Framed curves and knotted DNA

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Abstract
The present mini-review covers the local and global geometry of framed curves and the computation of twist and writhe in knotted DNA circles. Classical inequalities relating the total amount of bending of a closed space curve and associated knot parameters are also explained.

Introduction

The physics of DNA can be modelled in a variety of ways ranging from smaller to larger length scales including: (i) at atomic resolution; (ii) as a collection of discrete bases; (iii) as discrete basepairs; (iv) by averaging over short segments (decamers/dodecamers); (v) as double continuum elastic filaments (called bi-rods); and (vi) as semi-flexible polymers (single continuum elastic filaments). For a recent comparison of these methods in the context of a full literature review, see [1], and for a wider discussion of DNA geometry and topology, see [2–4].

The present article reviews the classical geometry and framing of curves, the concepts of twist and writhe, and inequalities relating the local geometry of curves and global topological properties of knots. The motivating application is knotted DNA mini circles.

Representing the DNA backbone as a space curve

A curve in three-dimensional space can be described as the set of points given by co-ordinates

$$\mathbf{x}(s) = \begin{bmatrix} x(s) \\ y(s) \\ z(s) \end{bmatrix} = [x(s), y(s), z(s)]^T,$$

where T denotes the transpose (which changes a row vector into a column vector), and s is the curve parameter. In the present context, s is the arc length (length measured along the curve from a fixed starting point where $s = 0$). I discuss only finite curve segments defined by arc length values in the range $0<s<L$, where L is the total length of the segment, and take $\mathbf{x}(0) = 0 = [0,0,0]^T$.

Space curves and Frenet–Serret framing

Frenet–Serret apparatus (developed c.1849) extracts two functions: curvature and torsion from a curve, and assigns a unique reference frame to each point. Given $\mathbf{x}(s)$, then the curvature and torsion are respectively defined by the equations

$$\kappa^2(s) = \frac{\mathrm{d}^2\mathbf{x}}{\mathrm{d}s^2} \cdot \frac{\mathrm{d}^2\mathbf{x}}{\mathrm{d}s^2}$$

and

$$\tau(s) = \frac{1}{\kappa^2(s)} \frac{\mathrm{d}\mathbf{x}}{\mathrm{d}s} \cdot \left(\frac{\mathrm{d}^2\mathbf{x}}{\mathrm{d}s^2} \times \frac{\mathrm{d}^3\mathbf{x}}{\mathrm{d}s^3} \right).$$

Here, a centred dot is the dot product defined for any two three-dimensional vectors as $\mathbf{a} \cdot \mathbf{b} = a_1 b_1 + a_2 b_2 + a_3 b_3$.

The Euclidean norm (or length) of a vector is

$$\|\mathbf{a}\| = \sqrt{\mathbf{a} \cdot \mathbf{a}}.$$

A Frenet–Serret reference frame specifying an orientation at each value of s along the curve can be defined as

$$R_{\mathrm{FS}}(s) \stackrel{\Delta}{=} [\mathbf{t}(s), \mathbf{n}(s), \mathbf{b}(s)],$$

where the columns of this orthogonal matrix (which are respectively called the tangent, normal and bi-normal) are

$$\mathbf{t}(s) = \frac{\mathrm{d}\mathbf{x}}{\mathrm{d}s},$$

$$\mathbf{n}(s) = \frac{1}{\kappa} \frac{\mathrm{d}\mathbf{t}}{\mathrm{d}s}$$

and

$$\mathbf{b}(s) = \mathbf{t}(s) \times \mathbf{n}(s).$$

Here, the cross product produces a vector $\mathbf{b}$ that is perpendicular to both $\mathbf{t}$ and $\mathbf{n}$ in accordance with the right-hand rule.

It can be shown that $[\mathbf{t},\mathbf{n},\mathbf{b}]$ is, in fact, a rotation matrix, and the orientation of the Frenet–Serret frame attached to the point $\mathbf{x}(s)$ can be viewed as a rotation from the identity reference frame to the orientation $[\mathbf{t},\mathbf{n},\mathbf{b}]$.

Global properties of closed curves

Some theorems relating the integrals of curvature and torsion of 'nice' closed curves in three-dimensional space to global

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topological properties are reviewed in the present article without proof. The closed curves are all assumed to be smooth and self-avoiding. An integral with a superimposed circle is standard notation for an integral over a closed curve where $s = 0$ and $s = L$ correspond to the same point in space.

Theorem 1 (Fenchel [5])

The following constraint bounds from below the total curvature of a closed curve

$$\oint \kappa(s)\mathrm{d}s \geqslant 2\pi,$$

with equality holding only for some kinds of planar curves (which are distinguished by the fact that they have zero torsion).

