Statistical topology of closed curves: Some applications in polymer physics

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Topological entanglement in polymers and biopolymers is a topic that involves different fields of science such as chemistry, biology, physics, and mathematics. One of the main issues in this topic is to understand how the entanglement complexity can depend on factors such as the degree of polymerization, the quality of the solvent, and the temperature or the degree of confinement of the macromolecule. In this respect a statistical approach to the problem is natural and in the last few years there has been a lot of work on the study of the entanglement complexity of polymers within the statistical mechanics framework. A review on this topic is given here stressing the main results obtained and describing the tools most used with this approach.

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I. INTRODUCTION

Long linear polymer molecules have two main characteristic features: their connectivity and flexibility. In addition, the monomers take up space so that the polymer chain cannot cross itself. These features imply that polymer molecules can be self-entangled and, if a ring closure reaction occurs, the entanglement can be trapped as a knot in the resulting ring polymer molecule. If the ring polymer is knotted, the knot cannot be removed without breaking chemical bonds in the polymer. Knots and other entanglements are important in many areas of polymer physics and there has been considerable interest and research activity on this subject. Knots in ring polymers have been studied using rigorous approaches, computationally and experimentally, though we focus on the first two areas in this review.

When linear polymers in solution crystallize entanglements can be trapped in the crystallization process and they can affect the properties of the crystal and the degree of crystallinity (de Gennes, 1984; Bayer, 1994; Saitta *et al.*, 1999; Saitta and Klein, 2002). It is likely that entanglements become localized in the amorphous regions of the crystal. Rheological properties are also affected by entanglements between polymer chains and these can contribute to the elasticity of a polymer network (Edwards, 1967, 1968).

As we will show, the probability of being knotted depends on the degree of polymerization of the polymer as well as on the solvent quality and polymer flexibility. DNA molecules are typically enormously long and the probability of knotting is high, in spite of the fact that DNA is a very stiff molecule. Knots and entanglements in DNA can affect the efficiency of cellular processes such as replication and transcription (Wasserman *et al.*, 1986; Sumners, 1990, 1992, 1995) and knotting in DNA has been well studied by molecular biologists (Dean *et al.*, 1985; Liu *et al.*, 2006). Organisms have special enzymes, the topoisomerases, which can pass one strand of DNA through another and knot and unknot the DNA molecule, to facilitate these cellular processes (Goto and Wang, 1982; Wang, 1996; Rybenkov *et al.*, 1997; Yan *et al.*, 1999). There are also topoisomerases which act on RNA (Wang *et al.*, 1996). In bacteria the DNA molecules are often circular so the action of the enzymes can be studied directly on circular DNA molecules with a particular knot type and the change in knot type after the action of the enzyme can be determined. Understanding the mechanism of action of these enzymes has led to a fruitful collaboration between topologists and molecular biologists (Sumners, 1995; Sumners *et al.*, 1995).

The knot probability in DNA molecules has been studied by Shaw and Wang (1993, 1994) and by Rybenkov *et al.* (1993). They took linear DNA molecules with different lengths in solutions of different ionic strengths, and carried out a cyclization reaction. They then determined the proportion of the resulting circular DNA molecules which were knotted. This is perhaps the most direct measurement of knot probability that has been carried out. The knot probability also depends on the extent to which the DNA molecule is geometrically confined. For instance, DNA molecules confined to viral capsids have a very high probability of being knotted and the distribution of knot types is different from the knot distribution for free DNA in solution (Arsuaga *et al.*, 2002; Micheletti *et al.*, 2006). The importance of entanglements in DNA for cellular processes has led to a general interest in the effects of stiffness and geometrical constraints on knot probabilities.

Knotted ring polymers have a smaller radius of gyration than unknotted ring polymers with the same degree of polymerization. For polyelectrolytes this means that the molecules move at different speeds in an electric field. *In vitro* gel electrophoresis experiments can be used to separate circular DNA molecules with different knot types and such experiments can be used to determine the types of knots produced by the action of an enzyme (Stasiak *et al.*, 1996; Levene and Tsen, 1999; Trigueros *et al.*, 2001).

In linear polymers, as opposed to ring polymers, the molecule is not knotted in the topological sense. Nevertheless, we are used to thinking of linear pieces of string as being knotted, or containing a knot. The string, or linear polymer, can certainly be entangled but how do we make sense of the idea of knotting in linear polymers? This question arises in proteins which are not usually cyclic and so are not knotted in the topological sense. Taylor and co-workers (Taylor, 2000; Taylor *et al.*, 2003) have addressed the problem of deciding if a protein is "knotted," though even with their definition, clearly knotted proteins are not common (Taylor *et al.*, 2003).

Modern micromanipulation techniques such as atomic force microscopy (AFM) and optical tweezers allow single molecules to be manipulated (Bustamante *et al.*, 2000; Strick *et al.*, 2003). For instance, a single molecule can be stretched and the stress-strain curve can be measured (Bustamante *et al.*, 1994; Cluzel *et al.*, 1996). In addition, the molecule can be stretched and then released so that its relaxation behavior can be studied (Bohbot-Raviv *et al.*, 2004), or can be stretched until a chemical bond breaks so that the influence of knotting on the breaking strength can be studied. Recently knots have been tied in single-actin filaments (Arai *et al.*, 1999) and DNA (Meiners and Quake, 2000; Bao *et al.*, 2003) using optical tweezers in combination with beads attached to the macropolymers as handles and it has been suggested (Arai *et al.*, 1999) that molecular-scale knots might function as micromanipulation tools in biological systems.

Experimental evidence for knots in DNA and for their influence on cellular processes is unequivocal. Knots and entanglements must also be ubiquitous in synthetic polymers. The growth in interest in knotting in the last 20 years is enormous and this review discusses the rigorous results and numerical simulations which have contributed to our understanding of the area.

Polymers in solution are flexible objects and, to understand their configurational properties, one must carry out an averaging procedure over the space of configurations. The obvious approach is to use statistical mechanics though this field has also attracted interest from combinatorialists and probabilists. The first papers which investigated knotting in polymers from a theoretical point of view were by Edwards (1967, 1968). Edwards pointed out the importance of carrying out a restricted average over the topologically available region of the configuration space. These papers are highly original and insightful and require careful study. They had an enormous influence on the development of the field, even though the invariant proposed by Edwards is not a topological invariant.

The first numerical studies of knotting in polymers were by Frank-Kamenetskii and co-workers in a series of papers (Vologodskii *et al.*, 1974, 1975; Frank-Kamenetskii *et al.*, 1975). They were the first to use the Alexander polynomial to characterize the knot type of the ring polymer. This approach is still used today though other knot polynomials (e.g., the Jones polynomial and the HOMFLY polynomial) are becoming more widely used since they are better discriminators of knots. See Adams (1994) for an approachable discussion of the Jones and HOMFLY polynomials.

The idea that long ring polymers in dilute solution will be knotted with high probability is due to Frisch and Wasserman (1961) and to Delbruck (1962). This is the

famous Frisch-Wasserman-Delbruck conjecture. The basic idea behind the modern proof of this conjecture can be traced back to Frisch and Klempner (1970) though a detailed proof does not seem to have been given until much later (Sumners and Whittington, 1988; Pippenger, 1989). This theorem and the idea behind the proof are discussed in Sec. III.A.1. Rigorous results about knotting of ring polymers in various environments are discussed in Sec. III.A. This requires some basic knot theory which is outlined in Sec. II. Many questions cannot be answered rigorously and much of our knowledge comes from numerical approaches. In Sec. III.B we describe the main Monte Carlo methods which have been useful in this field, and survey the results obtained.

If we know that a ring polymer will be knotted, we can ask how badly knotted it will be. This is the question of topological entanglement complexity which is the subject of Sec. III.A.2. It is closely connected to geometrical entanglement complexity which is discussed in Sec. IV.

There are interesting questions about how tightly a knot is tied in a polymer ring. Is the knot a local object or is it delocalized over the whole ring? This notion of tightness has important consequences for the dimensions of polymer rings and also for the dependence of entropy on the degree of polymerization, and will appear in several places in this review.

In the same way that a polymer ring can be knotted, two or more polymer rings can be linked. Linking can have deleterious effects on cellular processes, just as knotting can. The problem of linking is discussed in Secs. III.A.7 and III.B.7.

Molecules like duplex DNA consist of two polymer chains which wind around each other. These systems can be modeled as ribbons. If the ribbon is closed then the appropriate kind of ribbon to model circular DNA has two boundary curves. These curves can be knotted or linked and these properties are discussed in Secs. III.A.8 and III.B.8.

Finally, we introduce the idea of ideal knots in Sec. VII.

II. SOME BASIC KNOT THEORY

If one takes a piece of string and identifies the two ends, either it is possible to lay the string down so that it lies entirely in a plane (say on a flat table) or this is impossible and the string must cross itself at least three times. In carrying out this operation one is allowed to move the string around and deform it at will. The string is a model of a simple closed curve in Euclidean three-space, R^3. In the first case we say that the simple closed curve is *unknotted* and in the second that it is *knotted*. Knot theory is concerned with embeddings of a simple closed curve in three-space and these embeddings are called *knots*. If two different embeddings can be smoothly deformed into one another then we say that the two embeddings have the same *knot type*. So a knot type is an equivalence class of embeddings. Embeddings which can be deformed so that they are planar are unknotted embeddings, and each of them is the unknot. It is easy to see that there are different knotted embeddings which cannot be deformed into one another so there are different knot types. A little experimentation shows that the simplest knot type has at least three crossings when we attempt to deform it to lie in a plane; see Fig. 1. Another way of looking at this is to project the embedding of the simple closed curve onto a plane and count the number of crossings in the projection. If we minimize over all smooth deformations and over all projection directions then the minimum number of crossings is the *crossing number*. If we neglect enantiomers there is only one knot type, the trefoil, which has crossing number 3, one (the figure-eight knot) with crossing number 4 but two with crossing number 5. We shall use a symbol which is based on the crossing number but has a subscript which distinguishes between different knots with the same crossing number. The first few knots have symbols 3_1, 4_1, 5_1, and 5_2 (since there are two knots with crossing number 5). These are sketched in Fig. 1. There is an arithmetic of knots something like the idea of factorization of integers into their prime factors. Some knots (like the granny knot) can be factored into simpler knots. The granny knot is two trefoils, one tied after the other as sketched in Fig. 1. We write the granny knot as $3_1\#3_1$, and say that it is the *connect sum* of two trefoils. If a knot cannot be factored in this way we say that the knot is *prime*. Otherwise it is *composite*.

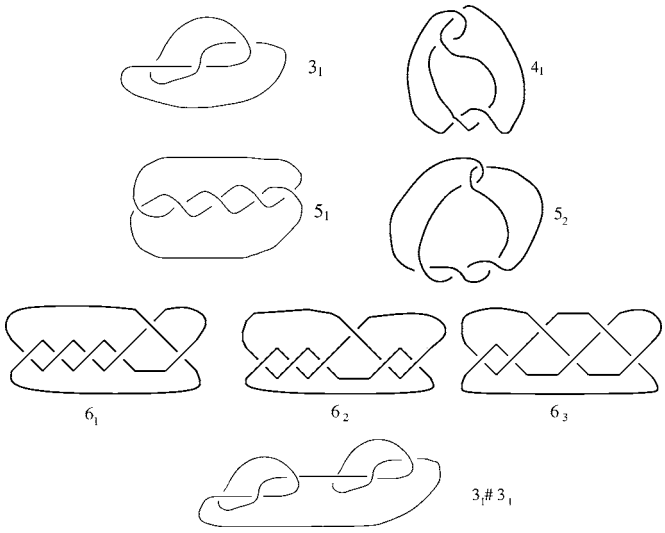

FIG. 1. Knot diagrams for some knots.

There is an extra complication because sometimes a knot and its mirror image are distinct in that one cannot be deformed into the other. This is true for 3_1, 5_1, 5_2, 6_1, and 6_2 but not for 4_1 and 6_3, for instance. If a knot can be smoothly deformed into its mirror image, we say that the knot is *achiral*. We call the two enantiomers of the trefoil the $3_1(+)$ and $3_1(-)$ knots if we want to emphasize the difference between the enantiomers. The composite knots $3_1(+)\#3_1(+)$ and $3_1(-)\#3_1(-)$ are two enantiomers of the granny knot. The knot $3_1(+)\#3_1(-)$ is achiral and is the square knot. (This is analogous to the meso stereo-

isomer of tartaric acid. The molecule has two chiral centers but has a plane of symmetry so it is achiral.) Counting enantiomers there are three composite knots with six crossings, the (+) and (−) granny knots, and the achiral square knot.

Tables giving pictures of prime knots (in fact, of one enantiomer of each knot when the knot is chiral) with up to nine crossings can be found in Livingston (1993) and Adams (1994). Prime knots with up to 16 crossings have been enumerated by Hoste *et al.* (1998); see also Jacobsen and Zinn-Justin (2002) and Rankin *et al.* (2004). It is known that the number of knots with n crossings increases exponentially rapidly with increasing n (Ernst and Sumners, 1987; Welsh, 1991).

We can convert a knot into an unknot by reversing one or more crossings in the knot. If we draw the trefoil in its simplest form so that it only has three crossings, and reverse any of its three crossings, we obtain the unknot. We call the minimum number of crossing reversals needed to obtain the unknot the *unknotting number*. The trefoil and figure-eight knots each have unknotting number 1. Of the two five crossing number knots, 5_2 has unknotting number 1 and 5_1 has unknotting number 2. The granny knot has unknotting number 2 (essentially because each trefoil has to be unknotted). It turns out that if a knot has unknotting number 1 then it is automatically prime (Scharlemann, 1985).

We can ask for the minimum number of crossing changes needed to convert one knot into another. This gives a distance on the space of knots and this has been studied by Darcy (2001). Sometimes it is possible to compute the distance exactly but sometimes only upper and lower bounds are available. These numbers are of interest in understanding topoisomerase action on circular DNA (Flammini *et al.*, 2004).

It is useful to be able to make changes to a projection of a knot (a *knot diagram*) which correspond to smooth deformations of the three-dimensional object. Reidemeister showed that any smooth deformation (isotopy) can be represented by a sequence of modifications to the projection. These are called Reidemeister moves and are sketched in Fig. 2.

