Macromolecules **1994,** *27,* 3843-3849

Semiflexible Chain Molecules with Nonuniform Curvature. 1. Structural Properties

Christer Håkansson and Christer Elvingson*

Department of Physical Chemistry, Chalmers University of Technology,
S-412 96 Göteborg, Sweden

Received March 30, 1994⊛

ABSTRACT: The structure of polymers with nonuniform curvature has been calculated for a semiflexible chain model, and a general expression for the persistence length and end-to-end distance is derived for a freely rotating chain. The statistical properties of molecules with one or more static bends or having a locally changed flexibility are analyzed in terms of the persistence length, but also the influence from heterogeneity of the molecular structure for an ensemble of chains is considered. Assuming the change in chain structure is caused, e.g., by the binding of ligand molecules, the effect of cooperativity on the molecular configuration is also treated.

Introduction

Many polymers, both synthetic and biological, may be characterized as semiflexible, showing an almost rigid rod behavior at low molecular weights which gradually changes toward a random coil behavior with increasing molecular mass. The structure of such molecules is often analyzed using the wormlike chain model. In this model the polymer is represented by a curve for which the curvature varies smoothly in space.[1] It is, however, known that for a biopolymer like DNA, interaction with proteins, e.g., in nucleosomes where the DNA is wrapped around the core histone proteins,[2] as well as the binding of low molecular weight ligands[3] is often associated with a change in curvature of the corresponding DNA tracts. Also, the presence of poly(dA) sequences in DNA results in changed structural properties, compared with mixed-sequence B-DNA.[4] These changes in the DNA structure can be measured by the retardation during gel electrophoresis[5] or by the enhanced ability for circularization.[6] The increased DNA curvature can also be observed by methods sensitive to the hydrodynamic properties of the molecules, such as the orientation in an electric[7] or shear flow field.[8] The results of such measurements are often presented in terms of the persistence length, the magnitude being a sum of contributions from thermal fluctuations and a sequence-dependent or ligand-induced static bending.[9,10] The resulting DNA structure as a result of binding of a drug molecule is, however, not always easy to interpret, since the orientation in an external field can be anticipated to be changed either due to the introduction of static bends or by a locally changed flexibility. The effect of a changed curvature on the structure of polymer molecules has been analyzed in various detail by different authors,[11-18] and in the present paper we have extended the work of Schellman[11] using the wormlike chain model. Such an analysis is important for understanding the large-scale structure of semiflexible chain molecules like DNA when introducing kinks and different flexibilities along the molecule. A detailed analysis of the equilibrium statistical properties of such chain molecules is also important when interpreting the dynamical behavior of the corresponding molecules.

Methodology

Being primarily interested in the long-range structure of DNA, we will use the freely rotating chain model shown in Figure 1, which can be thought of as a discrete wormlike chain. The main advantage of this model is that a number of cases can be treated analytically,[19] and careful use of the theory gives good agreement with experimentally determined persistence lengths.[20,21] It can also readily be used in simulations of the corresponding dynamic properties.[22-24] The molecule is here represented by a string of beads, or subunits, held together by harmonic forces.[24] The bending motion is restricted, but all torsional angles are equally probable. In earlier Brownian dynamics simulations, the stiffness of the chain was invoked by using the following expression for the free energy of bending

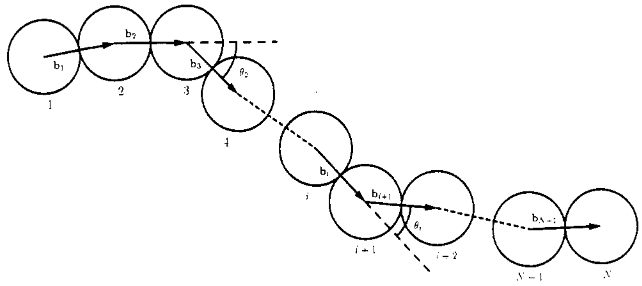

Figure 1. Polymer molecule modeled as a discrete wormlike chain. It consists of N subunits and two of the bending angles (θ_2 and θ_i) have the minimum in bending free energy at a bending angle (θ^0) different from zero.

$$U_b^{(1)} = k_b^{(1)} \sum_{j=1}^{N-2} [1 - \cos(\theta_j - \theta_j^0)] \qquad (1)$$

where N is the number of subunits and $k_b^{(1)}$ is the bending force constant, θ_j being the angle between bond vectors $\mathbf{b}_j$ and $\mathbf{b}_{j+1}$, where $+\mathbf{b}_j$ is the distance vector from subunit j to $j + 1$, and θ^0 the angle at the minimum in potential energy which in earlier work was set equal to zero.[22-24] Since DNA is a rather stiff molecule, the fluctuations in θ were assumed to be small and using $\sin\theta \approx \theta$ gave the same expression for the restoring force as a harmonic bending potential. In the present paper, however, we will also be looking at molecules having kinks along the chain with $\theta^0 \neq 0°$, and U_b will in most cases instead be given by

$$U_b^{(2)} = \frac{k_b^{(2)}}{2} \sum_{j=1}^{N-2} (\cos\theta_j - \cos\theta_j^0)^2 \qquad (2)$$

The latter potential is advantageous to use in dynamics

⊛ Abstract published in *Advance ACS Abstracts,* May 15, 1994.

