Ring closure in actin polymers

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We present an analysis for the ring closure probability of semiflexible polymers within the pure bend Worm Like Chain (WLC) model. The ring closure probability predicted from our analysis can be tested against fluorescent actin cyclization experiments. We also discuss the effect of ring closure on bend angle fluctuations in actin polymers.

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I. INTRODUCTION

In the past two decades, there has been much interest in the theoretical study of semiflexible polymer elasticity. These studies are motivated by micromanipulation experiments [1,2] on biopolymers. In particular, in recent years there have been experiments involving stretching DNA molecules [1] which give us information about the bend elastic properties of DNA. There have also been experiments on fluorescently tagged actin filaments [3].

More recently, there have been fluorescence experiments on cyclization of actin filaments [5]. In these papers they measure the bend persistence length of actin. There have also been experiments on fluorescently tagged actin filaments [4] where they measure the bend persistence length of actin.

Our starting point is the pure bend Worm Like Chain (WLC) model. The ring closure probability predicted from our analysis can be tested against fluorescent actin cyclization experiments. We also discuss the effect of ring closure on bend angle fluctuations in actin polymers.

II. RING CLOSURE PROBABILITY DISTRIBUTION

Our starting point is the pure bend Worm Like Chain (WLC) model [7]. In this model, the polymer configuration is viewed as a space curve \( \vec{x}(s) \). There is a tangent vector associated with each point on the polymer of contour length \( L \) and the energy of configuration is given by:

\[
E[\mathcal{C}] = \frac{A}{2} \int_0^L ds r^2
\]

where \( \mathcal{C} \) stands for the polymer configuration. \( A \) is the bending elastic constant and the curvature \( \kappa = |\vec{r}/r| \).

One of the key quantities characterizing the elasticity of a biopolymer is \( \bar{Q}(\vec{r}) \), the probability distribution for the end to end distance vector \( \vec{r} \) between the two ends of the polymer as it gets jiggled around by thermal fluctuations in a cellular environment [9]. In [7] we use a method for solving the wormlike chain model for semiflexible polymers to any desired accuracy over the entire range of polymer lengths to determine \( \bar{Q}(\vec{r}) \).

Here \( \mathcal{N} \) is the normalization constant and \( k_B T \), the thermal energy at temperature \( T \). As mentioned in [7], we solve for \( \tilde{Q}(\vec{r}) \) by first considering a related end to end distance measure:

\[
P(z) = \int d\vec{r} \tilde{Q}(\vec{r}) \delta(r_3 - z),
\]

which is \( \bar{Q}(\vec{r}) \) integrated over a plane of constant \( z \). This in turn is related to \( \tilde{P}(f) \), the Laplace transform of \( P(z) \) given by:

\[
\tilde{P}(f) = \int_{-L}^{L} P(z) e^{-ifz} dz
\]

\( f \), the variable conjugate to \( z \) has the interpretation of a stretching force and thus \( \tilde{P}(f) \), can be written as the ratio \( Z(f)/Z(0) \) of the partition functions in the presence and absence of an external stretching force \( f \). We do an eigenspectrum analysis of \( \tilde{P}(f) \) and determine \( Q(\vec{r}) \) using tomographic transformations outlined in [7].

Here we address a question which is of current interest to application of polymer physics to biology: cyclization of actin filaments [3]. Within the pure bend Worm Like Chain (WLC) Model we compute the ring closure probability (RCP) by considering \( Q(\vec{r} = 0) \).
III. METHOD

In Fig. 4 of [7] we display a family of curves of $Q(\vec{\rho})$ versus $\rho$, with $\rho = |\vec{r}|$ for various values of $\beta$. $Q(\rho)$ is a theoretically convenient quantity expressed in terms of scaled units ($\vec{\rho} = \vec{r}/\beta$). In order to compute the ring closure probability density $\tilde{Q}(\vec{r} = 0) = Q(0)$ versus $\beta$, setting $Q(\vec{r}) = Q(r)$, we get:

$$\int Q(\vec{\rho}) d\vec{\rho} = \int Q_r dr$$ (4)

or

$$\int \frac{Q(\vec{\rho})}{\beta^3} d\vec{\rho} = \int Q_r dr$$ (5)

which in turn implies

$$\frac{Q(0)}{\beta^3} = Q_0$$ (6)