One of the basic questions in knot theory is to find an algebraic way of distinguishing a knot from the unknot or distinguishing two knots from one another. The idea is to find an *invariant* such that if the value of the invariant differs for two different embeddings then the two embeddings have different knot types. An example, which has a venerable history and is still much used today, is the Alexander polynomial. This is a polynomial in a variable t which can be calculated for any embedding. We explain how to compute the Alexander polynomial for a given embedding though we will not show why it is an invariant. Consider the figure-eight knot as an example. Attach an orientation to the curve as shown in Fig. 3. Classify the crossings as positive or negative by a right-hand rule (so the figure-eight knot has two positive crossings and two negative crossings). The crossings divide the curve into four arcs. At each crossing there is an overcrossing arc, an incoming arc, and an outgoing arc.

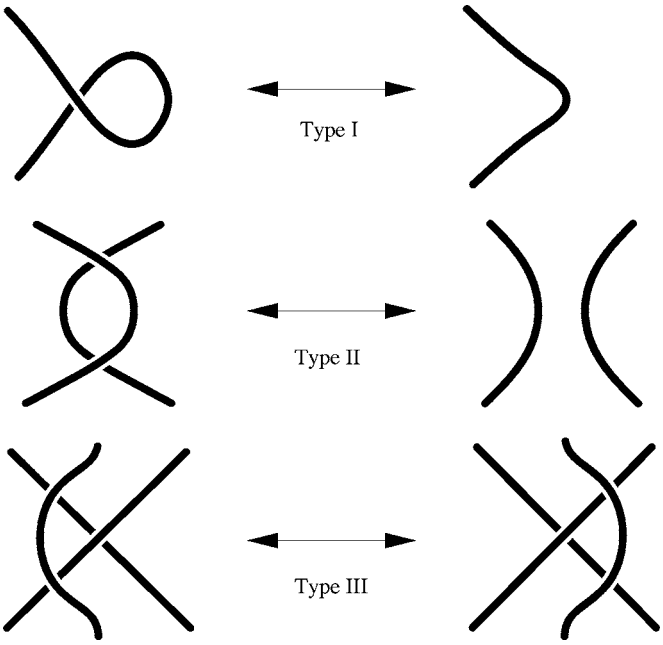

FIG. 2. The three Reidemeister moves.

Number the arcs and the crossings. Write down a determinant with rows corresponding to the crossings and columns corresponding to the arcs, with arc parameters as shown in Fig. 4. If the crossing is positive, the entry corresponding to the overcrossing arc is $1-t$, the entry corresponding to the incoming arc is -1, and to the outgoing arc is t. Similarly if the crossing is negative, the three corresponding entries are $1-1/t$, -1, and $1/t$. For the figure-eight knot shown in Fig. 3 the determinant has the form

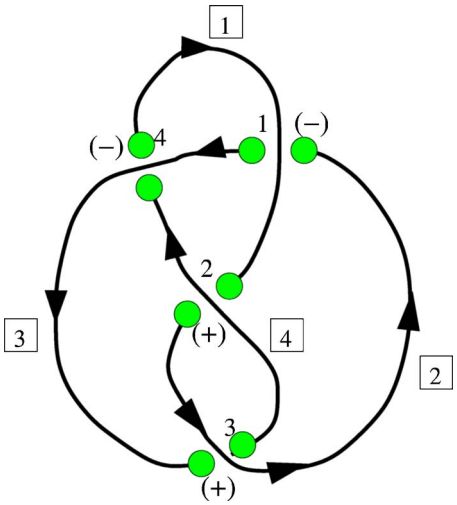

FIG. 3. (Color online) Oriented knot diagram for the knot 4_1. The numbers in boxes refer to the labeling of the four arcs. For clarity the arcs are delimited by filled circles.

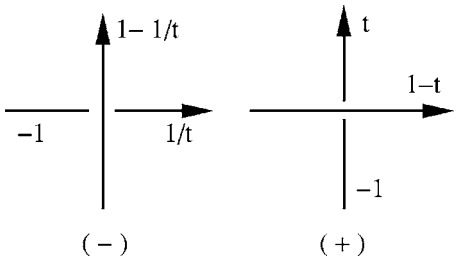

FIG. 4. The sign convention for signed crossings and the arc labelings for computation of the Alexander polynomial.

$$D(t) = \begin{vmatrix} 1-\frac{1}{t} & -1 & \frac{1}{t} & 0 \\ -1 & t & 0 & 1-t \\ 0 & 1-t & -1 & t \\ \frac{1}{t} & 0 & 1-\frac{1}{t} & -1 \end{vmatrix}. \quad (1)$$

One then computes any principle minor and multiplies or divides by powers of t and $1-t$ to obtain a polynomial in t which has a constant term. This is the Alexander polynomial, $\Delta(t)$. In this case we obtain

$$\Delta(t;4_1) = t^2 - 3t + 1. \quad (2)$$

If we repeat the procedure with the trefoil (see Fig. 5), we get the determinant

$$D(t) = \begin{vmatrix} -1 & \frac{1}{t} & 1-\frac{1}{t} \\ \frac{1}{t} & 1-\frac{1}{t} & -1 \\ 1-\frac{1}{t} & -1 & \frac{1}{t}. \end{vmatrix}. \quad (3)$$

If, for example, we take as the principle minor (order 2 in this case) the one at the bottom-left corner, we get an expression that, after multiplication by t^2, gives the polynomial

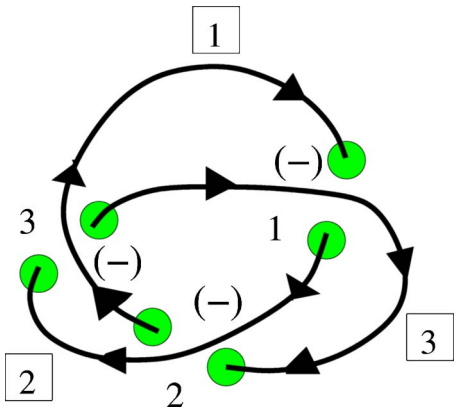

FIG. 5. (Color online) Oriented knot diagram for the knot -3_1.

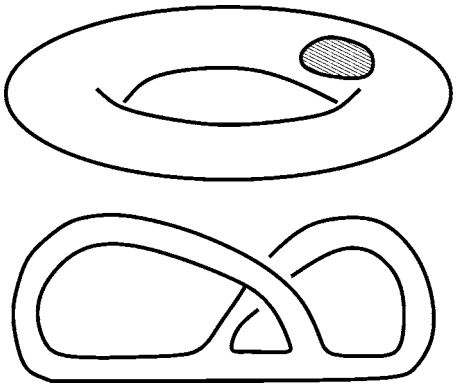

FIG. 6. Two drawings of a punctured torus whose boundary curve is the unknot.

$$\Delta(t;3_1) = t^2 - t + 1. \quad (4)$$

A comparison between $\Delta(t;4_1)$ and $\Delta(t;3_1)$ tells us that the trefoil and figure-eight knots are indeed distinct. The unknot has an Alexander polynomial equal to 1. Composite knots have Alexander polynomials which are the products of the Alexander polynomials of their prime components, so that

$$\Delta(t,3_1 \# 4_1) = (t^2 - t + 1)(t^2 - 3t + 1). \quad (5)$$

The Alexander polynomial is not a perfect discriminator since there are several pairs of knots with the same Alexander polynomial. For instance, the knot 8_{20} has an Alexander polynomial $(t^2-t+1)^2$, which is the same as the granny knot $3_1\#3_1$, and 8_{21} has the same Alexander polynomial as $3_1\#4_1$. Examples of knots with trivial Alexander polynomial are known (e.g., the Kinoshita-Terasaka knot which has 11 crossings) so these cannot be distinguished from the unknot by computing the Alexander polynomial.

Other polynomials are known which are better discriminants of knots. Examples are the Jones polynomial and the HOMFLY polynomial; see, for instance, Adams (1994).

One can also use geometrical ideas to characterize knots. The boundary of a punctured sphere is necessarily the unknot. If we puncture a higher genus surface (e.g., a torus), the boundary curve can be knotted. The lowest genus (orientable) surface which when punctured can have a particular knot as the boundary curve defines the genus of a knot and is called the *Seifert surface* of the knot. For instance, the trefoil and figure-eight knots both have genus 1 since they can each be the boundary curve of a punctured torus. In Fig. 6 we show two drawings of a punctured torus where the boundary curve is the unknot. The Seifert surface of the figure-eight knot is sketched in Fig. 7. The two bands in Fig. 6 have been twisted and it is easy to check that the resulting boundary curve is a figure-eight knot. It is not difficult to prove that genus adds under the connect sum operation so the granny knot has genus 2. We end this section with descriptions of some types of knots which play a particular role in what follows. Consider the standard solid torus T,

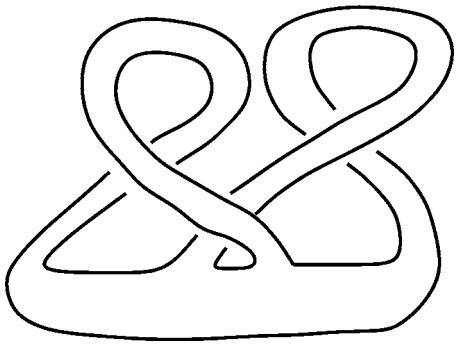

FIG. 7. The Seifert surface of the figure-eight knot. This surface is a punctured torus and the figure-eight knot has genus one.

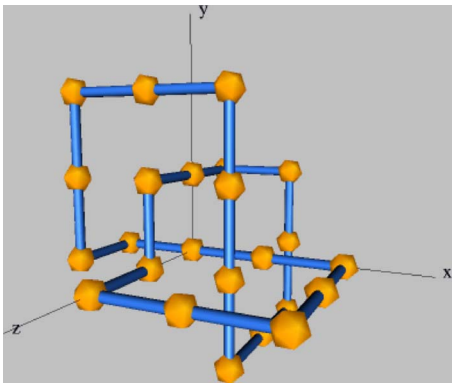

FIG. 8. (Color online) The shortest trefoil knot on a cubic lattice.

i.e., the surface and interior of an "unknotted" torus. A torus knot $T_{p,q}$ wraps around the surface of T, ∂T, p times in the meridinal direction and q times in the longitudinal direction. We often describe $T_{p,q}$ as the (p,q)-torus knot. For instance, the trefoil, 3_1, is the $(2,3)$-torus knot and 5_1 is the $(2,5)$-torus knot.

We say that a disk D in a solid torus T is *meridinal* if its boundary ∂D is a nontrivial curve (i.e., cannot be shrunk to a point) in the boundary of T, ∂T. A curve in the interior of T is *geometrically essential* if it intersects every meridinal disk in T. Consider a curve in the interior of the standard torus T which is geometrically essential and which has knot type K_1. Now knot the solid torus T so that its center line is a knot of type K_2. This converts K_1 to a new knot K_3. We say that K_3 is a *satellite knot* with K_2 as *companion*.

This gives only a brief account of some basic facts about knots. Many good knot theory books are available which give detailed but not too technical accounts of the subject (Livingston, 1993; Adams, 1994).

III. KNOTTING PROBABILITY IN RING POLYMERS

A. Rigorous results

In order to make progress in understanding the probability of knotting in ring polymers we have to make a choice of how to model the system. Several different models have been considered and these have their own specific advantages and disadvantages. Below we list some of them.

(i) Lattice polygons: A simple model which captures the fact that monomers take up space to the exclusion of other monomers is a *lattice polygon*. The model is discrete so that one is simply counting objects and combinatorial ideas and methods can be used. Consider the simple cubic lattice as an example. A lattice polygon is an embedding of a simple closed curve in this lattice. That is, it is an alternating sequence of vertices and edges in the lattice so that no vertex of the lattice is visited more than once, and the zeroth and last vertices of the sequence are identical (see Fig. 8 for an example of a knotted lattice polygon). It can also be thought of as a walk which revisits its zeroth vertex at its last step and is otherwise self-avoiding. Polygons are regarded as being distinct if they cannot be superimposed by translation. Clearly the smallest polygon has four edges and there are three ways to embed a square in the lattice [in the (x,y), (x,z), and (y,z) planes]. If we write p_n for the number of polygons with n edges then $p_4=3$. Similarly it is not difficult to see that $p_6=22$ and $p_8=207$. Note that all polygons on the simple cubic lattice have an even number of edges.

(ii) Equilateral random polygons: These are closed (piecewise linear) curves in R^3 where all the edges making up the curve have equal length. Successive edges are equally likely to point in any direction. One can think of them as random walks (with all steps of equal length) in R^3 conditioned to return to their starting point on their last step. Notice that with probability 1 an equilateral random polygon is a simple closed curve (i.e., it has no self-intersections) and knotting is well defined.

(iii) Gaussian random polygons: These are similar to equilateral random polygons but where each edge is a Gaussian random vector.

(iv) Continuum models with balls at the vertices: To account for the fact that monomers take up space and exclude other monomers one can add hard balls at each vertex of either of the previous two models. One then conditions on the balls being disjoint. These are sometimes called rod-bead models (Chen, 1981a, 1981b, 1981c).

(v) Thick continuum models: In a similar way one can thicken the edges in equilateral or Gaussian random polygons, and insist that these thick edges are disjoint except around a vertex where two edges meet. Effectively this is a tubular neighborhood of an equilateral or Gaussian random polygon.

(vi) Wormlike chains: This model is also a continuum

model but with continuous curvature of the chain, where the curvature direction is random at every point along the chain. It can be thought of as a limiting version of the freely rotating chain. (The freely rotating chain is a piecewise linear, equilateral model, where the angle between adjacent edges is fixed, but where all dihedral angles are equally likely.) The wormlike chain (WLC) was first invented by Kratky and Porod (1949) and a useful description can be found in Flory (1969). In contrast to the previous cited models the WLC is a useful model for stiff chains, such as double stranded DNA, where the persistence length is relatively large. For example, the WLC model has proven to be very useful in understanding the force-extension diagram of a DNA molecule (Smith *et al.*, 1992; Bustamante *et al.*, 1994; Marko and Siggia, 1995).

