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On the mean and variance of the writhe of random polygons

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Abstract

We here address two problems concerning the writhe of random polygons. First, we study the behavior of the mean writhe as a function length. Second, we study the variance of the writhe. Suppose that we are dealing with a set of random polygons with the same length and knot type, which could be the model of some circular DNA with the same topological property. In general, a simple way of detecting chirality of this knot type is to compute the mean writhe of the polygons; if the mean writhe is non-zero then the knot is chiral. How accurate is this method? For example, if for a specific knot type K the mean writhe decreased to zero as the length of the polygons increased, then this method would be limited in the case of long polygons. Furthermore, we conjecture that the sign of the mean writhe is a topological invariant of chiral knots. This sign appears to be the same as that of an “ideal” conformation of the knot. We provide numerical evidence to support these claims, and we propose a new nomenclature of knots based on the sign of their expected writhes. This nomenclature can be of particular interest to applied scientists. The second part of our study focuses on the variance of the writhe, a problem that has not received much attention in the past. In this case, we focused on the equilateral random polygons. We give numerical as well as analytical evidence to show that the variance of the writhe of equilateral random polygons (of length n) behaves as a linear function of the length of the equilateral random polygon.

1. Introduction

In the early 1960’s, polymer scientists conjectured that in long polymer chains knots would occur with almost sure certainty (Frisch-Wasserman- Delbrück Conjecture [15, 26]). This conjecture was proved for several polymer models [17, 21, 55, 68] and verified experimentally on randomly circularized DNA chains [6, 46, 57, 60]. This result has important implications on the study of long polymer chains in the physical and natural sciences.

How a circular DNA molecule is knotted and the extent of its topologically entanglement are important questions in the study of DNA. Many biochemical processes can be characterized by the topological changes they induce in their DNA substrates. Examples include the topological mechanism of site- specific recombinases (reviewed in [8, 67]) and of topoisomerases (*e.g.* [58, 73]), and the packing of DNA in certain bacteriophages [5, 7, 48].

The knot type and complexity of a circular polygonal chain can often be determined theoretically [1, 12, 14]. In the case of circular DNA such information is not always easy to retrieve, specially for long DNA molecules. In this case, one turns to measures of complexity that are easier to observe experimentally and yet still can be used to detect the average overall knot complexity of the molecules. The average crossing number (ACN) is one such example. The ACN of a fixed polygonal realization of a certain knot type is defined as the average of the number of crossings over all possible projections of the polygon. When the ACN is averaged over all realizations of the knot type (or a well defined statistical ensemble of such realizations), we refer to the resulting number as the *mean ACN* and denote it by $\langle \text{ACN} \rangle$. Another appropriate name for the mean ACN is *expected crossing number*. Although the ACN is not a knot invariant, its average over the entire statistical ensemble of polygons with a given length (mean ACN) correlates well with the expected sedimentation coefficient of different types of DNA knots of equal length [72]. In other words, if we see a polygon with a high ACN, then there is a good chance that the polygon has a complicated knot type. Furthermore, the ACN of knotted DNA molecules can be detected experimentally [45, 62, 70] and a number of theoretical properties are known about the mean ACN [4, 18, 19, 22, 61]. In this paper, we are interested in a different measure, also motivated by biological problems, called the writhe.

The writhe provides a measure of chirality. The writhe of unknotted DNA molecules is a direct measure of their level of supercoiling. In the case of knotted DNA, the writhe is believed to influence DNA packing [7] and to play an important role in the biological activity of certain enzymes such as condensins [41, 66] and topoisomerases [65]. The writhe of random polymer models has been studied under different settings [20, 27, 33, 43, 44, 49, 52, 69], and topological invariants have been proposed to predict it [13]. In particular, the behavior of the writhe of ideal knots has been studied in [13, 23, 39, 40, 54, 53].

Let K be a knotted polygonal chain in $\mathbb{R}^3$. The *writhe* of K , denoted by $w(K)$, is the average of the projected writhe taken over all projections of K . Given a knot diagram D_K (i.e. a regular projection of K distinguishing over- and under-crossings) the *projected writhe* of D_K is computed by assigning a ± 1 to each crossing according to the convention in Figure 1. We define the *mean writhe* of a knot K for some specific length n as the writhe averaged over all n -edge realizations of the knot. We define the *overall mean writhe* of K as the writhe averaged over all realizations of K (over all lengths).

Mathematically, the writhe and the ACN are similar in terms of their definition and ease of computation. The writhe of a knot can be thought of as the signed generalization of the ACN. Like the ACN, the writhe of a knot is not a knot invariant, but is a measure that traps geometrical and topological information about the knot. In general, the writhe contains more topological information than the ACN. For example, the mean ACN of all polygons with the same knot type and length (which is likely to be a large positive number if the polygons are long) cannot tell us whether the polygons are knotted, nor how complicated the knots are. On the other hand, a nonzero mean writhe of an ensemble of polygons of the same length and knot type would indicate that the knot type of these polygons is nontrivial and is in fact chiral.

This paper focuses on two important issues regarding the writhe of random polygons. First, we study the behavior of the mean writhe of random polygons as a function of length. Random polygons are sampled from the ensemble of polygons of fixed length L and knot type K . Second, we study the variance of the writhe (when the writhe of a random polygon is treated as a random variable).

The motivation for studying how mean writhe changes with respect to length is to establish a correspondence between the knot type of a population of random knots and its mean writhe. Given a population of knotted DNA molecules of fixed unknown knot type, estimating its mean writhe could help determine the chirality and knot type of the molecules. Here we generate large ensembles of random polygons with a given knot type with eight or less crossings, and we study the relationship between the sign of their mean writhe and their knot type.

Consider the ensemble of all polygons of fixed length and knot type. We conjecture that the sign of the mean writhe of this ensemble is a topological invariant of chiral knots. Our numerical data, presented in section 3, give support to this claim. In view of this we propose a new nomenclature of chiral knots as follows: consider a chiral pair (K_1, K_2) of a given knot type K , K_i will be called K if the mean writhe of K_i is positive, otherwise it is called the mirror image of K and is denoted by K^* . Furthermore we conjecture that if the writhe of an “ideal knot” with knot type K is a nonzero constant $w_I(K)$, then the mean writhe of the random polygons with knot type K and length n approaches a constant that is close to $w_I(K)$ as n goes to infinity. This gives rise to the following question: is $\text{sign}(w_I(K))$ the same as the the sign of the mean writhe of the population of all random polygons of same length and knot type? The concept of an ideal shaped polygon is similar to that of “maximally inflated knots” defined in [29] where knotted ring polymers were studied. Early introductions to the concept of an ideal knot include [29, 51, 63]. Related studies can be found in the various articles collected in [64]. For lattice knots we here define an ideal conformation to be one with minimum step number. Minimum step number conformations are described in [36, 59]. This definition of ideal lattice knot is related to that given in [36].