On the other hand, when considering knotted curves that have restrictions on their ability to bending (as would be the case for an elastic filament), which is described by the curvature at each point on the curve being less than a specific constant curvature (denoted by κ_0), then the following upper bound results,

$$\kappa_0\, L \geqslant \oint \kappa(s)\,\mathrm{d}s,$$

where L is the length of the curve. For example, when double-helical DNA is modelled as an elastic rod, there will be limits on its ability to bend until to kinks.

Theorem 2 (Fary–Milnor [6,7])

For closed space curves forming a knot,

$$\oint \kappa(s)\,\mathrm{d}s \geqslant \mathbf{4}\pi.$$

Many extensions of these theorems exist in which quantities such as the bridging number can be included to provide sharper bounds. See, for example, [8].

Frames with minimal twist

The Frenet–Serret apparatus reviewed above is not the only way to frame a curve. Rather than starting with the curve and attaching an orientation at each point, it is possible to start with an orientation [or rotation matrix, $R(s)$] for $0<s<L$, and define a curve from it. Given $R(s)$ and the tangent defined to be in the local x direction, and then using the notation $\mathbf{e}_1 = [1,0,0]^T$, the formula

$$\mathbf{x}(s) = \int_0^S R(\sigma)\mathbf{e}_1\mathrm{d}\sigma$$

defines an arc-length-parameterized curve that 'grows' along the local x-axis, which is the tangent to the curve.

The body-fixed description of angular velocity (with respect to s, since there is no time variable in this formulation) can be related to the skew-symmetric matrix

$$\begin{pmatrix} 0 & -\omega_3 & \omega_2 \\ \omega_3 & 0 & -\omega_1 \\ -\omega_2 & \omega_1 & 0 \end{pmatrix} \triangleq R^T \frac{\mathrm{d}R}{\mathrm{d}s}$$

as

$$\omega = [\omega_1, \omega_2, \omega_3]^T \triangleq \Omega^\nu$$

(which serves to define the 'vector operation' that extracts an angular velocity vector from the above skew-symmetric matrix). Measuring the amount that the reference turns around the x-axis gives

$$\rho(s) = \int_0^S \omega_1(\sigma)\mathrm{d}\sigma.$$

This local 'twist' will be called 'roll' so as not to confuse it with torsion or any other words starting with the letter 't'. The minimally twisting frame can be obtained directly from the Frenet–Serret frame by observing that the roll associated with that frame is

$$\rho_{FS}(s) = \int_0^S \tau(\sigma)\mathrm{d}\sigma$$

Therefore the framing with minimal twist is

$$R_B(s) \triangleq R_{FS}(s)R_1[-\rho_{FS}(s)],$$

where the subscript 1 denotes the rotation matrix describing anticlockwise rotation around the local x-axis by the angle $-\rho_{\mathrm{FS}}(s)$ inside the brackets. A curve $\mathbf{x}(s)$ with attached frame defined by the orientation given in the above equation is sometimes called the Bishop frame after [9].

Figure 1 depicts a three-dimensional framed curve and the twisting/roll degree of freedom around the tangential (local x) direction, which distinguishes Frenet–Serret and minimal-twist frames. The concept of a minimally twisting frame for a given curve is important in the context of DNA because it provides a datum. Superimposed on this is the natural twist of the double helix, from which under-twisting and over-twisting can be measured.

Twist, writhe and linking number

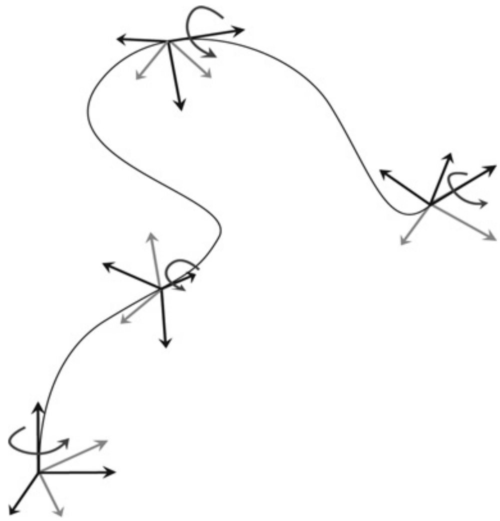
Given two closed curves, $\mathbf{x}_1(s)$ and $\mathbf{x}_2(s)$, where $\mathbf{x}_i(0) = \mathbf{x}_i(L_i)$ and $\mathbf{t}_i(0) = \mathbf{t}_i(L_i)$, then the Gauss integral is a functional defined as

$$G(\mathbf{x}_1, \mathbf{x}_2) = \frac{1}{4\pi} \oint_{C1} \mathrm{d}s_1 \oint_{C2} \mathrm{d}s_2 [\dot{\mathbf{x}}_1(s_1) \times \dot{\mathbf{x}}_2(s_2)] \cdot \frac{\mathbf{x}_1(s_1) - \mathbf{x}_2(s_2)}{\|\mathbf{x}_1(s_1) - \mathbf{x}_2(s_2)\|^2},$$

where an overdot is shorthand for the derivative $\mathrm{d}/\mathrm{d}s$.