1. A rigorous proof of a conjecture

In the early 1960s Frisch, Wasserman, and Delbruck (Frisch and Wasserman, 1961; Delbruck, 1962) conjectured that sufficiently long ring polymers would be knotted with high probability. Although this conjecture was investigated numerically it was not until 1988 that it was established rigorously for well-defined models (Sumners and Whittington, 1988; Pippenger, 1989; Soteros, Sumners, and Whittington, 1992; Diao, Pippenger, and Sumners, 1994; Diao, 1995). The simplest case to study is lattice polygons. Suppose that we write p_n for the number of n-edge polygons on the simple cubic lattice, then it is known that p_n increases exponentially rapidly as the number of edges increases. In fact, Hammersley (1961) showed that

$$0 < \lim_{n\to\infty} n^{-1} \log p_n \equiv \kappa < \infty \tag{6}$$

which means that

$$p_n = e^{\kappa n + o(n)}. \tag{7}$$

The quantity κ is called the connective constant of the lattice and, for the simple cubic lattice, it is easy to see that

$$\log 3 \le \kappa \le \log 5. \tag{8}$$

Numerical estimates show that $\kappa \approx \log(4.68) \approx 1.54$. κ is the limiting entropy per edge of the polygon in reduced units. If c_n is the number of n-edge self-avoiding walks on the lattice (so that $c_1=6$, $c_2=30$, $c_3=150$, $c_4=5\times150-3\times2\times4=726$), then Hammersley (1961) also showed that

$$\lim_{n\to\infty} n^{-1} \log c_n = \kappa, \tag{9}$$

so the numbers of polygons and self-avoiding walks grow at the same exponential rate. The equality of the connective constant for self-avoiding walks and polygons is the basis for the inequalities in Eq. (8). The upper bound comes from the fact that the set of walks with no reverse steps contains the set of self-avoiding walks. The lower bound comes from the subset of self-avoiding walks with steps only in positive coordinate directions.

If we write p_n^o for the number of unknotted polygons with n edges then Diao (1993) showed that $p_n^o = p_n$ for $n \le 23$ so that all polygons in the simple cubic lattice with less than 24 edges are unknotted. At 24 edges the only knot which can occur is the trefoil (see Fig. 8). We note that the probability that a polygon with n edges is unknotted P_n^o can be written as

$$P_n^o = \frac{p_n^o}{p_n} \tag{10}$$

and the Frish-Wasserman-Delbruck conjecture says that P_n^o goes to zero as n goes to infinity. In fact, Sumners and Whittington (1988) and independently Pippenger (1989) showed that

$$\lim_{n\to\infty} n^{-1} \log p_n^o = \kappa_o \tag{11}$$

and that $\kappa_o < \kappa$, so the limiting entropy per edge of an unknotted polygon is strictly less than that of a polygon where there is no restriction on the knot type. This implies that

$$P_n^o = e^{-(\kappa-\kappa_o)n + o(n)} = e^{-\alpha_0 n + o(n)}, \tag{12}$$

where $\alpha_0 > 0$. Hence P_n^o goes to zero as n goes to infinity (the Frisch-Wasserman-Delbruck conjecture) and goes to zero exponentially rapidly. There are no useful rigorous results about the magnitude of the constant α_0.

The proof is technical but the basic ideas are quite simple. We want to show that most sufficiently long polygons contain a knot which is tied so tightly that there is no space available for the polygon to rethread through this region and unknot the polygon. In fact the proof uses only three main ideas:

(i) The first idea is purely topological. For any knot type k there does not exist a knot type k' such that the connect sum $k\#k' = \emptyset$, the unknot. This means that there are no *antiknots* which will unknot a given knot. If you tie a knot in a hose pipe there is no point in then tying an additional knot in the hope that the two will cancel. The proof of this statement relies on the additivity of genus. If a knot has two components then the genus of the knot is the sum of the genuses of the two components. Since every nontrivial knot has positive genus the nonexistence of antiknots follows immediately.

(ii) If we have a local knot in a polygon, we still have to worry about the remainder of the polygon reentering this local region and untying the knot. For lattices this problem is easy to handle in the following way. Every vertex has an associated dual three-cell (the Wigner-Seitz cell) so every subwalk has an associated neighborhood made up

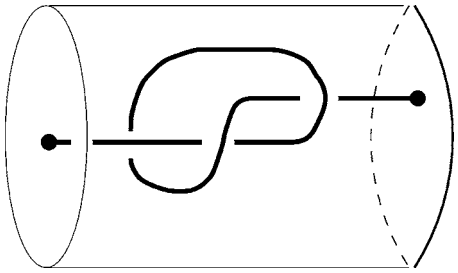

FIG. 9. A sketch of the knotted ball pair corresponding to the trefoil.

of the union of these dual three-cells. If we consider a subwalk then its associated set of dual three-cells might be a three-ball. If so, we have a *ball pair* (a three-ball and a properly embedded one-ball). We can ask if this ball pair is knotted. See Fig. 9 for a sketch of a knotted ball pair whose knot type is 3_1. (A ball pair is *unknotted* if the ball pair can be smoothly deformed to give the standard geometrical three-ball with the one-ball as a diameter. Otherwise it is *knotted*.) If the polygon contains a subwalk such that the walk and its dual three-cell neighborhood form a knotted ball pair then the polygon cannot reenter this region (the three-ball) so we are guaranteed that the polygon is knotted.

(iii) Finally we need to guarantee that these subwalks corresponding to knotted ball pairs occur on most sufficiently long polygons. For this we use a pattern theorem due to Kesten (1963). Consider a subwalk ω which can occur at least three times on a sufficiently long self-avoiding walk. Let $p_n(\bar{\omega})$ be the number of n-edge polygons which do not contain ω as a subwalk. Then

$$\limsup_{n\to\infty} n^{-1}\log p_n(\bar{\omega}) < \kappa \tag{13}$$

so we are guaranteed that the subwalk occurs at least once on all except exponentially few sufficiently long polygons.

Now we are ready to prove the theorem. Suppose that ω is a subwalk corresponding to a tightly tied trefoil, so that the knot type of the ball pair corresponding to ω and its associated three-ball neighborhood is 3_1; see Fig. 9. Write $p_n(\bar{3}_1)$ for the number of n-edge polygons which do not contain a trefoil as part of the knot decomposition. We have the following set of inequalities:

$$p_n^o \le p_n(\bar{3}_1) \le p_n(\bar{\omega}). \tag{14}$$

We then use Kesten's pattern theorem to obtain

$$\lim_{n\to\infty} n^{-1}\log p_n^o \equiv \kappa_o < \kappa. \tag{15}$$

Although these results are for the simple cubic lattice they can be extended to some other lattices in three dimensions, such as the face-centered-cubic lattice.

Similar results have been obtained for Gaussian random polygons and for equilateral random polygons (Diao *et al.*, 1994; Diao, 1995). For these models there are additional technical difficulties since for off-lattice models we do not have an excluded volume (the dual three-cell) for each vertex. Instead one must consider three-balls which are large enough that they contain a knotted subwalk with high probability but small enough that the ball will be revisited with low probability. Otherwise the idea of the proof is similar to the lattice case.

For extensions of these continuum models (where the edges are thickened or balls are associated with each vertex) no such rigorous results exist.

Embeddings of graphs in lattices can also be knotted and there are extensions of these kinds of results to knotted graphs (Soteros *et al.*, 1992).

2. Measures of knot complexity

Given that sufficiently long ring polymers are knotted with high probability one can ask how badly knotted the polymer is likely to be. This introduces the idea of measures of knot complexity. For instance, one could ask for the probability that the knot is prime, or how many components there are likely to be in the knot type. One can also ask for the typical crossing number or the typical unknotting number, or for the span of the Alexander or Jones polynomial. Another useful measure of knot complexity is $\log|\Delta(-1)|$. The results of the previous section can be extended to give some partial answers to these questions.

As it stands the argument given in the last section for lattice polygons guarantees that all but exponentially few sufficiently long polygons will contain a trefoil as part of their knot decomposition. In addition, one can consider a pattern corresponding to a pair of trefoils and then the argument shows that most polygons contain at least two trefoils and so are composite. This implies that prime knots are exponentially rare. There is nothing special about the trefoil in the above argument so the argument can be extended to show that sufficiently long polygons contain any given knot type with high probability.

Kesten's theorem tells us more. It says that not only do all except exponentially few polygons contain a given subwalk ω but that the subwalk occurs with positive density. That is, there is a positive number $\epsilon=\epsilon(\omega)$ such that with high probability the polygon will contain at least ϵn copies of ω for large enough n. So sufficiently long polygons contain a positive density of knots of every fixed knot type, with high probability. This kind of argument can be used to show that the expected value of the crossing number increases at least linearly with n as n goes to infinity, with similar results for other measures of knot complexity (Soteros *et al.*, 1992). In particular $\langle\log|\Delta(-1)|\rangle$ increases at least linearly with increasing n.

There are no corresponding results for any continuum models. However, for Gaussian random polygons and for equilateral random polygons we know that the knot

is a satellite knot with high probability (Jungreis, 1994; Diao *et al.*, 2001).

3. Ring polymers with specified knot type

A somewhat different kind of question is to ask for the probability that a ring polymer has a particular knot type. For instance, how likely is it that the polymer is a trefoil? (This is not the same as asking for the probability that the ring contains a trefoil as part of its knot decomposition.)

We present some results for the trefoil but the same arguments work for any other given knot type. Since everything which is known rigorously about this question is for lattice polygons, we shall restrict ourselves to this case.

Let $p_n(3_1)$ be the number of n-edge polygons whose knot type is the trefoil. Since all except exponentially few polygons contain at least one copy of, say, the knot 4_1,

$$\limsup_{n\to\infty} n^{-1}\log p_n(3_1) < \kappa \tag{16}$$

so polygons with a particular knot type are exponentially rare (Whittington, 1992). We can also ask how they compare with unknots. A subset of trefoil polygons with n edges can be constructed by concatenating trefoil polygons with m edges and unknots with $n-m$ edges (Whittington, 1992). This gives the inequality

$$p_n(3_1) \geq \tfrac{1}{2} p_m(3_1) p_{n-m}(\emptyset). \tag{17}$$

Taking logarithms, dividing by n, and letting n go to infinity with m fixed gives the inequality

$$\liminf_{n\to\infty} n^{-1}\log p_n(3_1) \geq \kappa_o \tag{18}$$

so that to exponential order there at least as many trefoils as unknots.

These results are expressed using lim inf and lim sup because the existence of the limit $\lim_{n\to\infty} n^{-1}\log p_n(3_1)$ is an open question. It would be interesting to establish whether Eq. (18) is an equality or a strict inequality. This would give useful information about the relative abundance of unknots and ring polymers with a particular knot type.

4. Rings in confined geometries

Polymers are often confined in some way. For instance, DNA can be confined in a cell, in the nucleus, or in a viral capsid. Polymers used in steric stabilization of dispersions can be confined between two large colloidal particles, and polymers can be confined in capillaries. These geometrical constraints can affect the properties of the polymer in many ways. For instance, the entropy of the polymer is decreased, and its size and shape can be affected.

Tesi, Janse van Rensburg, Orlandini, and Whittington (1994) considered lattice polygons in a slab of the simple-cubic lattice. That is, they considered polygons confined between two parallel planes $z=0$ and $z=L$. It is possible to have knotted polygons whenever $L>0$. Let $p_n(L)$ be the number of n-edge polygons with this constraint where two polygons are considered distinct if they cannot be superimposed by translation in the x and y directions. It can be shown that

$$\lim_{n\to\infty} n^{-1}\log p_n(L) \equiv \kappa(L), \tag{19}$$

where $\kappa(L)$ is a strictly increasing function of L and

$$\lim_{L\to\infty} \kappa(L) = \kappa. \tag{20}$$

If $p_n^o(L)$ is the number of n-edge *unknotted* polygons in a slab of width L then Tesi, Janse van Rensburg, Orlandini, and Whittington (1994) showed that

$$\lim_{n\to\infty} n^{-1}\log p_n^o(L) \equiv \kappa_o(L) \tag{21}$$

and that $\kappa_o(L)<\kappa(L)$ for all $L\geq 1$. This means that sufficiently long polygons with this slab constraint are knotted with high probability.

Soteros (1998) proved a pattern theorem for polygons in prisms using transfer-matrix methods and used this result to show that sufficiently long polygons in prisms are knotted with high probability.

5. Adsorbing ring polymers

When a ring polymer in solution adsorbs at an impenetrable surface one might expect that the probability that the ring is knotted would decrease in the adsorbed phase compared to in the desorbed phase. The problem has been studied for lattice polygons by Vanderzande (1995) and by Janse van Rensburg (2002a). The model is as follows. Consider the simple cubic lattice with vertices having integer coordinates (x,y,z) and the half space $z\geq 0$. The plane $z=0$ corresponds to a plane at which adsorption can occur and the space $z>0$ corresponds to the solution in contact with this plane. We call vertices in the plane $z=0$ visits. Consider n-edge polygons in the half space $z\geq 0$ with at least one visit. Let $p_{n,m}$ be the number of polygons with n edges and with m visits. We can construct the partition function

$$Z_n(\alpha) = \sum_{m=1}^{n} p_{m,n} e^{\alpha m}, \tag{22}$$

where $\alpha=-\epsilon/k_BT$. T is the absolute temperature, k_B is Boltzmann's constant, and $\epsilon<0$ is the energy associated with a visit, i.e., with an adsorbed monomer. There exists an $\alpha_c>0$ such that the reduced limiting free energy

$$\mathcal{F}(\alpha) = \lim_{n\to\infty} n^{-1}\log Z_n(\alpha) \tag{23}$$

is equal to κ, independent of α, for all $\alpha\leq\alpha_c$ and is strictly greater than κ for all $\alpha>\alpha_c$. Suppose that $\langle m\rangle$ is the mean number of visits. Then

$$\rho(\alpha) = \lim_{n\to\infty} \frac{\langle m \rangle}{n} \tag{24}$$

is the limiting fraction of vertices in the plane $z=0$, i.e., the limiting fraction of vertices which are visits. Then $\rho(\alpha)=0$ for all $\alpha<\alpha_c$ and $\rho(\alpha)>0$ for all $\alpha>\alpha_c$.

The critical value α_c corresponds to the adsorption transition. With fixed $\epsilon<0$ there is a critical temperature T_0 above which the polymer is desorbed and below which it is adsorbed. It is not known rigorously whether the transition is first order (ρ discontinuous) or higher order (ρ continuous), though there is convincing numerical evidence that the transition is not first order (Hegger and Grassberger, 1995). There are also convincing scaling arguments describing the adsorption transition [see, for example, de Gennes (1979) and Vanderzande (1998)].

Vanderzande (1995) showed that for every finite value of α, as n goes to infinity the probability that the polygon is knotted goes to 1. So except in the limiting case of infinite α (i.e., zero temperature) when the polygon lies completely in the plane $z=0$ the polygon is knotted with high probability. Of course, the knot probability for finite n will depend on α and this has been investigated numerically (see Sec. III.B.4).

