Maximum-entropy calculation of end-to-end distance distribution of force stretching chains

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Using the maximum-entropy method, we calculate the end-to-end distance distribution of the force stretched chain from the moments of the distribution, which can be obtained from the extension-force curves recorded in single-molecule experiments. If one knows force expansion of the extension through the \((n - 1)\)th power of force, it is enough information to calculate the \(n\) moments of the distribution. We examine the method with three force stretching chain models, Gaussian chain, free-joined chain and excluded-volume chain on two-dimension lattice. The method reconstructs all distributions precisely. We also apply the method to force stretching complex chain molecules: the hairpin and secondary structure conformations. We find that the distributions of homogeneous chains of two conformations are very different: there are two independent peaks in hairpin distribution; while only one peak is observed in the distribution of secondary structure conformations. Our discussion also shows that the end-to-end distance distribution may discover more critical physical information than the simpler extension-force curves can give.

I. INTRODUCTION

Recent advances in the molecules manipulation have made it possible to measure and characterize molecular properties at a single molecule level. One of basic characteristics is the extension-force curves (EFCs)\( ^{[1, 2, 3]} \). These curves have provided lots of interesting and useful physical information about studied molecules, going from the detailed elastic properties\( ^{[1]} \) to complex structure transitions\( ^{[4, 5, 6]} \). On theoretical side, many kinds of models have been constructed to character and explain the recorded various EFCs of different molecules\( ^{[7, 8, 9, 10, 11]} \). Except computer simulations, e.g., molecular dynamic or Monte Carlo sampling, the calculation of the end-to-end distance distributions (EEDDs) of the force stretched molecules is the center problem in using statistical mechanical method. In principle, EEDDs can be obtained by partition function. But two questions must be faced firstly: one is what physical interactions should be taken into account; the other is what mathematical technique is needed to solve the EEDDs. It is not easy to describe physical interactions in complex molecules, such as polyelectrolytes or proteins. While specific mathematical technique is not always useful in different molecular systems.

In contrast to traditional mind, in this paper we try to extract EEDDs from the recorded EFCs in experiments using the maximum-entropy (or least-biased) method (MEM). Our motivations are that, first, to our knowledge, little concern about EEDDs has been given in previous force stretching models. Although EEDDs of simpler molecules may be simpler enough, it is no reason to assume that they are still simple for complex molecules, such as secondary structure RNA; second, because the EEDDs are the results of interplay between intra-molecule and force, they can be seen as primitive examining for more realistic physical models. In addition, our studies also show that the EEDD at vanishing force calculated by MEM keeps almost all characteristic of the exact distribution without force. Therefore this method may provide a possible way to directly “measure” EEDDs by force spectroscopy.

The organization of this paper is as follows. We first, in Sec. IID, briefly review the maximum entropy method. In Sec. III, the basic relations between the distance moments and EFCs are demonstrated. In Sec. IV, MEM is examined by reconstructing EEDDs of three force stretching chain models: Gaussian chain, free-joined chain and self-avoiding chain on 2-dimension lattice. We also show in Sec. V that the method is capable of resolving EEDDs of complex chain molecules stretched by force. As an illustration, the model of force unzipping double-stranded chain molecules is used to provide exact EFCs and EEDDs\( ^{[12]} \); these results are necessary to calculate and compare EEDDs solved by MEM. Section VI is our conclusion.
II. MAXIMUM ENTROPY METHOD

Given a finite set of the moments of a distribution function, how to construct the function is an old mathematical problem. The MEM has been proved to be useful in this problem. From a normalized distribution function \( P(z) \) on the interval \((0, 1)\), the power moments are calculated as

\[
\mu_n = \int z^n P(z) dz. \tag{1}
\]

On the other hand, given a set of \((M + 1)\) moments, from \(\mu_0\) to \(\mu_M\), it is not always possible to find a positive, well-behave function \( P(z) \) that will have these moments. The necessary and sufficient conditions for the existence of a function \( P(z) \) with a set of \((M + 1)\) moments on interval \((0, 1)\) are the Hausdorff relations:

\[
\sum_{m=0}^{k} (-1)^m \binom{k}{m} \mu_{n+m} \geq 0, \quad \text{for } (n, k) = (0, 0) \text{ to } n + k \leq M. \tag{2}
\]

The MEM offers a definite procedure for the construction of the approximate distribution \( P_M(z) \) based on \((M + 1)\) moments as the following form:

\[
P_M(z) = \exp \left[ - \sum_{n=0}^{M} \lambda_n z^n \right]. \tag{3}
\]

The \(\lambda_n\) are a set of \((M + 1)\) constants determined by the \((M + 1)\) known \(\mu_n\). This involves a straightforward nonlinear iterative procedure that usually converges rapidly.