The second question, which involves the variance of the writhe, is motivated by computer simulations of DNA packing in bacteriophages that suggest that the DNA molecule inside the bacteriophage capsid is chirally organized [7]. Simulations of random polygons biased by the writhe have been performed in order to establish the interplay between the values of the writhe and the knotting probability and distribution [7, 9, 11, 56]. However these simulations were performed without estimating the variance of the writhe. By a symmetry argument it is easy to see that the mean writhe of all random polygons of the same length is zero (regardless of which model is used, so long as the model is not biased toward any particular configuration). In the case of lattice polygons, it has been shown that the mean absolute writhe (namely the expected value of the absolute value of the space writhe) is bounded below by $O(\sqrt{n})$ where n is the number of edges of the polygons [33, 35, 50]. Similar observations have been made for the wormlike chain [42]. In the case of uniform random polygons (URPs) in a confined volume, it has been shown that the variance of the writhe behaves as $O(n^2)$ [52]. However, there has not been any specific study on the variance of the writhe in the case of equilateral random polygons. We here provide

numerical evidence that the mean writhe can be used to detect the chirality of random polygons with fixed knot type (and length). In order to have an accurate estimate of the mean writhe, one needs to generate large uncorrelated ensembles which uniformly explore the space of all configurations. Understanding the behavior of the variance of the writhe in general will be helpful in increasing the power of the chirality detection method. Partial analytical results lead us to conjecture that the variance of the writhe (of all equilateral random polygons of length n) behaves as $O(n)$, where n is the length of the polygon. Our numerical results strongly support this conjecture.

The paper is organized as follows. In Section 2, we give a brief introduction to key concepts in knot theory. In Section 3, we present the results of our numerical study on the mean writhe of polygons with fixed knot type on and off-lattice. From the observations of these numerical results we outline several questions and conjectures. In Section 4, we discuss the variance of the writhe of equilateral random polygons. In Section 5 we discuss the findings in the context of the conjectures proposed in earlier sections, and we pose some questions for future study.

2. Basic concepts and terminology of Knot Theory

In this section we offer an informal discussion of basic knot theory. The interested reader is referred to [1, 12, 14] for more precise definitions.

Throughout this paper, a *knot* K means a simple closed curve in 3- dimensional space $\mathbb{R}^3$. Two knots K_1 and K_2 are topologically equivalent if one can be continuously deformed into the other without self-intersection. The collection of all knots that are *topologically equivalent* is called a *knot type* and is denoted by K .

For a fixed knot embedding K , a knot diagram D_K is a regular projection of K onto a plane with over and under-crossings specified. A projection is regular if every crossing is at most a double crossing (*i.e.* no more than 2 strands cross at any point in the projection) and all crossings are transverse. The number of crossing points in D_K is called the *crossing number* of that diagram. The crossing number of D_K not only depends on the knot type of K , it also depends on the geometrical shape of K and the projection direction chosen. The minimal number of crossings over all regular projections of all embeddings of the knot K is called the *crossing number* of the knot K and is denoted by $Cr(K)$. By this definition, if K_1 and K_2 have the same knot type, then $Cr(K_1) = Cr(K_2)$. Note that there will always be embeddings of K for which none of the regular projections has crossing number $Cr(K)$.

Upon assigning an orientation to the knot embedding K , one can assign a ± 1 at each crossing in a regular diagram D_K of K using the rule shown in Figure 1. The *writhe* of D_K is the sum of these signed crossing numbers and is denoted by w_{D_K} . The average of w_{D_K} over all possible projections of K is defined as the *writhe* of K and is denoted by $w(K)$. The writhe of a knot K depends on the geometry of K and is not a knot invariant. Note that the writhe of a knot diagram is independent of the chosen orientation of the knot, while a knot diagram and its mirror image have opposite writhe values, since a crossing and its mirror image have opposite signs (Figure 1).

Empirically, the writhe of a knot K in $\mathbb{R}^3$ is estimated by taking a set of regular projections of K chosen uniformly over all possible directions, and averaging the writhes of the corresponding diagrams. Alternatively, one can use the following Gaussian integral formula to compute the writhe directly:

$$w(K) = \frac{1}{2\pi} \int_K \int_K \frac{(\dot{\gamma}(t), \dot{\gamma}(s), \gamma(t) - \gamma(s))}{|\gamma_1(t) - \gamma_2(s)|^3} dt ds, \quad (1)$$

where γ is the arclength parameterization of K and $(\dot{\gamma}(t), \dot{\gamma}(s), \gamma(t) - \gamma(s))$ is the triple scalar product of $\dot{\gamma}(t)$, $\dot{\gamma}(s)$, and $\gamma(t) - \gamma(s)$.

If a knot K is topologically equivalent to its mirror image, then K is said to be *achiral*. Otherwise, K is *chiral*. If a knot K is chiral, then any K' equivalent to K is also chiral. In [34] it was shown that if the expected value of the writhe of a knot is not zero, then the knot is chiral. This implies that the mean writhe is a good measure for detecting the chirality of the knot type of random polygons. Furthermore, one can ask whether the writhe of an ideal conformation of a knot K is always different than 0 for chiral knots. This question is further discussed in section 3. In the following lemma we reformulate the theorem from [34] for random polygons.

Lemma 1

[34] *Let $P(K, n)$ be the set of all polygons of length n and of knot type K . If the mean writhe of the polygons in $P(K, n)$ is nonzero, then K is a nontrivial knot and is chiral. Here polygons can be self-avoiding polygons in the simple cubic lattice, equilateral random polygons, Gaussian random polygons, uniform random polygons or any other random polygons that do not favor any polygon over its mirror image.*

Proof

If K is achiral (which would include the trivial knot), then for each realization of a nonzero writhe value by a polygon, there is a writhe value of the opposite sign by the mirror image of the polygon (since the mirror image of the polygon is also in $P(K, n)$ given that K is achiral). Thus the mean writhe of $P(K, n)$ is zero.