How can we understand this result? For any $\alpha<\infty$ one can show that there are very large excursions (i.e., out-of-plane subwalks). This means that the number of vertices between successive visits can be very large. If these excursions are large enough then they will be knotted with high probability by an argument similar to that used in Sec. III.A.1. In addition, one can think of the adsorbed polygon as having some typical span in the z direction so that, roughly speaking, it lies in a slab (see Sec. III.A.4). If the slab has width of at least 1, then this is wide enough for knots to form and one can appeal to the results of Sec. III.A.4 to understand the knotting.

6. Semiflexible polymers

Different polymer molecules can have very different degrees of flexibility and biopolymers such as DNA are in fact very stiff. One would expect that the flexibility might affect the probability of knotting. Orlandini and Tesi (1998) considered a lattice model of ring polymers with an additional term to account for a bending energy. They considered polygons on the simple cubic lattice where they kept track of the number of right angles between adjacent pairs of edges (meeting at a vertex). Suppose that $p_n(k)$ is the number of n-edge polygons with k right angles. One can construct a partition function

$$Q_n(\gamma) = \sum_k p_n(k) e^{\gamma k}. \tag{25}$$

Here γ can be thought of as a flexibility parameter. The free energy $\mathcal{Q}$ is given by

$$\mathcal{Q}(\gamma) = \lim_{n\to\infty} n^{-1} \log Q_n(\gamma). \tag{26}$$

If we write $p_n^o(k)$ for the number of unknotted polygons with n edges and k right angles, we can define the corresponding partition function and free energy

$$Q_n^o(\gamma) = \sum_k p_n^o(k) e^{\gamma k} \tag{27}$$

and

$$\mathcal{Q}^o(\gamma) = \lim_{n\to\infty} n^{-1} \log Q_n^o(\gamma). \tag{28}$$

Orlandini and Tesi (1998) showed that

$$\mathcal{Q}^o(\gamma) < \mathcal{Q}(\gamma) \tag{29}$$

for all finite γ. This means that even semiflexible polygons are knotted in the infinite n limit though the knot probability at finite n will of course depend on γ, as we show later. The effect of increasing the stiffness is to decrease the effective number of edges. Although this affects how the limiting behavior is approached, it does not affect the behavior in the infinite n limit. As far as we know no corresponding results are available for any continuum models.

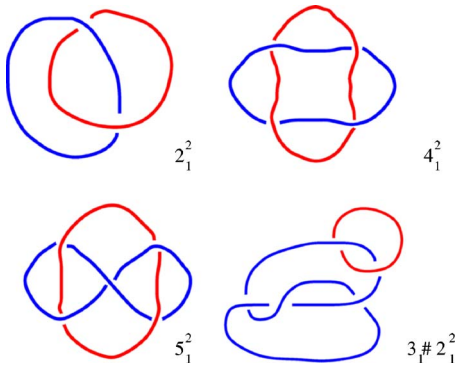

FIG. 10. (Color online) Some link diagrams. The links shown are the Hopf link, the (2,4)-torus link, the Whitehead link, and the connect sum of the trefoil and the Hopf link.

7. Linked rings

In the same way that a simple closed curve can be self-entangled to form a knot, two simple closed curves can be mutually entangled. If the two curves cannot be deformed so that they lie on two different sides of a plane, we say that they are *linked* or that they form a *link*. Sometimes we call this *topological linking*. The simplest kind of link has two crossings, and is called the *Hopf link* 2_1^2. It is sketched in Fig. 10. Links (or catenanes) are of interest chemically in their own right (Frisch and Wasserman, 1961; Dietrich-Buchecker and Sauvage, 1984). In addition, linked pairs of DNA rings occur in the mitochondria of malignant cells (Hudson and Vinograd, 1967) and are intermediates in the replications of circular DNA (Adams *et al.*, 1992), so linking can have important biological consequences.

The simplest link invariant is the *linking number*. To compute this we first orient both curves. At each crossing of the two curves (note that we ignore places where a curve crosses itself) we attach a sign (i.e., ±1) according to a right-hand rule as in Fig. 4. If we have K crossings

numbered $i=1,2,\ldots,K$ with crossing i having sign σ_i, the linking number of the link is

$$Lk = \frac{1}{2}\sum_{i=1}^{K} \sigma_i. \tag{30}$$

Since the sign of Lk depends on the orientations attached to the two curves, we are often interested only in $|Lk|$. For the Hopf link $|Lk|=1$. In Fig. 10 we also sketch the (2,4)-torus link 4_1^2 with $|Lk|=2$. If $|Lk|\neq 0$ then the two curves are linked but if $|Lk|=0$, this invariant does not definitely tell us that they are unlinked. For instance, for the Whitehead link 5_1^2, sketched in Fig. 10, the two curves are linked but $|Lk|=0$. If $|Lk|\neq 0$, we say that the two curves are *homologically linked* so if they are homologically linked, they are topologically linked but not vice versa.

One can form a link between two closed curves, one or both of which can be knotted. For instance, the trefoil can be linked to the unknot as shown in Fig. 10 to give the connect sum of the trefoil and the Hopf link $3_1\#2_1^2$. One can also have links with k simple closed curves, $k>2$. We say that the link has k *components*.

Little is known rigorously, but some work has been done on the linking probability for random embeddings of circles in R^3 (Duplantier, 1981; Pohl, 1981) and in the cubic lattice (Orlandini, Janse van Rensburg, *et al.*, 1994).

Consider, for example, two simple closed curves which are embedded in the simple cubic lattice so that (i) neither of the two curves is knotted, (ii) each curve has length n, so that each of them is an n-edge polygon, and (iii) the pair of curves forms a link of some particular link type τ.

We can ask for the number of such embeddings $p_{n,n}^{(2)}(\tau)$ where the superscript tells us that the link has two components and the subscripts tell that each polygon has n edges. Orlandini, Janse van Rensburg, *et al.* (1994) investigated this question and proved that

$$\lim_{n\to\infty} (2n)^{-1}\log p_{n,n}^{(2)}(\tau) = \kappa_0 \tag{31}$$

independent of the two component link type τ. This means that the numbers of embeddings of two equal sized polygons linked as the Hopf link, the $(2,4)$-torus link, the Whitehead link, etc., all grow at the same exponential rate. If k unknotted polygons form a k-component link of type τ, so that each polygon has n edges then

$$\lim_{n\to\infty} (kn)^{-1}\log p_{n,n,\ldots}^{(k)}(\tau) = \kappa_0 \tag{32}$$

independent of the k-component link type τ. Some extensions of these results can be found in Soteros *et al.* (1999).

It is interesting to compare these results about the exponential growth rate being independent of link type with the situation of single polygons with fixed knot type, where no such result is available (see Sec. III.A.3).

Diao (1994) and Diao and Janse van Rensburg (1998) have looked at the opposite extreme case where there is a large density of simple closed curves and one asks for the probability that they form an unsplittable link. This means that there is no smooth deformation (ambient isotopy) whereby some of the simple closed curves can be separated from others by placing them on opposite sides of a plane.

As the simplest possible case Diao (1994) considered two geometrical circles with unit radius, oriented at random in three-space but with the distance between their centers fixed at r. He showed that $P(r)$, the linking probability, is given by

$$P(r) = 1 - r/2, \tag{33}$$

when $0\leq r\leq 2$ and zero otherwise. This is a remarkably simple result.

We call $B(O,R)$ the three-ball of radius R centered at O. Suppose we have n unit radius circles with centers randomly distributed in $B(O,R)$ and with random orientations. Diao (1994) showed that the probability that these n circles form an unsplittable link is at least $1-e^{-\beta n}$ for some $\beta>0$.

Diao and Janse van Rensburg (1998) considered a collection of unit radius circles with their centers generated by a Poisson process in three-space and with random orientations. They showed that there is a critical value δ_c of the density (δ) of circles such that for $\delta<\delta_c$ the probability that there is an infinite unsplittable link is zero. For $\delta>\delta_c$ this probability is positive. This work on many linked rings may be relevant to understanding the arrangement of DNA circles in trypanosomes. These micro-organisms are associated with serious diseases such as leishmaniasis and Chagas disease. They have an organelle called the kinetoplast which houses thousands of DNA circles which can be interlinked to form a network resembling chain mail (Chen *et al.*, 1995).

8. Ribbon models

Some polymer molecules, such as double stranded DNA, consist of two polymer chains which wind around one another. These molecules can be modeled as ribbons in three-space where the two polymer chains form the two boundary curves of the ribbon. If the two ends of the ribbon are glued together, we have a *closed ribbon*. The closed ribbon can have two boundary curves (i.e., it is homeomorphic to a cylinder) and it is then an *orientable ribbon* (see Fig. 11 for some examples) or one boundary curve (i.e., it is homeomorphic to a Mobius band) and it is then a nonorientable ribbon (see Fig. 12). In the case of DNA the two polynucleotide chains run antiparallel and the chemistry then requires that when the chain ends join to form a closed ribbon the ribbon must be orientable.

When the ribbon is orientable we can ask if the center line of the ribbon is knotted or whether the boundary curves are knotted. In fact, the knot type of the center line is the same as the knot type of either boundary curve (because the pushoff across the ribbon is an ambi-

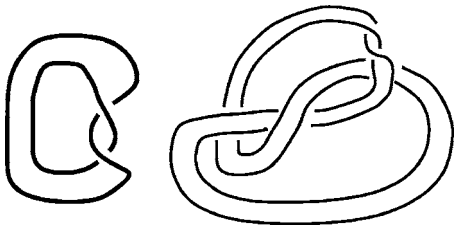

FIG. 11. Some orientable ribbons. In the sketch on the left the two boundary curves form the Hopf link. On the right they are a satellite link of the trefoil.

ent isotopy). But there is an additional complication because the two boundary curves can be linked. If the center line is unknotted then the only possible link types are the $(2,2k)$-torus links. The simplest example is the Hopf link and the next most complicated is the $(2,4)$-torus link shown in Fig. 10. If the center line is knotted then the two boundary curves can form a *satellite link*. See Fig. 11 for an example of a satellite link when the knot type of the center line is the trefoil.

When the ribbon is nonorientable there is only one boundary curve. If the center line is unknotted then the knot type of the boundary curve must be a $(2,2k+1)$-torus knot (unless it is unknotted). If the center line is knotted, the boundary curve is a satellite knot. See Fig. 12 for an example of a satellite knot when the knot type of the center line is the trefoil.

Janse van Rensburg *et al.* (1994, 1996) considered a lattice version of a ribbon. Consider the simple cubic lattice. A *plaquette* is a unit square whose vertices are at vertices of the simple cubic lattice. Plaquettes can be attached so that they share a common edge and a sequence of plaquettes can form a closed ribbon, which can be orientable or nonorientable. One can count the number of embeddings of an orientable closed ribbon with n plaquettes and show that this number increases exponentially rapidly with n. The rate of increase (to exponential order) is the same for orientable and nonorientable ribbons. Janse van Rensburg *et al.* (1996) showed that all except exponentially few sufficiently long orientable ribbons have a knotted center line so the boundary curves are knotted. Nonorientable ribbons also have knotted center lines with high probability so, with high probability, the boundary curve is a satellite knot. These proofs are an extension of the proof sketched in Sec. III.A.1 for lattice polygons.

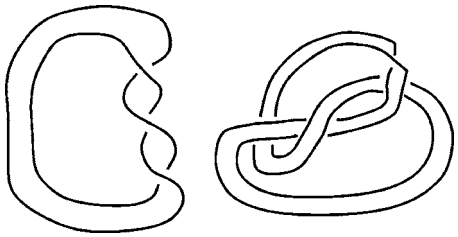

FIG. 12. Some nonorientable ribbons. The left figure shows a ribbon whose boundary curve is the trefoil, i.e., the $(2,3)$-torus knot. The right is a satellite knot of the trefoil.

In the case of orientable ribbons the boundary curves can be linked and it is reasonable to ask how badly linked they are likely to be. One measure of the link complexity is the linking number Lk (see Sec. III.A.7). Janse van Rensburg *et al.* (1996) showed that

$$\langle |Lk| \rangle \geq An^{1/2} \tag{34}$$

for some positive constant A, and n sufficiently large.

For any smooth orientable ribbon the linking number of the two boundary curves can be written as the sum of two geometrical quantities, the twist Tw and the writhe Wr so that

$$Lk = Tw + Wr. \tag{35}$$

This is White's theorem (White, 1969). Twist characterizes the local crossings between the two boundary curves and writhe characterizes the nonlocal (or distant) crossings of one curve with itself. Writhe is a useful measure of the degree of supercoiling in molecules like DNA. In the continuum the twist and writhe can be computed by integrating around the closed curve (Călugăreanu, 1959; Pohl, 1968; Fuller, 1971). For lattice models there is a convenient way to calculate the writhe by computing linking numbers of the curve with its pushoffs in certain directions (Lacher and Sumners, 1991; Garcia *et al.*, 1999; Laing and Sumners, 2006). Janse van Rensburg *et al.* (1996) showed that

$$\langle |Wr| \rangle \geq Bn^{1/2} \tag{36}$$

and

$$\langle |Tw| \rangle \geq Cn^{1/2} \tag{37}$$

for some positive constants B and C, and n sufficiently large.

For the nonorientable case the writhe of the center line of the ribbon satisfies the inequality (36).

9. Some open problems

We end this section on rigorous results with a short list of open problems which we regard as being especially interesting.

(i) We know that the constant α_0 in the expression for the unknotting probability is positive but little else is known. Provide good upper and lower bounds on α_0. This is equivalent to providing bounds on the entropy difference between all polygons and unknotted polygons.

(ii) Does α_0 depend on the lattice? For example, is α_0 different for the simple cubic and face centered cubic lattices? One might expect α_0 to be lattice dependent since κ certainly depends on the lattice. However, α_0 is a *difference* between two nonuniversal quantities.

(iii) Although we know that the limit

$$\lim_{n\to\infty} n^{-1} \log p_n^o$$

exists, we do not know that the limit

$$\lim_{n\to\infty} n^{-1}\log p_n(3_1)$$

exists. Of course, the situation is the same for all nontrivial knot types.

(iv) Does the number of trefoils increase at the same exponential rate as unknots or does the number of trefoils increase exponentially more rapidly?

(v) We know (Whittington, 1992) that the number of granny knots increases at least as rapidly (on an exponential scale) as the number of trefoils. Do they increase at the same exponential rate?

(vi) Do ring polymers with fixed knot type collapse at the same temperature as unrestricted ring polymers?

(vii) When a ring polymer collapses to form a compact structure below the θ temperature, there is strong numerical evidence that the knot probability increases. Can we say anything rigorously about this?