In general, a real distribution is not always defined on interval \((0, 1)\). Hence the first step in using MEM is to convert the distribution to a function on this interval. Given that the power moments of the original distribution \( f(x) \) are \(\gamma_m\), and the lower and upper bounds are designated as \(\alpha_1\) and \(\alpha_2\) respectively. Defining the extent of the distribution

\[
L = \alpha_2 - \alpha_1. \tag{4}
\]

First, shift the moments \(\gamma_m\) to interval \((0, L)\) by

\[
\overline{\mu}_n = \sum_{m=0}^{n} (-\alpha_1)^{n-m} \binom{n}{m} \gamma_m. \tag{5}
\]

Then scale these moments \(\overline{\mu}_n\) to interval \((0, 1)\) by

\[
\mu_n = \overline{\mu}_n / L^n. \tag{6}
\]

Thus MEM can be used to calculate distribution \( P(z) \).

Conversely, if the approximate distribution \( P(z) \) is solved from moments \(\gamma_m\), the distribution can be first rescaled from interval \((0, 1)\) to \((0, L)\) by the change of variable \( y \)

\[
g(y) = \frac{1}{L} P \left( \frac{y}{L} \right), \quad y \in (0, L). \tag{7}
\]

Then shift the distribution \( g(y) \) to interval \((\alpha_1, \alpha_2)\) by

\[
f(x) = g(x - \alpha_1), \quad w \in (\alpha_1, \alpha_2). \tag{8}
\]

III. MOMENTS FROM EXTENSION-FORCE CURVES

Assuming that one end of a chain consisting of \(N\)-links is fixed at origin, and external force \( f \mathbf{z}_0 \) is exerted on the other end, where unit vector \( \mathbf{z}_0 \) is along \(z\)-axis. Let \( P_N(\mathbf{R}, f) \) be the probability distribution function that the end-to-end vector of the force stretched chain is \( \mathbf{R} = (R_x, R_y, R_z) \). Then the power moments of component \( R_z \) distribution
The first moment is just the average extension \( Z \)

\[
P_N(R_z, f) \text{ are calculated by}
\]

\[
\overline{R_z^m}(f) = < (R \cdot z_0)^m > \\
= \int dR_z(R_z)^m P_N(R_z, f) \\
= \int d^3R (R \cdot z_0)^m P_N(R, f).
\]

In order to illustrate expressions more seriously and explicitly, distribution function of the ideal chains is used \[15, 16\]

\[
P_N(R, f) = Q^{-1}[f] \int \mathcal{D}[r(s)] \delta^3 \left( R - \int_0^L ds v(s) \right) \\
\times \exp \left[ -\frac{1}{k_B T} \int_0^L ds \rho_c(r, s) + \frac{f}{k_B T} z_0 \cdot \int_0^L ds v(s) \right],
\]

where \( k_B \) is Boltzmann constant, \( T \) is temperature, \( L \) is arclength of the chain, “vector” \( r(s) \) describes the local state at arclength point \( s \), e.g., in the case of a flexible Gaussian chain, \( r \) is a three-dimensional position vector; while in case of a wormlike chain, \( r \) is the unit tangent vector \[17\]. Vector \( v(s) \) is also different according to concrete chain model, e.g., \( v = d\text{d}r/\text{d}s \) for Gaussian chain, and \( v = r(s) \) or the tangent vector for wormlike chain. The normalization factor \( Q[f] \) is

\[
Q[f] = \int dR \int \mathcal{D}[r(s)] \delta \left( R - \int_0^L ds v(s) \right) \\
\times \exp \left[ -\frac{1}{k_B T} \int_0^L ds \rho_c(r, s) + \frac{f}{k_B T} z_0 \cdot \int_0^L ds v(s) \right] \\
= \int \mathcal{D}[r(s)] \exp \left[ -\frac{1}{k_B T} \int_0^L ds \rho_c(r, s) + \frac{f}{k_B T} z_0 \cdot \int_0^L ds v(s) \right].
\]

