using Eq. (8) it is not difficult to realize that the assumption in Eq. (23) leads to a Gibbs partition function in form of a power of N

$$Z_{\vec{f}}(\vec{f}, T) = [A(\vec{f})]^N, \tag{24}$$

where the base is

$$A(\vec{f}) = \left(\frac{2\pi m}{\beta}\right)^{3/2} \frac{4\pi}{\beta \|\vec{f}\|} \int_0^\infty \exp[-\beta V(x)] \sinh(\beta \|\vec{f}\| x) dx. \tag{25}$$

From now on we assume $\beta = 1/(k_B T)$. Of course, Eqs. (24) and (25) are only valid for systems without confinements [39–41]. This mathematical form of $Z_{\vec{f}}(\vec{f}, T)$ will be very useful in the next section to approach the problem of the ensembles equivalence for large molecules. From now on we suppose to work with functions $V(x)$ yielding partition functions $Z_{\vec{r}}(\vec{r}, T)$ and $Z_{\vec{f}}(\vec{f}, T)$ convergent everywhere. From Eq. (25) it is not difficult to prove that if the integral is convergent with a continuous function $V(x)$, then $A(\vec{f})$ is a differentiable function of \vec{f} . This property is important to develop the following calculations. We remark that the determination of the Helmholtz partition function cannot be performed in closed form but, however, we can exploit the property stated in Eq. (16).

3.1. Particular cases

Although we will prove the equivalence of ensembles for an arbitrary potential $V(x)$, we introduce here some specific polymer models, as examples useful in several applications. Three important chains belonging to such a class of polymers are the following:

- freely jointed chain (FJC) model;
- flexible model with extensible bonds;
- chain model consisting of domains which can exhibit conformational transitions between two states.

The corresponding partition functions for the Gibbs ensemble are reported in Table 1.

The Gibbs partition function for the FJC model is a standard result in polymer theory [11,12] and, for the sake of completeness, it is reported in the first line of Table 1. This mathematical form can be recovered by taking into consideration a spring like interaction potential $V(x) = (1/2)k(x - l)^2$ and by performing the limit for the constant k approaching infinity. So doing, we impose the constant length l to all bonds between adjacent monomers, as discussed in Ref. [19].

The second model considers an extensible bonds chain (EBC) described by harmonic interactions. 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 and l is the equilibrium bond length (both quantities assuming finite values). The potential is set to infinity for $x \notin (l - \Delta, l + \Sigma)$ in order to impose a limited extension of the spring both for expansion and compression (see Fig. 2, top panel). The correspondent Gibbs partition function is given in second line of Table 1. Other details concerning this model can be found in the literature [19].

Table 1

Partition functions of the polymer models described in Section 3: FJC (freely jointed chain), EBS (extensible bonds chain) and TSC (two-state chain). The function Π is defined as $\Pi(\alpha, \gamma, x_0, a, b) = 2 \int_a^b x e^{-\frac{\alpha}{2}(x-x_0)^2} \sinh(\gamma x) dx$.
 Source: For its closed form expression see Refs. [19,20].

Polymer model	Gibbs partition function
FJC	$Z_{\vec{f}}(\vec{f}, T) = \text{const.} \times \left[\frac{\sinh(\beta \ \vec{f}\ l)}{\beta \ \vec{f}\ l} \right]^N$
EBC	$Z_{\vec{f}}(\vec{f}, T) = \left(\frac{2\pi m}{\beta} \right)^{3N/2} \left(\frac{2\pi}{\beta \ \vec{f}\ } \right)^N \times \left[\Pi(\beta k, \beta \ \vec{f}\ , l, l - \Delta, l + \Sigma) \right]^N$
TSC	$Z_{\vec{f}}(\vec{f}, T) = \left(\frac{2\pi m}{\beta} \right)^{3N/2} \left(\frac{2\pi}{\beta \ \vec{f}\ } \right)^N \times \left[\Pi(\beta k, \beta \ \vec{f}\ , x_f, 0, x_1) + e^{-\beta M} \Pi(-\beta k, \beta \ \vec{f}\ , x_0, x_1, x_2) + e^{-\beta \Delta E} \Pi(\beta k, \beta \ \vec{f}\ , x_u, x_2, +\infty) \right]^N$

To conclude, we consider a two-state chain (TSC) consisting of N domains, able to describe conformational transitions of the polymer structure. The internal state of each domain is described by a potential energy $V(x)$, which exhibits two minima corresponding to the lengths $x = x_f$ (folded conformation) and $x = x_u$ (unfolded conformation), connected via an energy barrier M at $x = x_0$ (see Fig. 2, bottom panel). The energy is written as a \mathcal{C}^2 piecewise function, constructed by imposing continuity and differentiability at the joining points x_1 and x_2

$$V(x) = \begin{cases} \frac{1}{2}k(x - x_f)^2 & 0 < x < x_1 \\ -\frac{1}{2}k(x - x_0)^2 + M & x_1 < x < x_2 \\ \frac{1}{2}k(x - x_u)^2 + \Delta E & x > x_2. \end{cases} \quad (26)$$

For chosen values of the lengths x_f and x_u , the domain spring constant k , and the energy difference ΔE between the two conformations, all the other parameters are simply calculated as follows. The domain length variation generated by the force-induced conformational transition is given by

$$\delta = x_u - x_f, \quad (27)$$

the energy barrier position and amplitude are

$$x_0 = \frac{x_u + x_f}{2} + 2 \frac{\Delta E}{k\delta}, \quad (28)$$

$$M = \frac{k}{4} \left[\frac{\delta}{2} + 2 \frac{\Delta E}{k\delta} \right]^2, \quad (29)$$

and the extremes of the domains x_1 and x_2 can be evaluated through the expressions

$$x_1 = x_f + \frac{\delta}{4} + \frac{\Delta E}{k\delta}, \quad (30)$$

$$x_2 = x_u - \frac{\delta}{4} + \frac{\Delta E}{k\delta}. \quad (31)$$

We remark that this model properly gives a barrier with $x_f < x_0 < x_u$ only for $|\Delta E| \leq k \frac{\delta^2}{4}$. When x_f , x_u , k and ΔE are fixed, the model is completely defined and we get the partition function given in the third of Table 1. The application of this model to several conformational transitions observed in polymers of biological origin (DNA [44], large protein domains such as the Ig units in titin [45], and polysaccharides such as the dextran [53]) can be found in a recent paper [20].

