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Quantifying non-primary DNA formations through mechanical and geometric models

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Abstract

In this article, mechanical and geometric models for DNA strains (regarded as a helical structure in 3 dimensions, embedded into surfaces of various shapes (straight or curved cylinders, spheres, or projected into planes), are analyzed in order to obtain parameter estimates for DNA characteristics which can be used to detect the formation of secondary and tertiary formations in the presence of disorder. The models allow for the explicit representation of the DNA shape on constrained geometries and can therefore be implemented directly into {\it{ab initio}} or synthetic simulation studies.

Keywords

DNA models, thermodynamics, statistical ensembles

QUANTIFYING NON-PRIMARY DNA FORMATIONS THROUGH MECHANICAL AND GEOMETRIC MODELS

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Abstract. In this article, mechanical and geometric models for DNA strains (regarded as a helical structure in 3 dimensions, embedded into surfaces of various shapes (straight or curved cylinders, spheres, or projected into planes), are analyzed in order to obtain parameter estimates for DNA characteristics which can be used to detect the formation of secondary and tertiary formations in the presence of disorder. The models allow for the explicit representation of the DNA shape on constrained geometries and can therefore be implemented directly into *ab initio* or synthetic simulation studies.

1. Statement of the problem

The essential role played by DNA in living organisms can hardly be overstated. From a biological point of view, it provides the core structure through which information needed for every cell function is stored, duplicated, searched, and retrieved. From a biochemical point of view, DNA was considered a "simple" molecule [1], a point of view which may be simply reduced to the fact that, while DNA is represented as a double helix, other molecules participating in cell processes form triple helical structures, and so on. An open problem in rigorous modeling of DNA is understanding the precise relationship between its geometric properties and functionality on one had, and the mechanism for emergence of secondary and tertiary structures and molecular dynamics, on the other.

If the primary DNA structure is taken to be its straight double-helix structure (mathematically, embedded into a straight cylindrical surface), then its non-primary structures would correspond to the occurrence of multiple points on this helix, once it is bent or wrapped around other embedding surfaces, such as by mapping the original cylindrical surface onto a half-circle, or twisting it around into a secondary helix. It becomes then a relevant question to explore these deformations from the point of view of optimization theory, either for a geometric functional or a thermodynamic potential.

In this paper, we explore the exact geometric characteristics of such shapes in three dimensions and compute a number of characteristic quantities that are relevant in setting up the model for optimization analysis.

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3. The mathematical model

3.1. **Helix on a straight circular cylinder.** In order to set up the geometric models for a helix-shaped molecule, we introduce the straight helix as the graph of the vector-valued function

$$\vec{F} : [-\tau, \tau] \to C_r \subset \mathbb{R}^3,$$

where $\tau > 0$ is used to parametrize the curve and $r > 0$ is the radius of the straight cylinder symmetric along the $z-$axis,

$$C_r := \{(x, y, z) \in \mathbb{R}^3 | x^2 + y^2 = r^2, \, z \in \mathbb{R}\} \tag{3.1}$$

With these definitions, and arc of the helix on a straight cylinder is then given by the graph of the function

$$\vec{F}(t) = \langle r\cos(\omega t), r\sin(\omega t), p \cdot t\rangle, \quad t \in [-\tau, \tau], \tag{3.2}$$

up to reparametrization. Here, the model parameters $\omega \geq 0$, $p \geq 0$ describe the angular frequency of turning in the xy plane and the pace of displacement along the $z-$axis, respectively.