Replacing Eq. (10) into Eq. (9) and performing \( R \) integral we have

\[
\overline{R_z^m}(f) = Q^{-1}[f] \int \mathcal{D}[r(s)] \left( z_0 \cdot \int_0^L ds v(s) \right)^m \\
\times \exp \left[ -\frac{1}{k_B T} \int_0^L ds \rho_c(r, s) + \frac{f}{k_B T} z_0 \cdot \int_0^L ds v(s) \right].
\]

It is easy to prove that Eq. (12) can be rewritten as

\[
\overline{R_z^m}(f) = \frac{(k_B T)^m}{Q[f]} \frac{\partial^m}{\partial f^m} Q[f].
\]

The first moment is just the average extension \( Z(f) \) recorded in experiments as a given force \( f \),

\[
\overline{R_z^1}(f) = Z(f) = \frac{k_B T}{Q[f]} \frac{\partial}{\partial f} Q[f].
\]

We can alternatively relate the partition function \( Q[f] \) to derivatives of \( Z(f) \) with respect to \( f \) as follows:

\[
\frac{1}{k_B T} \frac{\partial}{\partial f} Z(f) = -\left( \frac{Q^{(1)}}{Q} \right)^2 + \frac{Q^{(2)}}{Q},
\]

\[
\frac{1}{k_B T} \frac{\partial^2}{\partial f^2} Z(f) = 2 \left( \frac{Q^{(1)}}{Q} \right)^3 - 3 \left( \frac{Q^{(1)}}{Q} \right) \left( \frac{Q^{(2)}}{Q} \right) + \left( \frac{Q^{(3)}}{Q} \right),
\]

\[
\frac{1}{k_B T} \frac{\partial^3}{\partial f^3} Z(f) = -6 \left( \frac{Q^{(1)}}{Q} \right)^4 + 12 \left( \frac{Q^{(1)}}{Q} \right)^2 \left( \frac{Q^{(2)}}{Q} \right) - 3 \left( \frac{Q^{(2)}}{Q} \right)^2 - 4 \left( \frac{Q^{(1)}}{Q} \right) \left( \frac{Q^{(3)}}{Q} \right) + \left( \frac{Q^{(4)}}{Q} \right),
\]
According to Eq. the moments \( R^2_z(f) \) can be solved in terms of derivatives of \( Z(f) \) with respect to force \( f \) as follows:

\[
\begin{align*}
R^2_z &= Z(f), \\
R^2_z &= k_B T \frac{\partial}{\partial f} Z(f) + \left( R^1_z \right)^2, \\
R^2_z &= (k_B T)^2 \frac{\partial^2}{\partial f^2} Z(f) - 2 \left( R^1_z \right)^3 + 3 \left( R^2_z \right) \left( R^1_z \right), \\
R^2_z &= (k_B T)^3 \frac{\partial^3}{\partial f^3} Z(f) + 6 \left( R^1_z \right)^4 - 12 \left( R^2_z \right)^3 \left( R^1_z \right)^2 + 3 \left( R^2_z \right)^2 + 4 \left( R^2_z \right) \left( R^1_z \right). 
\end{align*}
\]

The above relations show that if one has the first \((n-1)\) derivatives of \( Z(f) \), then this is enough information to calculate the first \(n\) moments of the distribution \( P_N(R_z, f) \). These derivatives of \( Z(f) \) can be obtained by expanding the extension \( Z(f) \) in a Taylor series about the reference force \( f_0 \) as

\[
Z(f) = Z(f_0) + \frac{\partial}{\partial f} Z(f_0) \Delta f + \frac{1}{2} \frac{\partial^2}{\partial f^2} Z(f_0) \Delta f^2 + \frac{1}{6} \frac{\partial^3}{\partial f^3} Z(f_0) \Delta f^3,
\]

where

\[
\Delta f = f - f_0.
\]

In general, no analytical \( Z(f) \) is used in real situation; only the EFCs are recorded in experiments. All the derivatives have to be calculated by numerical methods.

Before beginning the next section, we clarify our procedure: first calculate different derivatives of \( Z(f) \) from EFCs by numerical method; then use Eq. to obtain necessary power moments of \( P_N(R_z, f) \); and finally, apply MEM presented in Sec. to construct approximate EEDDs.