A key issue in knot theory (and this paper) is how to identify different knots. A polynomial invariant of knots can be computed from any knot projection and is invariant so long as the projections represent the same knot type. The Alexander polynomial and the HOMFLY polynomial are a few of the well known and commonly used knot polynomials. We will not go into the details about how these polynomials are defined and computed. The reader is referred to a standard knot text for more information [1, 12, 14]. Each of these polynomials has its own strengths and weaknesses. For example, the Alexander polynomial is reasonably good at distinguishing knots and links of up to 8 crossings but does not distinguish between a knot and its mirror image. The HOMFLY polynomial unambiguously distinguishes all knots (including mirror images) with 9 or fewer crossings except for 9.42 which has the same HOMFLY as its mirror image (despite being chiral). On the other hand the Alexander polynomial is much easier to compute than the HOMFLY polynomial. We use the HOMFLY polynomial in section 3.3 to separate ERPs by knot type. Polynomial invariants

are reviewed in [1, 14], the HOMFLY polynomial was first introduced in [25], we use implementations from [28, 38] in our work.

3. The mean writhe of random polygons with fixed knot types

In this section, we explore the mean writhe of random polygons with fixed knot type. In order to carry out a numerical study with significant results, we need to generate, for various lengths, large ensembles of random polygons with fixed knot types. Unfortunately, there are no known fast algorithms that generate such data for the off-lattice random polygons. The case of off-lattice polygons is discussed in section 3.3. In section 3.1, we focus on polygons in $\mathbb{Z}^3$. For the lattice polygons, there is a well known and fast algorithm called BFACF [2, 3, 10]. In section 3.2, we discussed questions and conjectures arising from this study.

3.1. The case of self-avoiding polygons on the cubic lattice

The BFACF algorithm is a dynamic Monte Carlo method that operates on paths in $\mathbb{Z}^d$ and samples along the realization of a Markov chain (reviewed in [47]). In 3D, the Monte Carlo method generates a Markov chain that is reducible and whose ergodicity classes are the knot types [37]. The BFACF has one adjustable parameter, z . Fixing z results in a specific mean length. We used the BFACF algorithm to generate ensembles of lattice polygons for all knot types up to eight crossings. Independent runs were performed for polygonal lengths ranging from 75 to 350. This process is also described in [30]. We computed the mean writhe of lattice polygons for all knot types up to 8 crossings and for polygonal lengths ranging from 75 to 350. We ran a standard independence test to ensure that all polygons in our study are essentially independent. Different runs were used to generate ensembles of polygons of different lengths, z values were optimized for each mean length and for each knot type. For achiral knots (*i.e.* $0_1, 4_1, 6_3, 8_3, 8_9, 8_{12}, 8_{17}, 8_{18}$) the mean writhe is zero and our numerical estimates are in strong agreement with this expected value, hence are omitted from the Table 1. For each given chiral knot type, we sampled 5000 uncorrelated lattice polygons with length L , where $L \in \{75, 100, 150, 200, 250, 300, 350\}$. In each of these cases, the mean writhe is clearly either positive or negative. Is this true in general? This is a very difficult question to answer. We believe that knot types which are counterexamples to this question are rare (if they ever exist). This suggests that chiral knots can be naturally organized and named according to the sign of their mean writhe. In this new *naming convention* we propose that a knot be denoted by K if its mean writhe is positive, and by K^* if its mean writhe is negative. For example, the results summarized in Table 1 are for all chiral knots K (up to 8 crossings) with $L \in \{75, 100, 150, 200, 350\}$. Although in theory, the mean writhe of a chiral knot K and the mean writhe of K^* differ only by a sign, our numerical studies include both of them to ensure that our sampling algorithm is unbiased. This is indeed the case. In all cases in our study, the mean writhe of K^* is within the negative 99% confidence interval of the mean writhe of K (with similar confidence interval lengths).

For the purpose of cross reference, in Table 2 we compare our results with those reported in [34, 35]. The first column in Table 2 shows the overall mean writhe of self-avoiding polygons in the cubic lattice averaged over fixed knot types of lengths 75, 100, 150, 200, 250, 300, and 350, while the last column in Table 2 shows published numerical estimates of the overall mean writhe for lengths up to 250 segments in [34, 35]. The error bars reported

here are set at the 68% confidence level as in [34]. In [35] the authors provide comparisons with experimental data and ideal knot data from [39]. Our results are in very good agreement with those data.

From our numerical data we observe that the mean writhe values are stable, *i.e.* as the lengths of the polygons increase, the mean writhe values only fluctuate within a narrow interval. The interval does not include zero for any of the chiral knots in our study (which include all knots up to 8 crossings). This was also observed in [9, 34, 35]. These results suggest that the mean writhe of a set of random polygons (of fixed knot type) fluctuates around an “ideal” mean writhe. This is similar to the results of [39], where the ACN of simulated DNA chains was compared with that of “ideal” forms with the same knot type.

The random polygons studied in this section are self-avoiding polygons in the cubic lattice. In this context we consider minimal edge polygons of a given knot type to be “ideal” shapes for that knot type. This concept of “ideal” lattice polygons is related to the one suggested in [36]. Theoretical and computational studies of minimal lattice knots include [16, 31, 32, 36]. Our group reported numerical estimates for the number of minimal edge conformations of lattice polygons with 9 and less crossings in [59]. For example, an ideal polygon for the trefoil knot has length 24 and there are 1664 such configurations for the right-hand trefoil [16, 59]. We define the *ideal mean writhe* of K , and denote it by $w_I(K)$, as the writhe averaged over all minimal edge conformations of the knot. We computed $w_I(K)$ values based on the data from [59] (Table 3). Comparison of tables 1 and 3 suggests that for each knot type the mean writhe of the random knots fluctuates around the ideal mean writhe. No claim is made that ideal shapes have any direct resemblance to the random knots, instead properties of the ideal are reflected in ensemble averages of the random simulations.

Figure 2 is a comparison between the mean writhe values for different lattice knots of length 200 and the ideal mean writhe of lattice polygons of same knot type. Specific knot types are not shown in the figure.

3.2. Some questions and conjectures

From these observations we state the following questions and conjectures.

