

# An Elastic Model of the Large-Scale Structure of Duplex DNA

CRAIG J. BENHAM,\* *Department of Mathematics, Lawrence University, Appleton, Wisconsin 54912*

## Synopsis

A general model for the large-scale, time-independent structure of duplex DNA is developed based on elastic considerations. The general conditions of elastic equilibrium are given. These equations are solved for the equilibrium shape of stressed duplex DNA, based on the assumption that the double helix behaves mechanically as a symmetric, linearly elastic rod. It is shown that, in general, two orders of superhelicity will arise at equilibrium. Several possible applications of this approach to the supercoiling of closed circular DNA are described.

## INTRODUCTION

A previous paper by the author<sup>1</sup> introduced an elastic model of large-scale duplex DNA structure. The purpose of the present contribution is to develop this approach in detail, deriving explicit expressions for the elastic equilibrium shapes of stressed DNA and suggesting applications to questions of supercoiling.

A linear section of unstressed double-helical DNA remains straight (neglecting kinetic effects) with a twist angle of about  $34^\circ$  per base pair.<sup>2</sup> The present theory posits that deviations from this conformation give rise to elastic restoring forces directed towards a return to the unstressed shape. If the segment is free in solution, then it may bend and twist so as to relieve these stresses. That is, the (time-independent) elastic equilibrium shape of a linear segment of unconstrained duplex DNA is straight.

If the strands of the duplex close on themselves to form a circular molecule, however, the DNA is constrained by the constancy of its linking number  $Lk$ .<sup>3,4</sup> (The linking number measures the extent to which one closed strand links through the circle formed by the other strand. In the absence of nicks,  $Lk$  for a given molecule is a fixed integer.) In this case the molecule cannot relieve the imposed stresses by unconstrained twisting and bending. More precisely,  $Lk$  may be decomposed into terms  $Wr$ , the writhing number, and  $Tw$ , the total twist<sup>3</sup>:

$$Lk = Tw + Wr \quad (1)$$

$Wr$  measures the shape of the central axis of the molecule, hence varies as the molecule bends;  $Tw$  measures the number of times either strand twists

\* Present address: Department of Mathematics, University of Kentucky, Lexington, Kentucky 40506.

around the central axis. Both  $T_w$  and  $W_r$  may vary continuously as the shape of the molecule changes, even though the molecule is closed so that  $Lk$  is fixed. From Eq. (1) it follows that the constraint imposed by the constancy of  $Lk$  for a covalently closed, circular molecule consists of a coupling between bending and twisting.

Within the limitations of Eq. (1), however, closed circular molecules may assume whatever structure is energetically most favorable in their local environment. This could involve partitioning energy among bending and twisting of duplex regions, denaturation,<sup>5,6</sup> breathing modes, or interconversion between forms of the DNA. As the  $Lk$  is altered (by a nicking-closing event, for instance), the relative contributions of these effects may change.<sup>7,8</sup>

The purpose of the present paper is to determine the elastic equilibrium shapes possible for double-helical portions of such a constrained molecule. If there is no denaturation, then the whole molecule may be regarded as an elastic ring deforming to equilibrium subject to constraints. In the presence of locally denatured sections, the present theory applies to the segments of double helix between adjacent regions of denaturation. Thus the elastic deformations both of linear segments subject to forces and torques on their ends and of closed-ring structures are relevant to the problems of supercoiling.

The primary assumption of the present theory is that duplex DNA has the mechanical properties of a symmetric, linearly elastic rod. The condition of symmetry states that there is no preferred direction of bending. That is, the double helix is equally stiff to bending in any direction. In this case DNA has a unique bending stiffness (as has been tacitly assumed by all workers in this field to date).<sup>9-11</sup>

This assumption is probably not precisely correct at the scale of the double helix. But in situations where any bending is spread over several turns of the helix (such as occurs in supercoiling), the assumption of symmetry is probably reasonable. The theory presented in this paper is limited to such situations for other reasons that will be described below.

The present theory generalizes to nonsymmetric structures without sacrificing numerical computability, as will be shown. In that case, the single bending stiffness is replaced by two. We confine our attention primarily to symmetric elastic properties because this is the simplest case. Furthermore, no measurement has been made of a second bending stiffness for DNA to date.

The assumption of linear elasticity states that the relationships between deformations (i.e., curvatures) and loads (i.e., stresses) are linear, with the constants of proportionality being the appropriate stiffnesses. Again, generalization to nonlinearly elastic models is feasible. However, the application of such a theory would require the measurement of second-order effects. These would only become appreciable at large curvatures, a situation excluded in the present model.

The tacit assumption is made that the radius of curvature of any bend in the structure is large compared to the radius of the double helix. This is necessary so that deformations and shear of the cross section relative to the helix axis do not have to be considered.