**IV. TEST OF MEM: THREE FORCE STRETCHING CHAIN MODELS**

In this section, the MEM is examined with three force stretching chain models which have different statistical properties: Gaussian chain, free-joined chain and excluded-volume (EV) chain on two dimension. The main reason to choice these model is that their EEDDs with forces have exact expressions. EEDDs and EFCs of the models are solved by statistical mechanical methods firstly. Then seeing the obtained EFCs as experiment data, approximate distributions is computed by MEM according to procedure mentioned in above section. Distributions solved by two methods are compared finally.

For each chain model, EEDDs at three nonzero forces are calculated respectively. In addition, distributions at zero force are also solved. Because that EEDD without force is important in polymer research, such as the calculation of root-mean-square end-to-end distance, it is interesting to see whether the distributions calculated by MEM at zero force can keep main characteristic of the exact EEDD. Though our method only solve \( P_N(R_z, 0) \), the length distribution \( P_N(R, 0) \) could be obtained from the numerical relations provided by Domb et al. early.

**A. Gaussian model**

As the simplest \(N\)-link chain model, the energy with force \( f z_0 \) in Gaussian model is expressed as

\[
\mathcal{E} = \frac{3k_B T}{2b} \int_0^{L=Nb} ds \left( \frac{\partial \mathbf{r}}{\partial s} \right)^2 - f z_0 \cdot \int_0^{N} ds \frac{\partial \mathbf{r}}{\partial s},
\]

where \( b \) is effective bond length, \( \mathbf{r} \) is position vector. Using path integral method, the EEDD of Gaussian chain stretched by force is derived as

\[
P_N(R, f) = \left( \frac{3}{2\pi Nb^2} \right)^{3/2} \exp \left\{ -\frac{3}{2Nb^2} \left( R - \frac{N f z_0}{3k_B T} \right)^2 \right\}.
\]
Correspondingly, the component $R_z$ distribution in $z_0$ direction can be integrated by

$$P_N(R_z, f) = \int dR_x dR_y P_N(R, f) = \left( \frac{1}{2\pi Nb^2} \right)^{3/2} \exp \left\{ -\frac{3}{2Nb^2} \left( R_z - \frac{Nb^2 f}{3k_BT} \right)^2 \right\}. \quad (22)$$

The extension versus force then is calculated as

$$Z(f) = \int dR_z R_z P_N(R_z, f) = \frac{Nb^2}{3k_BT} f. \quad (23)$$

As an illustration, we choose $N = 16$ and plot the function in Fig. 1. This function will be viewed as EFCs “measured” in experiments.

Before applying MEM, firstly expand Eq. (23) in Taylor series about force $f_0$ as

$$Z(f) = Z(f_0) + \frac{Nb^2}{3k_BT} (f - f_0), \quad (24)$$

or $Z(f_0) = Nb^2 f_0 / 3k_BT$ and $\partial Z / \partial f_0 = Nb^2 / 3k_BT$. Three moments can be obtained at any given force $f_0$ through Eq. (22) directly. Then approximate distributions are solved by MEM. Three distributions calculated by MEM and their comparing with exact Eq. (22) are shown in Fig. 2. Considering that the extension is linear with force, three moments approximation is used in this model. Obviously, MEM can precisely reconstruct distributions of the Gaussian chain. In fact, because the approximation function $P_2(R_z, f)$ is just the Gaussian distribution, it is not unexpected that MEM reconstruct EEDDs of Gaussian chain perfectly. In addition, EEDD at $f = 0.0k_BT/b$ is the same with distributions at nonzero forces, since the first-order derivate of $Z(f)$ is constant at any force,

**B. Free-joined chain model**

Free-joined chain model has been used to fit the observed EFCs of force stretching single-stranded DNA experiments[7]. The model is defined as a chain with N-link of length $b$ in which all rotational angles occur with
FIG. 2: Comparing EEDDs solved by MEM (the black lines) with exact EEDDs calculated by Eq. 22 (the blue lines) for force stretching Gaussian chain model: (a) \( f = 0.0 \) \( k_B T / b \); (b) \( f = 1.0 \), \( 2.0 \) and \( 3.0 \) \( k_B T / b \). Here three moments approximation is used in MEM. Overlapping of two color lines demonstrates that the MEM can precisely reconstruct the exact EEDDs of Gaussian chain at any force value.

