Studies on a DNA Double Helicoidal Structure Immersed in Viscous Bio-Fluid

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ABSTRACT

The paper aims at extending, utilising and generalising research in nonlinear dynamics of (i) spiral/helicoidal structures, and (ii) viscous, low speed fluid to biomechanical DNA fluid-structure interaction. Employing a nonlinear helicoidal model, the energy stored in a distorted Watson-Crick DNA model subjected to viscous, low speed organic fluid loading is examined. An efficient recursive numerical scheme based on the variational principle is presented. Significant dynamical responses such as energy distribution, bending and twisting of DNA model under organic fluid excitations are discussed. Matching of DNA sequential characteristics with respect to the nonlinear dynamical responses is outlined in order to reveal information regarding DNA sequencing by means of a fluid-structure dynamical approach.

Keywords: Biomechanical DNA model, nonlinear helicoidal model, fluid-structure interaction, nonlinear dynamical responses, DNA sequential characteristics.

1 INTRODUCTION

Although Deoxyribonucleic acid (DNA) was first identified as a kind of acid in a cell nucleus over 100 years ago, the way by which two polynucleotide chains are held together in a helical manner with A-T and G-C pairing bases was only discovered by James Watson and Francis Crick [1] in 1953. This model has been widely discussed and several alternative models have also been proposed [2]. In general, DNA is constructed from two inconceivably long and heavily supercoiled helical polymers, commonly referred to as the Watson-Crick double helix model. It is known as one of the most interesting and mysterious biological molecules having an ability to conserve, replicate and transfer genetic information. It has been discovered as an acid in a cell nucleus for more than 100 years, and its biological aspects have been established to a certain advanced level today. However, the understanding of non-linear physical properties of DNA is still far from sufficient for accurate prediction of its dynamical responses. The knowledge of molecular biomechanics is important because almost all aspects of life are engineered at that level. As Francis Crick mentioned "*All approaches at a higher level are suspect until confirmed at the molecular level*" [3].

There exists intensive research in biological and chemical DNA analyses [4]. A comprehensive review of the essential works is out of scope, and will not be presented. Three events stimulated the appearance and rapid development of non-linear DNA physics [5,6]. The first was the success of non-linear mathematics and its application to many physical phenomena. The second was the emergence of new results in the dynamics of biopolymers, which has led to an understanding of the important role of dynamics in the biological functioning of biopolymers. The third event was the publications of Davydov [5] where, for the first time, the achievements of non-linear mathematics were applied to biology and the occurrence of solitons in biopolymers was hypothesized. One of the earliest research works on the non-linear physics of DNA was attributed to Englander *et al*. [6] who introduced the non-linear conformational excitations and presented the first non-linear Hamiltonian of DNA, which gave a powerful impulse for theoretical investigations. A number of investigators [2] improved the Hamiltonian model and its dynamical parameters, by investigating corresponding non-linear differential equations and their soliton-like solutions with consideration of DNA solitons and calculation of corresponding correlation functions. The results [5,6] formed a theoretical basis for the non-linear physics of DNA.

DNA is not motionless. It is in a constantly wriggling dynamic state in a medium of bioorganic fluid in the nucleus of a cell. DNA can be modelled as a double twisted helicoidal structure [2,4] constantly interacting with surrounding viscous, organic fluid. Almost all-existing DNA analyses assume a very coarse dynamical model. Among them are the rod-like models, the double rod-like models and the nonlinear higher-level models [2]. Complexity was introduced by adding the effects of environment, inhomogeneity, helicity and nonlinear excitations [2]. The rod-like models disregard DNA helical effects, and assume a coiled double helix as a single rod. They are only good if we are interested in examining the global responses of DNA at a coarser level. As the Watson-Crick model features a double helix, the rod-like models are too crude to study the interior twisting, deformation and distribution of energy.

For the reasons above, we present a new innovative approach to investigate the non-linear dynamics of DNA in this paper. The DNA molecule is modelled, from a physical viewpoint, as an interactive fluid-structure complex dynamical system, having a two-dimensional

helicoidal structure [7-12]. The model proposed here is more refined than the rod-like models. It can be developed from expertise in the modelling of helicoidal structures, because the model can be formed by limiting the width of a drill [11,12]. In other words, a helix is a special subset of a drill, and therefore the dynamic responses of a double helix can be investigated from the knowledge of dynamics of drilling structures. The viscous bio-fluids surrounding DNA are considered as Low-Reynolds number fluids, and fundamental solutions can be obtained by solving the unsteady Stokes flow equation [13]. The fluid-structure system can be characterised by specific distributions of internal forces and energy, and determining internal motions (including bending, twisting and oscillation) resulting from unsteady viscous flow loadings. These dynamical characteristics and responses will assist in the classification of various types of DNA.

