Biophysical Chemistry 11 (1980) 321–328
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THE FLEXIBILITY OF DNA.
I. THERMAL FLUCTUATIONS ☆

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The theory of the flexibility of DNA makes use of a worm-like coil model which implies an isotropic bending potential. This paper investigates the influence of non-isotropic bending which is cased by the real, lower symmetry of a DNA molecule. Formulas are developed for the persistence and mean square length of a molecule in terms of DNA symmetry elements, i.e., a helical screw operation and perpendicular dyad axes. It is shown that the low symmetry of a DNA helix leads to mean propagation properties which differ from the static equilibrium properties. The worm-like coil model may be justified in terms of the mean, thermally averaged, properties of the DNA but not in terms of its static equilibrium properties. Changes in helix angle and displacement with temperature and solvent are a natural result of the asymmetric potential of DNA.

1. Introduction

This paper will deal with the statistical flexing of DNA from its straight helical form. The method of analysis which is employed can be applied to a number of helical systems but it will be helpful to use double stranded nucleic acid as a specific example. The force field for the bending of DNA is not known experimentally, but there have been recent calculations using empirical energy parameters [1,2]. In order to provide a foundation for discussion of flexibility, this paper will be restricted to results which can be obtained from the symmetric of DNA; i.e., conclusions which can be drawn from the presence of a helical axis and a set of transverse dyad axes. The results are formal rather than practical but they eventually justify the use of an isotropic model (the Kratky–Porod model) for a non-isotropic bending potential and provide a clear explanation for the variability of the helical parameters of DNA with temperature and environment.

2. The link model for DNA

The statistical properties of DNA can be interpreted either by means of the worm-like coil model [3] or a model in which the molecule is considered as a chain of virtual links connecting equivalent points on the helical axis in each base pair [4]. If one is considering statistical properties of the chain, it makes little difference which model is used. Formulas for the chain dimension are very simple in both cases and agree with one another remarkably well even down to quite short chains. (It was intended here to include a comparative graph of the rms dimensions calculated by the two models but the differences are too small for moderate sized DNA chains to be visualizable on a graph.) Which of the models is used depends on the application. The continuum approach has been instrumental in solving a number of hydrodynamic problems by Yamakawa and coworkers [5–7]. On the other hand, the link model offers advantages when one is attempting to relate chain statistical properties with structural features of the DNA. In previous papers [4,8] we have used the link model to compare the case of isotropic bending with local hinge bending. We now present a more general discussion.

Treating a DNA double helix as a series of simple chain links is tantamount to assigning only three degrees of freedom per unit (base pair) in the chain: the length

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☆ Research supported in part by grants from the National Institutes of Health (GM 20195, GM 15423, GM 00715) and the National Science Foundation (PCM 76-80741).

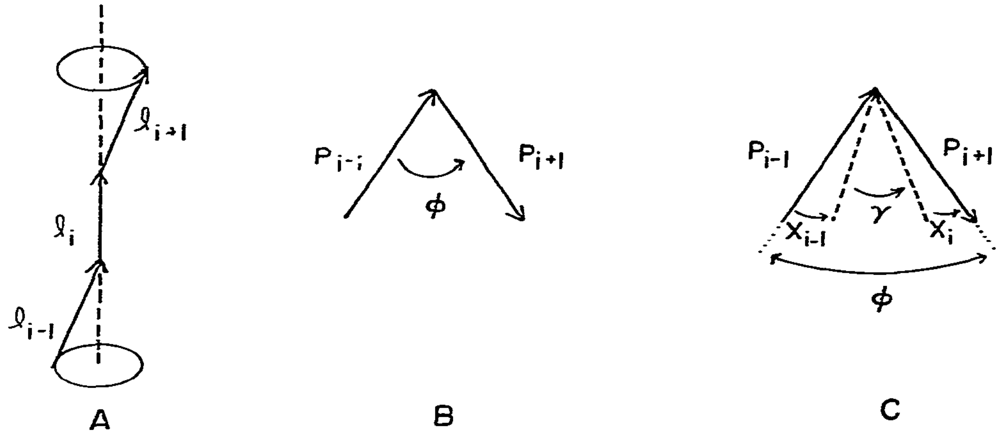

Fig. 1. A. Three consecutive links in a chain. In the static equilibrium conformation the links are colinear. B. Projection of fig. 1A onto the equatorial plane of link i to define the torsional angle ϕ_i. P_{i+1} and P_{i-1} are the projections of l_{i+1} and l_{i-1}. C. The relationship of the instantaneous torsional angle ϕ to the helix angle γ_0 and the stochastic bending angles χ_i and χ_{i-1}.