Question 1—Can the mean writhe of random polygons of a given knot type and fixed length be approximated by the mean writhe of the corresponding ideal minimum step conformation? This will be numerically checked in a future study by enumerating all random polygons of a given knot type with a fixed (but not minimum) length. The current work supports the following conjecture.

Conjecture 1—Let K be a knot and $w_I(K)$ be the mean writhe of the ideal minimal step conformations of K (*i.e.* in the lattice). There exists a constant α_K such that the mean writhe of a random lattice polygon of the same knot type K with length n belongs to $(w_I(K) - \alpha_K, w_I(K) + \alpha_K)$, independently of the value of n .

Question 2—Is it true that $w_I(K) = 0$ for any chiral knot K ?

Although this appears to be true for all knots we have studied, our study only covered knots with eight or less crossings. It is important to point out that the ideal lattice knot conformations are not easy to enumerate in general. The ideal lattice polygons used in Table 3 were obtained in [59] by numerical simulations. The polygonal lengths thus obtained are upper bounds of the true minimum step number. Precise minima supported by analytical proofs are only known for 3_1 , 4_1 and 5_1 [16, 59]. Likewise the list of ideal polygons obtained numerically has not been proven to be exhaustive. Furthermore, we do not have a good theoretical explanation or intuition to support an affirmative answer to this question for knots with more than eight crossings. However, in order to use the mean writhe as a way to detect chiral knots, one does not need an affirmative answer to Question 2 (which is perhaps too strong to be true). Instead, a confirmation of the following conjecture would be good enough.

Conjecture 2—Let K be a chiral knot and $w_I(K)$ be the mean writhe of the ideal conformations of K (on the lattice). Then in most cases $w_I(K) \neq 0$ and the constant α_K mentioned in Conjecture 1 is such that $0 < \alpha_K < |w_I(K)|$. That is, the mean writhe of a random lattice polygon of the same knot type K with length n belongs to an interval that does not contain 0, regardless how large n is.

Notice that the above conjecture is deliberately stated in a somewhat vague manner. One could interpret “most cases” in many different ways. It is obviously a very difficult problem to determine the proportion of chiral knots with the property stated in Conjecture 2. If Conjecture 2 were true in general, then the mean writhe would indeed be a very useful tool in detecting most chiral knots. Specifically, we propose the use of the sign of the mean writhe as a topological invariant to distinguish a chiral knot from its mirror image. As a convention, we propose the following nomenclature of knots: denote a chiral knot by K if its mean writhe is positive, and its mirror image by K^* (which would have a negative mean writhe). In this way a chiral knot is naturally associated with the sign of its mean writhe. Currently, knots are not presented uniformly in this manner in the literature. This paper (as well as [59]) uses this convention.

3.3. The case of off-lattice random polygons

Finally, let us end this section with some discussion on off-lattice knots in $\mathbb{R}^3$, more specifically on the equilateral random polygons that will be discussed in more detail in section 4. Conducting a thorough study like the one above for equilateral random polygons is very challenging. Although it is not difficult to generate large ensembles of equilateral random polygons of various lengths, it is extremely difficult to do so with fixed knot type. This is due to the fact that the commonly used crankshaft algorithm and the generalized hedgehog algorithm sample over the entire space of equilateral polygons [71]. To generate a large ensemble of polygons with a given knot type we take the following approach. First we use the crankshaft algorithm and run a standard independence algorithm to generate uncorrelated equilateral random polygons with the desired length, we then use the HOMFLY polynomial [25, 28, 38] to separate the polygons by knot type. One challenge is that for short lengths, the overwhelming majority of the sampled polygons are trefoils or simply unknotted, so it is difficult to get a large sample of knots with more complicated knot

types. In addition, for long polygons it becomes very difficult to compute the knot polynomials due to the high number of crossings in the knot diagrams.

We here present a limited numerical study and summarize the results in Table 4. The sample sizes for non-trivial knots ranged between 1000 (for 6_1 at length 125) and 55,000 (for the trefoils of length 225). Sample sizes for the unknot were much larger. The different sample sizes are due to the method used to generate these polygons as we have no direct control over the knot type of the polygon generated. Even though our numerical study in this case is limited, the trend shown in the results is still clearly in strong agreement with our observation in the lattice polygon case: the mean writhe values are stable, *i.e.* as the lengths of the polygons increase, the mean writhe values only fluctuate within a narrow interval. Again for the several chiral knots studied, the confidence intervals of the mean writhe values are far away from 0, and the sign of the mean writhe is invariant across the tested lengths. Therefore our off-lattice results are in line with the proposed conjectures.

4. The variance of writhe of the equilateral random polygons

Let EP_n be an equilateral random polygon with n edges. In this section we discuss the variance of the writhe of EP_n . We will denote the writhe of EP_n by $w(EP_n)$ and conjecture that the variance of $w(EP_n)$ behaves as $O(n)$, namely as the order of the mean average crossing number (mean ACN) of EP_n and provide some numerical evidence for this.

Let $\ell_1, \ell_2, \dots, \ell_n$ be the consecutive edges of EP_n . So if we let $X_0, X_1, \dots, X_n = X_0$ be the consecutive vertices of EP_n , then $\ell_k = \overline{X_{k-1}X_k}$ ($1 \leq k \leq n$). If we let w_{ij} be the mean writhe between ℓ_i and ℓ_j , then the writhe of EP_n is simply the sum of the w_{ij} 's:

$$w(EP_n) = \sum_{1 \leq i < j \leq n} w_{ij} = \frac{1}{2} \sum_{1 \leq i, j \leq n} w_{ij},$$

and its expected value is given by

$$E(w(EP_n)) = \sum_{1 \leq i < j \leq n} E(w_{ij}) = \frac{1}{2} \sum_{1 \leq i, j \leq n} E(w_{ij}).$$

By a simple symmetry argument, one has $E(w_{ij}) = 0$ (since ℓ_i and ℓ_j have equal chance to take the positions that are mirror images to each other which would produce opposite crossing signs as shown in Figure 1), therefore we must have $E(w(EP_n)) = 0$, where EP_n is taken over the entire ensemble of equilateral random polygons with length n , not some special ones with a fixed knot type. Figure 3 summarizes our numerical estimates of the mean writhe of equilateral random polygons of various lengths, which agrees with this theoretical observation.

