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The geometrical origin of the strain-twist coupling in double helices

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A simple geometrical explanation for the counterintuitive phenomenon when twist leads to extension in double helices is presented. The coupling between strain and twist is investigated using a tubular description. It is shown that the relation between strain and rotation is universal and depends only on the pitch angle. For pitch angles below 39.4° strain leads to further winding, while for larger pitch angles strain leads to unwinding. The zero-twist structure, with a pitch angle of 39.4°, is at the unique point between winding and unwinding and independent of the mechanical properties of the double helix. The existence of zero-twist structures, i.e. structures that display neither winding, nor unwinding under strain is discussed. Close-packed double helices are shown to extend rather than shorten when twisted. Numerical estimates of this elongation upon winding are given for DNA, chromatin, and RNA.
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I. INTRODUCTION

Imagine pulling a double helix by the end, would it simply unwind by the applied tension? In this paper we show why this is not always the case: A helix can unwind, wind, or it can stay at its current twist (which we denote a zero-twist structure). Winding is contrary to unwinding; unwinding is the de-twisting of the helices obtained by stretching in the longitudinal direction. For the zero-twist structure there is no coupling from strain to twist.

For the description of compact strings and tube models, a curvature measure of non-local nature has been suggested to have significance for optimum shape, see Gonzalez and Maddocks[1] and Maritan *et al.*.[2] A related suggestion for the best packing of proteins and DNA has been advocated by Stasiak and Maddocks,[3] for DNA this packing has a pitch angle of 45° which is significantly different from that of the sugar phosphate backbone. A detailed analysis of the geometry of helices, and of their self-contacts, has been given by Przybyl and Pieranski,[4] Neukirch and van der Heijden,[5] and Olsen and Bohr.[6] Przbył has applied the ideal-knot-criterion to helices,[7] and Banavar *et al.*[8] have considered tubes which interaction depends on the amount of buried surface area. They find various motifs, both helical and strand-like.

The geometrical investigation presented below is based on the study of double helices modeled as two flexible tubes with hard walls. The first requirement is that the strands are excluding each other from their volumes. This simply follows from the strands being treated as having hard walls. Secondly, we assume that the strands are in contact with each other, i.e. that the helices are packed. This is the first step of including the attractive forces. When estimating the extension of a specific helix, e.g. the RNA double helix, we use the ideal close-packed motif as a generic starting point. This means that for these molecules we make the conjecture that the net effect of all the molecular forces is to form a helix that to a good approximation optimizes its volume fraction.

For the α-helices and for DNA we have previously found that this conjecture reproduces the pitch angels of the molecular structures within $\sim 2^\circ$.[6] This was based on an analysis of the volume fraction of packed helices. Specifically by determining which of the packed helices has the largest

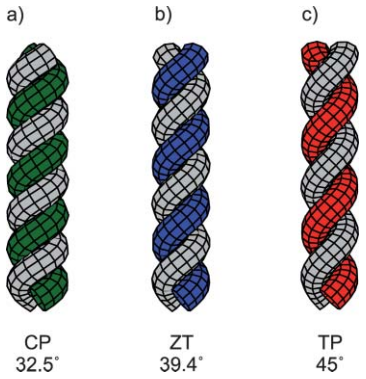

FIG. 1. *Different geometries of a double helix of tubes of fixed diameter D with an increasing pitch from left to right.* **a)** *Close-packed (CP) structure of pitch angle* 32.5° *measured from horizontal.* **b)** *Zero-twist (ZT) structure with a pitch angle of* 39.4°. *It is at the point between winding/unwinding.* **c)** *Tightly-packed (TP) structure of pitch angle* 45°. *Stretching provoke winding from a) to the b) confirmations, and unwinding from b) to c).*

volume fraction. This suggests that in these cases close-packing is at work as a principle for formation of molecular structures.