equal probability \[15, 16\]. When exerted external force \( f z_0 \) on one end of the chain, the force potential energy is written as

\[ E_f = -f z_0 \cdot \sum_{n=1}^{N} r_n, \quad (25) \]

where \( r_n \) are bond vectors with constant length \( |r_n| = b \). According to Eq. 10, the distribution function \( P_N(R, f) \) of the end-to-end vector \( R \) is

\[ P_N(R, f) = \frac{\exp [\beta f z_0 \cdot R] P_N(R, 0)}{\int dR \exp [\beta f z_0 \cdot R] P_N(R, 0)}, \quad (26) \]

where \( \beta = 1/k_B T \), and \( P_N(R, 0) \) is the EEDD without applied force, which has been given in literature \[17\]

\[ P_N(R, 0) = \frac{1}{2^{N+1} (N-2)! \pi b^2 R} \sum_{n=0}^{[N-(R/b)/2]} (-1)^n \binom{n}{N} (N - 2n - R/b)^{N-2}, \quad (27) \]

where \( R \) is the length of vector \( R \). The normalization factor or the partition function \( Q[f, T] \) can be calculated exactly as

\[ Q[f, T] = \int dR P_N(R, f) = \left( \frac{4 \pi}{\beta f b} \sinh (\beta f b) \right)^N. \quad (28) \]

Then EEDD of component \( R_z \) can be obtained by integral of Eq. 29 with respect to components \( R_x \) and \( R_y \) as

\[ P_N(R_z, f) = \frac{\exp (\beta f R_z)}{[4 \pi \sinh (\beta f b) / \beta f b]^N} P_N(R_z, 0), \quad (29) \]

where

\[ P_N(R_z, 0) = \frac{1}{2^N (N-2)! b} \int_{R_z/b}^{N} dx \sum_{0}^{[(N-x)/2]} (-1)^n \binom{n}{N} (N - 2n - x)^{N-2}, \quad R_z \geq 0. \quad (30) \]
FIG. 3: EFC of free-joined chain, here \( N = 16 \). The dot-dash and dash curves are asymptotic curves corresponding to large and small forces respectively. Three arrows point out different nonzero forces in which corresponding EEDDs are calculated by MEM.

The average extension \( Z(f) \) is then given as

\[
Z(f) = bN \left[ -\frac{1}{\beta fb} + \coth(\beta fb) \right].
\] (31)

Eq. 31 is served as experiment data to check our MEM. As an example, take \( N = 16 \), and its EFC is shown in Fig. 3. We expand Eq. 31 in Taylor series at different forces, \( 0.0, 0.5, 1.7, \) and \( 4.0k_B T/b \). EFC at these forces has different asymptotic formula; see dash curves in Fig. 3. Similarly to the case of of Gaussian model, EEDDs calculated by MEM and their comparing with exact distribution are shown in Fig. 4. At \( f = 0.0k_B T/b \), because the third-order derivative of \( Z(f) \) is not zero, EEDDs of three and five moments are solved by MEM respectively; see Fig. 4(a). The distributions of three and five moments are slightly different at origin: EEDD of three moments is the same with the distribution of Gaussian model; while distribution value at origin calculated by five moments is smaller, which is the same with prediction of exact EEDD. Our results show that MEM is sensitive enough to detect the fine difference of EEDDs from simple EFCs. When force is nonzero, EEDDs solved by MEM are the same with exact EEDDs.

C. Self-avoiding chain model

As a more realistic model, the self-avoiding chain which accounts for EV interactions plays very important role in polymer theory\[16, 19\]. But in force stretching problem, almost all theoretical models implicated that EV interaction can be negligible. This assumption is doubted at small force region. In this section, We try to simulate the force stretched EV chain of \( N \)-link as \( N \)-step self-avoiding walks (SAW) on two dimensional (2D) quadratic lattice. The early work of Domb et al. has demonstrated that EEDD of self-avoiding chain differ appreciably from Gaussian distribution\[20\]. It is interesting to see weather MEM can recover the EV properties exactly when the force tends to zero.

First we formulate the force stretching partition function \( Q[f, T] \) and EEDD \( P_N(n, f) \) as follows

\[
Q[f, T] = \sum_{n=-N}^{n=N} C_N^x(n) \exp(f\beta n),
\] (32)

and

\[
P_N(n, f) = \frac{C_N^x(n) \exp(f\beta n)}{Q[f, T]},
\] (33)
FIG. 4: Comparing EEDDs solved by MEM (the black lines) with exact EEDDs given by Eq. 29 (the blue lines) for force stretching free-joined chain model: (a) $f = 0.0k_B T/b$. We calculate the EEDDs using three (black dash line) and five moments (black solid line), respectively. The EEDD of five moments slightly derives from the distribution of three moment at origin, which is confirmed by exact EEDD. (b) $f = 0.5, 1.7$ and $4.0k_B T/b$. Here five moments are necessary. Unlike in Gaussian chain, not only the maximum values of EEDDs are movable, but also the distribution regions are variable at different forces. Overlapping of two color lines show that MEM can very precisely reconstruct the EEDDs of free-joined chain at any given force.

where $C^x_N(n)$ is the number of walks whose final $x$ coordinates are $n$. Extension function $Z(f)$ then can be calculated from EEDD accurately.