0024-9297/94/2227-3843$04.50/0

simulations of molecules with nonuniform curvature since the expression for the corresponding force does not suffer from numerical instabilities.[25] Comparing results obtained using eq 1 or 2 requires, however, the force constants to be determined in a self-consistent way. One way of doing this is to require the persistence length, P, to be the same for both potentials. For a molecule for which all θ_j^0 are equal, the persistence length in the freely rotating chain model is given by[26]

$$P_N = \langle b \rangle \frac{1 - \alpha^{N-1}}{1 - \alpha} \qquad (3)$$

where $\langle b \rangle$ is the average bond length and $\alpha = \langle \cos \theta \rangle$, which is obtained from the relation

$$\alpha = \frac{\int_0^{\pi} \cos \theta \mathrm{e}^{-U_\mathrm{b}(k_\mathrm{b})/kT} \sin \theta \, \mathrm{d}\theta}{\int_0^{\pi} \mathrm{e}^{-U_\mathrm{b}(k_\mathrm{b})/k\mathrm{T}} \sin \theta \, \mathrm{d}\theta} \qquad (4)$$

where k is the Boltzmann constant and T the temperature. For a large molecule, where eq 3 reduces to the corresponding expression for a continuous chain,[27] $P_\infty = \langle b \rangle / (1 - \alpha)$, $k_\mathrm{b}^{(1)}$ can be calculated analytically for a linear molecule[19] and is given by

$$k_\mathrm{b}^{(1)} = P_\infty k\mathrm{T} / \langle b \rangle \qquad (5)$$

One can, of course, choose b to be small enough for the limiting expressions to be valid and regarding P as an intensive property.[15] We have obtained this limit in our calculations, as shown in the next section, by choosing the molecules large enough compared to P.

Using eq 2 instead for the potential energy, we can determine the force constant (for a linear molecule) by an iterative procedure by combining eq 2 with eqs 3 and 4, giving $k_\mathrm{b}^{(2)}$ for a molecule with the same persistence length. By specifying P and thereby α, we have also determined the equilibrium structure of the corresponding molecules, since the end-to-end distance, R, and the radius of gyration are both functions of α. This means that the results presented in the next section for the end-to-end distance should also apply to the radius of gyration. The dynamics of the molecules, however, should in principle be different when using eqs 1 or 2, since assuming all $\theta^0 = 0°$, the leading term in θ when expanding eq 1 is θ^2 while for eq 2 it is θ^4. This is also the reason why we use the above procedure for determining $k_\mathrm{b}^{(2)}$ and not $k_\mathrm{b}^{(2)} = k_\mathrm{b}^{(1)} / \sin^2 \theta^0$, which is obtained for nonlinear molecules when comparing the first nonvanishing coefficients.[25]

The molecules discussed so far have been assumed to be smoothly bending linear chains. Semiflexible molecules like DNA, however, can be curved with a minimum in the free energy of bending at $\theta^0 \neq 0°$ or they can have locally changed flexibilities with a different k_b than the unperturbed bending sites. For these cases, the usual expressions for the persistence length and end-to-end distance are no longer valid, and instead the following relations can be derived (cf. Appendix):

$$P_N = \frac{\langle b \rangle}{1 - \alpha} \sum_{m=0}^{n} [\alpha^{p_m - m} (1 - \alpha^{p_{m+1} - p_m}) \prod_{q=0}^{m} \alpha_{p_q}] \qquad (6)$$

$$\langle R^2 \rangle = (N - 1) \langle b^2 \rangle + 2 \langle b \rangle^2 \left\{ \frac{\alpha}{1 - \alpha} \sum_{m=0}^{n} \left(p_{m+1} - p_m - \frac{1 - \alpha^{p_{m+1} - p_m}}{1 - \alpha} \right) + \sum_{m=0}^{n-1} \sum_{s=m+1}^{n} \left[(\prod_{q=m+1}^{s} \alpha_{p_q}) \alpha^{p_s - p_{m+1} - (s-m-1)} \times \frac{(1 - \alpha^{p_{m+1} - p_m})(1 - \alpha^{p_{s+1} - p_s})}{(1 - \alpha)^2} \right] \right\} \qquad (7)$$

In these equations there are n locations at positions p_j, given by the number of the corresponding bending angle θ_j, where a kink or a different bending force constant changes the average value of cos θ from α to α_{p_j}. For completeness, we must also define $p_0 = 0$, $p_{n+1} = N - 1$, and $\alpha_{p_0} = 1$.

There are a number of cases that could cause a DNA molecule to obtain a nonuniform curvature. One possibility is that AT-rich regions in the DNA introduce static bends.[28] These bends could then be distributed more or less randomly. Another possibility is that the nonuniformities are due to the binding of different ligand molecules which could occur either randomly or with a certain degree of cooperativity. We could also think of cases where the bound molecules tend to be as far apart as possible, e.g., if they have the same charge. In any of these cases, the persistence length and the end-to-end distance will change, and in the calculations presented in the next section, these changes in the molecular structure are assumed to be characterized either by a changed θ^0 or a changed bending force constant or a combination of both. For example, the binding of a ligand to DNA could induce an increased bending angle $\theta^0 \neq 0°$ or instead increase/decrease the local persistence length (force constant), or the ligand could change the flexibility or even reduce the bending angle at an originally bent DNA sequence.[29] In most calculations (except in Figures 3 and 6), *the force constant, k_b will be given in terms of the corresponding persistence length, P_∞, for an infinite unperturbed molecule* through eq 5 when using potential $U_\mathrm{b}^{(1)}$ and determined by an iterative procedure for $U_\mathrm{b}^{(2)}$. The actual persistence length and end-to-end distance for the finite size molecules are then calculated from eqs 6 and 7. For the special case of nonuniformities occurring at random with a certain probability, the limiting persistence length can also be evaluated analytically by a relation given by Schellman[11]

$$P_\infty = \frac{\langle b \rangle}{1 - (1 - p)\alpha - p\gamma} \qquad (8)$$

where $\alpha = \langle \cos \theta \rangle$ for the normal link and $\gamma = \langle \cos \theta \rangle$ for a deformation occurring with the probability p. If we define $\alpha_\mathrm{eff} = (1 - p)\alpha + p\gamma$, then eq 8 can be written $P = \langle b \rangle / (1 - \alpha_\mathrm{eff})$ and the "standard" equations for the structural properties of the uniform discrete wormlike chain, the end-to-end distance or radius of gyration, are valid using α_eff instead of α. For the other cases treated below (binding with cooperativity or other nonrandom distributions of deformations), we have not found any simple analytical expressions.