We first set out to compute the curvature κ and torsion χ [2] for the arc of helix and find their degenerate limits $p \to 0$, $\omega \to 0$. Since in the limit $p \to 0$, the helix becomes a circle (therefore planar), we have the corresponding limits

$$\lim_{p\to 0} \kappa = \frac{1}{r}, \ \lim_{p\to 0} \chi = 0 \tag{3.3}$$

while for $\omega \to 0$, the curve becomes a straight line, leading to the degenerate values

$$\lim_{\omega\to 0} \kappa = 0, \ \lim_{\omega\to 0} \chi = 0 \tag{3.4}$$

From computations, the arclength differential is found as

$$\frac{d\ell}{dt} = \left\| \frac{d\vec{F}}{dt} \right\| = \sqrt{r^2\omega^2 + p^2},$$

so the unit tangent vector is given by

$$\widehat{T} = \frac{d\vec{F}}{d\ell} = \frac{1}{\sqrt{r^2\omega^2 + p^2}} \langle -r\omega\sin(\omega t), r\omega\cos(\omega t), p\rangle,$$

Since

$$\frac{d\widehat{T}}{d\ell} = \frac{r\omega^2}{r^2\omega^2 + p^2} \langle -\cos(\omega t), -\sin(\omega t), 0\rangle,$$

using also the limit $p \to 0$ (3.3), we can identify the geodesic curvature and the normal unit vector as

$$\kappa = \frac{r\omega^2}{r^2\omega^2 + p^2}, \quad \widehat{N} = \langle -\cos(\omega t), -\sin(\omega t), 0\rangle.$$

The binormal vector is therefore equal to $\widehat{B} = \widehat{T} \times \widehat{N} = \frac{1}{\sqrt{r^2\omega^2+p^2}} \langle p\sin(\omega t), -p\cos(\omega t), r\omega\rangle$.

3.1.1. *Curvature, torsion, and elastic energy of a straight helix arc.* The arclength derivative of the binormal vector can now be used to compute the torsion of the straight helix as

$$\frac{d\widehat{B}}{d\ell} = \frac{p\omega}{r^2\omega^2 + p^2}\langle \cos(\omega t), \sin(\omega t), 0\rangle = -\chi \widehat{N},$$

so we get by introducing the vertical displacement $H = p\tau$, the total angular displacement $\Theta = \omega\tau$, and the total length L,

$$\chi = \frac{p\omega}{r^2\omega^2 + p^2} = \frac{H\Theta}{r^2\Theta^2 + H^2} = \frac{H}{L}\cdot\frac{\Theta}{L} = \frac{H}{\Theta}\cdot\left(\frac{\Theta}{L}\right)^2$$

For consistency, the geodesic curvature can be expressed through the vertical and angular displacements also, as

$$\kappa = \frac{r\omega^2}{r^2\omega^2 + p^2} = r\frac{\Theta^2}{r^2\Theta^2 + H^2} = r\frac{\Theta^2}{L^2}.$$

In order to derive the mechanical properties of a straight helix from its geometric data, consider the arc corresponding to the parametrization $0 \le t \le \tau$,

$$\vec{F}(t) = \langle r\cos(\omega t), r\sin(\omega t), p\cdot t\rangle, \quad t \in [0,\tau], \quad p \ge 0, \quad p \in \mathbb{R}.$$

We denote the total length of this arc of helix by L. If the helix is modeled as an elastic medium with torsion elastic coefficient ν, so that when twisted around its axis by a total angle $\varphi - \varphi_0$, it has elastic potential energy

$$W = \frac{\nu}{2}(\varphi - \varphi_0)^2,$$

then we can identify it to an elastic spring with *effective* elastic coefficient

$$k = \nu\frac{\kappa}{r} = 4\pi^2\nu n^2, \quad n = \frac{\omega\tau}{2\pi L} = \frac{\Theta}{2\pi L},$$

where n represents the number of turns per length. In order to compute this effective elastic coefficient, notice that for a given length L, the range of

$$t \in [0,\tau] \text{ is } \tau = \frac{L}{\sqrt{r^2\omega^2 + p^2}},$$

while its extent along the $z-$axis is

$$H = p\tau = \frac{pL}{\sqrt{r^2\omega^2 + p^2}} = \frac{\sqrt{r}\chi}{\sqrt{\kappa}}L = \sqrt{\frac{r}{\kappa}}\varphi \Rightarrow \varphi = \sqrt{\frac{\kappa}{r}}H.$$