In the next section we consider the class of polymers here introduced, and in particular the three examples described, in order to prove the equivalence between the Gibbs and Helmholtz ensembles.

4. Equivalence of the ensembles

We consider a polymer with the partition function given in Eq. (24) and we determine the Gibbs constitutive equation stated in Eq. (10)

$$\langle \vec{r}(\vec{f}, T) \rangle = k_B T \frac{\partial}{\partial \vec{f}} \log Z_{\vec{f}} = k_B T \frac{1}{Z_{\vec{f}}} \frac{\partial}{\partial \vec{f}} Z_{\vec{f}}, \quad (32)$$

which immediately assumes the simpler form

$$\langle \vec{r}(\vec{f}, T) \rangle = k_B T \frac{1}{A^N} \frac{\partial}{\partial \vec{f}} A^N = N k_B T \frac{1}{A} \frac{\partial A}{\partial \vec{f}}. \quad (33)$$

In order to take into consideration the Helmholtz ensemble we take advantage of Eq. (16). Therefore, by using Eq. (24), we easily get

$$Z_{\vec{r}}(\vec{r}, T) = \text{const.} \times \int_{\mathfrak{R}^3} [A(i\vec{\eta})]^N e^{-i \frac{\vec{\eta} \cdot \vec{r}}{k_B T}} d\vec{\eta}. \quad (34)$$

Consequently, the Helmholtz constitutive equation is given by Eq. (6)

$$\langle \vec{f}(\vec{r}, T) \rangle = -k_B T \frac{\partial}{\partial \vec{r}} \log Z_{\vec{r}} = -k_B T \frac{1}{Z_{\vec{r}}} \frac{\partial}{\partial \vec{r}} Z_{\vec{r}}, \quad (35)$$

or, by using Eq. (34), by the following expression

$$\langle \vec{f}(\vec{r}, T) \rangle = i \frac{\int_{\mathfrak{R}^3} \vec{\eta} e^{-i \frac{\vec{\eta} \cdot \vec{r}}{k_B T}} [A(i\vec{\eta})]^N d\vec{\eta}}{\int_{\mathfrak{R}^3} e^{-i \frac{\vec{\eta} \cdot \vec{r}}{k_B T}} [A(i\vec{\eta})]^N d\vec{\eta}}. \quad (36)$$

Now, we must compare the two ensembles through Eqs. (33) and (36). The Gibbs vision in Eq. (33) furnishes

$$\langle \vec{r} \rangle = \Phi(\vec{f}), \quad (37)$$

while the Helmholtz vision in Eq. (36) gives

$$\langle \vec{f} \rangle = \Psi(\vec{r}). \quad (38)$$

If we have the ensembles equivalence for $N \rightarrow \infty$ (i.e. the same constitutive equation), Φ must be the inverse function of Ψ (and vice versa) and, therefore, we must obtain

$$\lim_{N \rightarrow \infty} \Psi(\Phi(\vec{f})) = \vec{f}. \quad (39)$$

We begin by constructing the quantity $\Psi(\Phi(\vec{f}))$ as follows

$$\begin{aligned} \Psi(\Phi(\vec{f})) &= i \frac{\int_{\mathfrak{R}^3} \vec{\eta} e^{-i \frac{\vec{\eta} \cdot \Phi(\vec{f})}{k_B T} \cdot N k_B T \frac{1}{A(\vec{f})} \frac{\partial A(\vec{f})}{\partial \vec{f}}} [A(i\vec{\eta})]^N d\vec{\eta}}{\int_{\mathfrak{R}^3} e^{-i \frac{\vec{\eta} \cdot \Phi(\vec{f})}{k_B T} \cdot N k_B T \frac{1}{A(\vec{f})} \frac{\partial A(\vec{f})}{\partial \vec{f}}} [A(i\vec{\eta})]^N d\vec{\eta}} \\ &= i \frac{\int_{\mathfrak{R}^3} \vec{\eta} e^{-iN \left[\frac{\vec{\eta} \cdot \Phi(\vec{f})}{A(\vec{f})} \cdot \frac{\partial A(\vec{f})}{\partial \vec{f}} + i \log A(i\vec{\eta}) \right]} d\vec{\eta}}{\int_{\mathfrak{R}^3} e^{-iN \left[\frac{\vec{\eta} \cdot \Phi(\vec{f})}{A(\vec{f})} \cdot \frac{\partial A(\vec{f})}{\partial \vec{f}} + i \log A(i\vec{\eta}) \right]} d\vec{\eta}}. \end{aligned} \quad (40)$$

By defining the phase function

$$g(\vec{\eta}) = \frac{\vec{\eta} \cdot \Phi(\vec{f})}{A(\vec{f})} \cdot \frac{\partial A(\vec{f})}{\partial \vec{f}} + i \log A(i\vec{\eta}), \quad (41)$$

we can simply write

$$\Psi(\Phi(\vec{f})) = i \frac{\int_{\mathfrak{R}^3} \vec{\eta} e^{-iN g(\vec{\eta})} d\vec{\eta}}{\int_{\mathfrak{R}^3} e^{-iN g(\vec{\eta})} d\vec{\eta}}. \quad (42)$$