It is important to note that *neither* this assumption *nor* the assumption of linearity precludes large changes of geometry from the straight, unstressed shape. Indeed, the elastic equilibrium shapes arising from the present model can be highly coiled, as shown in Fig. 2. That a highly convoluted shape can still have large radius of curvature (hence small curvature) everywhere is simply an effect of scale. For instance, to bend a short segment of DNA to the shape shown in Fig. 2A would require high curvatures. In such a case, deformations of the cross section and possible nonlinearities in the governing elastic laws could be important. Yet a long segment may assume such a shape with only small curvatures everywhere. More precisely, the radius of curvature (which is the reciprocal of the curvature) is not invariant under changes of scale, but depends linearly upon the scale factor involved. We assume that the scale of any bends involved is large relative to the radius of the double helix.

This assumption of large scale can also be relaxed. The full generalization of the present theory to nonlinearly elastic structures at large curvatures, accounting for both shear and deformation of the cross section, will be developed in a subsequent contribution.

In the next section the conditions of elastic equilibrium are described. When applied to a linearly elastic, symmetric structure, these conditions yield three differential equations for the equilibrium shape expressed in terms of Euler angles. These equations are solved analytically using elliptic integrals of the first and third kinds. This gives an explicit description for the possible equilibrium shapes in terms of Euler angles as functions of distance along the rod.

It is shown that, in general, two orders of supercoiling will arise at elastic equilibrium. This theoretical prediction is supported by the low-angle x-ray scattering results of Brady et al.,<sup>12</sup> who found evidence for two orders of superhelicity in supercoiled PM2 viral DNA in solution. If the larger order has pitch angle zero, the equilibrium shape could approximate a toroidal helix. Evidence supporting this structure for supercoiled polyoma viral DNA at very low ionic strength has also been found.<sup>13</sup> Further considerations concerning the general properties of the equilibrium shapes are given in Ref. 1.

A method for the numerical solution of the equations of equilibrium on a computer is described below. This method applies both to nonsymmetric and symmetric linearly elastic rods. Computer-generated solutions are shown in Fig. 2 illustrating the two orders of superhelicity arising at equilibrium. A discussion of the possible role of elasticity in supercoiling follows.

## DERIVATION OF THE EQUILIBRIUM EQUATIONS

A double-helical DNA molecule has a central axis, along which distance is measured from some starting point (such as one end of a linear segment). At each distance  $s$  there is a cross section perpendicular to the central axis, which has two principal axes  $x(s)$ ,  $y(s)$ . The  $z(s)$  axis is defined by the tangent at  $s$  which points in the direction of increasing distance. In this manner a system of local, body axes is determined at each point along the molecule.

Two cross sections separated by an infinitesimal distance  $\Delta s$  have their body axes rotated by a vector  $\Delta\Phi$ . The vector curvature of the molecule is defined by

$$\kappa(s) = \lim_{\Delta s \rightarrow 0} \frac{\Delta\Phi}{\Delta s}$$

Expressed in component form in the local, body system of axes, the curvature is  $\kappa(s) = (\kappa_x(s), \kappa_y(s), \tau(s))$ . Here  $\kappa_x(s)$ ,  $\kappa_y(s)$  are the curvatures in the principal direction at distance  $s$ , whereas  $\tau(s)$  is the rate of rotation about the tangent.

The shape of the molecule may be described in an alternative manner by relating the local, body system of axes to a fixed set of space axes  $X$ ,  $Y$ ,  $Z$  using Euler angles  $\theta$ ,  $\phi$ ,  $\psi$  (Fig. 1.) Rotation through these angles brings the space axes into alignment with the body axes. When deformed, the orientation of the body axes may change with distance. Then the Euler angles become functions of distance  $\theta(s)$ ,  $\phi(s)$ ,  $\psi(s)$ .

One may express the curvature components in terms of Euler angles as

$$\kappa_x = \dot{\phi} \sin\theta \sin\psi + \dot{\theta} \cos\psi \quad (2a)$$

$$\kappa_y = \dot{\phi} \sin\theta \cos\psi - \dot{\theta} \sin\psi \quad (2b)$$

$$\tau = \dot{\phi} \cos\theta + \dot{\psi} \quad (2c)$$

Here the dot stands for differentiation with respect to the distance  $s$  in the

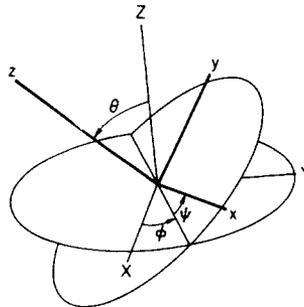


Fig. 1. The relationship between the fixed space axes  $XYZ$  and the local body axes  $xyz$  may be expressed using Euler angles  $\theta$ ,  $\phi$ ,  $\psi$ . By successively rotating through  $\theta$ ,  $\phi$ , and  $\psi$ , the space axes may be brought into coincidence with the local axes.

local body coordinates. (The notation  $d/ds$  is reserved for differentiation with respect to the fixed space axes.)