As an illustration, we exactly enumerate all 20-step SAWs on 2D lattice. According to Eq. 32, we calculate EFC and plot it in Fig. 5. The numerical expansions of extension of the chain at forces $0.0, 0.10, 0.25$, and $0.70k_B T/b$

FIG. 5: EFC of SAW chain, here $N = 20$. Three arrows point out different forces in which corresponding distributions are calculated by MEM.

are calculated respectively. Then using MEM, EEDDs at these forces are solved; see Fig. 6. At force $0.0k_B T/b$, distributions of three and five moments are different apparently. Domb et al. have pointed out that instead of Gaussian distribution, the distributions considering EV effect on 2D lattice can be well fitted by a function form of
\[ \exp(-|x|^4), \] which will be seen that the portion of the EEDD near to the origin is more “flat-topped”, and the decay of distribution for larger values of \( x \) is sharper.\(^2\) EEDD calculated by five moments at zero force precisely recovers these major aspects. However, it is unexpected that even a slight dip in the value of distribution can be recovered by the MEM; see Fig. 6(a). Because the origin of the dip arises from the restriction of no returns to the origin,\(^2\) the result demonstrates again that the MEM is very sensitive to detect the fine structure restrictions from the simple EFC. This characteristic in distribution is still preserved at small forces, such as at force 0.10\( k_B T / b \) in Fig. 6(b).

From the analysis of self-avoid chain, we conclude that EV may play important role even in force stretching problem. Especially, EV effect can be reflected more explicitly from EEDD, instead of simple EFCs.

![Graphs](image)

**FIG. 6:** Comparing EEDDs solved by MEM (lines) with exact EEDDs (symbols) given by Eq. 33 for force stretching self-avoiding chain. (a) \( f = 0.00k_B T / b \). We calculate EEDD using three and five moments respectively. Unlike EEDDs of Gaussian chain or free-joined chain at \( f = 0 \), two peaks in EEDD obtained by five moments (solid lines) appear in this model, which are demonstrated by exact enumeration (circles). (b) \( f = 0.10, 0.25 \) and 0.70\( k_B T / b \). Five moments are necessary. Good fitness of the lines and symbols shows that EEDDs calculated by MEM can recover real distribution precisely.

V. EEDDS OF FORCE STRETCHING COMPLEX MOLECULES: HAIRPIN AND SECONDARY STRUCTURE CONFORMATIONS

From the deduction of Eq. 15, the relations are independent of interactions between the units in a chain. On the other hand, units of any real polymer always interact with each other, e.g., the simple electrostatic repulsion of the phosphodiester backbone of DNA, and complex hydrophobic interaction in proteins. Hence it is valuable to see what MEM can tell us about the interactions in molecule. Because recent mechanical single molecular experiments have turn their attentions to molecular structure transitions induced by force, such as dsDNA or ssDNA (RNA) force unzipping,\(^6\) it is natural to apply MEM to these experiment data firstly. In particular, the EEDDs at critical force is of interest.\(^6\) However, considering that the MEM is very sensitive to the shapes of EFCs, and current experiment data are not fine enough, in this paper we do not ready to apply our method in experiment data directly. In this section we will make use of EFCs solved by an theoretical model of force stretching hairpin and secondary structures conformations in 2D plane\(^1\) as “experiment” data. Because our model also provide the exact EEDDs, comparing with EEDDs derived by MEM will ensure the availability of MEM when our method is applied to real scenario in future. In following section, we first give a brief overview about the statistical model of force stretching chain molecules of hairpin and secondary structure conformations. The details of the model are given elsewhere\(^1\).
A. A statistical mechanical model of force stretching chains of hairpin and secondary structure conformations