It follows that the variance of $w(EP_n)$ is simply

$$V(w(EP_n)) = E((w(EP_n) - E(w(EP_n)))^2) = E(w^2(EP_n)).$$

That is, the variance of the writhe is the same as the mean of the writhe squared. Therefore,

$$\begin{aligned} V(w(EP_n)) &= E(w^2(EP_n)) \\ &= \frac{1}{4} E \left(\sum_{1 \leq i, j, m, k \leq n} w_{ij} w_{mk} \right) \\ &= \frac{1}{4} \sum_{1 \leq i, j, m, k \leq n} E(w_{ij} w_{mk}). \end{aligned}$$

Although w_{ij} and w_{mk} are not independent and we cannot take their expected values separately, they are almost independent when the two pairs are reasonably far away from each other. And even when they are not, most configurations would have close counterparts that produce the opposite signs. Thus we suspect that the behavior of $E(w^2(EP_n))$ is dominated by the terms $E(w_{ij}^2)$ in the above. Since for each fixed pair of edges ℓ_i and ℓ_j , the sign of the crossing between them in any projection (where there is a crossing between them) is the same, it follows that $|w_{ij}| = a(\ell_i, \ell_j)$, where $a(\ell_i, \ell_j)$ is the average crossing number between ℓ_i and ℓ_j . Hence we have $w_{ij}^2 = a^2(\ell_i, \ell_j)$. In the following, we provide an analysis to show that $\sum_{1 \leq i, j \leq n} E(w_{ij}^2) = \sum_{1 \leq i, j \leq n} E(a^2(\ell_i, \ell_j))$ behaves as $O(n)$. For the convenience of our reader, we include some basic results about the density distribution functions of the vertices of an equilateral random polygon. More details can be found in [18].

Let X_k be the k -th vertex of an EP_n and let h_k be its density function, then

$$h_k(X_k) = \left(\sqrt{\frac{3}{2\pi\sigma_{nk}^2}} \right)^3 \exp \left(-\frac{3|X_k|^2}{2\sigma_{nk}^2} \right) + Err, \quad (2)$$

where the error term Err is of the order $O \left(\frac{1}{k^{5/2}} + \frac{1}{(n-k)^{5/2}} \right)$ and $\sigma_{nk}^2 = \frac{k(n-k)}{n}$. On the other hand, if X_1, X_{k+1} and X_{k+2} are the first, $(k+1)$ -st and $(k+2)$ -nd vertices of an EP_n ; then their joint probability density function $h_k(X_1, X_{k+1}, X_{k+2})$ can be approximated by

$$\varphi(X_1) \varphi(X_{k+2} - X_{k+1}) \left(\frac{3}{2\pi\sigma_{nk}^2} \right)^{\frac{3}{2}} \exp \left(-\frac{3|X_{k+1}|^2}{2\sigma_{nk}^2} \right), \quad (3)$$

where $\sigma_{nk}^2 = \frac{k(n-k)}{n}$ and the error term is at most of order $O \left(\frac{1}{k^{5/2}} + \frac{1}{(n-k)^{5/2}} \right)$.

Let ℓ'_1 and ℓ'_2 be two random edges (of unit length) in $\mathbb{R}^3$ with one end points fixed (they are NOT two consecutive edges along a random polygon). Let us consider $a(\ell'_1, \ell'_2)$. Assume that P and P_1 are the end point of ℓ'_1 and Q, Q_1 are the end points of ℓ'_2 and let $r = |P - Q|$, b , where b is some arbitrary positive constant. For example we can just pick $b = 4$. If we assume that P_1 and Q_1 are uniformly distributed on the spheres centered at P and Q respectively, then we have

$$E(a^2(\ell'_1, \ell'_2)) = \frac{1}{18\pi^2 r^4} + O\left(\frac{1}{r^5}\right). \quad (4)$$

Let us outline a proof of this fact. Without loss of generality, let us assume that $P = O$ and Q is on the positive z -axis. Let θ_1 be the angle between $U_1 = \overrightarrow{PP_1}$ and the z -axis and θ_2 be the angle between $U_2 = \overrightarrow{QQ_1}$ and the z -axis. Furthermore, let ϕ be the angle between the projections of U_1 and U_2 on the xy -plane. See Figure 4.

By [24], $a(\ell_1, \ell_2)$ is given by

$$\frac{1}{2\pi} \int_{\ell_1} \int_{\ell_2} \frac{|\dot{\gamma}_1(t), \dot{\gamma}_2(s), \gamma_1(t) - \gamma_2(s)|}{|\gamma_1(t) - \gamma_2(s)|^3} dt ds, \quad (5)$$

where γ_1 and γ_2 are the arclength parameterizations of ℓ'_1 and ℓ'_2 respectively, and $(\dot{\gamma}_1(t), \dot{\gamma}_2(s), \gamma_1(t) - \gamma_2(s))$ is the triple scalar product of $\gamma_1(t)$, $\gamma_2(s)$, and $\gamma_1(t) - \gamma_2(s)$. Using this, it was derived in [18] that

$$a(\ell'_1, \ell'_2) = \frac{1}{2\pi r^2} \sin \phi \sin \theta_1 \sin \theta_2 + O\left(\frac{1}{r^3}\right).$$

It follows that

$$a^2(\ell'_1, \ell'_2) = \frac{1}{4\pi^2 r^4} \sin^2 \phi \sin^2 \theta_1 \sin^2 \theta_2 + O\left(\frac{1}{r^5}\right).$$

It is known that ϕ is uniformly distributed over $[0, \pi]$ and that ϕ , θ_1 , and θ_2 are independent;

furthermore, the probability density functions for θ_1 and θ_2 are $\frac{1}{2} \sin \theta_1$ and $\frac{1}{2} \sin \theta_2$. Thus

$$\begin{aligned} E(a^2(\ell'_1, \ell'_2)) &= \int \int a^2(\ell_1, \ell_2) \varphi(U_1) \varphi(U_2) dU_1 dU_2 \\ &= \frac{1}{16\pi^3 r^4} \int_0^\pi \int_0^\pi \int_0^\pi \sin^2 \phi \sin^3 \theta_1 \sin^3 \theta_2 d\phi d\theta_1 d\theta_2 + O\left(\frac{1}{r^5}\right) \\ &= \frac{1}{18\pi^2 r^4} + O\left(\frac{1}{r^5}\right). \end{aligned}$$

