Relaxation dynamics of partially extended single DNA molecules

To cite this article: Ludger Harnau and Peter Reineker 1999 New J. Phys. 1 3

View the article online for updates and enhancements.

Related content
- On the dynamics of polymer melts: Contribution of Rouse and bending modes
  L. Harnau, R. G. Winkler and P. Reineker
- Global cross-over dynamics of semiflexible polymers
  M. Hinczewski and R. R. Netz
- Theoretical models for bridging timescales in polymer dynamics
  M G Guenza

Recent citations
- Anisotropic Hydrodynamic Mean-Field Theory for Semiflexible Polymers under Tension
  Michael Hinczewski and Roland R. Netz
- Static dynamics approach to relaxation modes and times for deformed polymers
  Roland Rzehak
- Force Spectroscopy of Molecular Systems—Single Molecule Spectroscopy of Polymers and Biomolecules
  York Oberdörfer et al
Relaxation dynamics of partially extended single DNA molecules

Ludger Harnau and Peter Reineker
Abteilung Theoretische Physik, Universität Ulm, 89069 Ulm, Germany
E-mail: harnau@physik.uni-ulm.de

New Journal of Physics 1 (1999) 3.1–3.6 (http://www.njp.org/)
Received 3 November 1998; online 15 January 1999

Abstract. Dynamical properties of chain molecules under tension are investigated using a functional integral formalism. The relaxation times of partially extended chain molecules are investigated on the basis of a Langevin equation approach and for the first time compared with experimental data of partially extended single DNA molecules. The hydrodynamic interaction as well as the semiflexibility of the molecules are taken into account. The theoretical approach quantitatively reproduces the experimental data. Furthermore, it is found that the normal mode concept also holds in the case of partially extended macromolecules.

1. Introduction

During the last six years a series of single DNA experiments has provided detailed insight into equilibrium and dynamic properties of DNA [1]–[7]. In these experiments the DNA molecules are stretched by various means such as optical tweezers or Stokes drag, and their extension and relaxation are measured. The equilibrium properties of stretched DNA molecules are mostly elucidated using a semiflexible chain model [8]–[11]. The dynamics is not yet as well understood as the equilibrium properties. Recently performed direct video microscope measurements of the dynamics of partially extended single DNA molecules reveal severe deviations from the theoretical predictions for both coiled polymers [12] and extended polymers [13]. The relaxation times characterizing the dynamics of the DNA molecules are smaller than the well known Zimm relaxation times [12] and exhibit a stronger mode number dependence. Thus, the question arises: is the classical theory of macromolecular hydrodynamics capable of interpreting the video microscope data on the dynamics of extended single DNA molecules? Here we show that these experimental data can be quantitatively described using a functional integral formalism together with a Langevin equation approach. The calculations demonstrate the importance of the normal mode concept in macromolecular science, and thereby provide a quantitative basis...
for the future investigations of questions of more biological interest such as the formation and breakdown of loops in single DNA molecules.

2. Relaxation times of extended macromolecules

DNA contains many base pairs within its persistence length of \(1/(2p) \approx 50\) nm. Equilibrium properties on length scales larger than the persistence length represent therefore averages over sequences and are usually described by a semiflexible chain model. The semiflexible chain model is represented as a space curve \(r(s)\) of total contour length \(L\) with \(s \in [-L/2, L/2]\) being the arclength. The unit tangent vector is \(u(s) = \partial r(s)/\partial s\). Using a mean field approach, the partition function of a semiflexible chain molecule under tension reads \([10, 14]\)

\[
Z = \int \mathcal{D}[u(s)] \exp \left( -\lambda \int_{-L/2}^{L/2} ds \, u^2(s) - \lambda_0 \left( u^2(-L/2) + u^2(L/2) \right) \right)
\]

\[
\times \exp \left( -\frac{3}{8p} \int_{-L/2}^{L/2} ds \left( \frac{\partial u(s)}{\partial s} \right)^2 - \int_{-L/2}^{L/2} ds \, f(s) \cdot u(s) \right). \tag{1}
\]