Therefore,

$$W = \frac{\nu}{2}(\varphi - \varphi_0)^2 = \frac{\nu\kappa}{2r}(H - H_0)^2 \Rightarrow k = \nu\frac{\kappa}{r} = \nu\frac{(\omega\tau)^2}{L^2} = 4\pi^2\nu n^2.$$

We conclude that a straight helix with angular displacement per arclength rate $2\pi n$ is characterized by an effective elastic constant

$$k = \nu\frac{\omega^2}{r^2\omega^2 + p^2} = \nu\frac{\Theta^2}{r^2\Theta^2 + H^2} = \nu\left(\frac{d\theta}{d\ell}\right)^2 = \frac{\nu}{r^2}\cdot\frac{\kappa^2}{\kappa^2 + \chi^2} \tag{3.5}$$

In the following sections, we will generalize these formulas to more general geometric models, with variable curvature and torsion.

3.2. **Helix on a cylinder wrapped around a circle.**

3.2.1. *The stereographic projection in two dimensions.* We recall that the stereographic projection in two dimensions maps the straight line onto the unit circle punctured at a point, through a differentiable bijection (diffeomorphism). To fix notation, we consider the unit circle in $\mathbb{R}^2$,

$$S^1 = \{(x, y) \in \mathbb{R}^2 | x^2 + y^2 = 1\}$$

We can define local charts via stereographic projection from the points $N \equiv (0, 1)$ and $S \equiv (0, -1)$. Let $U_N \equiv S^1 \setminus \{N\}$, $U_S \equiv S^1 \setminus \{S\}$, given by

$$f_N(x, y) = \frac{x}{1-y}, \quad f_S(x, y) = \frac{x}{1+y}$$

It can checked by elementary geometry that these differentiable functions are indeed bijections, and that

$$f_N(U_N) = f_S(U_S) = \mathbb{R}, \quad f_N(S) = f_S(N) = 0,$$

and moreover $f_N(U_N \cap U_S) = f_S(U_N \cap U_S) = \mathbb{R} \setminus \{0\}$, such that $\forall t \in \mathbb{R} \setminus \{0\}$,

$$f_N^{-1}(t) = \left(\frac{2t}{t^2+1}, \frac{t^2-1}{t^2+1} \right), \quad (f_S \circ f_N^{-1})(t) = \frac{1}{t}.$$

Since $t \to 1/t$ is a diffeomorphism on $\mathbb{R} \setminus \{0\}$, all the conditions are satisfied for the coordinate charts f_N, f_S to describe S^1 as a one-dimensional manifold embedded in $\mathbb{R}^2$.

Let $F : S^1 \to S^1$, given by the reflexion with respect to the $x-$axis, or $F(x, y) = (x, -y)$ in the embedding space $\mathbb{R}^2$. Obviously, $F(N) = S, F(S) = N$, and for $t \neq 0$,

$$(f_N \circ F \circ f_N^{-1})(t) = (f_S \circ F \circ f_S^{-1})(t) = \frac{1}{t}, \; (f_N \circ F \circ f_S^{-1})(t) = (f_S \circ F \circ f_N^{-1})(t) = t,$$

which are diffeomorphisms on $\mathbb{R} \setminus \{0\}$. The last two composition maps can be used at points N, S respectively, as well.