Let us now return to the estimation of $\sum_{1 \leq i, j \leq n} E(w_{ij}^2) = \sum_{1 \leq i, j \leq n} E(a^2(\ell_i, \ell_j))$. Observe that if ℓ_{i_1} , ℓ_{j_1} , ℓ_{i_2} , and ℓ_{j_2} are edges of an EP_n , then we have $E(a^2(\ell_{i_1}, \ell_{j_1})) = E(a^2(\ell_{i_2}, \ell_{j_2}))$ whenever $|j_1 - i_1| = |j_2 - i_2|$ or $|j_1 - i_1| = n - |j_2 - i_2|$ by symmetry. It follows that

$$\sum_{1 \leq i, j \leq n} E(a^2(\ell_i, \ell_j)) = n \sum_{3 \leq j \leq (n+1)/2} E(a^2(\ell_1, \ell_j)).$$

In the above summation, j starts at 3 since $a(\ell_1, \ell_2)$ is always 0. Let $r_j = |X_{j-1} - X_1|$. Since $a(\ell_1, \ell_j)$ depends only on X_1 , X_{j-1} and X_j , by (3) and (4), we have

$$\begin{aligned}
& E(a^2(\ell_1, \ell_j)) \\
&= \int \int \int a^2(\ell_1, \ell_j) h_{j-2}(X_1, X_{j-1}, X_j) dX_1 dX_{j-1} dX_j \\
&= \int \int a^2(\ell_1, \ell_j) \varphi(X_1) \varphi(X_j - X_{j-1}) dX_1 dX_j \\
&= \int \left(\left(\sqrt{\frac{3}{2\pi\sigma_{n(j-2)}^2}} \right)^3 \exp \left(-\frac{3|X_{j-1}|^2}{2\sigma_{n(j-2)}^2} \right) + O \left(\frac{1}{j^{5/2}} \right) \right) dX_{j-1} \\
&= \int \int a^2(\ell_1, \ell_j) \varphi(U_1) \varphi(U_2) dU_1 dU_2 \\
&= \int_{r_j < 4} \left(\left(\frac{3}{2\pi\sigma_{n(j-2)}^2} \right)^{\frac{3}{2}} \exp \left(-\frac{3|X_{j-1}|^2}{2\sigma_{n(j-2)}^2} \right) + O \left(\frac{1}{j^{5/2}} \right) \right) dX_{j-1} \\
&+ \int_{r_j \geq 4} \left(\left(\frac{3}{2\pi\sigma_{n(j-2)}^2} \right)^{\frac{3}{2}} \exp \left(-\frac{3|X_{j-1}|^2}{2\sigma_{n(j-2)}^2} \right) + O \left(\frac{1}{j^{5/2}} \right) \right) dX_{j-1} \\
&= O \left(\frac{1}{j^{\frac{3}{2}}} \right) + \frac{2}{9\pi} \int_4^{j-2} \left(\frac{1}{r_j^2} + O \left(\frac{1}{r_j^3} \right) \right) \\
&\quad \left(\frac{3}{2\pi\sigma_{n(j-2)}^2} \right)^{\frac{3}{2}} \exp \left(-\frac{3r_j^2}{2\sigma_{n(j-2)}^2} \right) dr_j \\
&= O \left(\frac{1}{j^{\frac{3}{2}}} \right),
\end{aligned}$$

where $U_1 = X_1$ and $U_2 = X_j - X_{j-1}$. Since $\sum_{3 \leq j \leq n/2} \frac{1}{j^{\frac{3}{2}}}$ converges, it follows that

$$\sum_{1 \leq i, j \leq n} E(a^2(\ell_i, \ell_j)) = n \sum_{3 \leq j \leq (n+1)/2} E(a^2(\ell_1, \ell_j)) = O \left(n \sum_{3 \leq j \leq (n+1)/2} \frac{1}{j^{\frac{3}{2}}} \right) = O(n).$$

Thus we conjecture that for equilateral random polygons of length n , the variance of the writhe behaves as $O(n)$. Table 5 shows the numerical estimate of the squared writhe for the chosen lengths of the polygons. Figure 5 is the corresponding plot for Table 5. The graph shows a near perfect linear relation, which strongly supports our conjecture.

5. Discussions and conclusions

DNA knots have been observed in a number of biological systems. In many of these studies the writhe of the molecule has played a key role as it is directly related to the supercoiling of the molecule and provides information on its level of entanglement. The present study is motivated by two questions. The first question asks whether one can distinguish the chirality of a knot population of the same knot type by its mean writhe, and the second question aims at estimating the growth of the variance of the writhe as a function of the length of the polygon. Our numerical results in section 3 support the hypothesis that the mean writhe is an effective way of detecting chirality. Mean writhe values vary only slightly as the polygonal length n increases. Hence, it is plausible that the sign of the mean writhe stays invariant for most chiral knot types. Indeed, inspection of the confidence intervals for the mean writhe of each knot type here generated using the BFACF algorithm shows no exception (Table 1). An analogous study was done for equilateral random polygons. Obtaining statistically meaningful data for all equilateral random polygons with eight or less crossings is challenging. We report preliminary results for knots with up to six crossings and short lengths. These results are consistent with the lattice data (Table 4). This does not necessarily

imply that the conjecture will hold for all chiral knots, since some chiral knots may have mean writhe values equal or very close to zero. Interestingly, the mean writhe values estimated numerically for lattice polygons are very close to the mean writhe values of ideal polygons of the same knot type, where ideal lattice polygons are defined as minimum step polygons of a given knot type. We suspect that this is a general trend for lattice knots with large crossing numbers. In the future we plan to carry out larger scale numerical studies of knots with nine or more crossings, complemented with more rigorous analysis.