II. MODEL

Certain helices have distinct properties. One example is the close-packed double helix briefly mentioned above. This unique helix has an optimized volume fraction and a pitch angle of 32.5°:[6] This structure that has a central channel is shown in Figure 1(a). Under a pull, the pitch angle is increased and the diameter of the central channel gets smaller, and eventually, the inner channel disappears at a pitch angle of 45°. Whether a helix winds or unwinds is then determined from the balance between the gain in length from the reduction in the helical radius versus untwisting. The crossing point – which we denote as the *zero-twist* angle – is at 39.4° (Figure 1(b)) and is smaller than the 45°, where the helical radius becomes equal to the diameter of the tubes, and is maintained for all pitch angles above 45°. The 45° motif, here denoted the tightly packed (TP) double helix, is shown in Figure 1(c).

Geometrically, the double helix is given by two tubes of diameter D, whose centerline defines two helices with simple parametric equations. A helix is a curve of constant curvature, κ, and torsion, τ, and it can be specified by two parameters, for example a and H, where a is the helix radius (the radius of the cylinder hosting the helical lines) and H the helical pitch (the raise of the helix for each 2π rotation). The tangent to each of the helical curves is at an angle $v_\perp$ (*the pitch angle*) with the horizontal axis, and it is determined by $\tan v_\perp = h/a$, where $h = H/2\pi$ is the reduced pitch. We say that the double helix is packed when the shortest distance between the centerline of one helical tube to the next one equals the diameter D of the tubes, i.e. the double helix is packed when the tubes are in contact.

The volume fraction can be calculated using, as a reference volume, an enclosing cylinder of height $H = 2\pi h$ and volume $V_E = 2\pi^2 h(a + D/2)^2$, and comparing it to the combined volume occupied by the two circumscribed helical tubes, $V_H = \pi^2 h D^2 / \sin v_\perp$. The volume fraction is the ratio of the two volumes, i.e. $f_V = V_H / V_E$, which reads

$$f_V = 2(1 + (\frac{a}{h})^2)^{1/2} \cdot (\frac{2a}{D} + 1)^{-2} \tag{1}$$

With this choice of reference volume the packing fraction depends only on the shape of the double helix structure, which can be described by one parameter, e.g. the pitch angle, $v_\perp$. The maximum of f_V defines the close-packed (CP) helix. For the double helix this maximum is at $v_{CP} = 32.5°$, where $f_{CP} = 0.769$.[6]

The diameter of the CP helix is larger than the strand diameter, i.e. $2a > D$. This means that the tubular CP double helix has a central channel; the channel radius is about 17 % of a.[6] Generally,

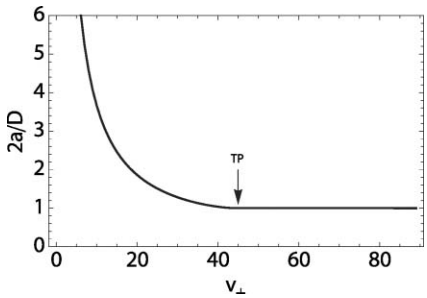

FIG. 2. *Graph showing the ratio $2a/D$ as a function of pitch angle, $v_\perp$ [deg.], where a is the helix radius and D the diameter of the helical tubes. The tightly packed double helix has a pitch angle of $v_{TP} = 45°$; it is the helix with the smallest pitch angle obeying the criterion that $2a = D$. The calculation is reproduced from ref. 6.*

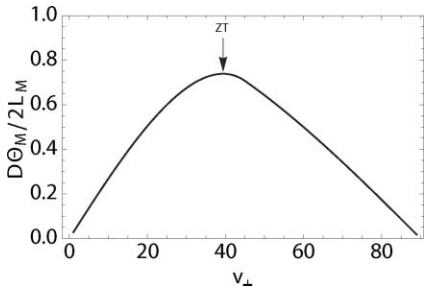

FIG. 3. *The total twist, θ_M, for a long segment of the double helix; the dimensionless quantity $D\theta_M/2L_M$ is shown as a function of the pitch angle, $v_\perp$ [deg.]. The maximum value is obtained for the pitch angle $v_{ZT} = 39.4°$ and mark the transition from winding to unwinding. At the ZT structure there is zero coupling between twist and strain.*