3.2.2. *Wrapping the infinite straight cylinder around a half-circle of radius $R \geq r$.* In this section, we will introduce a map between the straight cylinder C_r (3.1) and a surface $\Sigma_{r,R}$ we use to model a helix with non-constant curvature and torsion and constrained global geometry, parametrized by the radius $R \geq r$. Let Γ_R be the open half-circle

$$\Gamma_R := \{(x, y, z) \in \mathbb{R}^3 | x = 0, \, 0 \leq y < R, \, (y - R)^2 + z^2 = R^2\}, \tag{3.6}$$

then the $z-$axis maps onto Γ_R by the transformation

$$W(0, 0, z) = \left(0, R - \frac{R^2}{\sqrt{R^2+z^2}}, \frac{zR}{\sqrt{R^2+z^2}} \right)$$

The corresponding arclength transformation is given by

$$\tan \phi = \frac{z}{R} \Rightarrow \left| \frac{R d\phi}{dz} \right| = \frac{R^2}{R^2+z^2}$$

We can now extend this construction to every vertical line of the cylinder C_r and corresponding vertical half-circle centered on the $y-$axis and tangent to the line in the $x-y$ plane, by the transformation

$$W(r\cos\theta, r\sin\theta, z) = (X, Y, Z), \text{ where } \begin{cases} X &= r\cos\theta - \Delta(\theta, z)\sin\nu, \\ Y &= r\sin\theta + \Delta(\theta, z)\cos\nu, \\ Z &= \frac{z\delta(\theta)}{\sqrt{\delta^2(\theta)+z^2}}, \end{cases} \tag{3.7}$$

with

$$\begin{cases} \delta(\theta) &= \sqrt{R^2 + r^2 - 2Rr\sin\theta} \\ \Delta(\theta, z) &= \delta(\theta) - \frac{\delta^2(\theta)}{\sqrt{\delta^2(\theta)+z^2}} \\ \tan\nu &= \frac{r\cos\theta}{R - r\sin\theta}, \end{cases} \tag{3.8}$$

It is then easy to verify that the radius of the circle onto which the vertical line

$$\langle r\cos\theta, r\sin\theta, z\rangle, \quad z \in \mathbb{R}$$

is mapped is given by

$$\delta(\theta) = \sqrt{R^2 + r^2 - 2Rr\sin\theta}, \quad R - r \le \delta(\theta) \le R + r,$$

and the corresponding arclength transformation is given by

$$\tan\phi = \frac{z}{\delta(\theta)} \Rightarrow \left|\frac{\delta(\theta)d\phi}{dz}\right| = \frac{\delta^2(\theta)}{\delta^2(\theta) + z^2}$$

3.2.3. *Bijectivity.* From (3.8), we find the range of values for the angle ν, as

$$\tan\nu| < \frac{r}{R - r} < \infty \Rightarrow |\nu| < \frac{\pi}{2}, \ \cos\nu \ne 0,$$

therefore the extremal value corresponds to the critical values θ_c satisfying

$$\frac{d\nu}{d\theta} = 0 \Rightarrow \frac{d\tan\nu}{d\theta} = 0 \Rightarrow r^2\sin^2\theta - Rr\sin\theta = -r^2\cos^2\theta \Rightarrow \sin\theta_c = \frac{r}{R}.$$

The corresponding extremal value for $\tan\nu$ is then given by

$$\tan\nu(\theta_c) = \frac{r}{\sqrt{R^2 - r^2}}$$

For the range of values $\nu \in [-\nu(\theta_c), \nu(\theta_c)]$, the inversion

$$\tan\nu = \frac{r\cos\theta}{R - r\sin\theta} \Rightarrow \theta_\pm = \nu \pm \cos^{-1}\left(\frac{R}{r}\sin\nu\right),$$

along with

$$\delta(\theta_\pm) = \sqrt{R^2 + r^2 - 2Rr\sin\theta} = r\frac{\cos\theta_\pm}{\cos\nu}, \quad \delta(\theta_+) \le \delta(\theta_c) \le \delta(\theta_-),$$

shows that the mapping (3.7) is a bijection.