The first two terms in the exponent describe the flexible chain. Of particular importance is the term with the factor \(\lambda_0\). It expresses the fact that the translational symmetry along the chain contour is broken at the chain ends \([14]\). The third term represents the bending energy, which accounts for the molecular stiffness. It is assumed that in general the external field \(f(s)\), stretching the chain molecule, depends on \(s\) \([10]\). The auxiliary variables \(\lambda_0\) and \(\lambda\) are determined by the maximum entropy principle \([15]\). Since the entropy assumes an extremum at equilibrium, a variational calculation can be used. The extreme value has to be calculated under the constraint that \(u^2(s) = 1\). The Lagrangian multipliers are obtained by demanding the constraint to hold on average \([14]\). Exploiting an analogy between the path integral in equation (1) and the forced harmonic oscillator of mass \(3h^2/(4pk_BTL^3)\) and frequency \(2k_BTL\sqrt{2p\lambda/3}/\hbar\) in quantum mechanics \([16]\), the free energy \(\mathcal{F} = -k_B T \ln Z\) is easily calculated. \(\mathcal{F}\) is a generating functional which allows for the calculation of various expectation values. For example the mean square internal distance \(\langle (r(s) - r(s'))^2 \rangle\), which is necessary for the following calculations (equation (10)), is given by

\[
\langle (r(s) - r(s'))^2 \rangle = \int_{s'}^s ds_1 \int_{s'}^{s_2} ds_2 \frac{\partial}{\partial f(s_1)} \cdot \frac{\partial}{\partial f(s_2)} \mathcal{F}. \tag{2}
\]

We now specialize to the condition that \(f(s) = f\) is independent of \(s\). This situation applies for experiments on extended single DNA molecules \([1, 7]\). The comparison of the computed average elongation of a chain molecule under tension

\[
z = \frac{1}{|f|} \left\langle \int_{-L/2}^{L/2} ds \, u(s) \cdot f \right\rangle = -\frac{f}{|f|} \cdot \frac{\partial \mathcal{F}}{\partial f}
\]

\[
= \frac{4p|f|}{3\Omega^2} \left( L - \frac{16p\lambda_0}{3\Omega^2} \cosh \Omega L + \frac{8p\lambda_0/3\Omega}{\sinh \Omega L - 1} \right) \tag{3}
\]

\[
= \frac{4p|f|}{3\Omega^2} \left( L - \frac{16p\lambda_0}{3\Omega^2} \cosh \Omega L + \frac{8p\lambda_0/3\Omega}{\sinh \Omega L - 1} \right) \tag{4}
\]
\[ \Omega = 2\sqrt{\frac{2p\lambda}{3}} \] 

(5)

with experimental data for extended DNA molecules [1, 8] exhibits good agreement. Identifying the exponent in the partition function (1) as the intramolecular mean field potential energy of the chain molecules (multiplied by \(1/(k_B T)\)) and applying Hamilton’s principle, the following equation of motion along with the boundary conditions for a constant force \(f\) are obtained:

\[ \frac{\varrho}{k_B T} \frac{\partial^2}{\partial t^2} \mathbf{r}(s, t) = 2\lambda \frac{\partial^2}{\partial s^2} \mathbf{r}(s, t) - \frac{3}{4p} \frac{\partial^4}{\partial s^4} \mathbf{r}(s, t) \] 

(6)

\[ f = \left[ \frac{3}{4p} \frac{\partial^3}{\partial s^3} \mathbf{r}(s, t) - 2\lambda \frac{\partial}{\partial s} \mathbf{r}(s, t) \right] \pm L/2 \] 

(7)

\[ 0 = \left[ 2\lambda_0 \frac{\partial}{\partial s} \mathbf{r}(s, t) \pm \frac{3}{4p} \frac{\partial^2}{\partial s^2} \mathbf{r}(s, t) \right] \pm L/2 \] 