At a given cross section (say  $s = s_0$ ), that side for which  $s < s_0$  acts on the other side ( $s > s_0$ ) with a system of forces that is resolvable<sup>14</sup> into a force  $\mathbf{N}(s_0)$  and a torque  $\mathbf{M}(s_0)$ . (Of course, both sides act on each other with a system of forces that are equal and opposite.) At each cross section such a force and torque may be found, giving rise to (vector-valued) functions  $\mathbf{N}(s)$  and  $\mathbf{M}(s)$  describing the system of stresses on the rod.

Not all systems of stresses are compatible with the structure being in an equilibrium configuration. Many systems will cause acceleration, rotation, dynamic deformation, or a combination of all three. To occur at equilibrium, a system of stresses must be balanced. That is, if  $\mathbf{p}(s)$  [resp.  $\mathbf{q}(s)$ ] is the externally applied force (resp. torque) per unit length, the conditions of equilibrium are<sup>15,16</sup> (in the fixed, space coordinates)

$$\frac{d\mathbf{N}}{ds} + \mathbf{p}(s) = 0 \quad (3a)$$

$$\frac{d\mathbf{M}}{ds} + \mathbf{k}(s) \times \mathbf{N}(s) + \mathbf{q}(s) = 0 \quad (3b)$$

Here  $\mathbf{k}(s)$  is the unit tangent in the  $z(s)$  direction.

For the DNA in chromatin, external force and torque densities [ $\mathbf{p}(s)$  and  $\mathbf{q}(s)$ ] may arise through interaction with histones or nonhistone proteins. Alternatively, if a molecule crosses itself, it could exert contact forces resolvable into densities  $\mathbf{p}(s)$ ,  $\mathbf{q}(s)$ . In this latter case the problem becomes very difficult to solve, for the magnitude of the contact forces depends on the shape of the structure, whereas the shape is in part determined in response to the imposed forces. In what follows we confine our attention to the simplest case, where the molecule experiences no external forces so that  $\mathbf{p}(s) = \mathbf{q}(s) = 0$ . A subsequent contribution will treat more general problems.

The conditions for equilibrium are expressed as two first-order (vector), differential equations, Eqs. (3a) and (3b). A unique solution is determined when the force and torque are prescribed at a given cross section (such as one end). That is, one may specify the force and torque across one cross section at will. The differential equations Eqs. (3a) and (3b) then determine the system of stresses occurring at every cross section if the structure is at elastic equilibrium under the given load.

In order to determine the elastic equilibrium shape of the stressed structure, the stresses acting across the cross sections must be related by elastic laws to the deformations they cause. The simplest laws are linear:

$$M_x(s) = A\kappa_x(s), \quad M_y(s) = B\kappa_y(s), \quad M_z(s) = C\tau(s) \quad (4)$$

The constants  $A, B$  are called the bending stiffnesses, while  $C$  is the torsional stiffness. (If one wishes to regard the unstressed structure as curved, one must interpret the components  $\kappa_x$ ,  $\kappa_y$ ,  $\tau$  above as the deviations from the unstressed curvatures.)

Implicit in this choice is the assumption that the radius of curvature is large relative to the radius of the molecular cross section, so that the deformation and shear of the cross section are negligible. This may not be a reasonable assumption for problems of chromatin structure, where the curvature of the DNA is high. However, one expects that it is correct for supercoiled DNA.

In this paper we shall determine explicitly the elastic equilibrium shapes in the simplest possible case. We assume that double-helical DNA is linearly elastic, mechanically symmetric and deforms to elastic equilibrium without external forces. The symmetry condition means that the two bending stiffnesses are equal,  $A = B$ .

Then the conditions of equilibrium referred to the body axes are

$$\dot{\mathbf{N}} + \kappa(s) \times \mathbf{N}(s) = 0 \quad (5a)$$

$$\dot{\mathbf{M}} + \kappa(s) \times \mathbf{M}(s) + \mathbf{k}(s) \times \mathbf{N}(s) = 0 \quad (5b)$$

Substituting the elastic laws of Eq. (4) (with  $A = B$ ) into Eq. (5b) and expressing the result in component form yields

$$A\dot{k}_x + (C - A)\kappa_y\tau = N_y \quad (6a)$$

$$A\dot{k}_y + (A - C)\kappa_x\tau = -N_x \quad (6b)$$

$$C\dot{\tau} = 0 \quad (6c)$$

Note that Eq. (6c) states that the angular twist rate is constant along the length of the structure at equilibrium.