The integrals appearing in Eq. (42) can be asymptotically evaluated ($N \rightarrow \infty$) through the method of the stationary phase [42,43]. The underlying principle of the method is the assertion that the major contribution to the integrals comes from the points where the phase function $g(\vec{\eta})$ is stationary, i.e. $\partial g(\vec{\eta})/\partial \vec{\eta}$ vanishes. Therefore, we search the points (if any) that make the phase $g(\vec{\eta})$ stationary. We prove the existence of a single value $\vec{\eta}_0$ so that

$$\left[\frac{\partial g(\vec{\eta})}{\partial \vec{\eta}} \right]_{\vec{\eta}=\vec{\eta}_0} = 0. \quad (43)$$

Working out the derivative, we get

$$\frac{\partial g}{\partial \vec{\eta}} = \frac{1}{A(\vec{f})} \frac{\partial A(\vec{f})}{\partial \vec{f}} - \frac{1}{A(i\vec{\eta})} \left[\frac{\partial A(\vec{f})}{\partial \vec{f}} \right]_{\vec{f}=i\vec{\eta}}. \quad (44)$$

So, the condition in Eq. (43) is verified if and only if

$$\frac{1}{A(\vec{f})} \frac{\partial A(\vec{f})}{\partial \vec{f}} = \frac{1}{A(i\vec{\eta})} \left[\frac{\partial A(\vec{f})}{\partial \vec{f}} \right]_{\vec{f}=i\vec{\eta}}, \quad (45)$$

a condition proving the existence of the following unique stationary point

$$\vec{\eta}_0 = -i\vec{f}. \quad (46)$$

It is a remarkable result that we can obtain the position of the stationary point in closed form. Such an achievement allows us to apply the stationary phase method as follows. We develop the phase function in a power series centered in $\vec{\eta} = \vec{\eta}_0$ and we retain the terms up to the second order

$$g(\vec{\eta}) \simeq g(\vec{\eta}_0) + \frac{\partial g}{\partial \eta} (\vec{\eta} - \vec{\eta}_0) + \frac{1}{2} (\vec{\eta} - \vec{\eta}_0)^T \mathbb{H} (\vec{\eta} - \vec{\eta}_0), \quad (47)$$

where \mathbb{H} is the Hessian matrix of $g(\vec{\eta})$ calculated for $\vec{\eta} = \vec{\eta}_0 = -i\vec{f}$. Moreover, we observe that $\frac{\partial g}{\partial \eta} = 0$ for $\vec{\eta} = \vec{\eta}_0 = -i\vec{f}$, a condition leading to the simplified expression

$$g(\vec{\eta}) \simeq g(\vec{\eta}_0) + \frac{1}{2} (\vec{\eta} - \vec{\eta}_0)^T \mathbb{H} (\vec{\eta} - \vec{\eta}_0). \quad (48)$$

Returning to Eq. (42), for $N \rightarrow \infty$ we have

$$\Psi(\Phi(\vec{f})) \stackrel{N \rightarrow \infty}{\simeq} i \frac{\int_{\mathfrak{R}^3} \vec{\eta} e^{-iN[g(\vec{\eta}_0) + \frac{1}{2}(\vec{\eta} - \vec{\eta}_0)^T \mathbb{H}(\vec{\eta} - \vec{\eta}_0)]} d\vec{\eta}}{\int_{\mathfrak{R}^3} e^{-iN[g(\vec{\eta}_0) + \frac{1}{2}(\vec{\eta} - \vec{\eta}_0)^T \mathbb{H}(\vec{\eta} - \vec{\eta}_0)]} d\vec{\eta}}. \quad (49)$$

In this calculation we have considered an expansion up to the second order only. This can be justified by means of the following theorem: we consider an arbitrary integral $I(N) = \int h(\vec{x}) \exp[Ns(\vec{x})] d\vec{x}$ with $h(\vec{x})$ and $s(\vec{x})$ sufficiently regular. If $s(\vec{x})$ achieves its global maximum at a unique point \vec{x}_0 and the Hessian of $s(\vec{x})$ at \vec{x}_0 is negative definite, we have $I(N) = P(N) + R(N)$, where $P(N)$ is the standard approximated expression obtained by considering the second order expansion of $s(\vec{x})$ (as we did above) and $R(N)$ is the remainder term satisfying $\lim_{N \rightarrow \infty} R(N)/P(N) = 0$. It means that the terms of order larger than two in $s(\vec{x})$ generate vanishing terms in the limit $N \rightarrow \infty$. An exact proof of this property can be found in Ref. [42, Theorem 41, p. 56].

Now, performing the change of variable $\vec{\eta} - \vec{\eta}_0 = \vec{w}$ (yielding $d\vec{\eta} = d\vec{w}$), we get from Eq. (49)

$$\begin{aligned} \Psi(\Phi(\vec{f})) &\stackrel{N \rightarrow \infty}{\simeq} i \frac{\int_{\mathfrak{R}^3} (\vec{w} + \vec{\eta}_0) e^{-iN[\vec{w}^T \mathbb{H} \vec{w}]} d\vec{w}}{\int_{\mathfrak{R}^3} e^{-iN[\vec{w}^T \mathbb{H} \vec{w}]} d\vec{w}} \\ &= i\vec{\eta}_0 + i \frac{\int_{\mathfrak{R}^3} \vec{w} e^{-iN[\vec{w}^T \mathbb{H} \vec{w}]} d\vec{w}}{\int_{\mathfrak{R}^3} e^{-iN[\vec{w}^T \mathbb{H} \vec{w}]} d\vec{w}}. \end{aligned} \quad (50)$$

Now, we can use the standard results for the integration of multidimensional Gaussian functions

$$\int_{\mathfrak{R}^3} \vec{w} e^{-\vec{w}^T \mathbb{M} \vec{w}} d\vec{w} = \vec{0} \in \mathfrak{R}^3, \quad (51)$$

$$\int_{\mathfrak{R}^3} e^{-\vec{w}^T \mathbb{M} \vec{w}} d\vec{w} = \sqrt{\frac{\pi^3}{\det \mathbb{M}}} \neq 0, \quad (52)$$

which are valid for any symmetric complex matrix \mathbb{M} having all eigenvalues with strictly positive real part. These properties can be used in Eq. (50) by assuming $\mathbb{M} = iN\mathbb{H}$ and by supposing that all eigenvalues of $i\mathbb{H}$ have strictly positive real part. This condition will be studied in detail below. Finally, we get from Eqs. (50)–(52)

$$\Psi(\Phi(\vec{f})) \stackrel{N \rightarrow \infty}{\simeq} i\vec{\eta}_0 = i(-i\vec{f}) = \vec{f}, \quad (53)$$

and we have therefore proved the equivalence of the Helmholtz and Gibbs ensembles in the thermodynamic limit.