3.2.4. *The helix wrapping mapping.* To find the result of the mapping of the cylinder C_r by the wrapping transformation (3.7), we consider the parametrization

$$\theta(t) = \omega t,\ z(t) = pt,\ t \in \mathbb{R},$$

which leads to the result (deformed helix)

$$\begin{cases} X(t) &= r\sqrt{\frac{R^2+r^2-2Rr\sin(\omega t)}{R^2+r^2-2Rr\sin(\omega t)+p^2t^2}}\cos(\omega t), \\ Y(t) &= R\left[1-\sqrt{\frac{R^2+r^2-2Rr\sin(\omega t)}{R^2+r^2-2Rr\sin(\omega t)+p^2t^2}}\right] + r\sqrt{\frac{R^2+r^2-2Rr\sin(\omega t)}{R^2+r^2-2Rr\sin(\omega t)+p^2t^2}}\sin(\omega t), \\ Z(t) &= pt\sqrt{\frac{R^2+r^2-2Rr\sin(\omega t)}{R^2+r^2-2Rr\sin(\omega t)+p^2t^2}}, \end{cases}$$

Clearly, the limits $t \to \pm\infty$, we obtain the asymptotics

$$X \to 0,\ Y \to R,\ |Z| \in [R - r, R + r],$$

indicating that the wrapping map confines the deformed helix into a tubular neighborhood around the half-circle Γ_R (3.6). Moreover, in the limit $r \ll R$, this confinement is reduced to the half-circle to a first approximation.

It is instructive to consider other relevant limiting cases for this mapping, an analysis provided in the following sections.

3.2.5. *The case $R \gg L$.* In this case, the radius of curvature of the half-circle Γ_R is much smaller than the geodesic curvature of the helix, meaning that the helical structure is thin and narrow, slightly bent under the wrapping map. Therefore, the only meaningful expansion is with respect to the small parameter

$$\frac{p\tau}{R} \ll 1,$$

yielding

$$\sqrt{\frac{R^2 + r^2 - 2Rr\sin(\omega t)}{R^2 + r^2 - 2Rr\sin(\omega t) + p^2t^2}} \simeq 1 - \frac{p^2t^2}{2R^2} + O\left(\frac{p^2t^2}{2R^2}\right)^2,$$

which leads to the approximate mapping

$$\begin{cases} X(t) & \simeq & r\cos(\omega t)\left[1-\frac{p^2t^2}{2R^2}\right], \\ Y(t) & \simeq & \frac{p^2t^2}{2R}+r\sin(\omega t)\left[1-\frac{p^2t^2}{2R^2}\right], \\ Z(t) & \simeq & pt-\frac{p^3t^3}{2R^2}. \end{cases}$$

Therefore, to this order of approximation, the wrapped helix and the unperturbed helix are related by the transformation

$$\langle X,Y,Z\rangle(t)=\left[1-\frac{p^2t^2}{2R^2}\right]\langle x,y,z\rangle(t)+\frac{p^2t^2}{2R^2}\langle 0,R,0\rangle,$$

allowing to find the relation between their derivatives as well,

$$\langle \dot{X},\dot{Y},\dot{Z}\rangle(t)=\left[1-\frac{p^2t^2}{2R^2}\right]\langle \dot{x},\dot{y},\dot{z}\rangle(t)+\frac{p^2t}{R^2}\left[\langle 0,R,0\rangle-\langle x,y,z\rangle(t)\right],$$

$$\langle \ddot{X},\ddot{Y},\ddot{Z}\rangle(t)=\left[1-\frac{p^2t^2}{2R^2}\right]\langle \ddot{x},\ddot{y},\ddot{z}\rangle(t)-2\frac{p^2t}{R^2}\langle \dot{x},\dot{y},\dot{z}\rangle(t)+\frac{p^2}{R^2}\left[\langle 0,R,0\rangle-\langle x,y,z\rangle(t)\right],$$

leading to the perturbative form of the curvature of the wrapped helix, as

$$\widetilde{\kappa}=\frac{|\langle \dot{X},\dot{Y},\dot{Z}\rangle\wedge\langle \ddot{X},\ddot{Y},\ddot{Z}\rangle|}{|\langle \dot{X},\dot{Y},\dot{Z}\rangle|^3}$$