of the link, l_0, the inclination of each link with its predecessor, θ, and the "torsional" angle, ϕ, associated with three consecutive links (fig. 1a). For very small angles of bending the link length will be considered to be a constant leaving two degrees of freedom per link.

In the case of a real DNA chain, even if the possible distortions of bond lengths and angles are ignored, there are at least 12 torsional angles per base pair which must be considered as degrees of freedom. A detailed consideration of all operative degrees of freedom is required for an analysis of the molecular mechanism of flexing and bending and Olson has presented an analysis of a complete torsional model in a recent publication [1]. On the other hand, descriptions which include all degrees of freedom go far beyond the number of parameters available from real experiments. The simple model with θ and ϕ as the only degrees of freedom contains the possibility of local flexing and twisting modes and appears to be suitable for a phenomenological description of real DNA chains. In a work that is closely allied with the approach of the present paper, Zhurkin et al. [2] have calculated energy contours for the bending and azimuthal angles. This is essentially a projection of the many degrees of freedom of the real DNA molecule onto the two (or three) degrees of freedom of the link model.

3. The bending potential

The basic assumption is that the orientation of one link in the chain relative to the preceding link is governed by a local potential function, $V = V(\theta, \chi)$ where θ is the angle of bend and χ is the angle of the projection of link $(i+1)$ on the equatorial plane of link i relative to the dyad axis of link i (fig. 1). Since solvent interactions may vary as a function of bending, this potential surface is a free energy surface or potential of average force. The chain of links is defined such that the links are co-linear in the conformation of minimum potential. This conformation will be referred to later as the *static equilibrium conformation*, i.e., the conformation in which the bending forces vanish.

The only property of the potential which we wish to take into consideration is its symmetry. The symmetry elements of DNA are a helical screw operation with displacement l_0 and angle γ_0 and two sets of dyad axes perpendicular to the helix axis. γ_0 is the static equilibrium value for the helix angle, i.e., the value at which there is no torque. Since it is now becoming accepted that the DNA structure observed in fibers may not represent precisely the structure in solution, γ_0 will not in general be equal to the value obtained from fiber studies. (We shall see below that it is also not necessarily equal to the solutions value.)

The assumption of dyad axes and helical operations

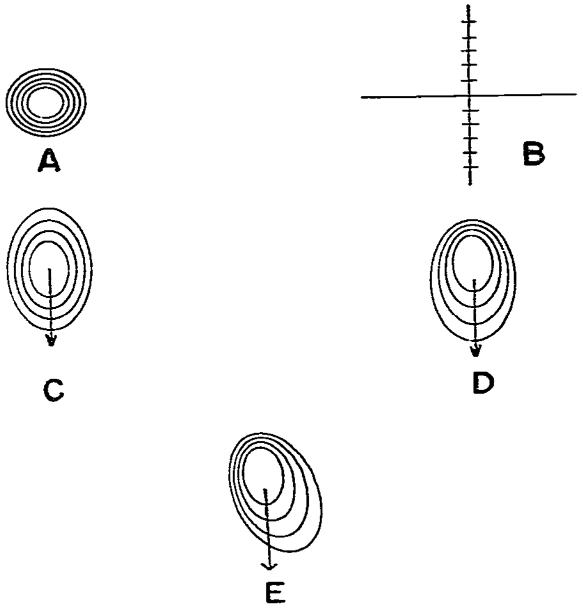

Fig. 2. Potential surfaces (free energy) for bending. The contours are constant potential energy; distance from the origin is angle of bend. A. Isotropic bending. B. Symmetric hinge bending, the contours are points on the dyad axis. C. Centrosymmetric bending. D. Biased bending with symmetry about the dyad axis, $\langle \sin\delta \rangle = 0$. E. Asymmetric bending $\langle \cos\delta \rangle \neq 0$, $\langle \sin\delta \rangle \neq 0$, see text.