Now, it is essential to investigate the sign of the real part of the eigenvalues of $i\mathbb{H}$. To this aim, from Eq. (41), we can write

$$\frac{\partial g}{\partial \eta_k} = \frac{1}{A(\vec{f})} \frac{\partial A(\vec{f})}{\partial f_k} + i \frac{1}{A(i\vec{\eta})} \frac{\partial A(i\vec{\eta})}{\partial \eta_k} \quad (54)$$

and

$$\begin{aligned} \frac{\partial^2 g}{\partial \eta_h \partial \eta_k} &= i \frac{\partial}{\partial \eta_h} \left(\frac{1}{A(i\vec{\eta})} \frac{\partial A(i\vec{\eta})}{\partial \eta_k} \right) \\ &= \frac{-i}{A^2(i\vec{\eta})} \frac{\partial A(i\vec{\eta})}{\partial \eta_h} \frac{\partial A(i\vec{\eta})}{\partial \eta_k} + \frac{i}{A(i\vec{\eta})} \frac{\partial^2 A(i\vec{\eta})}{\partial \eta_h \partial \eta_k}. \end{aligned} \quad (55)$$

So, we have

$$i\mathbb{H}_{kh} = \frac{1}{A^2(i\vec{\eta})} \frac{\partial A(i\vec{\eta})}{\partial \eta_h} \frac{\partial A(i\vec{\eta})}{\partial \eta_k} - \frac{1}{A(i\vec{\eta})} \frac{\partial^2 A(i\vec{\eta})}{\partial \eta_h \partial \eta_k}. \quad (56)$$

It is important to remark that $A(\vec{f})$ has a spherical symmetry (i.e. it depends only on the length $\|\vec{f}\|$ of the vector \vec{f}): this is manifest in Eq. (25) and in the partition functions of the examples presented in Section 3. Therefore, also the function $A(i\vec{\eta})$ exhibits a spherical symmetry, depending only on the quantity $\|\vec{\eta}\|$. Explicitly, from Eq. (25) we easily obtain

$$A(i\vec{\eta}) = \left(\frac{2\pi m}{\beta} \right)^{3/2} \frac{4\pi}{\beta \|\vec{\eta}\|} \int_0^\infty \exp[-\beta V(x)] \sin(\beta \|\vec{\eta}\| x) x dx. \quad (57)$$

By introducing the dimensionless quantity $\xi = \beta l \|\vec{\eta}\|$ (being l the equilibrium length of each bond) and the change of variable $x = ly$ (with y again dimensionless), we may define the real function $B(\xi) \triangleq A(i\vec{\eta})$ as follows

$$B(\xi) = \text{const.} \times \int_0^\infty \exp[-\beta V(ly)] \frac{\sin(\xi y)}{\xi} y dy. \quad (58)$$

We can now further develop the derivatives in Eq. (56). To do this we observe that

$$\frac{\partial A(i\vec{\eta})}{\partial \eta_h} = \frac{\partial B(\xi)}{\partial \xi} \frac{\partial \xi}{\partial \eta_h} = \frac{\partial B(\xi)}{\partial \xi} \beta l \frac{\partial \|\vec{\eta}\|}{\partial \eta_h} \quad (59)$$

and, by using the standard property $\partial \|\vec{\eta}\| / \partial \eta_h = \eta_h / \|\vec{\eta}\|$, we obtain the first result

$$\frac{\partial A(i\vec{\eta})}{\partial \eta_h} = \frac{\partial B(\xi)}{\partial \xi} \beta l \frac{\eta_h}{\|\vec{\eta}\|}. \quad (60)$$

We can similarly determine the expression for the second order derivative

$$\begin{aligned} \frac{\partial^2 A(i\vec{\eta})}{\partial \eta_h \partial \eta_k} &= \frac{\partial}{\partial \eta_k} \left(\frac{\partial B(\xi)}{\partial \xi} \beta l \frac{\eta_h}{\|\vec{\eta}\|} \right) \\ &= \beta l \frac{1}{\|\vec{\eta}\|^2} \left[\frac{\delta_{hk} \|\vec{\eta}\|^2 - \eta_h \eta_k}{\|\vec{\eta}\|} \frac{\partial B(\xi)}{\partial \xi} + \beta l \eta_h \eta_k \frac{\partial^2 B(\xi)}{\partial \xi^2} \right]. \end{aligned} \quad (61)$$

Summing up, these results can be used in Eq. (56), by eventually obtaining

$$i\mathbb{H}_{kh} = \frac{1}{B^2(\xi)} (\beta l)^2 \frac{\eta_h \eta_k}{\|\vec{\eta}\|^2} \left(\frac{\partial B(\xi)}{\partial \xi} \right)^2 - \frac{1}{B(\xi)} \beta l \frac{1}{\|\vec{\eta}\|^2} \left[\frac{\delta_{hk} \|\vec{\eta}\|^2 - \eta_h \eta_k}{\|\vec{\eta}\|} \frac{\partial B(\xi)}{\partial \xi} + \beta l \eta_k \eta_h \frac{\partial^2 B(\xi)}{\partial \xi^2} \right]. \quad (62)$$