Using the persistence length as a measure of the stiffness and rigid rod behavior of chain molecules, as is usually done, one must realize that the definition of the persistence length as the projection of the end-to-end distance on the first bond vector[30] will make P dependent on the nature of the first bond. When the structural properties of nonuniform molecules are calculated, it is therefore important to have good statistics and averaging over many different configurations to reduce any possible bias from the distribution of the nonuniformities. It should also be noted that a molecule having many static bends can also be very stiff in spite of having a small effective persistence length. It has been suggested[31] that the Kuhn length $l_K = \langle R^2\rangle/L$, L being the contour length, would be a more general measure of the extension or rectilinearity of a nonuniform polymer, and this parameter is also included in the calculations in the next section.

Results and Discussion

Molecules with Randomly Distributed Kinks. In Figure 2 is shown the persistence length, P, calculated using eq 6, as a function of θ^0 for molecules with 10, 30, and 50% randomly distributed kinks. The molecules consist of 200 subunits, each with a radius of 1.59 nm. The temperature is 20 °C, and the results are averages over 5000 generated molecules. The same chain length and number of molecules will be used for all results presented below, unless other figures are specifically given. The bending force constants for the molecules in Figure 2 are the same throughout a chain, irrespective of whether a certain bending angle has θ^0 equal to zero or not. In each figure, the results for two different sets of force constants are shown, corresponding to the potentials given in eqs 1 and 2 and expressed in terms of P_∞ for the unperturbed molecules. One first notices that the persistence length decreases considerably when θ^0 is increased, which is readily understood from the definition of P, being the projection of all consecutive bonds on the first. The decrease in P is also more pronounced for a stiff chain with a larger bending force constant than for a flexible molecule. This should be clear given the comparatively more coillike equilibrium structure for the flexible molecule. Increasing the number of kinks or their magnitude will result in a larger perturbation of the stiff molecule, and its persistence length will eventually reach about the same value as for the flexible molecule. The same features are also seen for the end-to-end distance (not shown), since this is also determined by α and α_p through eq 7. Formally, the qualitative behavior can be deduced, e.g., from eqs 3 and 8 by examining the limits $\theta^0 = 0°$ and $\theta^0 = 90°$. When $\theta^0 = 0°$, γ will be equal to α and P will be given by the same expression as for an unperturbed molecule. At $\theta^0 = 90°$, $\gamma = 0$ and $P = \langle b\rangle/[1 - (1 - p)\alpha]$, which means that increasing p or decreasing α (i.e., decreasing k_b) will reduce P. For $P_\infty = 80$ nm and $p = 0.50$ the limiting value at $\theta^0 = 90°$ will be $P = 6.1$ nm, while the corresponding result for $P_\infty = 40$ nm is 5.9 nm. Decreasing p to 0.10, the corresponding values will be 18.5 and 23.4 nm, respectively. Reaching almost the same value for P at $p = 0.50$, the force constant, however, is still much larger for the stiff molecule, and the persistence length thus tells us something about the extension but not necessarily about the stiffness of the molecule.

In Figure 2 is also shown the difference in persistence length obtained when using eq 1 or 2. The starting values, P_∞, for molecules described by either potential are equal, but $k_b^{(2)}$ will be larger than $k_b^{(1)}$ since the exponent in eq 2 is essentially the square of that in eq 1 for $\theta^0 = 0°$. Since k_b is assumed to be constant when introducing bends in the molecule, this makes potential 2 have a larger peak value and drop more rapidly at high θ values, which then results in the structural differences illustrated in Figure 2. In most model calculations and dynamic simulations a harmonic bending potential has been used,[22,24] which is an approximation of eq 1 valid at small θ as noted above. Equation 2, however, should work even better for larger fluctuations since higher powers of θ are included. One can also see in Figure 2 that although the bending force constants were calculated using the persistence length for an infinite chain, the P_N values at $\theta^0 = 0°$ for $N = 200$ agree very well with the corresponding P_∞. This is shown in