is an approximation since different bases are exchanged by these operations. These are pseudo-symmetries which at best apply only to the polyribose phosphate chain. If the bending potential does depend on local base composition, then the potential under discussion in this paper is an effective average that conforms to the bending statistics. The directions of the bond vectors and dyad axes provide a local set of coordinates for each link (fig. 1b). The potential function of one link is to be found from that of the previous link by the screw operators $S(l_0, \gamma_0)$.

A number of possible representations of the bending potential are given in fig. 2. These are presented as energy contours in polar coordinates. The polar angle χ is the bending azimuth relative to the dyad axis and the polar distance represents the angle of bend. The cases represented are isotropic bending, hinge bending, centrosymmetric bending, biased bending with the dyad axis as axymmetry axis, and asymmetric bending. These cases will be discussed in the next section. While this manuscript was being prepared, a paper appeared [2] in which the bending potential of a pair of stacked base pairs was calculated using empirical energy functions. These calculations show that flexing by bending into the large and small grooves is strongly favored. This corresponds to the hinge model discussed in previous papers [4,8].

4. Chain statistics

The parameters for a discussion of chain statistics are the link lengths, l_0, the bending angle, θ, between successive links, and the torsional angle associated with three consecutive links (fig. 1). The instantaneous torsional angle is conveniently divided into a helical part, γ_0, and a stochastic part, δ, which depends on thermal fluctuations, where $\delta = \chi_i + \chi_{i-1}$. χ_i and χ_{i-1} are depicted in fig. 1c. They measure the projected angle between the bond vectors and the local dyad axis.

The dimensional properties of a linked chain are describable in terms of products and series of the propagation matrix, A_i, for the chain, where

$$A_i = \begin{pmatrix} \cos\phi_i \cos\theta_i & \sin\phi_i & -\cos\phi_i \sin\theta_i \\ -\sin\phi_i \cos\theta_i & \cos\phi_i & \sin\phi_i \sin\theta_i \\ \sin\theta_i & 0 & \cos\theta_i \end{pmatrix}, \qquad (1)$$

is the matrix which transforms a vector in the frame of $l_i + 1$ into the coordinates of the link l_i. The coordinate system is defined in fig. 1. Note this coordinate system differs from that given in Volkenstein's book [9] in that the cis convention is used for torsional angles.

If it is assumed that the units are independent of one another (this means that the bend connecting link l_i and l_{i+1} is independent of the nature of the bend connecting l_{i-1} and l_i) then the propagation matrices may be averaged separately to give

$$\langle A \rangle = \begin{pmatrix} \langle \cos\phi \cos\theta \rangle & \langle \sin\phi \rangle & -\langle \cos\phi \sin\theta \rangle \\ -\langle \sin\phi \cos\theta \rangle & \langle \cos\phi \rangle & \langle \sin\phi \sin\theta \rangle \\ \langle \sin\theta \rangle & 0 & \langle \cos\theta \rangle \end{pmatrix}. \qquad (2)$$

We will further assume that the angles ϕ and θ are stochastically independent of one another, i.e., that the probability distribution in θ and ϕ can be represented by a product function $f(\theta)g(\phi)$. The large number of hidden degrees of freedom in the bending give some plausibility to this commonly made assumption. The average of products in eq. (2) can then be represented as

$$\langle A\rangle = \begin{pmatrix} \bar{\alpha}\bar{s} & \bar{s} & -\bar{S}\bar{c} \\ -\overline{\alpha s} & \bar{c} & \bar{S}\bar{s} \\ \bar{S} & 0 & \bar{\alpha} \end{pmatrix} \tag{3}$$

where $\bar{\alpha} = \langle\cos\theta\rangle$, $\bar{S} = \langle\sin\theta\rangle$, $\bar{c} = \langle\cos\phi\rangle$, and $\bar{s} = \langle\sin\phi\rangle$. The problem is solvable without this assumption but the results are more complicated than those presented below.