In the second part of the paper, we provide strong analytical and numerical evidence that the variance of the writhe of equilateral random polygons behaves as a linear function of n , where n is the length of the polygon. This information is important if we are to carry out numerical studies to make inferences on the mean writhe of equilateral random polygons under various constraints (such as confined volume or fixed knot type). Some technical challenges remain in proving this linear behavior rigorously. It is worth pointing out that one should not consider $E(w^2(EP_n)) = O(n)$ as something intuitive or obvious. For example, recall that for the case of confined uniform random polygons, it has been shown that the mean squared writhe behaves as $O(n^2)$. We strongly suspect that this is also true for confined equilateral random polygons. On the other hand, it can be shown that the mean ACN of an equilateral random polygon of n edges in a confined volume also behaves as $O(n^2)$. However, the mean ACN of an equilateral random polygon without confinement behaves as $O(n \ln n)$. So if we were to use the mean ACN (since it behaves the same as the mean squared writhe in the confined case) as a reference, we would guess that the mean squared writhe of an unconfined EP_n should behave as $O(n \ln n)$. Another observation is that the maximum $w^2(EP_n)$ value is of the order $O(n^4)$ since one can construct special EP_n 's with writhe in the order of $O(n^2)$. Thus the $w^2(EP_n)$ values have a wide range from 0 to $O(n^4)$. This wide range makes the prediction of $E(w^2(EP_n))$ harder without further information on the distribution of the $w^2(EP_n)$ values. Recently, a study has been done on the mean squared writhe of random knot diagrams [20]. There it is observed that the mean squared writhe behaves as $O(n)$, where n is the number of crossings in the diagram. However, the knot diagrams studied were mostly alternating (hence minimum) knot diagrams, which are very different from the knot diagrams obtained by projecting our random polygons. Hence a direct comparison cannot be made.

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Figure 1.
A positive and a negative crossing.

Figure 2.

Comparison between overall mean writhe values and the ideal expected writhes (*i.e.* the writhe averaged over all minimum length polygons for each individual knot type).

Figure 3.

99% confidence intervals for the mean writhe of equilateral polygons. The polygons are generated using the crankshaft algorithm. The sample size for each length is 500,000 and the error bars are at the 99% confidence level. The writhe is computed using the Gaussian formula given in (1).

Figure 4.

The relationship between two random edges ℓ'_1 and ℓ'_2 .

Figure 5.
The estimated mean squared writhe values compared to their linear regression line.

Table 1
The mean writhe of self-avoiding lattice polygons of fixed length and knot type

We computed the mean writhe for all knotted polygons with 8 and less crossings (including composites and mirror images) with lengths 75, 100, 150, 200, and 350. The knot $6c_1$ corresponds to $3_1 \# 3_1$ where $\#$ is the connected sum. Likewise, $3_1 \# 4_1$ is $7c_1$ etc... The numerical data for each knot and its mirror image were combined and are reported with the 99% confidence intervals.

K	75	100	150	200	350
3_1	3.45 ± 0.03	3.49 ± 0.03	3.47 ± 0.04	3.46 ± 0.05	3.42 ± 0.07
5_1	6.32 ± 0.02	6.31 ± 0.03	6.29 ± 0.04	6.29 ± 0.05	6.29 ± 0.07
5_2	4.57 ± 0.02	4.58 ± 0.03	4.61 ± 0.04	4.61 ± 0.05	4.51 ± 0.07
6_1	1.17 ± 0.02	1.19 ± 0.03	1.19 ± 0.04	1.22 ± 0.05	1.22 ± 0.06
6_2	2.89 ± 0.02	2.88 ± 0.03	2.89 ± 0.04	2.85 ± 0.05	2.90 ± 0.06
$6c_1$	6.96 ± 0.02	6.95 ± 0.03	6.95 ± 0.04	6.91 ± 0.05	6.89 ± 0.06
7_1	9.15 ± 0.02	9.14 ± 0.03	9.12 ± 0.04	9.07 ± 0.05	9.05 ± 0.06
7_2	5.76 ± 0.02	5.78 ± 0.03	5.82 ± 0.04	5.81 ± 0.04	5.83 ± 0.06
7_3	7.40 ± 0.02	7.41 ± 0.03	7.41 ± 0.04	7.40 ± 0.05	7.34 ± 0.06
7_4	5.68 ± 0.02	5.68 ± 0.03	5.72 ± 0.04	5.72 ± 0.04	5.72 ± 0.07
7_5	7.48 ± 0.02	7.49 ± 0.03	7.52 ± 0.04	7.48 ± 0.04	7.46 ± 0.06
7_6	3.40 ± 0.02	3.40 ± 0.03	3.41 ± 0.04	3.38 ± 0.04	3.38 ± 0.07
7_7	0.53 ± 0.02	0.54 ± 0.03	0.51 ± 0.04	0.53 ± 0.04	0.56 ± 0.06
$7c_1$	3.48 ± 0.02	3.47 ± 0.03	3.50 ± 0.04	3.48 ± 0.05	3.49 ± 0.06
8_1	2.35 ± 0.02	2.37 ± 0.02	2.40 ± 0.04	2.43 ± 0.04	2.45 ± 0.06
8_2	5.70 ± 0.02	5.70 ± 0.02	5.66 ± 0.04	5.65 ± 0.04	5.67 ± 0.06
8_4	1.73 ± 0.02	1.71 ± 0.02	1.69 ± 0.04	1.68 ± 0.04	1.65 ± 0.06
8_5	5.74 ± 0.02	5.75 ± 0.02	5.71 ± 0.04	5.76 ± 0.04	5.68 ± 0.06
8_6	4.07 ± 0.02	4.09 ± 0.02	4.08 ± 0.04	4.11 ± 0.04	4.06 ± 0.07
8_7	2.83 ± 0.02	2.83 ± 0.02	2.83 ± 0.03	2.78 ± 0.04	2.78 ± 0.06
8_8	1.20 ± 0.02	1.20 ± 0.02	1.22 ± 0.04	1.22 ± 0.04	1.24 ± 0.06
8_{10}	2.87 ± 0.02	2.87 ± 0.02	2.87 ± 0.04	2.85 ± 0.04	2.87 ± 0.06
8_{11}	3.98 ± 0.02	3.96 ± 0.02	3.98 ± 0.04	4.00 ± 0.04	3.98 ± 0.06