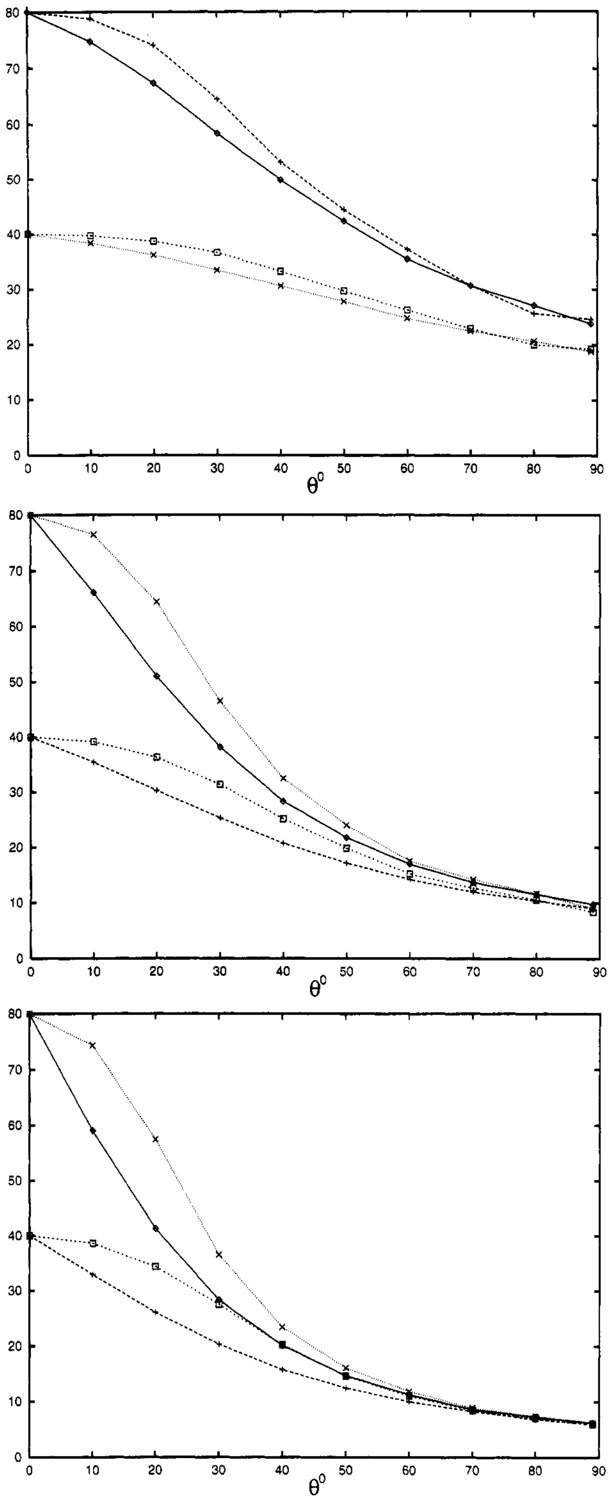

Figure 2. Persistence length P, in nm, as a function of θ^0 for two different sets of force constants representing each of the two potentials given in eqs 1 and 2. The different curves are given by (×) $U_b^{(1)}$,P_∞ = 40 nm; (□) $U_b^{(2)}$,P_∞ = 40 nm; (◇) $U_b^{(1)}$,P_∞ = 80 nm; and (+) $U_b^{(2)}$,P_∞ = 80 nm. The probability of kinks is (a, top) 10%, (b, middle) 30%, and (c, bottom) 50%.

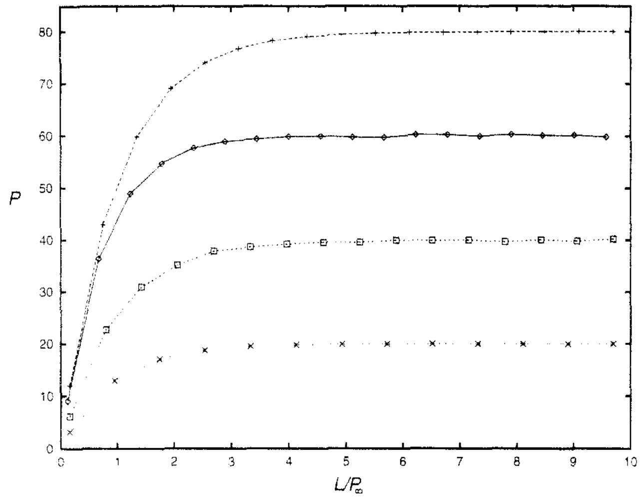

Figure 3. Persistence length P, in nm, as a function of chain contour length divided by P for the corresponding infinite chain: (×) $P_\infty = 20$ nm; (+) $P_\infty = 80$ nm; (□) $P_\infty = 40$ nm, chain containing 30% kinks with $\theta^0 = 30°$; (◇) molecule with 70% of the force constants corresponding to $P_\infty = 80$ nm and 30% corresponding to 37.9 nm.

more detail in Figure 3, where the persistence length is plotted as a function of L/P_∞. The results for two linear molecules are shown, as well as for a chain having 30% kinks with $\theta^0 = 30°$, and also for a molecule having locally changed flexibilities with 30% of the bending force constants corresponding to $P_\infty = 37.9$ nm and the rest having $P_\infty = 80$ nm (the corresponding overall persistence length will then be 60 nm for an infinite molecule). The force constant for the former molecule has in this case been determined by solving eq 8 for k_b (using eq 4 and assuming $k_{b,\alpha} = k_{b,\gamma} = k_b$). It is seen that for all four cases the convergence is fast, and the limiting value has been reached when the contour length is about 3 times the persistence length. The small noise seen for the two middle curves comes from the averaging over different randomly generated distributions of kinks, whereas the persistence lengths for the linear molecules are calculated analytically using eq 3.

In polymer chain statistics one often also uses the Kuhn length to describe the statistical behavior of a molecule, and it has been suggested[31] that one should use the Kuhn length as a measure for the extension of a molecule instead of the persistence length since the former does not explicitly depend on the nature of a specific reference bond (the first). In Figure 4 we show l_K for the same cases as in Figure 2b. For an infinite linear wormlike chain[30] $l_K = 2P$, but we can see that for $\theta^0 = 0°$ this is not fulfilled even for a chain with 200 subunits. This is due to the fact that the correction factor for a molecule with a finite length converges much more slowly for the Kuhn length than for the persistence length, which can be seen by combining the definition of l_K given in the previous section with eq A14.

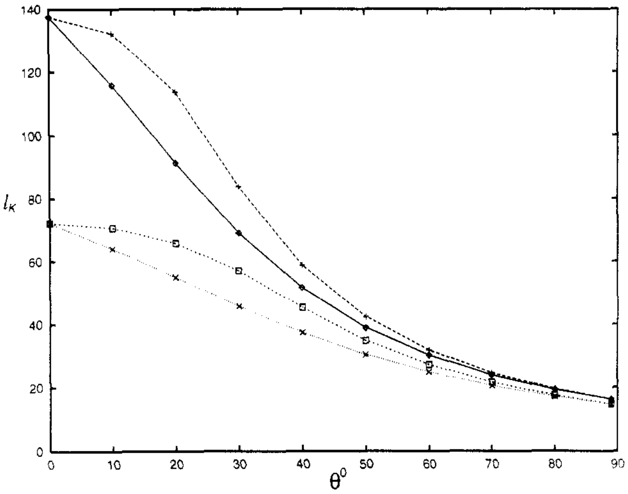

Figure 4. Kuhn length, in nm, as a function of θ^0. The meaning of the symbols is the same as in Figure 2b.