B. Numerical approaches

In order to investigate the topological properties of ring polymers we have to choose a suitable numerical approach. Knotting does not occur, or occurs with small probability for short ring polymers, in spite of the fact that we know that polygons are knotted with probability 1 in the infinite size limit. For instance, all polygons on the simple cubic lattice with less than 24 edges are unknotted and only the trefoil can occur on these polygons with 24 edges (Diao, 1993). This suggests that the most useful numerical methods will be those which can be applied directly to long polymer molecules, such as Monte Carlo methods and methods based on stochastic dynamics. Monte Carlo methods are designed to form a random sample of large polygons from which the properties of the complete set of polygons with that size can be estimated by statistical methods.

There are two problems to be faced. The first is to design an algorithm which will sample the space of polygons, either with a fixed number of edges or in an ensemble where the number of edges can vary. This in itself is a difficult problem but several algorithms exist and, especially for the lattice problem, the algorithms have been the subject of both rigorous analysis (to make sure that they sample the complete space and that they sample with the expected probability distribution) and stringent numerical tests. We describe two basic approaches for the lattice problem and some extensions which improve the sampling in some circumstances. At least some of the Monte Carlo methods which have been used for continuum models are closely related to methods for lattice problems.

The second problem is to identify the knot type. In practice one uses a topological invariant such as the Alexander polynomial $\Delta(t)$, even though this is not a perfect discriminator; see Sec. II. The computer time required grows like $O(n\log n)+O(k^2)$, where n is the number of edges in the polygon and k is the number of crossings. If less information is needed, it is sometimes sufficient to calculate $\Delta(-1)$. If more information is needed, it is possible to calculate additional polynomials such as the Jones polynomial or HOMFLY polynomial, although the computer time needed then grows exponentially with the number of crossings. One can also calculate Vassiliev invariants such as the derivatives of the Jones polynomial, which are less computationally intensive (Deguchi and Tsurusaki, 1993).

The identification of the knot type is necessary if one wants to sample the space of all polygons of a given size, and estimate the fraction of such polygons which are unknotted or which are trefoils, etc. Sometimes the question of interest is how to sample polygons with a fixed knot type and examine their properties, perhaps as a function of the number of edges. If one can construct an algorithm which samples the space of polygons with fixed knot type, this avoids the problem of computing a knot invariant but one then needs assurance that the algorithm samples appropriately from the polygon subspace. All these sampling issues will be addressed in the next sections.

1. Numerical studies of knot probabilities

We begin by describing an algorithm designed for systems with a fixed number (n) of edges where one wants to sample over the space of all knot types and estimate the relative frequency of occurrence of different knot types (especially the unknot). The calculation is then repeated for different values of n to estimate the knot probability as a function of n. We focus on the lattice case but similar methodology has been used to sample in continuum models.

The basic idea is to use a Markov chain to provide correlated samples. With n fixed the p_n polygons are the states $i=1,2,\ldots,p_n$ of a Markov chain. One constructs a Markov chain with transition matrix Q with elements q_{ij}, where q_{ij} is the transition probability from state i to state j. In the simplest situation where all polygons have equal weight (which is the typical situation when one is thinking of the good solvent regime and there are no flexibility terms or geometrical constraints) the limit distribution of the Markov chain should be uniform, and this limit distribution should be unique, independent of the initial state. Provided that the Markov chain is ergodic (i.e., any state can be reached from any other state in a finite number of time steps), aperiodic, and symmetric (i.e., $q_{ij}=q_{ji}$ for all i,j) the limit distribution will be unique and uniform.

How should one construct the Markov chain? One knows from experience with Markov chain sampling for self-avoiding walks that one cannot use only local moves (Madras and Sokal, 1987) and that one should aim for a Markov chain that has the possibility of making large changes in the conformation, even if these changes are only accepted infrequently. The pivot algorithm is known to work well for self-avoiding walks (Lal, 1969;

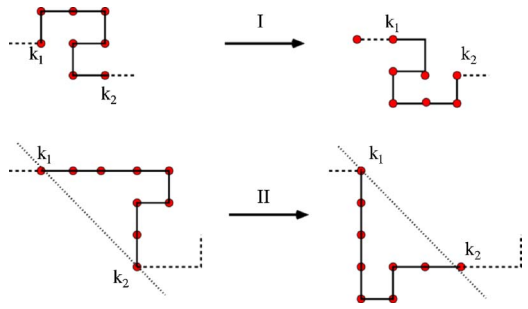

FIG. 13. (Color online) Examples of pivot moves: I, inversion. II, reflection through the $x=-y$ line.

Madras and Sokal, 1988). A modification of the pivot algorithm which is designed for polygons is the two-point pivot algorithm by Madras, Orlitsky, and Shepp (1990). The algorithm works as follows. Given a polygon with n edges label the vertices $k=1,2,\ldots,n$. Pick two vertices $k_1<k_2$ uniformly and independently. Split the polygon into two subwalks, one from k_1 to k_2 and the other from k_2 to k_1. Pick the shorter of these. Apply a lattice symmetry transformation to the shorter walk which leaves the end points of the walk invariant. (For example, one can invert or reflect the subwalk as shown in Fig. 13. One can always apply an inversion transformation but rotations and reflections can be applied only when the end points of the shorter walk are on particular lines in the lattice.) Reconnect the two subwalks at their (unchanged) end points. If the resulting object is a polygon, accept with probability 1 as the next state of the realization of the Markov chain. Otherwise reject it and the next state of the realization of the Markov chain is the current polygon. This Markov chain can be shown to be ergodic, aperiodic, and to have uniform unique limit distribution. Since the sequence of polygons generated is highly correlated, some care must be taken in forming reliable error estimates of the desired quantities. For continuum models such as equilateral random polygons in three-space one can use the same idea. One scheme which has been used is to pick two vertices at random, disconnect the polygon at these two vertices into two subwalks, and rotate the shorter walk about the line joining these two points through a randomly chosen angle. For equilateral random polygons the new object will be a polygon with probability 1 (although in principle one should worry about word length problems on the computer), so the new object is accepted. In variants where the equilateral polygon has thick edges or there are balls at the vertices one must check that the newly created object has no undesirable overlaps of balls or cylinders, etc. If not, the object is accepted as the new polygon. If there are overlaps (i.e., the excluded volume constraints are violated), the next polygon in the realization of the Markov chain is the old polygon. Modifications with other symmetry transformations in addition to rotation are also possible. The required ergodicity result for equilateral random polygons was proven by Millett (1994).

Next we describe the results for some Monte Carlo studies of knot probabilities. The first attempt to study numerically the knot probability for polymer rings was due to Frank-Kamenetskii's group who analyzed the frequency of knots for n-step polygons on the body-centered-cubic lattice (Frank-Kamenetskii *et al.*, 1975). Their results seemed to indicate that the constant α_0 is very small although the generation of relatively short polygons ($n\leq 160$) did not allow an estimate of its value. The first estimate of α_0 was by Janse van Rensburg and Whittington in 1990. They used a two-point pivot algorithm to study polygons on the face-centered-cubic lattice with up to 1600 edges. Using the Alexander polynomial they estimated the probability that a polygon is knotted for various values of n up to 1600 and fitted their data by the form

$$P_n^o = C_0 e^{-\alpha_0 n}. \tag{38}$$

They estimated that $\alpha_0=(7.6\pm0.9)\times10^{-6}$ and that C_0 is about 1. This means, of course, that κ and κ_o differ by only about 7.6×10^{-6} so it is quite hopeless to try to estimate the two connective constants separately. Moreover, even at $n=1600$ almost all knots found are trefoils (although we know from Sec. III.A.1 that in the large-n limit almost all knots must be composite). Yao *et al.* (2001) carried out a similar calculation for polygons with up to 3000 edges on the simple cubic lattice, using derivatives of the Jones polynomial to detect knotting, and estimated that $\alpha_0=(4.0\pm0.5)\times10^{-6}$. Janse van Rensburg (2002b) estimated α_0 on the simple-cubic, face-centered-cubic, and body-centered-cubic lattices, for polygons with up to 4000 edges, and obtained the values $\alpha_0=(4.15\pm0.32)\times10^{-6}$ (sc), $\alpha_0=(5.91\pm0.32)\times10^{-6}$ (fcc), and $\alpha_0=(5.82\pm0.37)\times10^{-6}$ (bcc). The first thing to notice is that these values are small. The second is that they indicate that α_0 is lattice dependent. Of course one can interpret α_0 as the inverse of a characteristic length n_0. For each of these lattices the value of n_0 is a little larger than 10^5. One can think of this length as roughly representing the length at which knotting starts to be important.

Since the incidence of knots is low in polygons, many studies have ignored the self-avoiding property of polymers and focused on polymers with Gaussian statistics instead (Vologodskii *et al.*, 1974; des Cloizeaux and Metha, 1979). Michels and Wiegel (1986) used a Langevin dynamics approach to study knotting in a continuum model where the polygon is represented by a sequence of up to 320 mass points joined by harmonic bonds. They estimated that the probability of being unknotted is roughly $P_n^o\approx\mu^n$, where $\mu=0.996\,40\pm0.000\,02$. This corresponds to $\alpha_0=(3.6\pm0.02)\times10^{-3}$. Consequently, α_0 is much larger for this off-lattice model with no excluded volume constraint (since the mass points have no size) than for lattice models, and this is borne out by other studies on knot probability for off-lattice models such as Gaussian random polygons and the rod-bead model. For Gaussian random polygons the exponential decay of the unknotting probability is confirmed with the constant α_0

being about 2.9×10^{-3} (i.e., $n_0\simeq340$) (Deguchi and Tsurusaki, 1993, 1997). For the rod-bead model the probability of being unknotted is still well represented by Eq. (38) but with α_0 increasing as the radius r of the beads decreases, ranging from 3.7×10^{-3} for $r=0.05$ (Deguchi and Tsurusaki, 1997) down to 1.25×10^{-6} for $r=0.499$ (Koniaris and Muthukumar, 1991a, 1991b), which is rather similar to the value found for the lattice calculation.

Another way to implement the excluded volume interaction is to consider polygons whose segments are given by cylinders of unit length with radius r (Shimamura and Deguchi, 2000). Two segments have no overlap if the distance between the central axis of the two cylinders is larger than $2r$ and allowed polygons are the ones with no overlaps between any pair of segments. By sampling polygons with a number of cylinders n up to 150 the authors were able to confirm the exponential decay behavior of the unknotting probability. Moreover, they showed that the characteristic length n_0 is roughly approximated by an exponential function of the cylinder radius (i.e., the chain thickness) r.

2. Rings in confined geometries

The first attempt to study ring polymers in a confined geometry was by Michels and Wiegel (1989). They were interested in the behavior of ring polymers in a slab geometry, i.e., confined between two parallel planes. As a simple model they considered closed curves in the plane in which the intersections were chosen to be + or − crossings at random. Their basic finding was that the knot probability was larger for this system than for ring polymers in three-space.

Tesi, Janse van Rensburg, Orlandini, and Whittington (1994) studied lattice polygons on the simple-cubic lattice confined so that the z coordinate of each vertex satisfied $0\le z\le L$, i.e., in a slab of width L. They used a two-point pivot algorithm coupled with rejection techniques to select polygons satisfying the slab constraint. At a fixed value of n they found that the knot probability first increased as L decreased and then decreased as L became close to 1. They estimated $\alpha_0(L)$ for $L=40$, 50, and 60. Their results for this range of L are consistent with $\alpha_0(L)=\alpha_0(\infty)+\beta/L$, where $\alpha_0(\infty)$ was found by Yao *et al.* (2001) for the complete simple-cubic lattice and β is a positive constant. Polygons in a prism were also studied in the same paper with qualitatively similar results.

Ring polymers have also been studied in cubes and spheres. The earliest study of this type was by Michels and Wiegel who found that the knot probability increases as the polymer becomes more constrained. For ring polymers with n monomers in a sphere of radius R the probability of being unknotted $P_n^o(R)$ appears to scale as

$$\frac{P_n^o(R)}{P_n^o(\infty)}=\frac{P_n^o(R)}{P_n^o}=g\left(\frac{n^\gamma}{R^3}\right), \tag{39}$$

with $\gamma\approx2.28$.

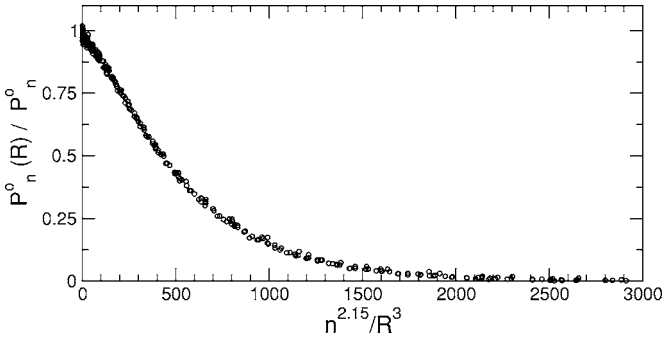

FIG. 14. Scaling of the unknotting probability for a ring confined to a sphere.

There has been a renewed interest in this geometrical constraint because of work on DNA in viral capsids. Recent Monte Carlo work on this problem for equilateral random polygons (Arsuaga *et al.*, 2002; Micheletti *et al.*, 2006) showed that the knot probability increases rapidly as the confining sphere decreases in radius. They found that their data scaled like Eq. (39) with $\gamma=2.15\pm0.04$; see Fig. 14. As R decreases the knot complexity increases and the distribution of knot types changes.

3. Semiflexible polymers

Polymers can have very different degrees of local flexibility and it is interesting to ask how the knot probability depends on the flexibility. The model discussed in Sec. III.A.6, where one keeps track of the number of right angles in the polygon and gives a weight to right angles, has also been studied by Monte Carlo methods for finite values of n (Orlandini *et al.*, 2005). Because different polygons can have very different weights the sampling procedure becomes more complicated. First one wants to sample from a Markov chain whose limit distribution is the appropriate Boltzmann distribution, not the uniform distribution. One can design a Markov chain with this limit distribution following the scheme originally proposed by Metropolis *et al.* (1953). If we have an underlying symmetric Markov chain with transition matrix Q with elements q_{ij} and we want to design a Markov chain with limit distribution $\{\pi_i\}$, we define a new Markov chain with transition matrix elements given by

$$p_{ij}=q_{ij}\min\left[\frac{\pi_j}{\pi_i},1\right] \tag{40}$$

when $j\neq i$ and

$$p_{ii}=1-\sum_{j\neq i}p_{ij} \tag{41}$$

for all i.