We compute $Q(0)$ for a range of values of $\beta$ using Mathematica. As we can see from the plot of the ring closure probability density $Q(0)$ versus $\beta$ (Fig. 1), that $Q(0)$ has a small value for short polymers which are hard to bend and form rings and it has a large value for long polymers which are easy to bend and thus the probability density of ring formation is high. We then compute and plot the ring closure probability density in physical space, $Q_0 = Q(0)/\beta^3$, as a function of $\beta$ (Fig. 2). The qualitative features of the plot shown in Fig. 2 are in agreement with our intuition. The ring closure probability density $Q_0$ in physical space, which is an experimentally measurable quantity is small for very small and large $\beta$ and peaks around an intermediate value $\beta \approx 3$. modes which do not contribute, we find that the contribution from the $x-y$ plane is given by

$$\langle \phi^2 \rangle_{xy}^{\text{ring}} = \frac{1}{12} \left( 1 - \frac{6}{\pi^2} \right) \frac{L}{L_P}$$ (7)

We need to add this contribution to the contribution coming from the $z$ direction where the ring closure condition is of the form

$$\int_0^L \phi_z(s) ds = 0.$$

In this case the Fourier expansion for $\phi_z(s)$ can be expressed as $\phi_z(s) = \sum_{n=2}^{\infty} \phi_n e^{2\pi i n s}$ which finally gives us

$$\langle \phi^2 \rangle_z^{\text{ring}} = \frac{1}{12} \left( 1 - \frac{6}{\pi^2} \right) \frac{L}{L_P}$$ (8)

Thus combining Eqs. 7 and 8 the net mean squared tangent angle fluctuation for a three dimensional ring is given by

$$\langle \phi^2 \rangle_{3d}^{\text{ring}} = \frac{1}{6} \left( 1 - \frac{6}{\pi^2} \right) \frac{L}{L_P}$$ (9)
the mean squared tangent angle fluctuation to be tested against future experiments on fluorescently tagged ring like and linear actin filaments in a three dimensional geometry.

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APPENDIX A: COMPUTATION OF $Q_0$

Our goal is to calculate $Q_0$, the ring closure probability. $Q_0$ is $\hat{Q}(\vec{r})$ for $\vec{r} = \vec{0}$. $\hat{Q}(\vec{r})$, the probability distribution for the end to end vector $\vec{r}$ for a semiflexible polymer has the following path integral representation:

$$\hat{Q}(\vec{r}) = N \int \mathcal{D}[\vec{f}(s)] \exp\left\{- \frac{1}{k_B T} \int_0^L \left( \frac{d\vec{f}}{ds} \right)^2 ds \right\} \times \delta^3(\vec{r} - \int_0^L \vec{f} ds) \quad (11)$$

Here $N$ is the normalization constant and $k_B T$, the thermal energy at temperature $T$.

Instead of $\hat{Q}(\vec{r})$ it turns out to be easier to first consider $P(z)$

$$P(z) = \int d\vec{r} \hat{Q}(\vec{r}) \delta(r_3 - z),$$

which is $\hat{Q}(\vec{r})$ integrated over a plane of constant $z$.

$P(z)$ in turn is related to $\hat{P}(f)$, the Laplace transform of $P(z)$ given by:

$$\hat{P}(f) = \int_{-L}^L P(z) e^{-f r_3} dz \quad (12)$$

$f$, the variable conjugate to $z$ has the interpretation of a stretching force and thus $\hat{P}(f)$, can be written as the ratio $Z(f)/Z(0)$ of the partition functions in the presence and absence of an external stretching force $f$.

$Z(f)$ is given by

$$Z(f) = N \int \mathcal{D}[\vec{f}(s)] \exp \left\{ -\frac{L_P}{2} \left[ \int_0^L \left( \frac{d\vec{f}}{ds} \right)^2 ds \right] \right\} \times \exp \left\{ \int_0^L \frac{f}{L_P} \int_0^L \vec{f}_z ds \right\}$$

which in turn can be expressed as

$$Z(f) = N \int \mathcal{D}[\vec{f}(\tau)] \exp \left\{ -\int_0^\beta d\tau \left[ \frac{1}{2} \left( \frac{d\vec{f}_z}{d\tau} \right)^2 - f\vec{f}_z \right] \right\}$$
which has the interpretation of the kernel of a quantum particle on the surface of a sphere at an inverse temperature \(\beta\). We now exploit the analogy between time imaginary quantum mechanics and classical statistical mechanics to re-express \(Z(f)\) as follows:

\[
Z(f) = \sum_n e^{-[\beta E_n] \psi_n (i_A) \psi_n (i_\beta)}
\]

where \(\{\psi_n (i_A)\}\) is a complete set of normalized eigenstates of the Hamiltonian \(H_f = -\frac{\Sigma^2}{2} - f \cos \theta\) and \(E_n\) are the corresponding eigenstates. For free boundary conditions for the end tangent vectors we can express \(Z(f)\) as

\[
Z(f) = \langle o | \exp -\beta H_f | o \rangle
\]