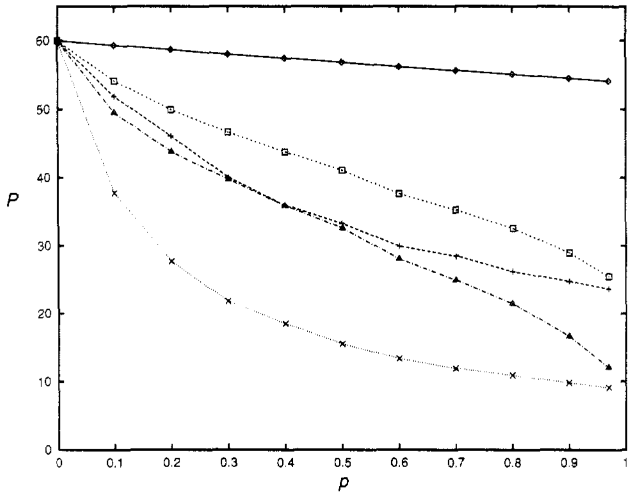

Figure 5. Persistence length P, in nm, as a function of p, the average fraction of kinks. The force constant for all curves corresponds to $P_\infty = 60$ nm. (◇) $\theta^0 = 10°$; (+) $\theta^0 = 30°$; (□) $\theta^0 = 30°$, cooperativity = 10^3; (×) $\theta^0 = 50°$; (△) $\theta^0 = 50°$, cooperativity = 10^3.

We have also calculated the change in P when increasing the fraction, p, of identical kinks in the molecules, corresponding, e.g., to the binding of ligands at different binding ratios, where a binding ratio of 1 means that all bending angles (see Figure 1) have been changed. Three different values of θ^0 have been used, and the results for potential $U_b^{(2)}$ are shown in Figure 5. For a small θ^0 the persistence length will change only marginally, even at binding ratios close to 1. When θ^0 increases, however, the persistence length decreases rapidly with increasing fraction of kinks (Figure 2). The binding of ligands inducing structural changes in a molecule could also be anticipated to occur with a certain degree of cooperativity. This is done here by increasing the probability for binding next to an already changed bending angle. In Figure 5 is also shown the effect of including cooperativity for the two largest θ^0 values by increasing the probability by a factor of 1000 compared to a completely random distribution. It is seen that the decrease in P is considerably slower if the introduction of kinks is a cooperative process instead of occurring randomly. This is because the effective number of kinks in the former case is smaller, being lumped together at certain locations along the molecules, the resulting effective bending angle not being the sum of the individual contributions. When more than half of the binding sites are occupied, however, the decrease in persistence length is faster for the cooperative binding, and the limiting value of P when p equals one must of course be the same in both cases.

When measuring the dynamical properties of DNA molecules, e.g., by fluorescence depolarization anisotropy, depolarized light scattering, or electric dichroism, it is important when interpreting the results to be aware of the effect of polydispersity. In Figure 6 we have compared the distribution of the persistence length for different fractions of kinks at two different equilibrium bending angles for a specific bending force constant by generating 50 000 molecules for each set of parameters. The force

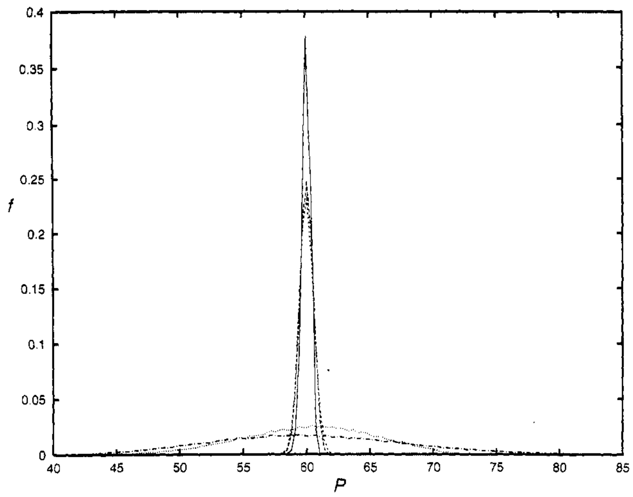

Figure 6. Relative frequency, *f*, for the distribution of the persistence length for five different types of molecules, all having an effective average persistence length equal to 60 nm. The different curves represent (—) $p = 0.10$, $\theta^0 = 10°$; (- - -) $p = 0.30$, $\theta^0 = 10°$; (- - -) $p = 0.50$, $\theta^0 = 10°$; (· · ·) $p = 0.10$, $\theta^0 = 30°$; and (- · -) $p = 0.20$, $\theta^0 = 30°$.

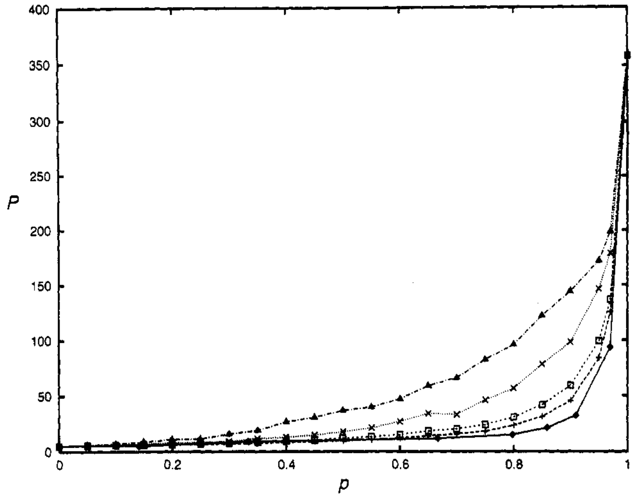

Figure 7. Persistence length *P*, in nm, for molecules originally having all k_b corresponding to $P_\infty = 5$ nm as a function of the fraction, *f*, of k_b corresponding to $P_\infty = 500$ nm: (+) randomly distributed (cooperativity = 1); (□) cooperativity = 10; (×) cooperativity = 10^2; (△) cooperativity = 10^3; (◇) evenly distributed along the chain.

constants have been determined by the same procedure used for the curve containing kinks in Figure 3. At a small equilibrium bending angle the distribution is rather narrow, and the width only increases slowly when increasing the fraction of kinks up to 50%. When the bending angle is becoming larger, however, the width of the distribution increases rapidly, even at a rather small fraction of kinks. Thus the standard deviation of the end-to-end distance and radius of gyration should increase rapidly when the binding of proteins or smaller ligand molecules changes the equilibrium bending angle at some parts of the molecules.