Keeping only up to quadratic terms in the perturbative parameter, we can write

$$\langle \dot{X},\dot{Y},\dot{Z}\rangle\wedge\langle \ddot{X},\ddot{Y},\ddot{Z}\rangle\simeq\left[1-\frac{p^2t^2}{R^2}\right]\langle \dot{x},\dot{y},\dot{z}\rangle\wedge\langle \ddot{x},\ddot{y},\ddot{z}\rangle+$$
$$+\frac{p^2}{R^2}\left[\langle \dot{x},\dot{y},\dot{z}\rangle(t)-t\langle \ddot{x},\ddot{y},\ddot{z}\rangle\right]\wedge\left[\langle 0,R,0\rangle-\langle x,y,z\rangle(t)\right]$$

We note that the straight helix has constant-modulus velocity $\langle \dot{x},\dot{y},\dot{z}\rangle$ as well as constant curvature

$$\kappa=\frac{r\omega^2}{r^2\omega^2+p^2}=\frac{|\langle \dot{x},\dot{y},\dot{z}\rangle\wedge\langle \ddot{x},\ddot{y},\ddot{z}\rangle|}{|\langle \dot{x},\dot{y},\dot{z}\rangle|^3},$$

which allows to expand the curvature of the deformed helix as

$$\widetilde{\kappa}\simeq\kappa\left[1-\frac{p}{\omega R}\left(\frac{2p\omega r}{p^2+r^2\omega^2}\cdot(\omega t)\cos(\omega t)+\frac{p}{r\omega}\sin(\omega t)\right)\right],$$

and by using the total number of turns of the helix (invariant under the transfror- mation)

$$N=\frac{\omega\tau}{2\pi},$$

we arrive at the first-order expansion in the small parameter $\frac{p\tau}{R} < \frac{L}{R} \ll 1$,

$$\frac{|\kappa - \widetilde{\kappa}|}{\kappa} = O\left(\frac{L}{NR}\right)$$

4. Energetic estimates for the helix wrapping transformation

Let us recall from § 3.1.1 that the total elastic energy of the unperturbed helix is

$$W_0 = \frac{1}{2} k H^2,$$

where $k = \frac{\nu}{r^2} \frac{\kappa^2}{\kappa^2 + \chi^2}$. Since the wrapping maps the helical axis onto the circular arc of length $R\phi$, where

$$\tan\phi = \frac{H}{R} \Rightarrow \phi = \arctan\left(\frac{H}{R}\right) \simeq \frac{H}{R} - \frac{1}{3}\left(\frac{H}{R}\right)^3 + \ldots,$$

the corresponding elastic energy of the deformed helix is estimated as

$$W = \frac{R^2}{2} \int_0^\phi \widetilde{\kappa}(t(\theta))\theta d\theta \Rightarrow \frac{W - W_0}{W_0} = O\left(\frac{L}{NR}\right) = O\left(\frac{1}{nR}\right)$$

,

using again the number of turns per length, n. Under the assumption of the Maxwell-Boltzmann distribution of an ensemble of DNA strings modeled by this mechanical helix, we obtain an equivalent estimate for the effective absolute temperature corresponding to a bending by radius R:

$$\frac{\Delta T}{T_0} \sim \frac{\Delta W}{W_0},$$

leading to the following estimate for the typical bending radius corresponding to a temperature change ΔT:

$$R \sim \frac{T_0}{n\Delta T},$$

with n the original number of turns per length of the helix at temperature T_0.

5. Conclusions

The analysis presented in this paper provides an estimate for the typical scale at which an elastic model of DNA would be deformed upon an effective relative temperature increase of $\Delta T/T_0$, at given number of turns per length. This result can be used for molecular dynamics modeling of ensembles of DNA molecules, which will be presented in an upcoming paper.