We remember that we defined $\xi = \beta l \|\vec{\eta}\|$ and that the Hessian matrix must be evaluated for $\vec{\eta} = \vec{\eta}_0 = -i\vec{f}$ (see Eq. (46)). Moreover, since the system is geometrically isotropic we can apply the force in an arbitrary spatial direction; to simplify the calculations we assume $\vec{f} = (0, 0, f)$ (leading to $\|\vec{f}\| = f$ and $\|\vec{\eta}\| = if$). In this case, from Eq. (62), we obtain the simpler form

$$i\mathbb{H} = \begin{bmatrix} \mu & 0 & 0 \\ 0 & \mu & 0 \\ 0 & 0 & \lambda \end{bmatrix}, \quad (63)$$

where

$$\mu = -\frac{\beta l}{if} \left[\frac{1}{B(\xi)} \frac{\partial B(\xi)}{\partial \xi} \right]_{\xi=i\beta fl}, \quad (64)$$

$$\lambda = \frac{(\beta l)^2}{B(\xi)} \left[\frac{1}{B(\xi)} \left(\frac{\partial B(\xi)}{\partial \xi} \right)^2 - \frac{\partial^2 B(\xi)}{\partial \xi^2} \right]_{\xi=i\beta fl}. \quad (65)$$

Since the matrix $i\mathbb{H}$ is now diagonal, λ and μ are its eigenvalues; moreover, they are manifestly real. The equivalence between the Helmholtz and Gibbs ensembles is therefore proved if $\lambda > 0$ and $\mu > 0$ for any value of the applied force f . We remark

that Eqs. (64) and (65) are valid for any kind of interaction potential $V(x)$ acting among adjacent monomers. Indeed, the function $B(\xi)$ appearing in Eqs. (64) and (65) is explicitly given in Eq. (58) as function of $V(x)$. To conclude our demonstration, we prove that $\lambda > 0$ and $\mu > 0$ for any admissible (with convergent partition functions) continuous potential $V(x)$. After some straightforward calculation we can obtain the following expressions (we neglect the non influential constant in Eq. (58))

$$[B(\xi)]_{\xi=i\beta f} = \int_0^\infty e^{-\beta V(y)} g_1(y) y dy, \tag{66}$$

$$-\frac{1}{i} \left[\frac{\partial B(\xi)}{\partial \xi} \right]_{\xi=i\beta f} = \int_0^\infty e^{-\beta V(y)} g_2(y) y dy, \tag{67}$$

$$-\left[\frac{\partial^2 B(\xi)}{\partial \xi^2} \right]_{\xi=i\beta f} = \int_0^\infty e^{-\beta V(y)} g_3(y) y dy, \tag{68}$$

where we defined the kernels

$$g_1(y) = \frac{\sinh(\beta l f y)}{\beta l f}, \tag{69}$$

$$g_2(y) = \frac{\beta l f y \cosh(\beta l f y) - \sinh(\beta l f y)}{\beta^2 l^2 f^2}, \tag{70}$$

$$g_3(y) = \frac{(2 + \beta^2 l^2 f^2 y^2) \sinh(\beta l f y) - 2 \beta l f y \cosh(\beta l f y)}{\beta^3 l^3 f^3}. \tag{71}$$

It is not difficult to verify that $g_1 > 0 \forall f \in \mathfrak{R}$, $g_2 > 0 \forall f > 0$ (and $g_2 < 0 \forall f < 0$), and finally, $g_3 > 0 \forall f \in \mathfrak{R}$. The proof that $\mu > 0 \forall f \in \mathfrak{R}$ becomes evident by multiplying Eqs. (66), (67) and the factor $\beta l/f$. Since $[B(\xi)]_{\xi=i\beta f}$ is always positive, to prove the same property for λ , we consider the term in square brackets in Eq. (65). We have to verify that

$$\left[\left(\frac{\partial B(\xi)}{\partial \xi} \right)^2 - B(\xi) \frac{\partial^2 B(\xi)}{\partial \xi^2} \right]_{\xi=i\beta f} > 0, \tag{72}$$

or, equivalently, that

$$\int_0^\infty e^{-\beta V(y)} g_1(y) y dy \int_0^\infty e^{-\beta V(y)} g_3(y) y dy > \left[\int_0^\infty e^{-\beta V(y)} g_2(y) y dy \right]^2. \tag{73}$$

In order to analyze this inequality we consider the following general expression

$$\left[\int x(t) y(t) dt \right]^2 = \int x^2(t) dt \int y^2(t) dt - \frac{1}{2} \iint [x(s) y(t) - y(s) x(t)]^2 ds dt, \tag{74}$$

which is valid for two arbitrary functions $x(t)$ and $y(t)$. Since the last integral term in Eq. (74) is always positive, we obtain the so-called Cauchy–Schwarz (or Cauchy–Bunyakovsky) inequality

$$\left[\int x(t) y(t) dt \right]^2 \leq \int x(t)^2 dt \int y(t)^2 dt, \tag{75}$$

where the equality holds exactly when one function is a scalar multiple of the other. Since g_1 is not proportional to g_3 we can affirm that

$$\begin{aligned} \int_0^\infty e^{-\beta V(y)} g_1(y) y dy \int_0^\infty e^{-\beta V(y)} g_3(y) y dy &> \left[\int_0^\infty \sqrt{e^{-\beta V(y)} g_1(y) y} \sqrt{e^{-\beta V(y)} g_3(y) y} dy \right]^2 \\ &= \left[\int_0^\infty e^{-\beta V(y)} \sqrt{g_1(y)} \sqrt{g_3(y)} y dy \right]^2, \end{aligned} \tag{76}$$

where we have used the property that g_1 and g_3 are always positive. To conclude we simply verify that

$$\int_0^\infty e^{-\beta V(y)} \sqrt{g_1(y)} \sqrt{g_3(y)} y dy \geq \int_0^\infty e^{-\beta V(y)} g_2(y) y dy \tag{77}$$

by observing that $g_1 g_3 \geq g_2^2$ (by using Eqs. (69)–(71) it is easy to prove that this inequality is equivalent to $\sinh^2(x) \geq x^2$, which is always verified $\forall x \in \mathfrak{R}$). Finally, we have eventually proved Eq. (73) and, therefore, the eigenvalue λ is positive for any value of the applied force f . This concludes the proof of equivalence of the considered statistical ensembles (under the simple hypothesis of continuity of $V(x)$).