2 ENGINEERING DNA MODEL

The geometry of a helix or a helicoil with length a, radius R, width b and projected angle θ_O are shown in Figure 1. When the condition $b < R << a$, where b is about an order smaller than R [2], is imposed, a helicoil (as shown in Figure 1(c)) is obtained. Although not shown in this figure, the thickness h of the helicoil considered *may not necessarily be a constant*. It could vary such that the cross section is *round* or *any other shape*, so that the helicoil model is more realistic. The Watson-Crick double helix DNA model can be constructed as a combination of such two parallel helicoils with internal bondings as shown in Figure 2(a), which can be used to model a DNA molecule as shown in Figure 2(b).

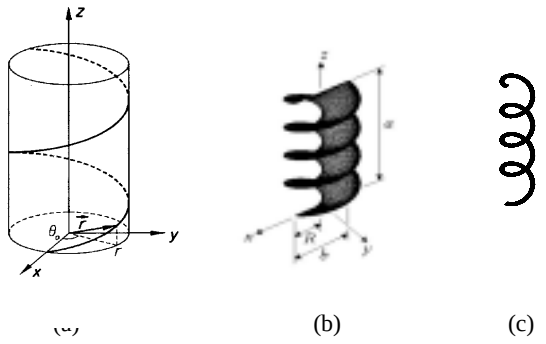


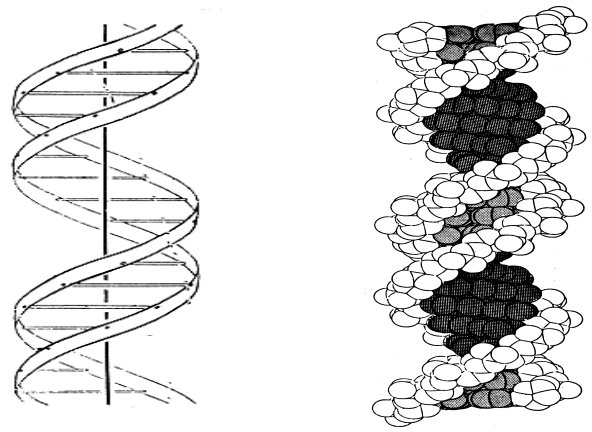
Figure 1: Geometry of (a) a helix, (b) a helicoidal structure, and (c) a helicoil.

A curvilinear coordinate system, perpendicular and tangential to the helix and lying in the osculating plane, $(\vec{\mathbf{r}}, \partial\vec{\mathbf{r}}/\partial\theta)$ is adopted. With the binormal vector to the helix $\vec{\mathbf{b}}$, it forms an orthogonal coordinate system $(\vec{\mathbf{r}}, \partial\vec{\mathbf{r}}/\partial\theta, \vec{\mathbf{b}})$, and its transformation with respect to the Cartesian system $(\vec{\mathbf{i}}, \vec{\mathbf{j}}, \vec{\mathbf{k}})$ is

$$\vec{\mathbf{r}} = r\left(\vec{\mathbf{i}}\cos\theta + \vec{\mathbf{j}}\sin\theta\right) + \frac{\theta}{\varphi}\vec{\mathbf{k}} \qquad (1)$$

where $\varphi = \theta_0/a$ is the rate of change of θ along the z-axis. Deriving from the theory of surfaces, a helicoil (Figure 1(c)) has infinite radius of curvature with respect to the coordinates (r,θ), whereas the radius of twist (or torsion of the space curve r) is finite [11,12],

$$\frac{1}{R_r} = 0; \qquad \frac{1}{R_\theta} = 0; \qquad \frac{1}{R_{r\theta}} = -\frac{\varphi}{1 + r^2\varphi^2} \qquad (2a,b,c)$$



(b)

Figure 2: (a) A double helicoidal DNA model with bonding and (b) a DNA molecule.