the radius of the central channel, which is given by $R_i = a - D/2$, is a decreasing function of $v_\perp$. Its variation with the pitch angle is important for the strain-twist coupling. Therefore $2a/D$ as a function of the pitch angle is shown in Figure 2. The details of the calculation is given in ref. 6, it involves finding the inter-strand contacts from the requirement that the centerline of the strands at these points are precisely a distance D apart

$$D^2 = \min_{t\in[-\pi;0]} (\,2a^2(1-\cos t) + h^2(t+\pi)^2\,) \tag{2}$$

where t defines the contact-point on the strand given with the parameterization

$$\vec{r} = (a\cos t, a\sin t, h(t+\pi)) \tag{3}$$

For $v_\perp \geq 45°$ the solution to the inter-strand contact problem is trivial and therefore $2a/D = 1$, see Figure 2.

III. RESULTS

Consider a long straight segment of a double helix consisting of two long molecular strands each of length L_M. The length of the double helix is $H_M = L_M \sin v_\perp$ and the total twist is $\Theta_M = L_M \cos v_\perp/a$. In Figure 3 the dimensionless ratio $D\theta_M/2L_M$ is shown as a function of the pitch angle. One can see that for $v_\perp < v_{ZT}$ there is winding while for $v_\perp > v_{ZT}$ there will be unwinding. We find numerically that $v_{ZT} = 39.4°$.

We can determine the amount of winding and unwinding in the following way. If a long double helical segment is stretched a bit the pitch angle, $v_\perp$, will change by a small amount $dv_\perp$, and hence H_M changes by

$$dH_M = L_M \cos v_\perp dv_\perp \tag{4}$$

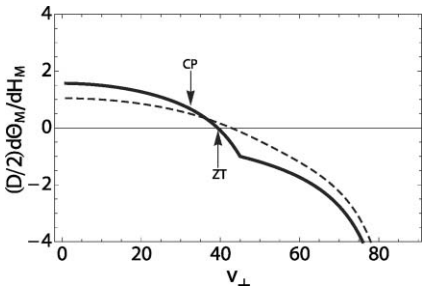

FIG. 4. *Differential twist calculated for double helices (solid line), i.e. Eq. (7) as a function of* $v_\perp$ *[deg.]. A positive value means that the double helix will exhibit further winding, while a negative value means that the double helix will exhibit unwinding. The zero-twist structure (ZT) is indicated with an arrow at* $v_{ZT} = 39.4^\circ$*, the close-packed structure (CP) is indicated by an arrow at* $v_{CP} = 32.5^\circ$*. The derivative is discontinuous at* $v_{TP} = 45^\circ$ *where the helix radius cannot get smaller. The dashed line is the corresponding calculation for a triple helix, which has a zero-twist angle of* 42.8°.

and Θ_M by

$$d\Theta_M = -L_M \frac{\sin v_\perp}{a} dv_\perp - \frac{L_M}{a^2} \cos v_\perp \frac{da}{dv_\perp} dv_\perp \tag{5}$$

so that

$$\frac{d\Theta_M}{dH_M} = -\frac{1}{a} \tan v_\perp - \frac{1}{a^2} \frac{da}{dv_\perp} \tag{6}$$

If this derivative is positive, then the helix will wind, and if it is negative, it will unwind. The derivative in Eq. (6) has dimension of inverse length. From a geometrical viewpoint it is more natural to look at the dimensionless function of $v_\perp$, obtained by multiplying with the common radius of the tubes, $D/2$, namely:

$$\frac{D}{2} \frac{d\Theta_M}{dH_M} = -\frac{D}{2a} \tan v_\perp + \frac{d}{dv_\perp} \left(\frac{D}{2a} \right) \tag{7}$$