The chain properties of chief interest will be the persistence length P_∞ and mean square end to end distance h^2. For a long chain

$$\langle h^2\rangle = \sum l_i \cdot \sum l_j \equiv C_\infty n l^2 \,. \tag{4}$$

n is the number of links in the chain and l is the length of a link, where C_∞ is the characteristic ratio. Evaluation of the persistence length and the characteristic ratio are equivalent to one another for long chains. We have

$$C_\infty = (1/nl^2)\sum_i \Big(l_i \cdot \sum l_j\Big) \,. \tag{5}$$

Defining a persistence P_i as the persistence based on the ith link vector,

$$C_\infty = (1/nl^2)\sum_i (P_i^+ + P_i^- - l^2) \,, \tag{6}$$

where P_i^+ is persistence propagating forward from i in the chain and P_i^- propagation backward. The $-l^2$ factor comes from the fact that l_i^2 is used twice in the forward and backward presistences. Note that P_i^+ and P_i^- are finite persistences (not necessarily P_∞, the standard persistence) because unit i may be near the end of a chain. If we assume that the chain propagates identically forward and backward and that the chain is so long that the fraction of links near the end where $P_i \neq P_\infty$ are negligible, then $P_i^+ = P_i^- = P_\infty$ and

$$C_\infty = 2P_\infty/l - 1 \,. \tag{7}$$

For a long chain the characteristic ratio is given by [9]

$$C_\infty = 2((I - A)^{-1})_{33} - 1 \,, \tag{8}$$

where I is the unit matrix, and the persistence length is

$$P_\infty/l = ((I - A)^{-1})_{33} \,. \tag{9}$$

It is not a difficult matter to invert the matrix $(I - A)$ and evaluate the 33 element.

The behavior of the chain depends strongly on the azimuthal properties of the potential. Expanding $\bar{c}$ and $\bar{s}$ to isolate the averages over the fluctuating angle δ we have

$$\begin{aligned} \bar{c} &= \langle\cos(\gamma_0 + \delta)\rangle = \cos\gamma_0\langle\cos\delta\rangle - \sin\gamma_0\langle\sin\delta\rangle \,, \\ \bar{s} &= \langle\sin(\gamma_0 + \delta)\rangle = \sin\gamma_0\langle\cos\delta\rangle + \cos\gamma_0\langle\sin\delta\rangle \,. \end{aligned} \tag{10}$$

If the potential is centrosymmetric, then $\langle\cos\delta\rangle = \langle\sin\delta\rangle = 0$, since δ is the sum of two angles with centrosymmetric distributions. Consequently $\bar{s} = \bar{c} = 0$. Substituting these values in eqs. (9) and (8)

$$P_\infty/l = 1/(1 - \bar{\alpha}) \,, \qquad C_\infty = (1 + \bar{\alpha})/(1 - \bar{\alpha}) \,. \tag{11}$$

These are the equations that have been obtained by a simpler analysis for the isotropic potential (fig. 2a) and the hinge model (fig. 2b). It can now be seen that it applies to any centrosymmetric potential, e.g. fig. 2c.

We now wish to introduce asymmetric elements in the analysis. For this we need the general solutions to eqs. (8) and (9), which are found to be

$$\begin{aligned} C_\infty &= \frac{(1+\bar{\alpha})(1-\bar{c}) + (1-\bar{\alpha}^2-\bar{S}^2)\bar{c} + \bar{s}^2(\bar{\alpha}+\bar{S}^2+\bar{\alpha}^2)/(1-\bar{c})}{(1-\bar{\alpha})(1+\bar{c}) - (1-\bar{\alpha}^2-\bar{S}^2)\bar{c} + \bar{s}^2(\bar{\alpha}-\bar{S}^2-\bar{\alpha}^2)/(1-\bar{c})} \,, \\ P_\infty &= \frac{(1-\bar{\alpha}\bar{c}) + \bar{s}^2\bar{\alpha}/(1-\bar{c})}{(1-\bar{\alpha})(1+\bar{c}) - (1-\bar{\alpha}^2-\bar{S}^2)\bar{c} + \bar{s}^2(\bar{\alpha}-\bar{S}^2-\bar{\alpha}^2)/(1-\bar{c})} \end{aligned} \tag{12}$$