Gauss showed that this integral is a topological invariant in the sense that its value only depends on the degree to which

Figure 1 | A three-dimensional curve framed in two ways



the curves intertwine. In the context of DNA, it is called the linking number of the two curves, and the notation $LW = G(\mathbf{x}_1,\mathbf{x}_2)$ is used.

Given a closed backbone curve of unit length, $\mathbf{x}(s)$, then a ribbon (or strip) associated with this backbone curve is any smoothly evolving set of line segments of fixed length $2r$ for $0<s<L$, with centres at $\mathbf{x}(s)$, such that the line segments point in a direction in the plane normal to the tangent. Then the tips of the line segments trace out closed curves. The tips of the ribbon can be described using the Frenet–Serret apparatus as the two curves

$$\mathbf{x}_{\pm}(s) = \mathbf{x}(s) \pm r\mathbf{v}(s),$$

where

$$\mathbf{v}(s) = \mathbf{n}(s)\cos\theta(s) + \mathbf{b}(s)\sin\theta(s)$$

and

$$\theta(0) = \theta(L).$$

When r is sufficiently small, it is useful to represent the linking number as the sum of two quantities: the writhe (or writhing number), denoted as Wr, and the twist (or twisting number), denoted as Tw. That is, the linking number can be decomposed as [10–13]:

$$Lw(\mathbf{x}, \mathbf{x} + r\mathbf{v}) = Wr(\mathbf{x}) + Tw(\mathbf{x}, \mathbf{v}),$$

which is often written more simply as $Lw = Wr + Tw$, where

$$Wr = \frac{1}{4\pi}\oint \mathrm{d}s \oint \mathrm{d}s'[\dot{\mathbf{x}}(s) \times \dot{\mathbf{x}}(s')] \cdot \frac{\mathbf{x}(s) - \mathbf{x}(s')}{\|\mathbf{x}(s) - \mathbf{x}(s')\|^3}$$

and

$$Tw = \frac{1}{2\pi}\oint \dot{\mathbf{x}}(s) \cdot \frac{[\mathbf{v}(s) \times \dot{\mathbf{v}}(s)]}{\|\dot{\mathbf{x}}(s)\|}\,\mathrm{d}s.$$

When the angle θ is zero for all values of s and so $\mathbf{v}(s) = \mathbf{n}(s)$, then

$$Tw = \frac{1}{2\pi}\oint \tau(s)\mathrm{d}s.$$

For a simple (non-self-intersecting) closed curve in the plane or on the surface of a sphere, it has been shown [14] that $Wr = 0$.

For any fixed unit vector $\mathbf{u}$ not parallel to the tangent to the curve $\mathbf{x}(s)$ for any value of s, the directional writhing number [14] is defined as

$$Wr(\mathbf{x}, \mathbf{u}) = Lk(\mathbf{x}, \mathbf{x} + \varepsilon\mathbf{u}),$$

where for sufficiently small ε, the value of the directional writhing number is independent of ε. The writhe can be calculated from the directional writhing number by integrating over all directions not parallel to the tangent of $\mathbf{x}$. This amounts to integration over the sphere (except at the set of measure zero where the tangent traces out a curve on the surface of the sphere) and so [14]

$$Wr(\mathbf{x}) = \int_{S^2} Wr(\mathbf{x}, \mathbf{u})\,\mathrm{d}\mathbf{u}.$$

Here the integral is normalized so that

$$\int_{S^2} \mathrm{d}\mathbf{u} = 1.$$

These relationships are reviewed in the present article because they play an important role in the study of DNA topology [2–4].

Conclusions

The differential geometry of space curves is an important tool for describing knotted DNA circles. The present mini-review covers some classical mathematical results that may find new applications in this area. These results include the definition of local geometric parameters such as curvature and torsion, the Frenet–Serret framing of space curves and the alternative minimal-roll framing. The relationships between global properties such as writhe, twist and linking number, and local properties such as the curvature and torsion are explained.

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