The  $z(s)$  component of Eq. (5a) is

$$\dot{N}_z - N_x\kappa_y + N_y\kappa_x = 0$$

Substitution of Eqs. (6a,b) into this expression gives

$$\dot{N}_z + A(\kappa_x\dot{k}_x + \kappa_y\dot{k}_y) + C\tau\dot{\tau} = 0$$

which integrates to an expression for conservation of "energy":

$$N_z + \frac{1}{2}A(\kappa_x^2 + \kappa_y^2) + \frac{1}{2}C\tau^2 = E = \text{const} \quad (7)$$

If  $|\mathbf{N}| = N$ , then  $N_z = N \cos\theta$  (where the space  $Z$  axis is chosen parallel to  $\mathbf{N}$ ).

A Lagrangian  $L$  may be constructed for this system. It is

$$L = \frac{1}{2}(A\kappa_x^2 + A\kappa_y^2 + C\tau^2) - N \cos\theta$$

Expressed with Euler angles by substitution of Eqs. (2a-c),  $L$  becomes

$$L = \frac{A}{2}(\dot{\phi}^2 \sin^2\theta + \dot{\theta}^2) + \frac{C}{2}(\dot{\phi} \cos\theta + \dot{\psi})^2 - N \cos\theta$$

Note that  $\phi, \psi$  are cyclic coordinates. (That is, they occur only in their derivatives  $\dot{\phi}, \dot{\psi}$ .) Therefore, from Lagrange's equation one sees that  $\partial L/\partial\dot{\phi} = p_\phi, \partial L/\partial\dot{\psi} = p_\psi$  are constants. These are

$$p_\phi = A\dot{\phi} \sin^2\theta + C(\dot{\phi} \cos\theta + \dot{\psi}) \cos\theta$$

$$p_\psi = C(\dot{\phi} \cos\theta + \dot{\psi}) = C\tau$$

Solving for  $\dot{\phi}, \dot{\psi}$  gives

$$\dot{\phi} = \frac{p_\phi - p_\psi \cos\theta}{A \sin^2\theta} \quad (8a)$$

$$\dot{\psi} = \frac{p_\psi}{C} - \frac{p_\phi - p_\psi \cos\theta}{A \sin^2\theta} \cos\theta \quad (8b)$$

Finally, substitution of Eqs. (2) and (8) into Eq. (7) for conservation of "energy" gives

$$N \cos\theta + \frac{1}{2} \left( \frac{(p_\phi - p_\psi \cos\theta)^2}{A \sin^2\theta} + A \dot{\theta}^2 \right) = \bar{E} = E - \frac{p_\psi^2}{2C}$$

or

$$\theta^2 = \frac{2}{A} \left( (\bar{E} - N \cos\theta) - \frac{(p_\phi - p_\psi \cos\theta)^2}{2A \sin^2\theta} \right) \quad (8c)$$

The substitution  $u = \cos\theta$  results in the equation

$$\dot{u}^2 = f(u) = \frac{2}{A} (\bar{E} - Nu)(1 - u^2) - \left( \frac{p_\phi - p_\psi u}{A} \right)^2 \quad (9)$$

The cubic equation  $f(u)$  has three real roots, which are ordered  $-1 \leq u_1 \leq u_2 \leq 1 < u_3$ . The physical range of  $u$  is  $u_1 \leq u \leq u_2$ , because there is only  $f(u) \geq 0$  and  $-1 \leq u = \cos\theta \leq 1$ , as required. We note that a single order of superhelicity arises only when  $u_1 = u_2 < 1$ , a special situation.<sup>1</sup> If there is a value  $\theta = \theta_0$  within this range such that  $p_\phi = p_\psi \cos\theta_0$ , then the direction of  $\phi$  changes sign at this value. If no such  $\theta_0$  exists,  $\dot{\phi}$  has the same sign throughout. In the next section this system of equations is solved for the possible elastic equilibrium shapes.

The Lagrangian arising in the linearly elastic but nonsymmetric case may be shown to lack cyclic coordinates. The equations arising in that case are not analytically solvable. Only in the symmetric, linearly elastic case can the differential equations expressing the elastic equilibrium shape, Eqs. (8) and (9), be solved analytically, as is done in the next section.

### SOLUTION FOR THE ELASTIC EQUILIBRIUM SHAPES

The solution of Eq. (9) for  $u = \cos\theta$  is obtained first, then the differential equations for the other Euler angles may be solved. These results express the elastic equilibrium shapes in terms of Euler angles.