5. Examples of equivalence

Now, we consider the three examples introduced in Section 3 and we briefly describe the ensembles equivalence in such cases.

5.1. Freely-jointed chain

We start with the FJC model described by the Gibbs partition function reported in Table 1. It corresponds to the Gibbs constitutive equation $r = Nl\mathcal{L}(\beta lf)$, where $\mathcal{L}(x) = \coth x - 1/x$ is the Langevin function [1,12]. We adopt the adimensional variables $\tilde{r} = r/(Nl)$ and $\tilde{f} = \beta lf$ and we show in Fig. 3 (top panel) the force–extension curve for the Gibbs ensemble ($\tilde{r} = \mathcal{L}(\tilde{f})$) and for the Helmholtz one. This latter has been obtained theoretically with the procedure described below and confirmed with the Monte Carlo method [54,19,55]. We assumed the parameters $l = 1, N = 4, 5, 10, 50$ and $k_B T = 1$ in arbitrary units. It is important to remark that the Gibbs curves with adimensional variables are independent of N since the partition function is an exact power with exponent N . Differently, the elastic response in the Helmholtz ensemble depends on the number of monomers N . The deviation between the Gibbs and the Helmholtz constitutive equations is evident for small values of N . On the contrary, they converge to the same curve when $N \rightarrow \infty$. In this simple case we can obtain the closed form expressions of the eigenvalues μ and λ

$$\mu = \frac{\beta l}{f} \left[\coth(\beta lf) - \frac{1}{\beta lf} \right] = \frac{\beta l}{f} \mathcal{L}(\beta lf), \quad (78)$$

$$\lambda = \frac{1}{f^2} \left[1 - \frac{(\beta lf)^2}{\sinh^2(\beta lf)} \right], \quad (79)$$

and we can define their adimensional versions $\tilde{\mu} = \mu/(\beta l)^2$ and $\tilde{\lambda} = \lambda/(\beta l)^2$, leading to

$$\tilde{\mu} = \tilde{f}^{-1} \mathcal{L}(\tilde{f}), \quad (80)$$

$$\tilde{\lambda} = \tilde{f}^{-2} - \sinh^{-2} \tilde{f}. \quad (81)$$

These results are represented in Fig. 3 (bottom panel), where we observe that $\tilde{\lambda} > 0$ and $\tilde{\mu} > 0$, as expected. Interestingly enough, we note that $\tilde{\lambda}(0) = \tilde{\mu}(0) = 1/3$.

We briefly describe the techniques for obtaining the force–extension curves for the FJC in the Helmholtz ensemble. We can start with the Gibbs partition function given in the first line of Table 1 and we can substitute it in Eq. (16). After some straightforward calculations we get the famous exact expression obtained by Rayleigh [56]

$$Z_{\vec{r}}(\vec{r}, T) = \frac{1}{2\pi r^2} \int_0^{+\infty} \sin \rho r \left(\frac{\sin \rho l}{\rho l} \right)^N \rho d\rho, \quad (82)$$

where $r = \|\vec{r}\|$. Now, we remark that $Z_{\vec{r}}(\vec{r}, T) = p(\vec{r})$ (to within a multiplicative function independent of \vec{r}), where $p(\vec{r})$ represents the density probability of the second end-terminal of the chain, being the first one grafted at the origin of the axes [1]. So, we obtain the polymer response as $\langle \vec{f} \rangle = -k_B T \frac{\partial}{\partial \vec{r}} \log Z_{\vec{r}} = -k_B T \frac{\partial}{\partial \vec{r}} \log p(\vec{r})$. Another exact finite expression was found by Treloar with a completely different probabilistic approach [57]

$$p(\vec{r}) = \frac{r}{2l^2} \frac{N^{N-2}}{(N-2)!} \sum_{s=0}^k (-1)^s \binom{N}{s} \left(\frac{1}{2} - \frac{r}{2Nl} - \frac{s}{N} \right), \quad (83)$$

which is valid in the sequence of intervals $Nl - 2(k+1)l \leq r \leq Nl - 2kl$ (covering the entire range from 0 to Nl), where $k = 0, 1, 2, 3$ and so on. It is not difficult to prove (numerically or analytically) the perfect agreement between Eqs. (82) and (83). Moreover, these curves have been also confirmed through standard Monte Carlo simulations for $N = 4, 5, 10, 50$. In several important works a series of approximations for $p(\vec{r})$ and for the corresponding force–extension curve have been elaborated [22,58–60]. Incidentally, it is interesting to observe that the authors of Ref. [22] obtained an approximated expression based on the eigenvalues μ and λ given in Eqs. (78) and (79), here used to check the equivalence of the ensembles. The interested reader can see Eqs. (25)–(29) in Ref. [22].

5.2. Chain with extensible bonds

Similar results for the chain with extensible bonds are shown in Fig. 4. In this case we adopted the parameters $l = 1, N = 4, 5, 10, 50, \Delta = 1, \Sigma = 1, k = 100$ and $k_B T = 1$ in arbitrary units. The series of curves representing the Helmholtz ensemble are converging to the Gibbs curve, as expected. Fig. 4 shows that differences between the two ensembles are considerable for short chains. As before we note that the eigenvalues are always positive, as predicted by the presented theory. A complete discussion about the polymer systems with extensible bonds can be found in Refs. [19,61]. In particular, it has been shown that the convergence to the thermodynamic limit upon increasing contour length is described by suitable power laws and some specific scaling exponents, characteristic of the model [19].