Eqs. (12) are related to chain statistical formulas which exist in the literature. Differences arise because the "bond angle" of DNA chain is statistical in nature and deviates from 180° only by virtue of thermal agitation. Bond angles in ordinary chain theory are fixed by assumption. For fixed angles the term $(1 - \bar{\alpha}^2 - \bar{S}^2)$ which appears in eqs. (12) vanishes providing the equations

$$\begin{aligned} C_\infty &= \frac{(1+\bar{\alpha})((1-\bar{c})^2 + \bar{s}^2)}{(1-\bar{\alpha})(1-\bar{c}^2-\bar{s}^2)} \,, \\ P_\infty &= \frac{(1-\bar{c})(1-\bar{\alpha}\bar{c}) - \bar{\alpha}\bar{s}^2}{(1-\bar{\alpha})(1-\bar{c}^2-\bar{s}^2)} \,. \end{aligned} \tag{13}$$

The first of these is a formula given by Sack [10] for a problem related to isolactic polymers. For another view of eq. (12) we assume $\bar{s} = 0$ which is a standard approximation for a broad class of polymer problems [9]. The result is

$$C_\infty = \frac{(1+\bar{\alpha})(1-\bar{c}) - (1-\bar{\alpha}^2-\bar{S}^2)\bar{c}}{(1-\bar{\alpha})(1+\bar{c}) - (1-\bar{\alpha}^2-\bar{S}^2)\bar{c}}. \qquad (14)$$

This is Taylor's equation with extra terms containing $(1-\bar{\alpha}^2-\bar{s}^2)$. This term is ignorable for most chains where the fluctuating part of the angle θ is small compared to θ itself. In DNA the term $(1-\bar{\alpha}^2-\bar{S}^2)$ is commensurate with $(1-\alpha)$ and must be retained in all calculations of the denominator. (See the appendix.) At any rate, $\bar{s} \neq 0$ for DNA because of the helical symmetry. Eqs. (13) and (14) have been presented only to demonstrate how eq. (12) reduces to known special cases. To clarify the interpretation it will be useful to consider first the two special cases $\langle \sin\delta \rangle = 0$ and $\langle \cos\delta \rangle = 0$.

First case $\langle \sin\delta \rangle = 0$. If the potential is not centrosymmetric but $\langle \sin\delta \rangle = 0$ it means that there is a statistical bias towards bending one way or the other along the dyad axis. At first sight this appears to be an excellent model for DNA since the C_2 symmetry of the dyad is equivalent to reflection symmetry of this kind. In addition bending along the dyad axes should be unsymmetrical since the degree of freedom represents bending into the small and large groove and there is nothing in the structure of DNA that suggests that these are symmetrical operations. There is, nevertheless, a missing feature in this model which will be discussed below.

If $\langle \sin\delta \rangle = 0$, then $\bar{c} = \cos\gamma_0 \langle \cos\delta \rangle$ and $\bar{s} = \sin\gamma_0 \times \langle \cos\delta \rangle$ from eqs. (10). Substituting in eq. (12)

$$\begin{aligned} C_\infty &= [(1+\bar{\alpha})(1-\cos\gamma_0\langle\cos\delta\rangle) \\ &\quad - \langle\cos\delta\rangle(\cos\gamma_0 - \langle\cos\delta\rangle)(\bar{\alpha}+\bar{S}^2+\bar{\alpha}^2)] \\ &\quad \times [(1-\bar{\alpha})(1-\cos\gamma_0\langle\cos\delta\rangle) \\ &\quad - \langle\cos\delta\rangle(\cos\gamma_0 - \langle\cos\delta\rangle)(\alpha-\bar{S}^2-\bar{\alpha}^2)]^{-1}, \\ P_\infty &= [1-\langle\cos\delta\rangle^2\bar{\alpha} + \cos\gamma_0\langle\cos\delta\rangle(1+\bar{\alpha})] \\ &\quad \times [(1-\bar{\alpha})(1-\cos\gamma_0\langle\cos\delta\rangle) \\ &\quad - \langle\cos\delta\rangle(\cos\gamma_0 - \langle\cos\delta\rangle)(\alpha-\bar{S}^2-\bar{\alpha}^2)]^{-1}. \end{aligned} \qquad (15)$$