Equation (9) may be factored into

$$\dot{u}^2 = a(u - u_1)(u - u_2)(u - u_3) \quad (10)$$

where  $a = 2N/A$  and  $-1 \leq u_1 \leq u_2 \leq 1 < u_3$ . If  $u = u_0$  at  $s = 0$ , then Eq. (10) yields an elliptic integral:

$$s = \int_0^s ds = \int_{u_0}^u [a(u - u_1)(u - u_2)(u - u_3)]^{-1/2} du \quad (11)$$

Let

$$z = (u - u_1)/(u_2 - u_1)$$

$$dz = du/(u_2 - u_1)$$

Then the physical range of  $z$  is  $0 \leq z \leq 1$ . Equation (11) becomes an elliptic integral of the first kind:

$$s = [a(u_3 - u_1)]^{-1/2} \int_{z_0}^z [z(1-z)(1-\lambda z)]^{-1/2} dz \quad (12)$$

where

$$\lambda = (u_2 - u_1)/(u_3 - u_1)$$

Thus

$$\begin{aligned} s &= [a(u_3 - u_1)]^{-1/2} \left( \int_0^z [z(1-z)(1-\lambda z)]^{-1/2} dz \right. \\ &\quad \left. - \int_0^{z_0} [z(1-z)(1-\lambda z)]^{-1/2} dz \right) \\ &= [a(u_3 - u_1)]^{-1/2} \left( \int_0^z [z(1-z)(1-\lambda z)]^{-1/2} dz - Q(z_0) \right) \end{aligned} \quad (13)$$

It can be shown<sup>17</sup> that

$$\int_0^v [t(1-t)(1-\lambda t)]^{-1/2} dt = 2F(\sin^{-1}(v^{1/2}), \lambda^{1/2})$$

where  $F$  is the elliptic integral of the first kind. By inversion<sup>18,19</sup> Eq. (13) may be written in terms of Jacobi's elliptic functions as

$$z^{1/2} = \operatorname{sn} \left( \frac{[a(u_3 - u_1)]^{1/2} s + Q(z_0)}{2} \right)$$

Hence the solution for the Euler angle  $\theta$  at elastic equilibrium is given by

$$u = \cos\theta = u_1 + (u_2 - u_1) \operatorname{sn}^2 \left( \frac{s[a(u_3 - u_1)]^{1/2} + Q(z_0)}{2} \right) \quad (14)$$

If, for example,  $u(0) = \cos\theta(0) = u_2$ , as happens when the initial torque is tangential to the axis of the rod,<sup>1</sup> then

$$Q(z_0) = 2K(\lambda^{1/2})$$

Here  $K(\lambda^{1/2})$  is the complete elliptic integral of the first kind with modulus  $\lambda^{1/2}$ .

Equation (14) shows that  $\theta$  oscillates periodically between  $\cos^{-1}(u_1)$  and  $\cos^{-1}(u_2)$ . The passage from  $u_1$  to  $u_2$  is completed in a distance along the structure of

$$\Delta s = 2[a(u_3 - u_1)]^{-1/2} K(\lambda^{1/2}) \quad (15)$$

In the sequel,  $\Delta s$  is called the semiperiodic distance and  $2\Delta s$  is the periodic distance of  $\theta$ .

Now a solution is sought to the differential equation for the Euler angle  $\phi$ . Expressed in terms of  $u$ , Eq. (8a) is

$$\dot{\phi} = \frac{p_\phi - p_\psi u}{A(1-u^2)} = \frac{p_\phi}{2A} \left( \frac{1}{1+u} + \frac{1}{1-u} \right) + \frac{p_\psi}{2A} \left( \frac{1}{1+u} - \frac{1}{1-u} \right)$$

Hence

$$\phi = \int_0^s \left( \frac{p_\phi}{2A} \left( \frac{1}{1+u} + \frac{1}{1-u} \right) + \frac{p_\psi}{2A} \left( \frac{1}{1+u} - \frac{1}{1-u} \right) \right) ds \quad (16)$$

From Eq. (11) it follows that

$$ds = [a(u-u_1)(u-u_2)(u-u_3)]^{-1/2} du$$

so that  $\phi$  may be expressed as an elliptic integral of the third kind in  $u$ :

$$\begin{aligned} \phi = & \frac{p_\phi + p_\psi}{2Aa^{1/2}} \int \frac{[(u-u_1)(u-u_2)(u-u_3)]^{-1/2}}{1+u} du \\ & + \frac{p_\phi - p_\psi}{2Aa^{1/2}} \int \frac{[(u-u_1)(u-u_2)(u-u_3)]^{-1/2}}{1-u} du \end{aligned} \quad (17)$$

Care must be taken concerning the limits of integration used in evaluating these integrals. Let  $\Delta\phi$  be the change in  $\phi$  experienced in one semiperiod of  $\theta$ :

$$\begin{aligned} \Delta\phi = & \frac{p_\phi + p_\psi}{2Aa^{1/2}} \int_{u_1}^{u_2} \frac{[(u-u_1)(u-u_2)(u-u_3)]^{-1/2}}{1+u} du \\ & + \frac{p_\phi - p_\psi}{2Aa^{1/2}} \int_{u_1}^{u_2} \frac{[(u-u_1)(u-u_2)(u-u_3)]^{-1/2}}{1-u} du \end{aligned} \quad (18)$$