(8)

where \(\varrho\) is the linear mass density. Since there is always strong damping in a macromolecular solution, the equation of motion is supplemented by frictional forces and the hydrodynamic interaction mediated by the motion of the solvent. Omission of the inertial term leads to the Langevin equation

\[ \frac{3\pi \eta}{k_B T} \frac{\partial}{\partial t} \mathbf{r}(s, t) = \int_{-L/2}^{L/2} ds' \left( 3\pi \eta H(s - s') + \delta(s - s') \right) \] 

\[ \times \left( 2\lambda \frac{\partial^2}{\partial s^2} \mathbf{r}(s', t) - \frac{3}{4p} \frac{\partial^4}{\partial s^4} \mathbf{r}(s', t) + \mathbf{g}(s', t) \right). \] 

(9)

\(\mathbf{g}(s', t)\) is a stochastic force and \(\eta\) the viscosity of the solvent. The hydrodynamic interaction tensor is given by the Rotne–Prager tensor \(H(s - s')\) [18]. In order to obtain an analytical solution of the Langevin equation (9) we apply the pre-averaging approximation [12, 19]:

\[ H(s - s') = \Theta(|s - s'| - d) \frac{3}{3\pi \eta} \sqrt{\frac{3}{2\pi \langle(r(s) - r(s'))^2\rangle}} \exp \left( -\frac{3d^2}{2 \langle(r(s) - r(s'))^2\rangle} \right) \] 

(10)

where \(d\) is the lateral diameter of the macromolecules. The Heaviside step function \(\Theta(|s - s'| - d)\) is introduced to exclude self-interaction. The quality of the pre-averaging approximation can only be estimated from a comparison with more sophisticated calculations. To solve equation (9) we use an expansion of the position vector and of the stochastic force in terms of the eigenfunctions \(\psi_l(s)\) of the eigenvalue problem without hydrodynamic interaction \((H(s - s') = 0)\):

\[ \mathbf{r}(s, t) = \sum_l \chi_l(t) \psi_l(s), \] 

(11)

\[ \mathbf{f}(s, t) = \sum_l \mathbf{f}_l(t) \psi_l(s). \] 

(12)

A numerical calculation exhibits that the transformed hydrodynamic interaction matrix

\[ H_{ln} = \int_{-L/2}^{L/2} ds \int_{-L/2}^{L/2} ds' \psi_l(s) H(s - s') \psi_n(s') \] 

(13)
3.4

is almost diagonal. Hence the amplitudes $\chi_l(t)$ can be considered as normal modes. Normal modes have also been calculated for boundary conditions where only one end of the polymer is fixed [17]. For rather flexible macromolecules ($pL \gg 1$) the solution of equation (9) reads approximately

$$ r(s, t) = \sqrt{\frac{2}{L}} \sum_{l_{\text{even}}}^{l_{\text{max}}} \chi_l(t) \cos \left( \frac{l\pi s}{L} \right) + \sqrt{\frac{2}{L}} \sum_{l_{\text{odd}}}^{l_{\text{max}}} \chi_l(t) \sin \left( \frac{l\pi s}{L} \right) - \frac{s^2}{2\lambda f}. \quad (14) $$

Assuming that the stochastic forces $g(s', t)$ are $\delta$-correlated in time the time correlation function of the amplitudes $\chi_l(t)$ and $\chi_k(0)$ in equation (14) is given by

$$ \langle \chi_l(t) \cdot \chi_k(0) \rangle = \frac{3L^2}{2\lambda l^2\pi^2} \delta_{lk} \exp \left( -\frac{t}{\tau_l} \right) \quad (15) $$

with relaxation times

$$ \tau_l = \frac{3\eta L^2}{2\pi k_B T l^2} \left( 1 + \frac{\sqrt{6}}{\sqrt{\pi} L} \int_{d}^{L} ds \frac{(L-s) \cos (\pi l s / L)}{\sqrt{(r(s) - r(0))^2}} \exp \left( -\frac{3d^2}{2(r(s) - r(0))^2} \right) \right)^{-1}. \quad (16) $$