Linear Molecules with Locally Changed Flexibilities. A change in the structure of linear chain molecules can also occur by locally changing the flexibility of the molecules, either by increasing or by decreasing the bending force constant. A change in DNA stiffness can, e.g., occur with the binding of proteins, like RecA, that form an outer helix wound around the DNA double helix[32] or upon binding of different dye molecules.[8,33] In Figure 7 is shown the effective persistence length when increasing the fraction of stiff parts of a chain by starting with a molecule having $P_\infty = 5$ nm and then increasing the percentage of bending force constants corresponding to $P_\infty = 500$ nm. Using a rather small initial persistence length and then a large increase in the local chain stiffness is motivated by the recent study of the complex formation between a peptide nucleic acid (PNA) and poly(dA), which forms a 2:1 triple helix at high enough concentrations of PNA.[34] The increased stiffness of these aggregates is, e.g., shown by a measurable orientation in a shear flow field, which the single-stranded poly(dA) does not show, due to its high flexibility.

The change in persistence length when increasing the fraction of stiff parts is very slow for binding ratios up to about 80% when distributing the stiffer parts randomly along the molecule as is seen in Figure 7. Including cooperativity, however, makes the effective persistence length start to increase at a lower binding ratio, and this effect is amplified when increasing the cooperativity. Decreasing the cooperativity from 1 to 0.001, though, hardly has any detectable effect on the persistence length compared to a random distribution (not shown). Forcing the stiff parts to be evenly distributed along the molecule instead has the opposite effect; i.e., the persistence length will have a smaller value compared to the random case. This is also in line with an earlier path integral calculation by Fredrickson[35] showing that a random copolymer is expanded relative to a homopolymer having the same average flexibility. These results then show that the sharp increase in stiffness of the poly(dA)–PNA complex at binding ratios close to the saturation point[34] comes from a random or possibly anticooperative binding. Figure 7 thus illustrates that it is the *number* of stiff parts of the molecule (for a chain without static bends) that determine the persistence length. When the cooperativity is increased, there will be patches of stiff parts and fewer (albeit longer) parts with high flexibility compared to the random case. This also explains the bottom curve representing evenly distributed parts with low flexibility. Being evenly distributed, the number of flexible parts will have a maximum and the persistence length will be smaller than for all other cases. The opposite situation when starting with a stiff molecule and increasing the number of flexible parts will then show the reverse behavior, the decrease in persistence length being slower when increasing the cooperativity.

Molecules with Kinks and Changed Flexibilities. The two different situations shown in Figures 5 and 7 can be combined by introducing kinks into a molecule while simultaneously changing the bending force constant at the corresponding locations. One way of doing this is presented in Figure 8, where *P* is shown as a function of the fraction of kinks for two different values of the equilibrium bending angle and where the introduction of a kink occurs simultaneously with an increased bending force constant. It is seen that since an increase in θ^0 decreases the effective persistence length, the final value at $p = 1.0$ rapidly becomes smaller when θ^0 is increased from 0° in Figure 7 to 10° and 20° in Figure 8. The small increase of the final value of *P* compared to the starting value at $p = 0$ also means that the difference when including cooperativity will be rather small when θ^0 is increased (since the final values must coincide). The steep increase of the persistence length of the poly(dA)–PNA complex close to saturation[34] discussed above is thus consistent with a stiffening of the nucleic acid chain without any significant bending at the binding sites.

We thus conclude that experiments sensitive to the statistical properties of chain molecules are important

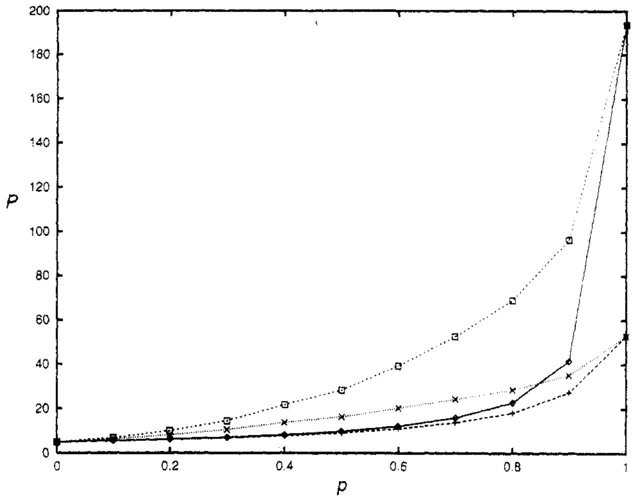

Figure 8. Same as in Figure 7 but with each k_b corresponding to P_∞ = 500 nm also having θ^0 = 10° or θ^0 = 20°; (◇) θ^0 = 10°, randomly distributed (cooperativity = 1); (□) θ^0 = 10°, cooperativity = 10^3; (+) θ^0 = 20°, randomly distributed; (×) θ^0 = 20°, cooperativity = 10^3.

when discriminating between different types of nonuniformities of the molecular configuration. The presence of static bends, or kinks, rapidly decreases the persistence length and the end-to-end distance, the effect being larger for originally more rodlike chains. The introduction of kinks also affects the polydispersity of the molecular structure, expressed, e.g., as the end-to-end distance, the distribution of which rapidly becomes broader with increasing bending angle. Changing the local flexibility at certain locations along the molecule, e.g., through binding of different ligand molecules, will, however, not affect the effective molecular size until rather large binding ratios unless the ligand binding is strongly cooperative. These observations can then be directly related to experimental studies of, e.g., the orientation of different DNA complexes in external fields,[36] which is strongly dependent on the extension and stiffness of the corresponding molecules.