It is known<sup>17</sup> that

$$\begin{aligned} \int_u^{u_2} \frac{dx}{(b-x)[(x-u_1)(x-u_2)(x-u_3)]^{1/2}} \\ = & \frac{2}{(b-u_3)(b-u_2)[(u_3-u_1)]^{1/2}} \\ & \times \left[ (u_2-u_3) \Pi \left( \sin^{-1} \left( \left( \frac{u_3-u_1}{u_2-u_1} \right)^{1/2} \left( \frac{u_2-u}{u_3-u} \right)^{1/2} \right), \lambda \left( \frac{b-u_3}{b-u_2} \right), \lambda^{1/2} \right) \right. \\ & \left. + (b-u_2) F \left( \sin^{-1} \left( \left( \frac{u_3-u_1}{u_2-u_1} \right)^{1/2} \left( \frac{u_2-u}{u_3-u} \right)^{1/2} \right), \lambda^{1/2} \right) \right] \end{aligned} \quad (19a)$$

$$\begin{aligned} \int_{u_1}^u \frac{dx}{(b-x)[(x-u_1)(x-u_2)(x-u_3)]^{1/2}} \\ = & \frac{2}{(b-u_1)[u_3-u_1]^{1/2}} \Pi \left( \sin^{-1}(z^{1/2}), \frac{u_2-u_1}{b-u_1}, \lambda^{1/2} \right) \end{aligned} \quad (19b)$$

where  $z, \lambda$  are as above,  $\Pi$  is the standard form of the elliptic integral of the third kind, and  $F$  is the standard form of the elliptic integral of the first kind. Therefore,

$$\Delta\phi = \frac{1}{A[a(u_3 - u_1)]^{1/2}} \left( \frac{p_\phi + p_\psi}{1 + u_1} \Pi\left(\frac{\pi}{2}, \frac{u_2 - u_1}{-1 - u_1}, \lambda^{1/2}\right) + \frac{p_\phi - p_\psi}{1 - u_1} \Pi\left(\frac{\pi}{2}, \frac{u_2 - u_1}{1 - u_1}, \lambda^{1/2}\right) \right) \quad (20)$$

To integrate Eq. (16) for  $\phi$ , we express  $s$  in terms of the periodic distance

$$s = n(2\Delta s) + \bar{s}$$

where  $n$  is an integer and  $\bar{s}$  is less than the periodic distance. Then

$$\phi(s) = n(2\Delta\phi) + \int_{[0, \bar{s}]} \dot{\phi} ds$$

Here the integral is that found in Eq. (16), evaluated on the interval  $0 \leq s \leq \bar{s}$ . This integral may have to be broken into several expressions of the form of Eq. (17) with appropriate limits, which are evaluated separately<sup>17</sup> according to Eqs. (19a,b). Thus the Euler angle  $\phi$  is given by expressions involving elliptic integrals of the third kind.

One may solve for the final Euler angle  $\psi$  in an analogous manner. However, knowledge of  $\psi$  is not required for the determination of the shape of the central axis of the elastic structure in space. For the position (relative to the space axes) of the point a distance  $s$  along the rod is

$$\mathbf{r}(s) = (X(s), Y(s), Z(s))$$

The unit tangent vector in these coordinates is

$$\mathbf{T}(s) = \frac{d\mathbf{r}}{ds} = (\sin\theta \sin\phi, -\sin\theta \cos\phi, \cos\theta) \quad (21)$$

Therefore,

$$X(s) = \int_0^s \sin\theta \sin\phi ds$$

$$Y(s) = - \int_0^s \sin\theta \cos\phi ds$$

$$Z(s) = \int_0^s \cos\theta ds$$

Thus knowledge of the two Euler angles  $\theta, \phi$  suffices to determine the shape of the structure.

It has been shown that  $\theta$  oscillates between the limits  $\cos^{-1}u_1$  and  $\cos^{-1}u_2$ . Furthermore,  $\phi$  completes one circuit of  $360^\circ$  in  $2\pi/\Delta\phi$  semi-periods of  $\theta$ , where  $\Delta\phi$  is given by Eq. (20). Thus, in general, the elastic equilibrium shapes of symmetric, linearly elastic rods have two orders of periodicity (i.e., superhelicity). The only case where one order may occur is when the two smallest roots  $u_1, u_2$  of the cubic equation  $f(u)$  are equal,  $u_1 = u_2 \neq 1$ . (The rod is straight if  $u_1 = u_2 = 1$ .) In particular, one may show that if the equilibrium shape is not straight and the torque  $\mathbf{M}$  is tan-

gential to the rod at some point, then two orders of superhelicity must occur.<sup>1</sup> Furthermore, if  $u_1$  and  $u_2$  have opposite signs and the semiperiod of  $\phi$  is an integral multiple of that of  $\theta$ , the elastic equilibrium shape can approximate a toroidal helix. This family of shapes could occur in the supercoiling of undenatured, closed-ring molecules.