<i>K</i>	75	100	150	200	350
8_{13}	1.12 ± 0.02	1.11 ± 0.02	1.12 ± 0.03	1.09 ± 0.04	1.13 ± 0.06
8_{14}	4.06 ± 0.02	4.07 ± 0.02	4.08 ± 0.04	4.06 ± 0.04	4.08 ± 0.06
8_{15}	7.99 ± 0.02	8.01 ± 0.02	8.01 ± 0.04	8.04 ± 0.04	7.98 ± 0.06
8_{16}	2.83 ± 0.02	2.83 ± 0.02	2.83 ± 0.03	2.82 ± 0.04	2.77 ± 0.06
8_{19}	8.80 ± 0.02	8.80 ± 0.03	8.78 ± 0.04	8.84 ± 0.05	8.80 ± 0.07
8_{20}	1.92 ± 0.02	1.92 ± 0.03	1.95 ± 0.04	1.93 ± 0.05	1.95 ± 0.06
8_{21}	4.68 ± 0.02	4.70 ± 0.03	4.73 ± 0.04	4.75 ± 0.05	4.67 ± 0.06
8_{c1}	9.80 ± 0.02	9.79 ± 0.03	9.79 ± 0.04	9.80 ± 0.05	9.69 ± 0.06
8_{c2}	2.84 ± 0.02	2.86 ± 0.02	2.82 ± 0.04	2.81 ± 0.04	2.83 ± 0.06
8_{c3}	8.04 ± 0.02	8.06 ± 0.03	8.06 ± 0.04	8.05 ± 0.04	8.02 ± 0.06
8_{c4}	1.09 ± 0.02	1.08 ± 0.02	1.10 ± 0.04	1.10 ± 0.04	1.13 ± 0.07

Table 2

The overall mean writhe of self-avoiding polygons in the cubic lattice averaged over fixed knot types of lengths 75, 100, 150, 200, 250, 300, and 350. The last column is the overall mean writhe averaged over lengths up to 250 segments, as reported in [34, 35]. The error corresponds to 68% confidence interval. In [35] the authors did not provide error bars.

K	Overall mean writhe	[34]
3_1^*	-3.447 ± 0.019	-3.441 ± 0.025
5_1^*	-6.291 ± 0.018	-6.254 ± 0.011
5_2^*	-4.577 ± 0.019	-4.548 ± 0.011
6_1^*	-1.205 ± 0.019	-1.159 ± 0.020
6_2^*	-2.868 ± 0.018	-2.830 ± 0.010
$6c_1^*$	-6.926 ± 0.018	-6.906 ± 0.027
7_1	9.107 ± 0.018	9.07
7_2	5.815 ± 0.018	5.74
8_1	2.408 ± 0.017	2.35
8_{19}^*	-8.822 ± 0.018	-8.731 ± 0.016
9_1	11.88 ± 0.017	11.89
9_2	7.001 ± 0.017	6.95
10_1	3.606 ± 0.017	3.55

Table 3

The *ideal mean writhe* of lattice knots with 8 or less crossings. In column 2, we report the number of minimum edge polygons for each knot type as in [59]. For knots 0_1 , 8_3 and 8_7 a unique minimum edge polygon was found (modulo rigid motion), thus explaining the absence of an error bar.

K	ideal mean writhe	# of polygons	chirality
0_1	0	3	achiral
3_1	3.441 ± 0.018	1664	chiral
4_1	0.000 ± 0.016	3648	achiral
5_1	6.228 ± 0.008	3336	chiral
5_2	4.528 ± 0.015	57456	chiral
6_1	1.096 ± 0.011	3072	chiral
6_2	2.789 ± 0.010	16416	chiral
6_3	0 ± 0.016	3552	achiral
7_1	9.215 ± 0.032	16980	chiral
7_2	5.752 ± 0.009	168180	chiral
7_3	7.475 ± 0.011	240	chiral
7_4	5.571 ± 0.012	84	chiral
7_5	7.271 ± 0.008	4728	chiral
7_6	3.441 ± 0.013	17016	chiral
7_7	0.512 ± 0.017	252	chiral
8_1	2.411 ± 0.014	11868	chiral
8_2	5.545 ± 0.009	45840	chiral
8_3	0	12	achiral
8_4	1.655 ± 0.007	23928	chiral
8_5	5.625 ± 0.011	576	chiral
8_6	4.008 ± 0.009	5520	chiral
8_7	2.750	24	chiral
8_8	1.081 ± 0.020	1560	chiral
8_9	0.000 ± 0.007	35280	achiral
8_{10}	3.007 ± 0.008	840	chiral
8_{11}	4.125 ± 0.013	96	chiral
8_{12}	0.000 ± 0.031	2592	achiral
K	ideal mean writhe	# of polygons [59]	chirality
8_{13}	1.183 ± 0.022	13056	chiral
8_{14}	3.983 ± 0.009	360	chiral
8_{15}	7.885 ± 0.014	40104	chiral
8_{16}	2.625 ± 0.018	48	chiral
8_{17}	0.000 ± 0.008	53184	achiral

K	ideal mean writhe	# of polygons	chirality
8_{18}	0.000 ± 0.024	3552	achiral
8_{19}	8.759 ± 0.009	6996	chiral
8_{20}	2.100 ± 0.011	120	chiral
8_{21}	4.535 ± 0.011	28020	chiral

Table 4

The mean writhe of self-avoiding polygons in $\mathbb{R}^3$ of fixed knot types at lengths 125, 150, 175, 200, and 225 with error bars set at the 99% confidence level. The knot $6c_1$ corresponds to $3_1 \# 3_1$ where $\#$ is the connected sum.

K	125	150	175	200	225
3_1	3.38 ± 0.03	3.36 ± 0.03	3.38 ± 0.03	3.40 ± 0.03	3.38 ± 0.04
5_1	6.18 ± 0.13	6.12 ± 0.13	6.07 ± 0.13	6.17 ± 0.13	6.19 ± 0.14
5_2	4.55 ± 0.09	4.58 ± 0.09	4.59 ± 0.10	4.59 ± 0.10	4.62 ± 0.10
6_1	1.16 ± 0.18	1.17 ± 0.18	1.13 ± 0.19	1.09 ± 0.19	1.15 ± 0.20
6_2	2.81 ± 0.18	2.88 ± 0.17	2.71 ± 0.17	2.82 ± 0.18	2.76 ± 0.20
$6c_1$	6.82 ± 0.13	6.78 ± 0.12	6.65 ± 0.12	6.72 ± 0.11	6.79 ± 0.11

Table 5

The plot of the estimated mean squared writhe.

polygon length	mean squared writhe	95% error bar
18	1.788	0.008
29	3.199	0.014
35	4.057	0.018
44	4.988	0.021
56	6.586	0.028
75	9.197	0.039
100	12.457	0.052
125	15.811	0.066
150	19.262	0.080
200	25.948	0.107
225	29.346	0.121