The derivation of nonlinear twisting curvature (2c) [11,12] is a benchmark, as it has generalized the conventional linear twisting curvature $1/R_{r\theta} \approx -\tan\varphi$ for a small φ [7,9,10]. Thus, it is possible to analyze a highly twisted helicoidal structure. There exist two inherent approximations in assuming $1/R_{r\theta} \approx -\tan\varphi$, the first being $\varphi \approx \tan\varphi$ and the second $r\varphi << 1$. For the first assumption, an approximately 10% error will occur for $\theta_0 = 30^0$; for the second assumption, $\theta_O(r/a) = 0.26 << 1$ for $r/a = 0.5$ is very unsatisfactory.

Let $\vec{\mathbf{u}}(t,r,\theta)$ be the time-dependent, t, displacement vector composing of u_r, u_θ in the osculating plane and u_b in the binormal direction, the linear normal and shear strains [11,12] are:

$$\varepsilon_{rr} = \frac{\partial u_r}{\partial r}; \varepsilon_{\theta\theta} = \frac{1}{h_\theta}\frac{\partial u_\theta}{\partial \theta} + \frac{r u_r}{h_\theta^2};$$
$$\gamma_{r\theta} = \frac{\partial u_\theta}{\partial r} - \frac{r u_\theta}{h_\theta^2} + \frac{1}{h_\theta}\frac{\partial u_r}{\partial \theta} - \frac{2u_b}{\varphi h_\theta^2} \quad (3a,b,c)$$

$$\kappa_{rr} = -\frac{3}{2\varphi h_\theta^2}\frac{\partial u_\theta}{\partial r} + \frac{3ru_\theta}{2\varphi h_\theta^4} - \frac{\partial^2 u_b}{\partial r^2} + \frac{1}{2\varphi h_\theta^3}\frac{\partial u_r}{\partial \theta} \quad (3d)$$

$$\kappa_{\theta\theta} = -\frac{3}{2\varphi h_\theta^3}\frac{\partial u_r}{\partial \theta} - \frac{1}{h_\theta^2}\frac{\partial^2 u_b}{\partial \theta^2} - \frac{r u_\theta}{2\varphi h_\theta^4} - \frac{r}{h_\theta^2}\frac{\partial u_b}{\partial r} + \frac{1}{2\varphi h_\theta^2}\frac{\partial u_\theta}{\partial r} \quad (3e)$$

$$\tau_{r\theta} = \frac{1}{h_\theta}\frac{\partial^2 u_b}{\partial r \partial \theta} + \frac{r}{h_\theta^3}\frac{\partial u_b}{\partial \theta} - \frac{1}{\varphi h_\theta^2}\frac{\partial u_r}{\partial r} - \frac{1}{\varphi h_\theta^3}\frac{\partial u_\theta}{\partial \theta} + \frac{r u_r}{\varphi h_\theta^4} \quad (3f)$$

where $h_\theta = (1/\varphi)\sqrt{1 + r^2\varphi^2}$ is the metric tensor of the helicoidal co-ordinate system. During deformation, the stretching strain energy and bending strain energy for constant thickness h can be expressed as

$$U = \frac{6D}{h^2}\iint_A \left[\varepsilon_{rr}^2 + \varepsilon_{\theta\theta}^2 + 2\nu\varepsilon_{rr}\varepsilon_{\theta\theta} + \frac{1-\nu}{2}\gamma_{r\theta}^2\right] h_\theta \, dr \, d\theta + \frac{D}{2}\iint_A \left[\kappa_{rr}^2 + \kappa_{\theta\theta}^2 + 2\nu\kappa_{rr}\kappa_{\theta\theta} + 2(1-\nu)\tau_{r\theta}^2\right] h_\theta \, dr \, d\theta \quad , \quad (4)$$

corresponding to the first and second integrals, respectively. Equations for varying $h(r,\theta)$ can be reformulated accordingly, by keeping the parameter in the domain integrals strain (first integral in Eq. (4)) and change of curvature (second integral in Eq. (4)). The work done due to external excitation is

$$W = \iint_A \vec{\mathbf{F}}(t,r,\theta) \bullet \vec{\mathbf{u}}(t,r,\theta) h_\theta \, dr \, d\theta \quad (5)$$

where $\vec{\mathbf{F}}(t,r,\theta)$ is the time-dependent external fluid loading. Assuming admissible displacement functions for u_r, u_θ, u_b, defining an energy functional as $F = U - W$, and integrating F in accordance with the variational principle result in a system of homogeneous equation as

$$[\mathbf{K}]\{\mathbf{c}\} - \{\mathbf{Q}\} = \mathbf{0} \quad (6)$$

where $[\mathbf{K}]$, $\{\mathbf{c}\}$, $\{\mathbf{Q}\}$ are the stiffness matrix, displacement coefficient and external loadings. Solving this homogeneous systems gives the response of the Watson-Crick DNA model subject to external fluid excitations.