In the present paper we have started by investigating the structural properties of chain molecules with kinks and locally changed flexibilities and will in future work extend this to the dynamics of semiflexible chains under equilibrium and nonequilibrium conditions.

Acknowledgment. This work was supported by the Swedish Natural Science Research Council by a research grant to C.E. and a postgraduate studentship to C.H. We also want to thank one of the referees for pointing out the possibility of using the matrix formalism of Flory to the systems studied in this paper.

Appendix

In this Appendix we outline the derivation of eqs 6 and 7. Although the final results should in principle be equivalent to the expressions one can obtain using the Flory matrix formalism,[30] we believe our derivation is somewhat more transparent and is an extension of the usually used method for homogeneous molecules.[19,26]

Persistence Length. The persistence length is defined as the average sum of the projections of all bonds (including the first bond) on the first bond vector.[26] For a molecule consisting of N subunits, this can be written

$$P_N = \sum_{i=1}^{N-1} \langle (\hat{\mathbf{b}}_1 \cdot \hat{\mathbf{b}}_i) b_i \rangle = \sum_{i=1}^{N-1} \langle b_i \cos \theta_{1i} \rangle \qquad \text{(A1)}$$

where $\cos \theta_{1i}$ is the angle between bond vectors 1 and i and a "hat" denotes a unit vector. Assuming the bond lengths and bending angles to be uncorrelated, we obtain

$$P_N = \langle b \rangle \sum_{i=1}^{N-1} \langle \cos \theta_{1i} \rangle \qquad \text{(A2)}$$

If all bond angles are equivalent, i.e., $\langle \cos \theta_i \rangle = \langle \cos \theta \rangle = \alpha$, eq A2 reduces to eq 3.

Let us now introduce a kink in the molecule at a position p between the bond vectors p and $p + 1$ (see Figure 1). The corresponding angle will then be θ_p and $\alpha_p = \langle \cos \theta_p \rangle$. P_N then becomes

$$P_N(p) = \langle b \rangle (1 + \alpha + \alpha^2 + ... + \alpha^{p-1} + \alpha_p \alpha^{p-1} + \alpha_p \alpha^p + ... + \alpha_p \alpha^{N-2})$$
$$= \frac{\langle b \rangle}{1-\alpha}[1 - \alpha^p + \alpha_p \alpha^{p-1}(1 - \alpha^{N-1-p})] \qquad \text{(A3)}$$

It is not difficult to see that in the general case with n kinks at positions $p_1, p_2, ..., p_n$ ($p_1 < p_2 < ... < p_n$)

$$P_N(p_1,p_2,...,p_n) = \frac{\langle b \rangle}{1-\alpha} \sum_{m=0}^{n} [\alpha^{p_m - m}(1 - \alpha^{p_{m+1} - p_m}) \prod_{q=0}^{m} \alpha_{p_q}] \qquad \text{(A4)}$$

where we have defined $p_0 = 0$, $p_{n+1} = N - 1$, and $\alpha_{p_0} = 1$.

End-to-End Distance. Assuming, as above, the bond lengths and bond angles to be uncorrelated, the mean square end-to-end distance $\langle R^2 \rangle$ can be written[19,30]

$$\langle R^2 \rangle = (N-1)\langle b^2 \rangle + 2\langle b \rangle^2 \sum_{i=1}^{N-2} \sum_{j=i+1}^{N-1} \langle \cos \theta_{ij} \rangle \qquad \text{(A5)}$$

If all angles are equivalent, characterized by $\langle \cos \theta \rangle = \alpha$, then $\langle \cos \theta_{ij} \rangle = \alpha^{|j-i|}$ and the double sum can easily be calculated.[19] Let us now, in the same way as for the persistence length above, introduce n kinks at positions $p_1, p_2, ..., p_n$. The summation in eq A5 can then be subdivided as follows:

$$\sum_{i=1}^{N-2} \sum_{j=i+1}^{N-1} =$$
$$\sum_{i=1}^{p_1} (\sum_{j=i+1}^{p_1} + \sum_{j=p_1+1}^{p_2} + \sum_{j=p_2+1}^{p_3} + ... \sum_{p_n+1}^{p_{n+1}}) +$$
$$\sum_{i=p_1+1}^{p_2} (\sum_{j=i+1}^{p_2} + \sum_{j=p_2+1}^{p_3} + ... \sum_{p_n+1}^{p_{n+1}}) + ... + \sum_{i=p_n+1}^{N-1} \sum_{j=i+1}^{N-1} \qquad \text{(A6)}$$

Using the same definitions for α_0, p_0, and p_n as in eq A4, the first column of double sums is equivalent to an unperturbed molecule. The second column becomes

$$\sum_{i=p_m+1}^{p_{m+1}} \sum_{j=p_{m+1}+1}^{p_{m+2}} \langle \cos \theta_{ij} \rangle = \alpha_{p_{m+1}} \sum_{i=p_m+1}^{p_{m+1}} \sum_{j=p_{m+1}+1}^{p_{m+2}} \alpha^{j-i-1} \qquad \text{(A7)}$$

and generally for $p_s \geq p_{m+1}$

$$\sum_{i=p_m+1}^{p_{m+1}} \sum_{j=p_s+1}^{p_{s+1}} \langle \cos \theta_{ij} \rangle = \prod_{q=m+1}^{s} \alpha_{p_q} \sum_{i=p_m+1}^{p_{m+1}} \sum_{j=p_s+1}^{p_{s+1}} \alpha^{j-i-(s-m)} \qquad \text{(A8)}$$