These are the formulas for biased helical bending. Random deviations in helical direction are expressed in the $(1-\bar{\alpha})$ and $(1-\bar{S}^2-\bar{\alpha}^2)$ factors, the helical structures in $\cos\gamma_0$, and the biased bending in $\langle\cos\delta\rangle$. Though eqs. (15) are perfectly straightforward, they would be difficult to employ in practice. The appendix shows that if a quadratic bending potential is assumed, that $\bar{S}$ and $\bar{\alpha}$ are expressible in terms of a single parameter, the bending force constant. On the other hand, nothing is known about $\langle\cos\delta\rangle$. Since experimental consistency has barely been achieved in recent years in the determination of a single chain parameter, the persistence length of the Kratky Porod model, it is unlikely that the field is ready for a complicated, multiparameter formulation. Nonetheless the results for the biased bending model will show the way for the simplification of the problem.

The helix parameters l_0, γ_0 that have appeared in the formulation of this problem are the static equilibrium helix parameters, i.e., the helix parameters which obtain if each link is in the conformation that minimizes the bending and twisting potential (local free energy). The meaning of the factor $\langle\cos\delta\rangle \neq 0$ is that the mean local conformation of a thermally activated helix is not the same as the static equilibrium conformation. The static equilibrium conformation, however, loses much of its significance if it does not coincide with the mean conformation. In the mean conformation each link is fixed in the direction of its mean orientation relative to neighboring links. Most experimental techniques, including X-ray diffraction, respond to the mean positions of atoms and in fact it is difficult to imagine an experimental procedure to determine the static equilibrium conformation of a system for the case of a skewed potential, which causes the mean conformation to deviate from the static equilibrium conformation. If we define the helix in terms of the mean local conformation then $\langle\cos\delta\rangle = 0$ by definition and eqs. (15) revert to the simple wormlike model with $C_\infty = (1+\alpha)/(1-\alpha)$ and $P_\infty/l = 1/(1-\alpha)$. This topic will be taken up again after the discussion of the next case.

Second case $\langle \sin\delta \rangle \neq 0$. The first question to consider is how this condition could arise. The assumption of the dyad axis would appear to eliminate this case since bending with orientation δ is converted to bending with orientation $-\delta$ by application of the dyad operator. The clue is to be found in the previous section. The assumption of the helical screw angle γ_0 is based on static equilibrium coordinates. A thermally agitated DNA molecule will have mean coordinates which differ

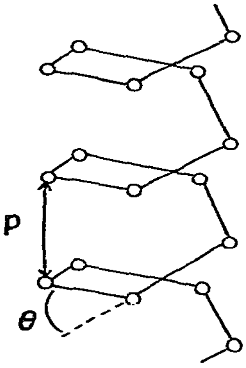

Fig. 3. The mean helical array formed by the static equilibrium bond vectors l_0 when $\langle\cos\delta\rangle \neq 0$. This figure is grossly exaggerated to present the helical structure. For DNA the mean orientations of the l_0 are only 5–6 degrees from the axis of the figure.

from the equilibrium coordinates since nothing in the structure of DNA suggests that the potential associated with structural twisting should be symmetric in the twist angle. This is a degree of freedom which is definitely present in a real DNA molecule [11–13], but which is hidden in the link model. As a result, the torsional angle for bending is expressible as $\gamma_0 + \delta' + \Delta$ where Δ is the deviation of the helical angle from the equilibrium angle and δ' is the bending azimuth relative to $\gamma_0 + \Delta$. Since Δ is not a symmetric variable, the result is equivalent to having a non-symmetric δ so that $\langle\sin\delta\rangle \neq 0$. The way out of this complication is the same as the previous case: Use the mean helical parameters $\bar{\gamma} = \gamma_0 + \bar{\Delta}$ to define the helix. $\langle\sin\delta\rangle$ then vanishes by definition. Together with the condition $\langle\cos\delta\rangle = 0$ which was achieved by using the mean link conformation as a basis, this permits the use of elementary wormlike chain formulas.