For nonlinear large deformation analysis, some linear relations such as the strain-displacement relationships (3a-f) and strain energy (4) must be reformulated. A number of nonlinear terms comprising $(\partial u_b/\partial r)^2$, $(\partial u_b/\partial \theta)^2$ *etc.* will be involved. Combining with the fluid flow excitations, the governing equation may have to be solved repeatedly and recursively. Some root-finding numerical procedures such as Powell's hybrid algorithm, an improved variation of Newton's method, may be employed.

If thickness h to width b is of the order $O(10^{-1})$ or higher, first-order or higher-order displacement functions, depending on the thickness coordinate, must be adopted [14]. A three-dimensional elasticity model [15] on *one unit* (360^o) of the repeating helicoil may also be solved for more accurate solutions. All formulation and equations derived for a modeling in Figure 1(b) are valid for a helicoil model in Figure 1(c).

3 LOW-REYNOLDS-NUMBER FLUID EXCITATION

The organic fluid in the nucleus of a living cell, in which DNA is submerged, is highly viscous and undergoes low speed motion. Precisely, it has a low Reynolds number defined as

$$R_e = \frac{\rho U L}{\mu} \quad (7)$$

where ρ, U, μ are respectively the fluid density, speed, dynamic viscosity and L is a typical dimension. In investigating flows at low Reynolds numbers, it is customary to linearize the Navier-Stokes equations, in order to obviate a prohibitively difficult problem of obtaining complete analytical solutions. A useful method for solving such linearized flows is the singularity method, where the solution is expressed in terms of discrete or continuous distributions of fundamental singularities. This approach has recently been further extended to unsteady, time-dependent Stokes flows and general fundamental solutions in an arbitrary temporal domain were presented [13]. For the analysis of DNA dynamics, the organic fluid flow is governed by:

$$\nabla \bullet \vec{\mathbf{v}} = 0 \quad (8)$$

$$\frac{\partial \vec{\mathbf{v}}}{\partial t} + \vec{\mathbf{V}} \bullet \nabla \vec{\mathbf{v}} - \nabla\left[(\vec{\mathbf{\Omega}} \times \vec{\mathbf{x}}) \times \vec{\mathbf{v}}\right] = -\nabla p + \nabla^2 \vec{\mathbf{v}} + \vec{\mathbf{F}}(t,\vec{\mathbf{x}}) \quad (9)$$

where $\vec{\mathbf{V}}, \vec{\mathbf{\Omega}}$ are the flow velocity and angular velocity; $\vec{\mathbf{v}}, p$ are the disturbed flow velocity and pressure, $\vec{\mathbf{F}}(t,\vec{\mathbf{x}})$ is the time-dependent fluid force in the flow field $\vec{\mathbf{x}}$, related to the quantity in Eq. (5). A fundamental solution for the force is [13]

$$\left\|\vec{\mathbf{F}}\right\| = \frac{8\pi}{1 + 2K_0(t/4; R_e/4)} \quad (10a)$$

where

$$K_n(t;\alpha) = \frac{1}{2}\left(\frac{\alpha}{2}\right)^n \int_0^t \frac{e^{-\beta - (\alpha^2/4\beta)}}{\beta^{n+1}} d\beta \quad (10b)$$

Decomposing $\vec{\mathbf{F}}$ into F_r, F_θ, F_b and substituting them into Eq. (5), the work done by the fluid loading on the helicoidal

structure can be determined. In conclusion, solving the equation system (5) determines the unsteady dynamics of a DNA model.

4 CONCLUDING REMARKS

The paper is devoted to a new and rapidly developing field of life sciences, the non-linear physics of DNA. A theoretical modelling for helicoidal structures subject to viscous fluid excitations at a low-Reynolds-number is presented herewith. It aims to model nonlinear DNA dynamics biomechanically from a fluid-structure interaction approach. Constructing a physical model for systematic and consistent analysis of the internal biomechanical structure of DNA is significant and valuable. Besides cultivating an understanding of life science, the matching of DNA sequential characteristics with respect to the dynamical responses derived in this paper will reveal information regarding DNA sequencing by means of its twisting and bending motions.

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