Hairpin and secondary structure conformations are the basic models for antiparallel β-sheet in protein and RNA molecules[21, 22]. The partition function \( Q_N(T; f) \) of a \((N+1)\) monomer \((N+1)\)-mer) chain molecules stretched by force \( f \) is formulated as

\[
Q_N(T; f) = \sum_{e} \sum_{\Delta} g_N(E; \Delta) e^{-\beta(E-f\Delta)},
\]

where \( \Delta \) is end-to-end distance (EED) of the chain along force direction, and \( g_N(E; \Delta) \) is the number of conformations having energy \( E \) and EED \( \Delta \). Because the energy contributed by force is only related with EEDs, we divide any conformation of the chain into two parts: one is main chain (MC), in which does not involve any contacts; the other is nested regions (NRs), which form hairpins, loops and turns. If only one NR is allowed in conformations, they are named hairpin, otherwise secondary structure conformations. On 2D lattice, the nested regions contribute whole EED value according their outmost contacts directions[12]. The EEDD value of the number of conformations of MC and NRs respectively. For hairpin conformations

\[
Q_N(T; f) = \sum_{n} \sum_{\Delta} C^{MC}(n, \Delta) C^{NRs}(n, E) e^{-\beta(E-f\Delta)},
\]

where \( n \) is the number of unrelated NRs in conformations, \( C^{MC}(n, \Delta) \) and \( C^{NRs}(n, E) \) are the number of conformations of MC and NRs respectively. For hairpin conformations \( n = 1 \).

Because our model is restricted on 2D lattice, the values of \( C^{MC}(n, \Delta) \) at given \( n \) can be counted exactly by enumeration and extrapolation method[22]. Whereas calculation of \( C^{NRs}(n, E) \) is modified and extended from nested polymer graph theory (NPGT) developed by Chen and Dill recently[21, 22]. The idea behind the NPGT is that the number of conformations of any arrangement of NRs is a product of each number of conformations of each NR restricted by EV requirement. In NPGT, different arrangement of NRs is represented by polymer graph, the diagrammatic representations of intrachain contacts, and each unrelated NR can be independently seen as a polymer graph or subpolymer graph. So the calculation of the number of conformations for any given subpolymer graph is the product of matrices:

\[
U \cdot S_{t_m} \cdot Y_{t_{m-1}} \cdots S_{t_1} \cdot U^t,
\]

where \( U = \{1, 1, 1, 1\} \), \( U^t \) is the transpose of \( U \), \( S_i \) is structure matrix of \( i \)th subunit, and \( Y_{ij} \) is viability matrix[21, 22]. We obtain EEDD from the partition function \( Q(T; f) \),

\[
P_N(\Delta, f) = e^{\beta f \Delta} \times \sum_{n} \sum_{E} C^{MC}(n, \Delta) C^{NRs}(n, E) e^{-\beta E / Q_N(T; f)},
\]

and the average extension function \( Z(f) \) is calculated exactly from above EEDDs. For comparing, we calculate EFCs of 70-mer homogeneous chains of hairpin and secondary structure conformations; see Fig. 3. Here the homogeneous chain means that any contact of two monomers in chain contributes energy \(-\varepsilon \) (\( \varepsilon > 0 \)). Considering to the importance of sequence in secondary structure molecules, we also give EFC of a 70-mer specific sequence, \( \Lambda \cdots ACCCCCCU \cdots UC \cdots CAAAAG \cdots G \), where the dots represent 15-mer \( \Lambda \), \( U \), \( C \) and \( G \) respectively; see Fig. 3(a). In contrast to homogeneous chain, only \( \Lambda-U \) or \( C-G \) pair contributes energy \(-\varepsilon \).

B. Single- and multipeak distributions

To be the same with previously section, we compute all EEDDs by numerical expansion of EFCs at different forces for different chain molecules; see Figs. 3 and 3(b).

The shapes of the EEDDs of the complex molecules are very different from those of simple molecules observed in Sec. IV. The most obvious feature is that the distribution regions of the complex chains expand in middle force whereas shrinking at smaller and larger forces. It is results of attracted interaction between monomers. Secondly, it seems that EFCs of homogeneous chains of hairpin and secondary structure conformations are similar except that extensions increase slowly or fast, however, the EEDDs calculated by MEM are completely different: only one peak is observed in the distribution at any force in secondary structure conformations; see Fig. 3(a); while in hairpin conformations,
FIG. 7: EFCs of 70-mer homogeneous chains of hairpin (blue lines) and secondary structure conformations (black line). Here temperature is $0.28\varepsilon/k_B$. Six arrows point out different forces in which corresponding distributions of two conformations are calculated by MEM.