### AN ALTERNATE APPROACH

We have found the elastic equilibrium (time-independent) shapes of stressed DNA under the assumption that the double helix has the elastic properties of a symmetric, linearly elastic rod. Furthermore, it was assumed that the curvatures of the shapes generated were small relative to the radius of the molecular cross section, so that deformations of the cross section could be ignored. If any of these assumptions is relaxed the problem becomes much more difficult, although still solvable in principle. (The only assumption that cannot be relaxed at present is that forces of self-contact do not arise.)

The nonlinear theory, including possible deformations of the cross section, will be discussed in a subsequent contribution. As a partial generalization, we describe an alternative and simpler approach to the problem applicable to nonsymmetric as well as symmetric structures. Basically, the technique is to generate solutions to the equations of equilibrium on a computer.

The conditions of equilibrium, Eqs. (5a,b), when expressed in coordinate form, become a system of six first-order differential equations. These are

$$\begin{aligned}\dot{N}_x + \kappa_y N_z - \tau N_y &= 0 \\ \dot{N}_y + \tau N_x - \kappa_x N_z &= 0 \\ \dot{N}_z + \kappa_x N_y - \kappa_y N_x &= 0 \\ \dot{M}_x + \kappa_y M_z - \tau M_y &= N_y \\ \dot{M}_y + \tau M_x - \kappa_x M_z &= -N_x \\ \dot{M}_z + \kappa_x M_y - \kappa_y M_x &= 0\end{aligned}$$

Substitution of the appropriate elastic laws, Eq. (4), gives a system of nonlinear equations in the curvature components  $\kappa_x$ ,  $\kappa_y$ ,  $\tau$  and the force components  $N_x$ ,  $N_y$ ,  $N_z$ . Prescription of the force  $\mathbf{N}$  on one cross section suffices to determine  $\mathbf{N}(s)$  everywhere, by Eq. (3a). Thus, to specify a single solution, one must simply specify the stiffnesses  $A, B, C$ ; the initial torque components  $M_x$ ,  $M_y$ ,  $M_z$ ; and the initial force  $\mathbf{N}$ . The system may be solved for this initial-value problem on a computer using, for example, the Runge-Kutta method. By suitable programming the computer can be instructed to plot the shape that it derives as its solution.

Figure 2(a,b), shows two representative equilibrium shapes for a rod under stress, as plotted by computer using the above technique. The two orders of superhelicity are evident.

The two shapes shown in Fig. 2 illustrate the biperiodic properties of the equilibrium geometry of stressed, linearly elastic rods. Such properties as the effective pitch angles and the ratio of the periods of the two orders will vary from case to case, depending on the forces, torques, and stiffnesses involved. Finally, as the elastic equilibrium shapes for the symmetric case are given by elliptic functions, they need not correspond exactly to coiled coils.

The present technique is both more general and simpler than the laborious derivation and solution of the previous section. It represents a step towards the fully general approach. However, for reasons described in the following section, it is expected that the symmetric, linear theory is the most important for questions of supercoiling.

### DISCUSSION AND CONCLUSIONS

The present paper develops a model of large-scale duplex DNA structure based on the assumption that the duplex has the elastic properties of a thin rod. The general conditions necessary for this rod to be in an elastic equilibrium (time-independent) shape are given in Eqs. (3a,b). The resulting equations are solved analytically for the simplest case, that in which

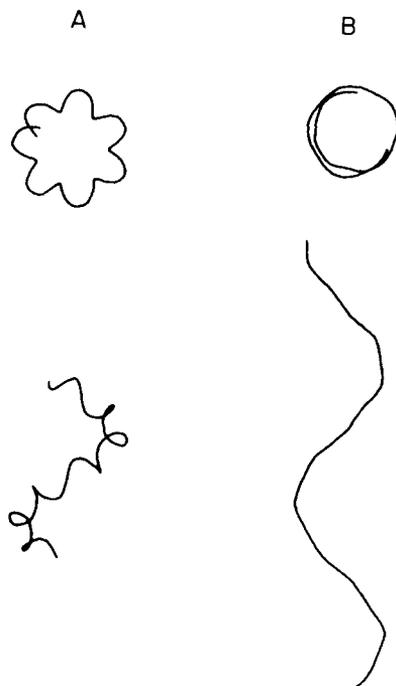


Fig. 2. Two shapes that arise at elastic equilibrium in a stressed, mechanically symmetric, linearly elastic rod. These solutions were generated and plotted by computer. The two orders of superhelicity are evident.

duplex DNA is assumed to be linearly elastic with identical bending stiffnesses in all directions (i.e., mechanically symmetric).