This is the original idea of Metropolis *et al.* (1953) and it works in principle and in many practical cases. However, when the system is strongly interacting, i.e., where there are energy terms which lead to large differences in the Boltzmann factors, the method can run into quasi-ergodic problems where the system gets trapped for long

periods, in particular regions of the configuration space. Worse still, the sampling procedure can appear to be working when this quasiergodic problem is present so the procedure can give erroneous results which are not apparently wrong. This can sometimes be recognized by careful data analysis and using different realizations of the Markov chain with different starting configurations. However, there are now methods available for dealing with quasiergodic problems which construct Markov chains with much higher mobility in the configuration space so that trapping is much less likely to occur. One method which works well in the kinds of problems described here goes by several different names: multiple Markov chain sampling, parallel tempering, and replica exchange. This method was originated by Geyer (1991) and described in the statistics literature. Tesi *et al.* (1996) used it in a polymer problem and it has now become a widely used method in statistical mechanics. Because it has been used in several random knotting problems we give a brief description here, though we focus just on the basic idea.

The method relies on sampling in a larger space where we have an auxiliary parameter such as temperature. It is often convenient to think of this parameter as being the fugacity associated with some property, like the number of right angles in the case of flexibility. Typically a standard Metropolis sampling procedure works well (i.e., gives fast convergence to the limit distribution with no quasiergodic problems) at high temperature but not as well at low temperature where one is often interested in extracting data. The idea behind multiple Markov chain sampling is to run several Markov chains in parallel at different temperatures and periodically attempt to swap configurations between different Markov chains at different temperatures. The swap probability (i.e., the probability that an attempted swap will be accepted) is chosen so that each of the Markov chains at different temperatures will have the limit distribution appropriate for that temperature. The realization of each Markov chain can then be analyzed separately to derive data at that temperature but one must remember that there are correlations between the data at different temperatures.

To understand why the method works, first focus on a particular temperature. Every time a successful swap occurs involving this temperature the state of the Markov chain will change drastically so that the sampling will then start again from a new region of the configuration space (Orlandini, 1998). Now focus on a configuration and how it changes. A configuration will move from one temperature to another, evolve to a different configuration at that temperature and then change temperatures again. When it returns to its original temperature it will have evolved at other temperatures and if these include higher temperatures, there will likely have been major changes to the configuration. The temperatures should be chosen such that adjacent temperatures should have a substantial overlap of their energy distributions so that swaps are frequently successful. This method has been widely used in statistical mechanics and was used to study knotting in semiflexible lattice polygons (Orlandini *et al.*, 2005). A related method which has not been tried for these problems but which would probably work well is umbrella sampling (Torrie and Valleau, 1977).

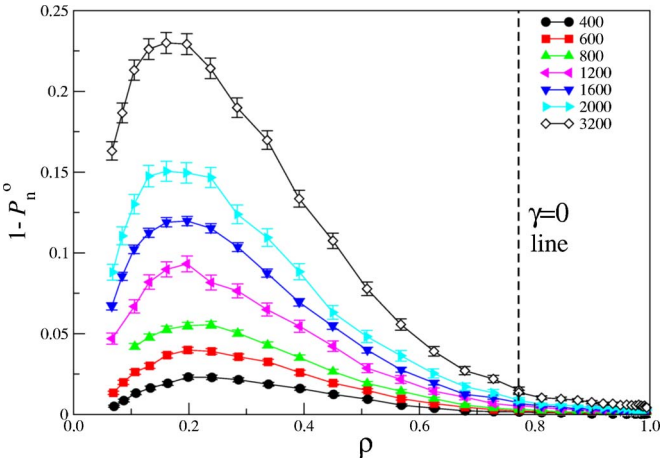

FIG. 15. (Color online) Knotting probability as a function of the density of right angles ρ. The dashed line represents the unweighted polygons.

Orlandini *et al.* (2005) studied knotting in polygons on the simple cubic lattice as a function of the flexibility parameter γ introduced in Sec. III.A.6. Larger values of γ correspond to a smaller persistence length. They considered polygons with up to 3200 edges. They computed the density of right angles $\rho=\langle k\rangle/n$ as a function of γ. At $\gamma=0$ (where we have polygons with uniform weight) the density of right angles ρ is about 0.77. At fixed ρ the knot probability increases as n increases and we know from Sec. III.A.6 that this probability goes to 1 as n goes to infinity. At fixed n the knot probability decreases as ρ increases beyond 0.77. As ρ decreases from 0.77 the knot probability at first increases, goes through a maximum, and then decreases as ρ decreases further; see Fig. 15. This means that there is an optimal degree of flexibility for knotting. At first the fact that the knot probability is a decreasing function of ρ seems counterintuitive. One might expect more flexible polygons (with a larger density of right angles) to be more easily knotted. Orlandini *et al.* argued that very flexible polygons have a high proportion of U turns which lead to a "wastage" of available edges for knotting. Removing these U turns (by replacing the sequence of three edges by a single edge) gives a polygon with less edges but the same knot type. Of course, when ρ becomes small enough the polygon becomes too stiff (i.e., has too few right angles) for knotting to occur effectively so the probability of knotting has to decrease at very low values of ρ.

Recently, inextensible wormlike polymer loops have been generated by the Fourier sums whose coefficients have random values whose amplitudes decay as $n^{-1}e^{-n/n_p}$ (Rappaport *et al.*, 2006). These Fourier knots have the property that locally they are similar to wormlike chains with persistence length that scales as $1/n_p$. By looking at the topological properties of Fourier loops it has been found that the unknotting probability decays exponen-

tially with the characteristic cutoff frequency of the Fourier expansion n_p.

4. Adsorbing ring polymers

The problem of knotting in adsorbing ring polymers has been investigated by Janse van Rensburg (2002a) using Monte Carlo methods. He estimated the exponent α_0 as a function of the interaction strength with the adsorbing surface (α, see Sec. III.A.5). The value of α_0 is independent of α in the desorbed phase and decreases with increasing α in the adsorbed phase.

One measure of knot complexity is $|\Delta(-1)|$. Janse van Rensburg estimated $\langle \log|\Delta(-1)|\rangle$ as a function of α and found that (i) $\langle \log|\Delta(-1)|\rangle$ increases roughly linearly with increasing n, (ii) is roughly independent of α in the desorbed phase, and (iii) decreases as α increases in the adsorbed phase. Consequently, polymers are less likely to be knotted in the adsorbed phase and the complexity of the knot decreases as the extent of adsorption increases.

5. Collapsing polymers

Polymers in a good solvent are expanded random coils but as the temperature decreases or the solvent quality decreases they typically undergo a transition to a collapsed conformation. The temperature at which this transition occurs is called the θ temperature. Above this temperature (in the good solvent regime) the radius of gyration S_n scales with the degree of polymerization as

$$S_n \sim An^{\nu}, \tag{42}$$

where $\nu \approx 0.588$ in three dimensions (Li *et al.*, 1995; Guida and Zinn-Justin, 1998). Below the θ temperature the radius of gyration scales as $S_n \sim Bn^{1/3}$ in three dimensions. Because the polymer is more collapsed below the θ temperature we would expect the knot probability to be higher than in the good solvent regime.

This phenomenon was first studied by Janse van Rensburg and Whittington (1990). They considered lattice polygons with an attractive pseudopotential between pairs of vertices which are unit distance apart but not joined by an edge of the polygon. At fixed n the knot probability increases dramatically in the collapsed phase. It appears that $P_n^o \sim e^{-\alpha_0 n}$ but α_0 is much larger in the collapsed phase than in the good solvent regime. There is no theoretical argument for this form for P_n^o in the collapsed phase.

Virnau *et al.* (2005) looked at a continuum model with the same phenomenon. Their model was a bead-spring model in which the bonds can stretch under a finite extensible nonlinear elastic (FENE) potential. In addition, the beads interact with a Lennard-Jones potential designed to mimic the behavior of polyethylene. As the temperature decreases they showed that the knot probability increases, in agreement with the results for the lattice model described above.

Mansfield (1994) examined the compact phase model in which the polygons are Hamiltonian cycles on the cubic lattice. This means that they are in the most compact state possible. To detect and identify knots he computed the Alexander polynomial $\Delta(t)$ at ten different values of t. By looking at n step Hamiltonian cycles with $n \le 1000$ he showed that the knot probability for such configurations was much higher than in the case of lattice polygons modeling the good solvent regime. In particular he estimated $n_0 \simeq 270$ giving $\alpha_0 \approx 3.7 \times 10^{-3}$, i.e., two orders of magnitude bigger than for polygons in the extended phase. More recently Lua *et al.* (2004) examined the knotting probability of Hamiltonian cycles on the cubic lattice with n up to 2774. The larger values of n and the use of more sophisticated knot detectors such as the Vassiliev invariants revised the estimate of the characteristic length from $n_0 \simeq 270$ to $n_0 \simeq 196$ corresponding to $\alpha_0 \simeq 5 \times 10^{-3}$.

6. Polyelectrolytes

DNA is a polyelectrolyte and its conformation is therefore sensitive to the ionic strength of the solution. The knot probability and distribution of knot types have been investigated experimentally by Rybenkov *et al.* (1993) and by Shaw and Wang (1993, 1994) as a function of ionic strength. Both groups found that the knot probability decreased as the ionic strength decreased. This reflects the fact that at low ionic strength the interionic repulsion is less screened so the polymer is stiffer. In a similar way more complex knots are seen at higher ionic strength. Rybenkov *et al.* modeled this by considering a closed chain of impenetrable cylinders with diameter d. The Hamiltonian also contained a bending rigidity term chosen to fit the Kuhn length of DNA. The value of d was then varied to give the best fit between the experimental and simulation results. The authors interpret d as an effective diameter. Although this treatment gives a nice (two-parameter) fit to the experimental data, it does not take into account the details of the screened Coulomb interaction.

Tesi, Janse van Rensburg, Orlandini, and Whittington (1994) investigated knotting in a simple model of a polyelectrolyte. They used the model of Janse van Rensburg and Whittington but added a screened Coulomb term (in fact, a Yukawa potential) to model the screened repulsion between like charges on the polyelectrolyte. Their potential can be written as

$$U = \sum_{i<j} \left[u(r_{ij}) + A \frac{e^{-\kappa r_{ij}}}{r_{ij}} \right]. \tag{43}$$

Here $u(r) = k_B T v$ if $r = 1$ and zero otherwise. κ is a screening parameter depending on the ionic strength of the solution. When κ is very large, the Coulomb repulsion is effectively negligible. They examined how the knot probability increased as κ increased, i.e., as the ionic strength increased. The results are in qualitative agreement with the experimental results of Shaw and Wang (1993, 1994) and of Rybenkov *et al.* (1993).

7. Linked rings

In Sec. III.A.7 we introduced two notions of linking, topological linking and homological linking. Homological linking is detected by computing the linking number Lk and two curves are homologically linked if $Lk \neq 0$ and homologically unlinked otherwise. If two curves are homologically linked, they are topologically linked but the converse is not necessarily true. Topological linking is more difficult to detect but there is a partial solution based on computing a two-variable Alexander polynomial (Torres, 1953). This idea was first used in polymer problems by Vologodskii *et al.* (1975) and by Klenin *et al.* (1988). The two-variable Alexander polynomial detects some links which would be missed by calculating the linking number, but it is not a perfect detector in that it also misses some links.

Orlandini, Janse van Rensburg, *et al.* (1994) examined the probability for a pair of polygons each with n edges, confined to a $L \times L \times L$ cube on the simple-cubic lattice, to be homologically linked. They found that the linking probability increased with increasing n at fixed L and decreased with increasing L at fixed n, as expected. They argued that there are two length scales in the problem: (i) the length (L) of the side of the cube and (ii) a typical dimension of the polygon in the absence of a spatial constraint n^{ν}, where $\nu \approx 0.588$. They also argued that the probability that the two polygons would be homologically linked would be a function of the ratio of length scales n^{ν}/L and found that their numerical results scaled in this way.

They approximated topological linking by having a nontrivial two-variable Alexander polynomial. They then asked what was the probability that two curves would be homologically linked, given that they are topologically linked. Again they argued that this conditional probability would depend on the ratio of length scales and found that their data scaled in this way. Two topologically linked curves are more likely to be homologically linked when n^{ν}/L is large and less likely to be homologically linked when n^{ν}/L is small. That is, homological linking is a good indicator of topological linking when the system is relatively dense but is not an effective indicator for sparse systems.

8. Ribbon models

The lattice ribbon model described in Sec. III.A.8 has been studied using Monte Carlo methods (Janse van Rensburg *et al.*, 1994; Orlandini, Janse van Rensburg, *et al.*, 1996). The Monte Carlo procedure is rather complicated but is based on grand canonical sampling where the length of the ribbon can vary. The results can be summarized as follows:

(i) For orientable ribbons the average of the absolute value of the linking number for two boundary curves increases roughly like $n^{1/2}$, where n is the number of plaquettes.

(ii) For orientable ribbons the probability that the two boundary curves are homologically linked increases to unity as n goes to infinity, linearly in $1/\sqrt{n}$.

(iii) For both orientable and nonorientable ribbons the average of the absolute value of the writhe for the center line increases like $n^{1/2}$.

These results are consistent with the rigorous bounds discussed in Sec. III.A.8 and indicate that the bound on the linking number and writhe might be best possible. It is unfortunate that we have no useful rigorous upper bounds on $\langle |Lk| \rangle$ or on $\langle |Wr| \rangle$.

In addition, the authors investigated the types of knots in the boundary curves of nonorientable ribbons and found 3_1 and 5_1 to dominate for relatively short ribbons. These are the torus knots discussed in Sec. III.A.8. Although we know that satellite knots must eventually dominate, the values of n required might be very large.