FIG. 8: Comparing between EEDDs solved by MEM (lines) and exact EEDDs given by Eq. 37 (symbols) for homogeneous chains. (a) Secondary structure conformations, where $f = 0.20, 0.50$ and $0.70\varepsilon/b$. (b) Hairpin conformations, where $f = 0.30, 0.46$ and $0.60\varepsilon/b$. Five moments are necessary. Two independent peaks in EEDD at force $0.46\varepsilon/b$ appear in hairpin model (triangle and dash line), while it does not present in secondary structure conformations.

two peaks located at shorter and longer EEDs present during narrow force range (between 0.42 to 0.49$\varepsilon/b$), but no conformations with other EEDs in between; see Fig. 8 (b). In addition, EEDDs of specific sequence show more complex shapes. At $f = 0.39\varepsilon/b$ the distribution has two peaks, then they quickly fuse into one peak with a small force increasing $0.03\varepsilon/b$, and finally the peak separates into two peaks at $f = 0.45\varepsilon/b$. To explore the phenomena of single- or multipeak, comparing with the exact EEDD is essential. These results are plotted in corresponding figures. We find that the two peaks in distributions predicted by MEM are consistent with exact EEDDs of specific sequence and homogeneous hairpin chain. At force $0.42\varepsilon/b$, however the exact distribution of specific sequence appears three peaks, whereas MEM predicts one peak only.

According to Eq. 15, the first-order derivative of the average extension $R_1^z(f)$ with respect of force $f$ can also be
written as \( \frac{dR_2^2}{df} = (R_2^2 - R_1^2)/k_B T \). The formula is the same with the definition of heat capacity \( C(T) \) except that the energy and temperature are replaced by EED and force, respectively. We believe that the EED plays important roles in force stretching chains problem, which is very similar with the roles played by energy in thermal melting biomolecules, at least in nucleic acids\(^{12}\). Many useful insights can be given through this analogy. Since the energy distribution can reveal molecular structure transitions induced by heating\(^{14}\), the EEDD might discover structure transitions driven by force. E.g., the EEDDs in Fig. 8 show that the transitions in secondary structure and hairpin conformations are “one-state” and “two-state”, respectively. These terms are borrowed from thermal melting case\(^{14, 23}\). The transition difference exhibited in two conformations warns us that the simpler EFCs may cover critical physical information; the investigation of EEDDs is necessary to determine physical properties in force “melting” chain molecules.

In traditional theory, physical properties of polymers only relate with the number of monomers, such as cooperativity or melting transition type\(^{16, 19}\). But in biomolecules, the monomer sequence may affect physical results dramatically. The apparent case in EEDDs is the number of peaks of the specific sequence in Fig. 8, though its EFC is simpler. The case of specific sequence warns us again that EFCs may be too simple to obtain real and useful information about the studied molecules. Because five moments cannot reconstruct three peaks in distribution\(^{14}\), we only solved a quick expansion in the distribution region. To explore three or more peaks in EEDDs, higher moments are necessary. Although our MEM fails to predict three peaks, the abnormal expansion of the distribution observed by MEM between two forces arising two peaks still can be seen as a sign of appearing of multipeak.

In this paper, contrary to the traditional mind, we calculate end-to-end distance distribution of force stretching chain molecules from the measured EFCs by using MEM. Because the method is independent of polymer energy formula or structure details, it provide a useful and simple way to detect the real physical information about complex molecules. Many results, such as the important role played by EV interactions, single- or multipeak in EEDDs can be obtained from the simple EFCs. It is interesting to see whether these results can be found in real stretching experiments.

**FIG. 9:** (a) EFC of 70-mer specific sequence of secondary structure conformations, where temperature is \( 0.28 \varepsilon/k_B \). Three arrows point out different forces in which corresponding distributions are calculated by MEM. (b) Comparing EEDDs solved by MEM (lines) with exact EEDDs (symbols), where \( f = 0.39, 0.42 \) and \( 0.45 \varepsilon/b \). Five moments are necessary. Unlike EEDDs of homogeneous chains, three peaks appear in the exact EEDD at \( f = 0.42 \varepsilon/b \) (triangles), while the EEDD calculated by MEM only shows an abnormal expansion at this force (dash line).

**VI. CONCLUSIONS**
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