The Hamiltonian \(H_f = -\frac{\Sigma^2}{2} - f \cos \theta\) is the Hamiltonian of a rigid rotor in a potential and \(|0\rangle\) is the ground state of the free Hamiltonian \(H_0 = -\frac{\Sigma^2}{2}\). We numerically evaluate \(Z(f)\) by choosing a suitable basis in which \(H_f\) has a tridiagonal symmetric matrix structure with

\[
H_{ll} = \frac{l(l + 1)}{2}
\]

\[
H_{l,l+1} = f(l + 1)\sqrt{1/[(2l+1)(2l+3)]}
\]

To summarize, after casting the problem analytically we use Mathematica programs to sequentially compute \(Z(f)\) and \(P(f)\), then \(P(z)\), then \(S(r) = -2rdP/(dr) = 4\pi r^2 Q(r)\) and finally \(Q(\rho)\). We then consider the scaled variable \(\rho = \frac{r}{\beta}\). \(Q(0)\) is then computed by considering \(Q(\rho)\) at \(\rho = 0\) and plotting it as a function of \(\beta\). \(Q_0 = Q(0)\). Below we display the programs for computing \(Q(\rho)\) and \(Q_0\). We have inserted some comments as part of the programs for clarity.

**Program for computing \(Q(\rho)\)**

```
ClearAll[h, f, Z, lmax, H, beta, Nmax, L1, L2, LPR, PR]
lmax = 10;
h = .005;
final = {};
For[k = 0, k < 50, k++,
beta = .25*k + 1;
Nmax = Piecewise[90000, beta <= 3, 9000, beta > 3];
L = {};
For[n = 0, n < Nmax + 1, n++, f = h*n*Pi;
H = Table[Switch[i-j, -1, f*(i+1)/Sqrt[(2i+1)(2i+3)], 0, (i+1)/2, 1, f*(i)/Sqrt[(2i-1)(2i+1)]], i, 0, lmax, j, 0, lmax];
M = MatrixExp[-beta*H];
(*Computation of Z(f)*)
Z = M[[1, 1]]; L = Append[L, Z] L = Re[L]; Pz = {};
P1z = {};
For[l = -2, l < 1200, l++, xi = .001*i;
P = (h*beta/Pi)*Sum[L[[n]]*Cos[(n-1)*h*xi*beta], n, Nmax];
Pz = Append[Pz, xi, P];
P1z = Append[P1z, P];
V = P1z;
QR1 = {};
L1 = Drop[V, 2]; L2 = Drop[V, -2];
LPR = (L1-L2)/(.001*2);
LPR = Drop[LPR, 1];
(*Computation of Q(r)*)
QR = Table[LPR[[i]] * 1/((i-1) * .001) * [-1/(2*Pi)],
i, 2, 1199];
(*Computation of Q(\rho)*)
QR1 = Table[(i-1) * .001, LPR[[i]] * (1/(i-1)) * 1/((i-1) * .001) * [-1/(2*Pi)],
i, 2, 2];
ListPlot[QR1]
```

**Program for computing \(Q_0\)**

```
ClearAll[h, f, Z, lmax, H, beta, Nmax, L1, L2, LPR, PR]
lmax = 10;
h = .005;
final = {};
For[k = 0, k < 50, k++,
beta = .25*k + 1;
Nmax = Piecewise[90000, beta <= 3, 9000, beta > 3];
L = {};
For[n = 0, n < Nmax + 1, n++, f = h*n*Pi;
H = Table[Switch[i-j, -1, f*(i+1)/Sqrt[(2i+1)(2i+3)], 0, (i+1)/2, 1, f*(i)/Sqrt[(2i-1)(2i+1)]], i, 0, lmax, j, 0, lmax];
M = MatrixExp[-beta*H];
Z = M[[1, 1]]; L = Append[L, Z] L = Re[L];
Pz = {};
P1z = {};
For[l = -2, l < 1200, l++, xi = .001*i;
P = (h*beta/Pi)*Sum[L[[n]]*Cos[(n-1)*h*xi*beta], n, Nmax];
Pz = Append[Pz, xi, P];
P1z = Append[P1z, P];
V = P1z;
QR1 = {};
L1 = Drop[V, 2];
```

L2 = Drop[V, -2];
LPR = (L1 - L2)/(.001*2);
LPR = Drop[LPR, 1];
QR = Table[LPR[[i]] * 1/((i - 1) * .001) * [-1/(2 * Pi)], i, 2, 1199];
QR1 = Table[(i - 1) * .001, LPR[[i]] * 
(1/(i - 1)) * 1/((i - 1) * .001) * [-1/(2 * Pi)], i, 2, 2];
final = Append[final, beta, (1/beta^3) * QR[[1]]]
ListPlot[final]

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