9. Entanglements in condensed phases

Linear and ring polymers in a dense phase such as concentrated solutions and melts (where the polymer is present at high density but is disordered) can be highly entangled. These entanglements can include both self-entanglements (i.e., the individual chain can be knotted) and mutual entanglements where different polymer chains can wind around one another. Although it is well established that entanglement (in any form) strongly affects the dynamical and rheological properties of the polymer network in condensed phases (de Gennes, 1979; Doi and Edwards, 1986), very little is known about the topological properties of such entanglements at equilibrium. Most of our knowledge on this subject comes from numerical studies in which several polymer chains are modeled in a restricted environment such as a box, and the behavior is investigated by molecular dynamics or Monte Carlo methods (see, e.g., Dickman and Hall, 1988; Smith *et al.*, 1998). However, efficient sampling of a system consisting of several polymers close to one another is an extremely difficult task and most numerical investigations have been restricted to relatively short chains. Another problem with these studies is a proper definition of topological entanglement if the melt consists of linear (open) chains. This is not the case for a melt of polymer rings where the topological entanglement is defined in terms of knotted and linked closed curves. Recently, several computational studies have been performed to explore the influence of topological constraints on the structure of ring polymers in melts. It has been found (Skolnick *et al.*, 1989; Müller *et al.*, 1996, 2000; Brown and Szamel, 1998) that unknotted and unlinked rings in melts are smaller than their linear chain counterparts, i.e., with observed radius of gyration scaling exponent ν between 0.4 and 0.42. This squeezing of the unknotted rings has been interpreted as an effect of the topological constraints imposed by neighboring rings. This effect has even stronger implications in the dynamical properties of such rings that do not follow the typical diffusion law (Rouse dynamics) for isolated ring polymers but a superdiffusion law (Brown *et al.*, 2001).

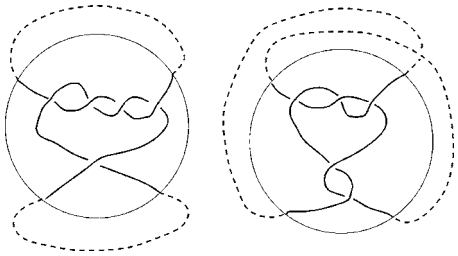

FIG. 16. Schematic representation of the projection of two chains properly embedded in a cube, and the completion of the chains to form two polygons by adding edges outside the cube.

Along these lines Kim and Klein (2004) have explored the evolution of a trefoil knot tied in a linear chain embedded in a melt of unknotted chains. In particular, they found that a tight open trefoil knot unravels via a sequence of expansions and contractions (early stage regime) followed by a slow migration of the whole knot along the backbone. It is interesting to notice that during the whole dynamics the knot maintains a definite size $\langle m \rangle$ that scales with chain length n as $n^{0.4}$ (see Sec. VI.B).

A quite different way of characterizing the entanglement complexity of concentrated polymer solutions and polymer melts has recently been proposed (Orlandini *et al.*, 2000; Orlandini and Whittington, 2004). The idea is to drill out a tube (prism) at random through a fixed polymer configuration to construct a random sample of polymer entanglements. Typically, chains will enter and leave the tube so that within the tube one will see many polymer subchains which begin and end in the boundary of the tube. If one cuts the tube into sections, each of which can be thought of as a cube, the cubes and k subchains within them will each form a tangle of k strings. Indeed these subchains can be both self-entangled and mutually entangled. One can then define knotting in such systems (by thinking of the cube and embedded chain as constituting a ball pair) and linking between two chains (for instance, by imagining joining up the ends of each chain outside the cube to form a simple closed curve); see Fig. 16. In this way a proper definition of topological entanglement is achieved in each cube and one can infer the topological properties of the entire system by reconnecting the cubes properly (i.e., by matching the subchains at the cube faces) to form the original tube. A possible model of this system is a set of k self-avoiding and mutually avoiding walks on a cubic lattice properly embedded in a cube of length D. This model has been explored by Monte Carlo simulations (Orlandini, *et al.*, 2000; Orlandini and Whittington, 2004). This work characterized the extent of mutual entanglement by calculating the linking number between two chains (properly embedded in the cube) with their ends joined up outside the cube to form two different simple closed curves. This was extended to k chains by computing the $\binom{k}{2}$ linking numbers between pairs of chains. The absolute values of these $\binom{k}{2}$ linking numbers were then added to form a measure L of entanglement complexity and this quantity was then averaged over realizations, to form $\langle L \rangle$. It turns out that $\langle L \rangle / \binom{k}{2}$ increases as the monomer density ρ increases and that $\langle L \rangle / \binom{k}{2}$ is roughly a universal function of $\rho D^{4/3}/k$, where D is the cube size. This comes from the following scaling argument. The entanglement complexity $\langle L \rangle / \binom{k}{2}$ should depend on the ratio of the two length scales R_F and D, where R_F is the free dimension of the polymer segment in the cube. If the typical segment length is m then $m = \rho D^3/k$. The ratio of length scales is then $\rho^{3/5} D^{4/5}/k^{3/5}$, so we see that the entanglement complexity is a function of $\rho D^{4/3}/k$ where we use the Flory value $\nu = 3/5$.

10. Some open problems

We end this section on numerical results with a short list of open problems which we regard as being especially challenging.

(i) The study of the knotting probability for highly confined polymer rings (or, in general, for polymers in a dense phase) is a difficult task, especially if the excluded volume interaction is included. There is a general problem of sampling efficiently for polymers in a highly compact state. Different Monte Carlo schemes have been proposed to handle this problem but none of them are effective when n is large. This is a general problem in Monte Carlo studies of polymers in dense phases and has applications outside knotting and linking.

(ii) There is a related topological issue. After generating a configuration of a ring polymer we have to check whether or not it is knotted and we might want to determine its knot type. In principle this can be done by computing knot invariants such as the Alexander or Jones polynomial. The difficulty is that for configurations that are highly compact the number of crossings (in a given projection) increases rapidly with n and the computation of such invariants becomes impracticable. Common approaches rely on algorithms that either reduce the number of crossings of a given projection (by Reidemeister moves) or simplify the configuration keeping its knot type unaltered. Again these strategies seem to work for relatively short ring polymers, but new methods are needed to extend current work to longer polymers.

IV. GEOMETRICAL MEASURES OF ENTANGLEMENT COMPLEXITY

Ring polymers with the same knot type can differ in the way in which they are geometrically embedded. For example, unknotted ring polymers and linear chains can be badly embedded in the sense that they can have many crossings in every projection.

A. Writhe

Linear DNA and unknotted circular DNA can be supercoiled (Vologodskii *et al.*, 1992). A useful measure of this type of entanglement is the *writhe* (Wr) of the molecule, introduced in Sec. III.A.8 in connection with a conservation theorem relating the writhe of the center line of a ribbon to the twist of the ribbon and the linking number of the two boundary curves. Although twist is only defined for double stranded molecules, writhe is well defined for a single curve (Călugăreanu, 1959; Pohl, 1968). For polygons in Z^3 Janse van Rensburg *et al.* (1993) showed that, for n sufficiently large,

$$\langle |Wr| \rangle \geq A\sqrt{n}, \tag{44}$$

where A is a positive constant. The square-root lower bound seems to be quite good since numerical estimates based on Monte Carlo simulations suggest a power-law dependence on n of the kind (Janse van Rensburg *et al.*, 1993)

$$\langle |Wr| \rangle \sim n^{\eta} \quad \text{with} \quad \eta = 0.522 \pm 0.004. \tag{45}$$

Writhe is also well defined for linear (open) polymers and numerical estimates of the absolute value of the writhe for self-avoiding walks in Z^3 (Orlandini, Tesi, *et al.*, 1994) give

$$\langle |Wr| \rangle \sim n^{\eta} \quad \text{with} \quad \eta = 0.500 \pm 0.005. \tag{46}$$

Unlike the lower bound, the only known rigorous upper bound on the absolute value of the writhe is quite far from the behavior observed numerically. The best upper bound known is given by Cantarella *et al.* (2001) and independently by Buck and Simon (1999) who have shown that

$$\langle |Wr| \rangle \leq An^{4/3}. \tag{47}$$

One might wonder if there are situations in random polymers in which the absolute value of the writhe can deviate drastically from square-root behavior. Possible candidates are polymers in dense phases such as the ones strongly confined in restricted volumes or undergoing a collapse transition. In the case of equilateral polygons confined in a sphere of radius R Micheletti *et al.* (2006) have shown that for R sufficiently small (compared to the typical extension of the chain)

$$\langle |Wr| \rangle \sim n^{\eta} \quad \text{with} \quad \eta \approx 0.75. \tag{48}$$

For highly constrained polymers the absolute value of the writhe seems to grow faster than that for unconstrained polymers in good solvents.

Gee and Whittington (1997) have investigated how linking can induce writhe in linked polygons.

B. Average crossing number

Another example of a geometrical measure of entanglement complexity is the *average crossing number*. Suppose we have a simple closed curve in R^3. If we project onto R^2 in some direction, we in general see crossings of the curve with itself. If we average the number of crossings over all possible projection directions, this is the average crossing number of the curve. Normally we are interested in a further average over realizations of the curve. This is sometimes called the *mean average crossing number* and sometimes simply the average crossing number $\langle \mathrm{ACN} \rangle$. For the case of equilateral random polygons Diao *et al.* (2003) proved that the mean average crossing number for equilateral random polygons with n edges behaves as

$$\langle \mathrm{ACN} \rangle = \tfrac{3}{16} n \log n + O(n). \tag{49}$$

The interesting feature is that it grows a little faster than linearly. If the knot type τ is fixed then a numerical investigation suggested that the behavior is

$$\langle \mathrm{ACN}(\tau) \rangle = a(n - n_0)\log(n - n_0) + b(n - n_0) + c, \tag{50}$$

where $n_0 = n_0(\tau)$ is a constant which depends on the knot type and a, b, and c are parameters independent of the knot type. In fact n_0 is the minimum number of edges need to form the knot τ. This has connections both to tight knots (Sec. VI.B) and to ideal knots (Sec. VII). A similar rigorous result was established for Gaussian random walks and polygons where now the constant $3/16$ is replaced by $1/(2\pi)$ (Diao and Ernst, 2005).

A numerical estimate of $\langle \mathrm{ACN} \rangle$ for self-avoiding walks in Z^3, with n up 1500 (Orlandini, Tesi, *et al.* 1994), gave

$$\langle \mathrm{ACN} \rangle \sim n^{1.1}, \tag{51}$$

where the deviation from linear behavior is due to the logarithmic correction enhanced by finite-size effects that in models with excluded volume interactions are quite severe. Indeed by going up $n = 4000$ Grassberger (2001) confirmed, also for self-avoiding walks, the $n \log n$ behavior. As for the absolute value of the writhe, a rigorous upper bound on $\langle \mathrm{ACN} \rangle$ has been found (Buck, 1998; Cantarella *et al.*, 1998),

$$\langle \mathrm{ACN} \rangle \leq n^{4/3}. \tag{52}$$

In this case, however, there are numerical indications (Grassberger, 2001) that this upper bound is a good one for compact polymers and one expects similar behavior also for dense polymers, i.e., confined in small spheres.

It is worth mentioning that in the case of protein chains the average crossing number provides an interesting measure of their compactness (Arteca, 1995) and several studies have been devoted to investigate how $\langle \mathrm{ACN} \rangle$ in proteins scales with the length n of the polypeptide chain (Arteca, 1993, 1994, 1997, 2002; Dobay *et al.*, 2004). Proteins have relatively short backbones and it is difficult to discriminate, for small n, between the $n \log n$ and $n^{4/3}$ behavior. It is then difficult to decide on those grounds if proteins, as far as the average crossing number is concerned, are more similar to random polymers in good solvents or to compact polymers.

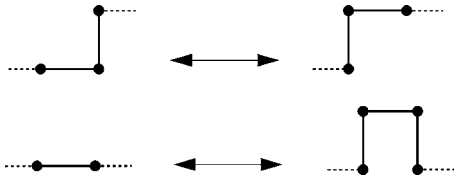

FIG. 17. The BFACF moves.

C. Some open problems

(i) We have seen that the upper bound on the absolute value of the writhe is quite far from numerical estimates. An improvement on that bound is clearly needed.

(ii) Up to now the only numerical result on the absolute value of the writhe for dense polymers is for a model of equilateral polygons confined to a sphere (Micheletti *et al.*, 2006). It would be useful to extend this investigation to other systems such as polymers in compact phases and to situations where the excluded volume interaction is taken into account.

V. ENTROPY AND DIMENSIONS OF KNOTTED RING POLYMERS

In previous sections we have been mainly concerned with the probability that a ring polymer is knotted. Now we turn our attention to the properties of ring polymers with a particular knot type. There are very few rigorous results for this kind of problem and we have to rely almost entirely on numerical methods.

There are two rather different Monte Carlo approaches for this type of problem. One is to use a two-point pivot algorithm and to classify configurations by knot type (e.g., by using the Alexander polynomial) and bin the data according to knot type. The second approach is to use a Monte Carlo scheme which samples polygons with a fixed knot type, perhaps at a range of values of n. We describe the idea behind a lattice version of the second scheme. This idea can be extended to an off-lattice model of the polymer provided that one makes sure that local moves do not result in a crossing change (Farago *et al.*, 2002).

One approach which samples at fixed knot type is to use the Berg, Foester, Aragao de Cavalho, Caracciolo, and Froelich (BFACF) algorithm (Berg and Foester, 1981; Aragao de Carvalho *et al.*, 1983; Aragao de Carvalho and Caracciolo, 1983). In this approach one uses a Markov chain defined on the set of all polygons, but the knot type of the initial polygon determines the knot type of all polygons in the (correlated) sample. The BFACF algorithm uses two types of local moves, sketched in Fig. 17. In the first move two adjacent edges at right angles are permuted. This is often called *flipping across a square*. In the second move an edge is replaced by three edges making a U turn or a U turn is replaced by a single edge. In the second move the number of edges in the polygon increases or decreases by 2, so the algorithm samples polygons with different sizes. There is a parameter in the algorithm which can be tuned to determine the typical range of values of n which is being sampled. Since neither move allows the polygon to pass through itself, the knot type cannot change so every polygon in the sample has the same knot type as the original polygon. A more delicate question is whether every polygon with a particular knot type can be obtained from a given initial polygon with the same knot type. This is the question of whether the ergodic classes of the Markov chain coincide with the knot types. This was established by Janse van Rensburg and Whittington (1991b) using an argument based on Reidemeister moves.

A. Entropic exponents

If we think of the class of all n-edge lattice polygons, it is expected that p_n will scale as

$$p_n = An^{\alpha-3}\mu^n\left(1+\frac{B}{n^{\Delta}}+\cdots\right). \tag{53}$$

Here $\mu=e^{\kappa}$, α is a critical exponent, and Δ is a correction to scaling exponent. The best estimate of α is 0.237 ± 0.005 (Li *et al.*, 1995).

It is at least plausible that for a fixed knot type τ

$$p_n(\tau) = A(\tau)n^{\alpha(\tau)-3}\mu(\tau)^n\left(1+\frac{B(\tau)}{n^{\Delta(\tau)}}+\cdots\right) \tag{54}$$

and we know that $\mu(\tau)<\mu$ for all knot types τ.