It is assumed that forces due to self-contact do not arise and that the radius of curvature of the bent structures is large relative to the cross-sectional radius of DNA. The latter assumption is required so that deformation and shear of the cross section (relative to the central axis) are negligible.

Under these assumptions it is found that the elastic equilibrium shape of the rod is given in terms of the Euler angles  $\theta$ ,  $\phi$  by elliptic integrals of the first and third kinds. Integration of the unit tangent, Eq. (21), gives the shape of the rod in Euclidean coordinates. It is found that at equilibrium the structure may be either straight, helical, or biperiodic. The helical case arises only in special situations, which are unlikely to be relevant in practice.<sup>1</sup>

Many of the assumptions of the present model can be relaxed. Specifically, nonlinearly elastic models of nonsymmetric rods will be developed in subsequent contributions. There, deformation and shear of the cross section will be accounted for explicitly. This generalized model will be relevant to situations of high curvature such as chromatin structure, where the presumed mechanical asymmetry of the double helix is important. The present symmetric, linear model is limited by the assumption of large scale to situations where the bending of the DNA is spread over numerous turns of the double helix, so that any asymmetries may be averaged out. Thus the present elastic model is relevant to questions of supercoiling.

To apply the present theory to supercoiling of DNA, we suggest a possible molecular basis for the elastic restoring stresses. One important (perhaps primary) source arises from the need for the constrained duplex to assume a conformation that minimizes the intramolecular potentials.<sup>2</sup> At the present, initial level of development we also subsume solvent, ionic, and electrostatic contributions into the effective elastic model. Hence it is possible that the values of the bending and torsional stiffnesses of DNA are not uniquely defined quantities, but might instead vary according to the nature of the local molecular environment and the sequence of bases. Indeed, the evidence of Gray<sup>13</sup> suggests that the shape of a supercoiled molecule may depend on the local ionic strength, indicative of changing elastic parameters.

The effective bending stiffness  $A$  of DNA (implicitly assumed to be symmetric) has been determined by several workers. One can show that<sup>10</sup>  $A$  is related to  $L$ , the statistical segment length of DNA, by the relationship  $A = kTL/2$ . The persistence length (which is half the statistical segment length  $L$ ) has been measured by both light-scattering and hydrodynamic techniques to be  $660 \pm 60$  Å. This gives a bending stiffness of about  $2.5 \times 10^{-10}$  erg Å under the experimental conditions.

The author is not aware of any published figure for the torsional stiffness  $C$  of DNA to date. In principle, one can evaluate  $C$  from the magnitude  $\bar{\theta}$  of the rms fluctuations in helical twist angle between base pairs. As-

suming neighboring angles fluctuate independently, the torsional stiffness is given by

$$C = kTl/\bar{\theta}^2$$

where  $l$  is the inter-base-pair distance of 3.4 Å. Again, values for  $\bar{\theta}$  have not appeared in the literature to date, although efforts are being made to evaluate it. Quantitative predictions of shape from the present theory will not be possible until the torsional stiffness of DNA is known.

Having developed an elastic theory for the large-scale structure of duplex DNA, it remains to incorporate this approach into specific models of supercoiling. Certainly other factors are important besides elastic bending and twisting.

It has been suggested that local denaturation occurs in supercoiled molecules.<sup>5,6</sup> Excessive torsional stress could be relieved through local denaturation, as a sort of local mechanical "failure." Such regions would have their elastic properties altered or destroyed, so that the present theory could not be applied to the molecule as a whole. Instead, the regions of double helix between adjacent sites of denaturation would be regarded as elastic rods, deforming to equilibrium through the action of forces and torques on their ends. The complete molecule would consist of a circular sequence of elastic "rods" joined by idealized universal joints (joints that can bend in any direction—the denatured segments).

Another factor that could be relevant to supercoiling is possible inter-conversion between the forms of DNA. If the A-form duplex has different elastic parameters than the B form (as one might expect), then a structure containing both would have to be modeled in pieces, with appropriate continuity conditions at the boundaries. The equations of equilibrium, Eqs. (3a,b), would still apply, but the difference in elastic laws would give rise to discontinuities in curvature at the junctions of the two forms.

Elastic considerations of the sort described in this paper could prove relevant to higher order chromosome structure.<sup>20-22</sup> Such structures might be regarded as elastic tubes or supersolenoids. Consideration of such models will be deferred until a subsequent contribution.

As stated previously, elastic models of chromatin structure require the generalization of the present model to high curvatures, nonsymmetric and possibly nonlinear elastic laws, and possible deformation and shear of the cross section. This generalization will be the subject of a future contribution.

In the present paper an elastic model of the time-independent equilibrium shapes of duplex DNA has been constructed on the assumption that the double helix is a symmetric, linearly elastic structure. Possible applications to supercoiling have been suggested. However, quantitative predictions of shapes must await the evaluation of the torsional stiffness of DNA.

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