The unsymmetrical twisting mode clearly changes the helical parameter γ. It is of some interest to investigate the effect of biased bending. With $\langle\cos\delta\rangle \neq 0$, the sequence of links in their mean orientations described a helix. This is illustrated in grossly exaggerated form in fig. 3. In fact, the helix of links for DNA will be very tight and look almost like a straight line. It should be emphasized that this helical array of links does not represent superhelix formation. In a superhelix the units of the fine grained helix are wound around a helix of greater pitch which serves as a local axis. The units are not all equivalent to one another being compressed or distended depending on whether they are on the inside or outside of the super helix. In the present case all of the units are equivalent and the result of the biased bending of fig. 3 is to change the helical parameters from their static equilibrium values to new mean values. The new helical parameters may be calculated from formulas published by Shimanouchi and Mizushima [14].

Table 1
Mean helical parameters for a systematically bent helix, γ_0 = 36°

θ, deg.	γ, deg.	d, Å
0	36.0	3.38
5	36.3	3.35
10	37.3	3.25
15	38.9	3.11

$$\cos\gamma_m = \tfrac{1}{2}\,[\cos\theta_m - \cos\phi_m - \cos\theta_m \cos\theta_m \cos\phi_m - 1],$$

$$l_m^2 = l_0^2(1+\cos\theta_m)(1+\cos\gamma_m)/2(1-\cos\beta)\,,$$

where γ_m and l_m are the helical screw angle and displacement of the mean conformation and θ_m and ϕ_m are the bending angle and torsional angle of the links in their mean conformation.

Table 1 shows the helical parameters which result from a DNA-like helix with original helical angle 36° as a function of the mean bending angle θ_m. $\langle\cos\delta\rangle$ has been set equal to unity to facilitate the calculation. This corresponds to bending which always takes place in one direction, for example into the large groove. The result is a new helical angle γ_m and translation, l_m. The effect of biased bending on the helical parameters is exaggerated because of the strong assumption $\langle\cos\delta\rangle = 1$, but the effect is real. If the potential is not centrosymmetric for bending and if bond vectors are based on the static equilibrium conformation, then the bond vectors for the mean helix will spiral around the static equilibrium helical axis. To avoid this complicated picture one need only define the helix in terms of the mean confrontation. One then has colinear bond vectors of length l_m and a helix angle γ.

What we have demonstrated is that the biased bending which results from a non-centrosymmetric potential automatically leads to changes in helical parameters. Since the magnitude of the effect depends on the amplitude of the bending, it is a function of the temperature and other solution properties. This helical distortion is superposed on the distortions which arise from the variation of the twist angle as discussed earlier.

5. Discussion

The purpose of this paper has been to explore the effect of the real structure of DNA on its statistical flexibility since previous models such as the wormlike coil or hingemodel assume a symmetry that DNA does not possess. In order to avoid special structural assumptions, the discussion has been based entirely on symmetry properties: the helical and dyad symmetry operation of the DNA molecule and the symmetry properties of the bending potential.

It is found that a local centrosymmetric bending potential, regardless of its form, is a sufficient condition for the validity of the Kratky–Porod equation or the related isotropic link model.

There is, however, no structural basis for a centrosymmetric potential since the symmetry of DNA only predicts a reflection symmetry in the local dyad axis. To treat the general case, formulas were derived (eqs. (12) et seq.) for the statistical properties of a chain where the bending potential from link to link is generated by a helical screw axis. In these formulas two parameters appear $\langle \cos \delta \rangle$ and $\langle \sin \delta \rangle$ where δ is the difference between the torsional angle for bending and the equilibrium helix angle. Both of these quantities vanish if the mean conformation of the molecule corresponds with the static equilibrium conformation, which is true for a centrosymmetric potential. The former is related to biased bending of the helix and the latter to biased torsion about the helix axis. The effects of thermal agitation can be considered as a superposition of a mean deviation from the static equilibrium conformation and a stochastic variation about this mean.