This equation can be given a simple interpretation. The first term is negative and determines the amount of unwinding, while the second term is positive and determines the amount of winding. The graph of this derivative, that dictates the coupling between strain and twist, is depicted in Figure 4. Notice that the CP double helix will always wind since $d\Theta_M/dH_M > 0$. At the close-packed structure, $v_{CP} = 32.5^\circ$, the differential twist is $(D/2)d\Theta_M/dH_M = 0.665$. The extension is therefore universally determined just by giving the diameter, D, of the tubes making up any close-packed double helix. At the zero-twist structure, $v_{ZT} = 39.4^\circ$, there is neither winding, nor unwinding. For larger pitch angles $(D/2)d\Theta_M/dH_M$ is negative and the double helix will unwind under strain. It is therefore crucial, that the pitch angle is below that of the zero-twist (39.4°) for winding to be observed, and it shows that elastic properties of the material are not essential to understanding the phenomenon.

IV. MOLECULAR EXAMPLES

In the following we discuss some molecular examples and estimate the elongation based on our simple model. For small deformations, DNA winds when stretched, i.e. it rotates counter to unwinding. This phenomenon for DNA was first observed in 2006, see Lionnet *et al.*[9] and Gore *et al.*[10] using magnetic tweezers to control the wringing[9] and optical tweezers to control the pulling;[10] it has been denoted *overwinding* by Gore *et al.* During overwinding the extension of a long chain of DNA-B has been reported to be 0.42 ± 0.2 nm per 2π rotation[9] and 0.5 nm per 2π rotation.[10] It follows from the discussion below that using a double helix tubular description for DNA leads to a theoretical estimate which is about one order of magnitude larger. There is an ongoing discussion about some of the mechanical properties of DNA. Mathew-Fenn *et al.* have suggested that in the

absence of tension DNA is an order of magnitude softer than previously assumed.[11] For a current discussion of the flexibility of DNA, see Peters and Maher III.[12]

Using the above mathematical solution for the symmetric double helical structure we find the change of length ΔH to be determined by

$$\Delta H = \frac{dH_M}{d\Theta_M}\Delta\Theta \tag{8}$$

The diameter of the molecular tubes that make up the DNA helix is $D = 1.15$ nm, which is given from our previous analysis of the close-packed structures.[6] We therefore estimate ΔH per full 2π turn to be $\pi(0.665)^{-1} \times 1.15$ nm $= 5.4$ nm, see Figure 4. The geometrical restriction imposed by base pairing and its influence on $d\Theta_M/dH_M$ has not been taken into account. The numerical analysis has been performed for the symmetrical double helix where the close-packed structure has a pitch angle of 32.5°. The asymmetrical DNA-B has a close-packed pitch angle of 38.3° and, as one can show, a zero-twist angle of 41.8°.

For chromatin, the above results can be related to recent experiments in twisting chromatin fibers, see Bancaud *et al.*[13] and Celedon *et al.*.[14] For a close-packed 30 nm chromatin fiber, in the so-called two-start geometry, we estimate a tube diameter of $30/(2a/D + 1)$ nm$= 30/(1.2 + 1) =$ 14 nm, where $2a/D$ is determined from Figure 2. For the close-packed 30 nm chromatin structure we then estimate ΔH per full 2π turn to be $\pi(0.665)^{-1} \times 14$ nm $= 66$ nm. It is interesting to note that the numbers reported in ref. 14 are measurements of ΔH for *Xenopus* chromatin per turn at a pulling force of 0.3 pN. Using the depicted data in ref. 14 we have estimated an average extension of $\sim 60 \pm 40$ nm per turn. Above, we have assumed the two-start helix to behave like a tubular packed double helix – that is a view which ignores the intricate details of the structure, such details are discussed for chromatin by Barbi *et al.*,[15] with elaborate mechanical models, including one which maintain its twist while being stretched.