Evaluating this double sum, we obtain

$$\sum_{i=p_m+1}^{p_{m+1}} \sum_{j=P_s+1}^{p_{s+1}} \alpha^{j-i-(s-m)} = \frac{\alpha^{1-(s-m)}}{(1-\alpha)^2}(1-\alpha^{p_{s+1}-p_s})\alpha^{p_s-p_{m+1}}(1-\alpha^{p_{m+1}-p_m}) \quad \text{(A9)}$$

and combining eqs A5, A6 and A9, we obtain eq 7, where the first sum comes from the first column in eq A6 and the double summation is equal to the number of remaining terms. Equation 7 can also can be written

$$\langle R^2(p_1,p_2,\ldots,p_n)\rangle = (N-1)(\langle b^2\rangle - \langle b\rangle^2) + \langle b\rangle^2 \times \left\{\sum_{m=0}^{n} (p_{m+1}-p_m)C_{p_{m+1}-p_m} + 2\sum_{m=0}^{n-1} \sum_{s=m+1}^{n} \left[\left(\prod_{q=m+1}^{s} \alpha_{p_q}\right)\alpha^{p_s-p_{m+1}-(s-m-1)} \frac{(1-\alpha^{p_{m+1}-p_m})(1-\alpha^{p_{s+1}-p_s})}{(1-\alpha)^2} \right]\right\} \quad \text{(A10)}$$

where C_{p_m} is the characteristic ratio.[30] For a homogeneous chain with $n = 0$ this reduces to the well-known expression[26]

$$\langle R^2\rangle - (N-1)[\langle b^2\rangle + \langle b\rangle^2(C_{N-1}-1)] \quad \text{(A11)}$$

References and Notes

(1) Kratky, O.; Porod, G. *Recl. Trav. Chim. Pay-Bas* **1949**, *68*, 1106.
(2) Thomas, J. O.; Kornberg, P. D. *Proc. Natl. Acad. Sci. U.S.A.* **1975**, *72*, 2626.
(3) Reinert, K.-E. *J. Biomol. Struct. Dynam.* **1991**, *9*, 331.
(4) Rhodes, D.; Klug, A. *Nature* **1981**, *292*, 378.
(5) Hagerman, P. J. *Nature* **1986**, *321*, 449.
(6) Ulanovsky, L.; Bodner, M.; Trifonov, E. N.; Choder, M. *Proc. Natl. Acad. Sci. U.S.A.* **1986**, *83*, 862.
(7) Levene, S. D.; Wu, H.-M.; Crothers, D. M. *Biochemistry* **1986**, *25*, 3988.
(8) Hiort, C.; Nordén, B.; Rodger, A. *J. Am. Chem. Soc.* **1990**, *112*, 1971.
(9) Reinert, K.-E. *Biophys. Chem.* **1981**, *13*, 1.
(10) Trifonov, E. N.; Tan, R. K.-Z.; Harvey, S. C. In *Structure & Expression*, Vol. 3: *DNA Bending and Curvature*; Olson, W. K., Sarma, M. H., Sarma, R. H., Sundaralingam, M., Eds.; Adenine: Guilderland, 1988.
(11) Schellman, J. A. *Biophys. Chem.* **1980**, *11*, 329.
(12) Mansfield, M. L. *Macromolecules* **1986**, *19*, 854.
(13) García Molina, J. J.; García de la Torre, J. *J. Chem. Phys.* **1986**, *84*, 4026.
(14) Prévost, C.; Louise-May, S.; Ravishanker, G.; Lavery, R.; Beveridge, D. L. *Biopolymers* **1993**, *33*, 335.
(15) Hagerman, P. J. *Annu. Rev. Biophys. Biophys. Chem.* **1988**, *17*, 265.
(16) Lavery, R.; Sklenar, H. *J. Biomol. Struct. Dynam.* **1989**, *6*, 655.
(17) Poncin, M.; Piazzola, D.; Lavery, R. *Biopolymers* **1992**, *32*, 1077.
(18) Song, L.; Schurr, J. M. *Biopolymers* **1990**, *30*, 229.
(19) Schellman, J. A. *Biopolymers* **1974**, *13*, 217.
(20) Roitman, D. B.; McAdon, M. *Macromolecules* **1993**, *26*, 4381.
(21) Zhang, R.; Mattice, W. L. *Macromolecules* **1993**, *26*, 4384.
(22) Allison, S. A. *Macromolecules* **1986**, *19*, 118.
(23) Allison, S. A.; Sorlie, S. S.; Pecora, R. *Macromolecules* **1990**, *23*, 1110.
(24) Elvingson, C. *Biophys. Chem.* **1992**, *43*, 9.
(25) Schlick, T. *J. Comput. Chem.* **1989**, *10*, 951.
(26) Yamakawa, H. *Modern Theory of Polymer Solutions*; Harper & Row: New York, 1971.
(27) Porod, G. *Monatsh. Chem.* **1949**, *2*, 251.
(28) Sundaralingam, M.; Sekharudu, Y. C. In *Structure & Expression*, Vol. 3: *DNA Bending and Curvature*; Olson, W. K.; Sarma, M. H., Sarma, R. H., Sundaralingam, M., Eds.; Adenine: Guiderland, 1988.
(29) Reinert, K.-E. *J. Biomol. Struct. Dynam.* **1993**, *10*, 973.
(30) Flory, P. *Statistical Mechanics of Chain Molecules*; Interscience: New York, 1969.
(31) Jung, B. *Makromol. Chem.* **1991**, *192*, 1667.
(32) Nordén, B.; Elvingson, C.; Kubista, M.; Sjöberg, B.; Ryberg, H.; Ryberg, M.; Mortensen, K.; Takahashi, M. *J. Mol. Biol.* **1992**, *226*, 1175.
(33) Satyanarayana, S.; Dabrowiak, J. C.; Chaires, J. B. *Biochemistry* **1992**, *31*, 9319.
(34) Kim, S. G.; Nielsen, P. E.; Egholm, M.; Buchardt, O.; Berg, R. H.; Nordén, B. *J. Am. Chem. Soc.* **1993**, *115*, 6477.
(35) Fredrickson, G. H. *Macromolecules* **1989**, *22*, 2746.
(36) Nordén, B.; Kubista, M.; Kurucsev, T. *Q. Rev. Biophys.* **1992**, *25*, 51.