There are two ways in which the problem can be visualized. In the first the helix is defined in terms of its static equilibrium coordinates and the link model in terms of the l_0 which are colinear in the static equilibrium conformation. Then for the thermally activated helix het chain statistics are given by eq. (15) and the mean position of the bond vector l_0 describe a helix as shown in fig. 3. The second approach is to define the helix in terms of the thermally activated mean conformation. The chain statistics are then those of the isotropic wormlike coil, eqs. (11), but now the parameters γ_m and l_m are variable and depend on temperature, ionic environment, etc.

There is no question but that the second approach is not only the simplest but the more physically realistic since most experiments respond to the average conformation and the static equilibiurm conformation is really unknown. It is a corollary of the results that helices with asymmetric bending and twisting potentials, like DNA, have mean helical properties which are functions of environmental factors like temperature and counterions. This effect is amply established in recent investigations [11,12,15,16].

Our final result is a vindication of the wormlike coil model regardless of the asymmetry of the binding potential. The price that is paid for this simplification is that we are dealing with a statistically defined, thermally activated helix and not a helix in mechanical equilibrium.

Acknowledgement

The author is grateful for the generous hospitality of the Laboratory for Structural Studies, MRC, Cambridge, England and the Department of Chemical Physics, Weizmann Institute, Rehovot, Israel during the course of this investigation.

Appendix.

Persistence averages with a quadratic bending potential.

If the local free energy of bending (potential of average restoring force) is quadratic in the angle of bend [17]

$$g(\theta) = (g''/2)\theta^2 , \qquad \text{(A1)}$$

then the Boltzmann weighting function is $e^{-b\theta^2}$ with $b = g''/2\theta^2$. Integrals which are required to evaluate $\bar{\alpha}$ and $\bar{S}$ are [18]

$$\int_0^\infty \sin\theta \; e^{-b\theta^2} d\theta = \frac{1}{\sqrt{b}} D\left(\frac{1}{2\sqrt{b}}\right) , \qquad \text{(A2)}$$

$$\int_0^\infty \cos\theta \sin\theta \; e^{-b\theta^2} d\theta = \frac{1}{2\sqrt{b}} D\left(\frac{1}{\sqrt{b}}\right) , \qquad \text{(A3)}$$

and

$$\int_0^\infty \sin^2\theta\, \mathrm{e}^{-b\theta^2}\,\mathrm{d}\theta = \frac{1}{4}\sqrt{\frac{\pi}{b}}\,(1-\mathrm{e}^{-1/b})\,, \tag{A4}$$

where $D(x)$ is Dawson's integral, $D(x) = \mathrm{e}^{-x^2}\int_0^x \mathrm{e}^{t^2}\,\mathrm{d}t$ which is tabulated [18]. The use of infinite limits in the integrals implies the assumption that the chains are sufficiently stiff that large angles have negligible weighting. With these formulas

$$\bar{\alpha} \equiv \langle\cos\theta\rangle = \frac{1}{2}\,\frac{D(1/\sqrt{b})}{D(1/2\sqrt{b})}\,, \tag{A5}$$

$$\bar{S} \equiv \langle\sin\theta\rangle = \frac{\sqrt{\pi}}{4}\,\frac{(1-\mathrm{e}^{-1/b})}{D(1/2\sqrt{b})}\,. \tag{A6}$$

The quantity $\bar{\alpha}$ can be determined experimentally from the relation $1-\bar{\alpha} = l_0/P_\infty$ and this permits the determination of the force constant via (A5). It was shown earlier [4] that the force constant can also be determined with good accuracy for stiff chains with the relation $P_\infty/l_0 = g''RT$. For a chain with $P_\infty = 600$, $\bar{\alpha} = 0.99436$, $1-\bar{\alpha} = 0.00564$, $\bar{S} = 0.093807$ and $1-\bar{S}^2 - \bar{\alpha}^2 = 0.0024$. Thus for chains which bent only because of thermal agitation the term $(1-\bar{S}^2-\bar{\alpha}^2)$ in the denominator of eq. (12) is commensurate with $1-\bar{\alpha}$ and cannot be ignored.

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