The relationship between the chain elongation and $\lambda$ is given by equation (3). The mean-square internal distance becomes with equation (2)

$$ \langle (r(s) - r(s'))^2 \rangle = \frac{3}{2\lambda} |s - s'| - \frac{3}{4\lambda} \sqrt{3} \frac{3}{2p\lambda} \left( 1 - \exp \left( -2 \sqrt{\frac{2p\lambda}{3}} |s - s'| \right) \right) $$

$$ + \left( 1 - \sqrt{\frac{3p}{2\lambda}} \right) (s - s')^2. \quad (17) $$

For an unextended flexible chain molecule the $\tau_l$ reduce to the Zimm relaxation times for a $\Theta$-solvent and vary as $l^{-1.5}$ [19]. Figure 1 displays the computed relaxation times according to equations (16) and (17) together with experimental data of partially extended single molecules of DNA [7]. In addition the first ten Zimm relaxation times for a $\Theta$-solvent are plotted in the figure. The inset displays the scaling behaviour $\tau_l \sim l^\alpha$. From the comparison of the experimental and theoretical data it is obvious that the calculations describe the measured relaxation times well. Please, note that the theoretical results are compared directly, i.e. without any fit procedures, with the experimental results. The contour length and the hydrodynamic diameter used in the numerical evaluation are given by $L = 20 \mu m$ and $d = 2.5 \text{ nm}$, respectively [7, 19]. Due to the use of the pre-averaged hydrodynamic tensor for the extended chain geometry the calculated relaxation times are smaller than the Zimm relaxation times for a $\Theta$-solvent and exhibit a stronger mode number dependence, as shown in the inset in figure 1. Using the mean-square internal distance of a highly extended chain molecule $\langle (r(s) - r(0))^2 \rangle = s^2$ the relaxation times (16) are approximately evaluated as

$$ \tau_l \approx \frac{3\eta L^2}{2\pi k_B T \lambda l^2} \left( 1 - \sqrt{\frac{6}{\pi}} C - \sqrt{\frac{6}{\pi}} \ln \left( \frac{l\pi d}{L} \right) \right)^{-1}. \quad (18) $$

where $C = 0.577...$ is Euler’s constant. Hence there are logarithmic corrections to the Rouse relaxation times $\tau_l \sim l^{-2}$. These corrections cannot be neglected [22] and lead to the observed exponents $\alpha < 2$. 

New Journal of Physics 1 (1999) 3.1–3.6 (http://www.njp.org/)
3.5

Figure 1. Relaxation times $\tau_i$ of partially extended single molecules of DNA (filled squares, $10 \mu m$ extension; filled down triangles, $12 \mu m$ extension; filled diamonds, $14 \mu m$ extension; filled up triangles, $16 \mu m$ extension) reported by Quake et al [7]. Open symbols represent the theoretical calculations according to equations (16) and (17). The stars correspond to the Zimm relaxation times for a $\Theta$-solvent. The length of the DNA fragments and the lateral diameter are given by $L = 20 \mu m$ and $d = 2.5 \text{ nm}$ [7, 19]. The inset displays the scaling behaviour $\tau_i \sim l^\alpha$. The experimental data (filled circles) are displayed with error bars. Open circles represent the theoretical calculations (for $z = 6 \mu m$ the experimental and theoretical values coincide).

3. Conclusion

In this paper we have investigated the relaxation dynamics of single DNA molecules on the basis of Langevin equations which take into account the semiflexibility of the molecules, damping and fluctuation as well as the hydrodynamic interaction via the pre-averaged Rotne–Prager tensor. Answering the initial question, our calculations show that the normal mode concept describes the relaxation times of partially extended single DNA molecules. If improved experimental data yield deviations from our calculations, possibly anisotropic pre-averaged or unpre-averaged hydrodynamic interaction has to be considered. Further experimental studies of shorter and therefore stiffer DNA fragments under tension should be very interesting in order to observe directly the bending modes which dominate the internal dynamics of rather stiff macromolecules [20]. These are necessary for the interpretation of recent measurements on loop formation and breakdown in short DNA molecules [21].
Acknowledgments

This investigation is part of a project of the Sonderforschungsbereich 239. The support of the Deutsche Forschungsgemeinschaft is gratefully acknowledged.

References

[22] Pincus P 1977 Macromolecules 10 210