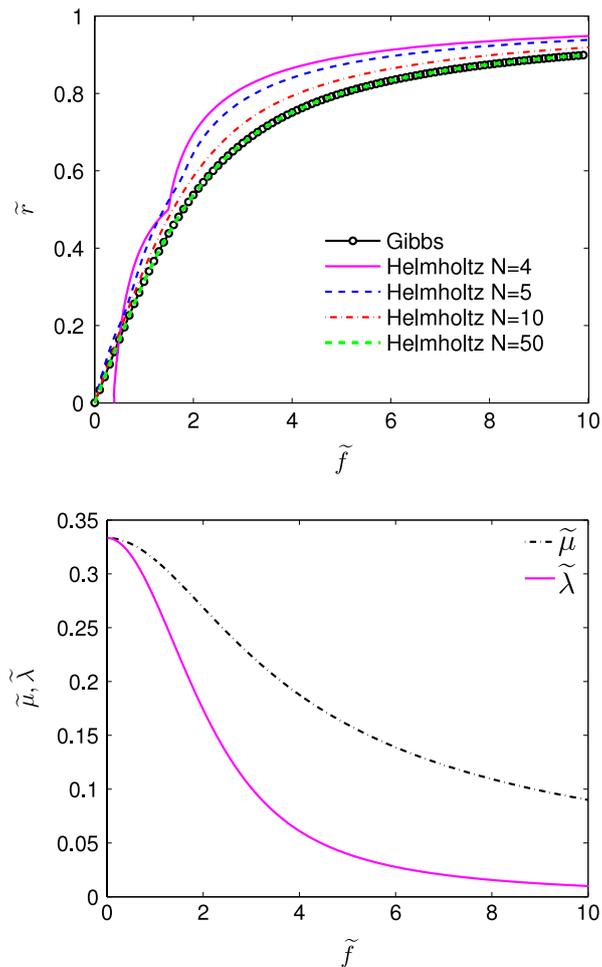


Fig. 3. Force–extension curves for Gibbs and Helmholtz ensembles (top panel) and adimensional eigenvalues (bottom panel) for the freely jointed chain (FJC) model.

5.3. Chain with conformational transitions

Finally, we take into consideration a chain of domains that can exhibit conformational transitions. We adopt the parameters $x_f = l = 1$, $x_u = 3$, $N = 4, 6, 10, 300$, $\Delta E = 50$, $\delta = 2$, $k = 50$ and $k_B T = 1$ in arbitrary units. In Fig. 5 (top panel) one can find the force–extension curves for the two ensembles. The response at constant applied force (a realization of Gibbs ensemble) shows that the conformational transition occurs simultaneously for all the domains at a given threshold force $f = \Delta E / \delta$ (plateau curve, cooperative behavior) [20]. This behavior has been observed in the over-stretching of DNA [44], and in polysaccharides such as the dextran [53]. On the other hand, the response at constant displacement (a realization of the Helmholtz ensemble) shows that the domains exhibit a sequence of independent conformational transitions to the unfolded configuration, generating a series of N peaks (sawtooth pattern, non-cooperative behavior) [20]. This kind of response has been observed in large protein domains such as the Ig units in titin [45]. Typically, all experimental results can be subdivided in these two separated classes showing cooperative and non-cooperative mechanically induced unfolding. It is therefore interesting to observe that the two-state polymer system is able to capture at the same time the main features of both responses. In other words, the experimental force–extension curves for short and long polymers are described by a unique universal model, which can be used with different boundary conditions. From the point of view of the Helmholtz force–extension curve (in our case with $N = 4, 6, 10, 300$ peaks), when the chain length is increased, the width of the peaks is decreased until, at a large enough N , the force–extension curve approaches again the plateau curve of the Gibbs ensemble [20]. Such a behavior can be easily identified in Fig. 5 (top panel). This is a further proof of the equivalence between the considered statistical ensembles. The behavior of the eigenvalues for this system is shown in Fig. 5 (bottom panel). In spite of the more complex shape of the curves representing the eigenvalues versus \tilde{f} , they are positive for any value of the applied force, confirming the equivalence of ensembles also in this case.

A similar dependence of the response on the type of loading devices (Helmholtz versus Gibbs) has been found in recent literature for a chain of bistable elements [62–64]. In addition to the above biophysical applications, discrete sequences of bistable (or multi-stable) elements are indeed largely used to model several physical systems: discrete phase transformations of small-scale specimen of standard materials, Hamiltonian dynamics of Fermi–Pasta–Ulam chains, elasticity of shape memory alloys and so on.

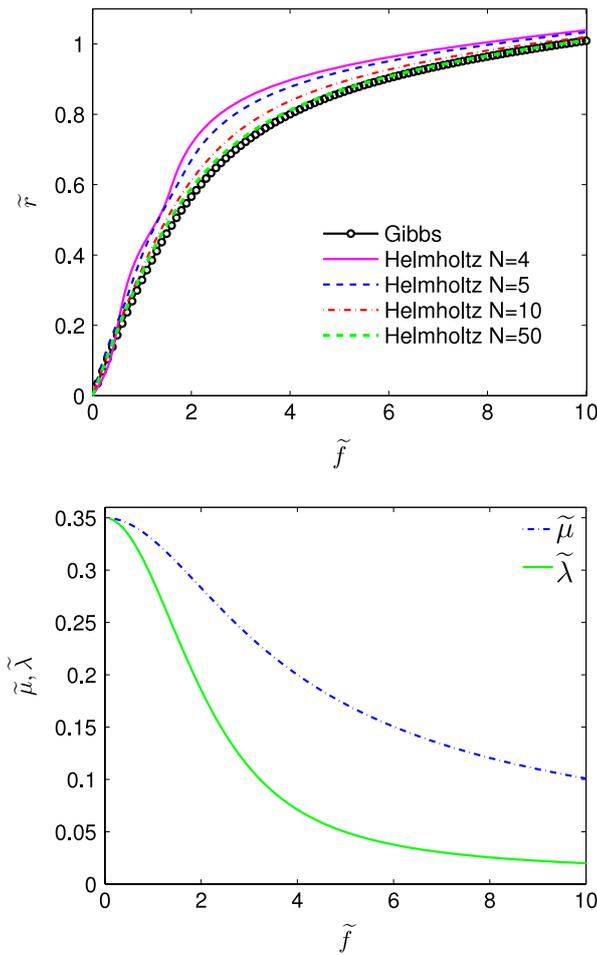


Fig. 4. Force–extension curves for Gibbs and Helmholtz ensembles (top panel) and adimensional eigenvalues (bottom panel) for the extendible bonds chain (EBC) model.