Necturus chromatin fibers, see Williams *et al.*,[16] are known to pack akin to double helix with a pitch angle of $v_\perp = 32 \pm 3°$, a value suggestive of being close-packed. Thus it follows that these chromatin fibers will wind-up (this would not necessarily be the case for chromatin fibers with a different linker length). For the RNA double helices, see Baeyens *et al.*,[17] we predict that winding will occur. Using a value of ~ 26 Å for the molecular diameter of the RNA double helix, from Varshavsky,[18] we estimate an elongation of 5.6 nm per 2π rotation. For an overview of how to use magnetic traps for the study of winding and unwinding of single biomolecules see Meglio *et al.*.[19]

Theoretical work on understanding the overwinding of DNA has focused on constructing elastic models which show a negative twist-stretch coupling, see Sheinin and Wang,[20] and Bernido and Carpio-Bernido[21] has incorporated stochastic effects. One elastic model was considered by Gore *et al.*,[10] and consists of a rod with a stiff helical wire attached to its surface. As this system is stretched, the inner rod decreases in diameter and the helix will overwind. Smith and Healey has argued that a linear material law is inadequate for the description and suggest a non-linear elastic rod.[22]

How would our estimates change if we included elastic terms? Tube models offer two simple ways of introducing elastic terms. One is to maintain hard walls but to introduce an elastic energy typically with quadratic terms in the curvature and in the torsion of the individual strands. This leads to the same packed helices. However, which one of these packed helices minimizes the energy will depend on the chosen Hamiltonian. This is in contrast to our approach where we assume that the net result of all the molecular forces is well described by close-packing. By taking a geometrical approach we stress that some of the properties simply originate from having a double helical structure.

The other way to introduce elasticity is to relax the hard wall criterion and introduce distance dependent forces perhaps with a typical van der Waals parameterization. If the interaction is only perpendicular to the strand one obtains structures that optimize the line defining the interactions between the strands (akin to the contact line for tubes with hard walls). Presumably, if van der Waals like forces are implemented fully in three dimensions one would get a structure which is in fair agreement with the close-packed structure.

For the DNA structure it is worthwhile to consider the base pairing. The pitch of the DNA helix is such that there is a channel. It is in this channel that the base pairing takes place, i.e. the structure

takes advantages of having the channel for additional features, e.g. base pairs. Their length must be approximately right for close-packing. Can the theoretical estimate for DNA and the experimental numbers be in better agreement if the base pairing geometry is considered? In the tube model there is an additional freedom, namely, the screw operation (combined translation and rotation) of one strand upon itself. With base-pairs that can tilt this will change their angle and therefore allow for the central channel to adjust its width proper. On the other hand, if the base pairs are not allowed to tilt then they would enforce a constant channel diameter, thereby prevent packing of the strands. In this case only unwinding will transpire.

V. CONCLUSION

Our intend with this paper is to see if we can understand the phenomenon of winding from simple assumptions without free parameters for adjustment. The result is a simple geometrical explanation based on the behavior of tubular double helices. The winding of helices under tension is an effect which has been observed before for the double helix of DNA and for chromatin, and which is contrary to usual unwinding. Our model of unwinding and winding can be applied to any symmetric double helix which is packed in the sense that the two helices touch and remain at the distance D from each other. Packed double helical structures will show a winding behavior similar to those already observed, as long as their initial pitch angle is sufficiently small, i.e. below 39.4°. In particular this is the case for double helices that are close-packed. Perhaps, the analysis will be relevant for other helical structures such as nanofabricated quartz cylinders, see Deufel *et al.*,[23] fabricated twisted polymer nanofibers, see Gu *et al.*,[24] and for the beautiful double helical structures formed from helical carbon nanotubes, see Liu *et al.*.[25] Further, the phenomenon may be important for some aspects of the working of molecular motors during gene expression and regulation, for a review see Michaelis *et al.*.[26]

The derived geometrical expressions for double helices are straightforwardly extended to helices with more than two strands. In Figure 4 we have shown also the solution for a triple helix (dashed line) which has a zero-twist angle of 42.8°. Maybe one will even find examples, where Nature has build zero-twist structures, i.e. structures that display neither winding, nor unwinding. Chromatin with an appropriate linker length, and collagen are possible candidates for structures with such properties. The case of collagen is discussed in details in ref. 27.

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