6. Conclusions

In this work we investigated the equivalence between the Gibbs and Helmholtz ensembles in the thermodynamic limit for single polymer chains in absence of any form of confinement. In particular, we rigorously proved the equivalence for the class of polymer models characterized by a continuous pairing interaction between neighboring monomers. To verify this property, we directly compared the force–extension curves of the two different ensembles, by obtaining the accordance for large molecules. To do this, we exploited the stationary phase method, applied to the integrals defining the Helmholtz force–extension response. We thoroughly analyzed the sign of the eigenvalues of the Hessian matrix of the phase function in order to accurately justify the applicability of stationary phase method. The results are in perfect agreement with those in Ref. [31], which is a recent work of great importance to clarify this subject. However, we adopted a completely different methodology since we directly compared the force–extension responses while, in Ref. [31], the entropies and free energies are examined utilizing the maximum entropy principle. The attainment of the same conclusion, obtained with two completely different methods, represents the unequivocal proof that the conjugated ensembles are equivalent in the thermodynamic limit.

We add some further comments about the controversy concerning the ensembles equivalence emerged in earlier literature. We remember that the constitutive laws given in Eqs. (37) and (38) map different quantities: $\langle \vec{f} \rangle$ and \vec{r} for the Helmholtz ensemble and $\langle \vec{r} \rangle$ and \vec{f} for the Gibbs one. As consequence, in Figs. 3–5 we plotted on the same graph $|\vec{r}|$ versus $|\langle \vec{f} \rangle|$ for the Helmholtz results and $|\langle \vec{r} \rangle|$ versus $|\vec{f}|$ for the Gibbs ones (we adopted scalar dimensionless variable for convenience). For $N \rightarrow \infty$ the two ensembles converge to the same curve, because of the proved equivalence. Following the theoretical works of Neumann [24,26] and the numerical verification of Süzen, Sega and Holm [37], we observe that different comparisons, based on different average values, can be taken into consideration. For spherically symmetric systems we can consider the force–extension responses $|\langle \vec{f} \rangle| = \alpha(|\vec{r}|)$ or $\langle |\vec{f}| \rangle = \gamma(|\vec{r}|)$ for the Helmholtz case and the relations $|\langle \vec{r} \rangle| = \beta(|\vec{f}|)$ or $\langle |\vec{r}| \rangle = \delta(|\vec{f}|)$ for the Gibbs one. The functions α and β are the scalar counterparts of those defined in Eqs. (37) and (38). Hence, we have $\beta = \alpha^{-1}$ (or $\alpha = \beta^{-1}$) in the thermodynamic limit. On the contrary, it is easy to prove that $\gamma^{-1} \neq \beta$, $\alpha^{-1} \neq \delta$ and $\gamma^{-1} \neq \delta$ for any polymer length N and, therefore, also for systems in the thermodynamic limit. The different behavior between γ and β or between α^{-1} and δ is not related to the length of the polymer but rather to the

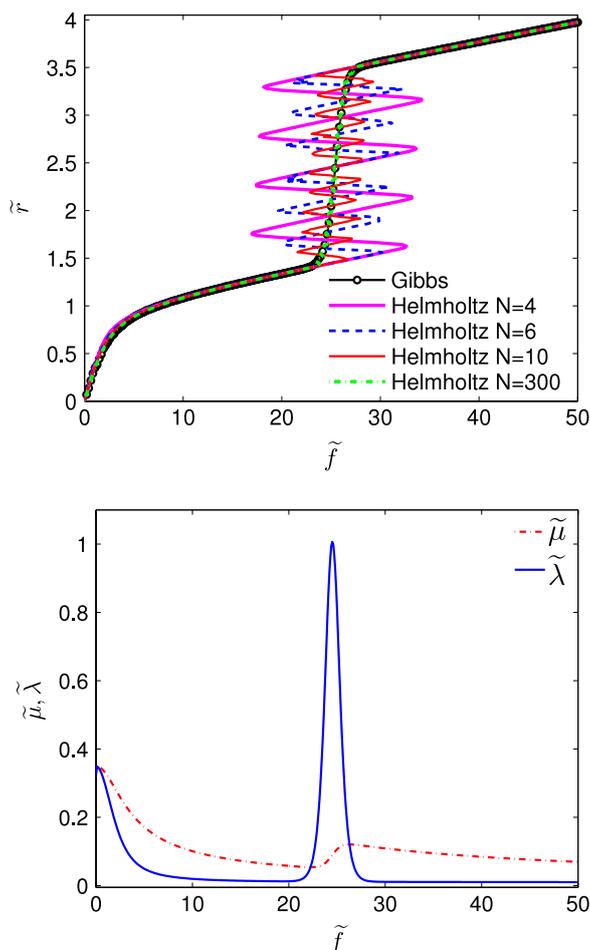


Fig. 5. Force–extension curves for Gibbs and Helmholtz ensembles (top panel) and adimensional eigenvalues (bottom panel) for the two-state chain (TSC) model.

transformation of random variables introduced to determine the average value of the modulus of the vectors \vec{r} and \vec{f} (in general $|\langle \vec{w} \rangle| \neq \langle |\vec{w}| \rangle$). To conclude, some forms of inequivalence have been observed by defining different observables. This point has generated the controversy largely discussed in the literature. However, these deviations do not indicate statistical ensemble inequivalence, because the introduced variables are just different average values with a clearly distinct behavior.

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