Using a BFACF algorithm coupled with multiple Markov chains Orlandini, Tesi, *et al.* (1996, 1998) investigated this scaling behavior and found evidence that $\alpha(\bigcirc)=\alpha$ and that

$$\alpha(\tau) = \alpha + N(\tau), \tag{55}$$

where $\bigcirc$ denotes the unknot and $N(\tau)$ is the number of prime components in the knot decomposition of τ. This implies that $\alpha(\tau)$ is independent of τ if τ is a prime knot. Within the confidence limits of the statistical analysis the authors found that $\mu(\tau)$ is independent of τ for the knots considered. Deguchi and Tsurusaki (1997) found very similar results for Gaussian random polygons and for a continuum rod-bead model.

One can understand the result in Eq. (55) if we assume that knots are tied relatively tightly. What do we mean by this? Suppose that ω is a simple closed curve in three-space with knot type τ. Suppose that S is a sphere which cuts ω at exactly two points, thus dividing ω into two one-balls, ω_1 and ω_2. Suppose that ω_1 meets S at its two boundary points but is otherwise inside S and that ω_2 meets S at its boundary points but is otherwise outside S; see Fig. 18. Convert ω_1 into a simple closed curve ω_1' by adding a curve on the sphere S to join the end points of ω_1. The same construction converts ω_2 to a simple closed curve ω_2'. Suppose that ω_1' has knot type τ and ω_2' is unknotted. Then we can say that the knot is *localized* inside S. Technically ω_1 and S form a knotted ball pair (see Figs. 9 and 18). Now minimize the number of edges in ω_1 over all possible spheres S and all possible pairs of intersection points. Call this minimum number

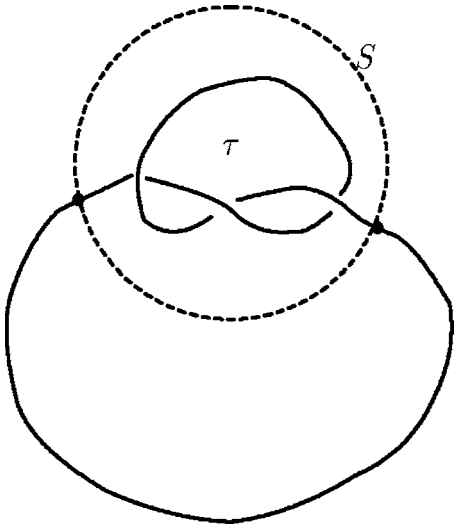

FIG. 18. Localization of a knot in the interior of a sphere S.

of edges m_τ. If $m_\tau = o(n)$ then the knot is said to be *tight*. An extreme case would be when m_τ is a constant independent of n. Returning to the lattice case, we first assume that τ is prime. When the knot is tight there are of order ϵn places where such a knot could be created by concatenating a small polygon with m edges and knot type τ and an unknotted polygon with n edges. From this one can argue that

$$p_{m+n}(\tau) \sim \epsilon n p_n(\emptyset) \tag{56}$$

so from the assumed scaling form (54) we have

$$\alpha(\tau) = \alpha(\emptyset) + 1 \tag{57}$$

if $\mu(\tau) = \mu(\emptyset)$. [We know that $\mu(\tau) \geq \mu(\emptyset)$ but not that they are equal.]

If τ is composite and has $N(\tau)$ prime components, we can give a similar argument. We can choose $N(\tau)$ of ϵn locations in about $(\epsilon n)^{N(\tau)}$ ways and the rest of the argument is the same and yields Eq. (55).

B. Metric properties

This assumption has implications for dimensions of polygons with fixed knot type. Suppose that $\langle R_n^2(\tau)\rangle$ is the mean-square radius of gyration of polygons with n edges and knot type τ. We might expect the mean-square radius of gyration to scale as

$$\langle R_n^2(\tau)\rangle = A_\nu(\tau) n^{2\nu(\tau)}[1 + B_\nu(\tau) n^{-\Delta_\nu(\tau)} + \cdots]. \tag{58}$$

If knots are tight in the above sense then a knotted polygon will resemble an unknotted polygon with small local additions of tightly knotted prime components. The effect of these additions should be to change the corrections to scaling terms but not the exponent ν or the amplitude A. This implies that $\nu(\tau) = \nu(\emptyset)$ and $A_\nu(\tau) = A_\nu(\emptyset)$ for all τ.

There is general agreement that $\nu(\tau)$ is independent of τ (Janse van Rensburg and Whittington, 1991a; Quake, 1994, 1995; Orlandini *et al.*, 1998; Matsuda *et al.*, 2003). Although there has been some disagreement about the constancy of the amplitude, there is a growing amount of numerical evidence that it is constant.

If we consider rings without excluded volume in three-space, such as equilateral or Gaussian random polygons, then the radius of gyration for the set of all rings scales like $n^{1/2}$. The object is just a random walk conditioned to return to the origin. Grosberg (2000) used scaling arguments to investigate the dimensions of this sort of model if the ring was conditioned to be unknotted. He argued that the radius of gyration would then scale as n^ν with $\nu \approx 0.588$, the value appropriate for self-avoiding polygons or for rings with excluded volume. While this *topological expansion* might seem surprising at first sight there is growing evidence that the prediction is correct (Dobay *et al.*, 2003; Matsuda *et al.*, 2003; Moore *et al.*, 2004).

The asymptotic behavior of the average size of ring polymers with fixed topology has also been studied for an off-lattice model in which self-avoiding polygons consist of N cylinders with radius r. By varying r Shimamura and Deguchi (2001, 2002) showed that the topological expansion strongly depends on the radius r. For small r (where the model is closer to the Gaussian random polygon) the effect is indeed significant, but it becomes less important as the radius r increases, i.e., as the self-avoidance becomes more and more relevant.

C. Some open problems

(i) There is a considerable amount of Monte Carlo data available on the number and dimensions of polygons with a particular knot type. The difficulty is to know how to analyze these data. Most of the existing analysis has used the functional forms (54) and (58) but in fact we do not know if the correction to scaling terms are of these forms. There will certainly be a term in n^{-1} and there could be terms which are more important than the assumed $n^{-\Delta}$ term (Marcone *et al.*, 2005).

(ii) Although there is growing evidence for the relations (55) and (57) in the expanded phase, are there corresponding relations for polygons in the compact phase?

VI. SIZE OF A KNOT WITHIN A KNOTTED POLYMER RING

In Sec. V we introduced the idea that knots might be tight. In this section we discuss this idea in more detail and review some numerical evidence both in the good solvent and poor solvent regimes. Since we are trying to identify the "knotted part" of a ring, i.e., where the essential aspect of the knot resides, we have to ask how to define knotting in an open chain or self-avoiding walk.

A. Knots in self-avoiding walks: Knotted arcs

If we consider an open chain then the standard definition of knotting says that all such open chains are unknotted. Technically this is because any one-ball is am-

bient isotopic to the standard one-ball. More informally it is because the chain can be deformed to convert it to a straight line without passing the chain through itself. In spite of this we talk about knots in pieces of string so the problem is to formalize this notion. For related work, and its application to knots in proteins, see Taylor (2000) and Taylor *et al.* (2003).

We first discuss some special cases. We introduced the idea of a knotted ball pair in Sec. III.A.1 and provide a more careful definition here (Sumners and Whittington, 1990). Consider a self-avoiding walk ω on the simple cubic lattice with vertices labeled $i=0,1,2,\ldots,n$. Vertex i is at the point $r_i=(x_i,y_i,z_i)$ where the coordinates are integers and $|r_i-r_{i-1}|=1$ for $1\le i\le n$. Associated with the ith vertex is a unit cube C_i centered at r_i, which we call the dual three-cube of the ith vertex. Let $C=\cup C_i$. Suppose that C is a three-ball [i.e., is homeomorphic to the standard three-ball $\{(x,y,x),x^2+y^2+z^2\le 1\}$]. All the vertices of ω are in the interior of C and we can add two half edges to extend ω to form ω' so that the end points of ω' are in the boundary of C, ∂C. This (unique) extension of ω is a one-ball properly embedded in the three-ball C so ω' and C form a ball pair (C,ω'). Now there is a standard ball pair, which is the standard three-ball defined above together with the line segment from $(1,0,0)$ to $(-1,0,0)$ which is a diameter of the standard three-ball. If (C,ω') is homeomorphic to the standard ball pair, we say that the ball pair (C,ω') is unknotted. Otherwise it is knotted. This can be used as a definition of knotting in an open curve but it only works when the union of the dual three-cells (C) is a three-ball.

Another special case which is worth considering is when the self-avoiding walk ω is *unfolded*. For instance, suppose that $x_0<x_i<x_n$ for $1\le i\le n-1$. Then we say that ω is x *unfolded*. In this situation we can add rays from r_0 to $(-\infty,y_0,z_0)$ and from r_n to (∞,y_n,z_n) and regard these rays as meeting at the point at infinity in the one-point compactification of R^3. We say that ω is knotted if this resulting simple closed curve is knotted, and unknotted otherwise. The number of these unfolded walks with n edges grows at the same exponential rate as the number of self-avoiding walks (Hammersley and Welsh, 1962) but they are still rare objects so this scheme is not generally useful. However, it does suggest some useful extensions:

(i) One idea is to join the two end points of the walk by a line segment to form a closed curve. The problem is that the closed curve might not be simple since this line segment will in general go through some lattice points which might be occupied by vertices of ω. One can get around this problem by first adding short parallel line segments (of length ϵ, say) to each end point of ω in a direction with irrational direction cosines, and then joining the end points of the resulting object to form a closed curve which is necessarily a simple closed curve. We say that ω is knotted if this simple closed curve is knotted. The answer might depend on the direction cosines chosen so an averaging over direction cosines might be necessary.

(ii) Another idea is to add parallel rays to the end points of ω and regard the rays as meeting at infinity to form a closed curve. If the rays have a randomly chosen direction, the rays will have irrational direction cosines with probability 1 and the closed curve will be simple, almost surely. Again it might be necessary to average over the direction cosines.

It has been shown (Janse van Rensburg *et al.*, 1992) that with each of these definitions of knotting in self-avoiding walks sufficiently long walks are knotted with high probability and the walks are very badly self-entangled with high probability.

Recently Millett *et al.* (2005) proposed a more *probabilistic* method to detect knots in linear chains. The idea consists in analyzing the spectrum of knots generated by multiple closures of the same open chain. Each closure is obtained by connecting the ends of the chain to a point chosen (randomly) on the surface of a sphere that contains the walk. Different closures correspond to different chosen points. For each fixed open chain a distribution of knots is estimated and the most probable knot gives the knot type of the open chain. Interestingly enough it turns out that the knot obtained by a simple direct end-to-end closure usually coincides with the knot type that dominates the random closure spectrum.

B. Tight knots

We met the idea of tight knots in the proof of the main theorem in Sec. III.A.1 and again when discussing the entropy and dimensions of rings with a specified knot type in Sec. V. In this section we examine the direct evidence as to whether or not a knot is tight and how this depends on solvent quality.

If we return to the definition of tightness given in Sec. V, we see that we really have three possibilities:

(i) If the average number $\langle m_\tau\rangle$ of edges in the part of the polygon localized in S increases more slowly than any power of n as n goes to infinity, we say that the knot is *strongly localized*. Note that this includes the situations where $\langle m_\tau\rangle$ is a constant or increases like $\log n$.

(ii) If $\langle m_\tau\rangle$ goes like $o(n)$ but at least like some power of n as n goes to infinity, we say that the knot is *weakly localized*.

(iii) If $\langle m_\tau\rangle$ goes like An for some positive constant A as n goes to infinity, we say that the knot is *delocalized*.

Katritch *et al.* (2000) carried out a Monte Carlo investigation of knot tightness in equilateral random polygons (in the good solvent regime). They used constructions related (i) to (ii) and described in Sec. VI.A to identify the shortest subwalk which, when closed to form a knot,

had the same knot type τ as the complete ring. We call this a *minimal knotted arc* and use its length to define the length m_τ of the knot in the ring. For polygons with 500 edges they found that the typical values of m_τ were about 6 to 8 for trefoils, about 15 for figure-eight knots, and about 20 for 5_1 and 5_2. They give results for the proportion of polygons with the knot localized in less than $n/10$ edges. Although it is difficult to put their results in the perspective described above (i.e., the three classes), their general conclusion was that knots were tight, in general agreement with the results described in Sec. V.

Marcone *et al.* (2005) carried out an analysis of tightness in self-avoiding polygons on the simple-cubic lattice using a variant of the above approach that allows one to minimize the risk of knot modifications or disentanglements during the closure of the subwalk in the resulting new ring. By detecting the minimal knotting arc for polygons having knot type 3_1 and with n up to 1500, they found

$$\langle m_\tau \rangle \sim n^t, \tag{59}$$

where $t \approx 0.75$ for the good solvent regime. This result turns out to be robust with respect to a change of prime knot type. For example, by replacing the 3_1 by a 4_1 or 5_1 knot, Eq. (59) remains valid with the same t within the confidence limits.

This approach works well in the good solvent regime but not for poor solvents where it turns out that the knot is delocalized. The closure schemes described above can introduce new extraneous crossings and, while this effect is minor in the good solvent regime, it causes serious problems for poor solvents where the polygon is compact. To get around this problem Marcone *et al.* (2005) used a different approach which works for both good and poor solvents. Consider a ring polymer which passes through a small slip ring (so that the ring polymer and slip ring are not linked). This essentially divides the ring into two subwalks each of which approximates a ring because their end points are close together. This is related to work by Edwards (1968) and by Metzler *et al.* (2002a). If we tie a trefoil in each of these subwalks and then simulate their behavior, in a good solvent typically one subwalk will grow and the other will shrink to maximize the total entropy. We can identify the length of the knot as the length of the shortest subwalk. Their results for this approach ($t \approx 0.75$) for good solvents agree with their results using the closure scheme. For poor solvents they estimated that $t \approx 1$. That is, they believe that knots are weakly localized in the good solvent regime but delocalized in the poor solvent regime.

These results for the good solvent regime are consistent with a molecular-dynamics study by Mansfield (1998) who found that maximally tight knots loosened somewhat in a molecular-dynamics simulation, suggesting that they are not strongly localized. Virnau *et al.* (2005) came to similar conclusions for an off-lattice model.

Another approach that in principle would work well either in the swollen or in the compact regime is the one introduced by Farago *et al.* (2002). The idea is to quantify the degree of tightness of knotted polymers by comparing the force-extension relations of knotted and unknotted chains. It turns out that, unlike unknotted configurations, knotted rings exhibit strong finite-size effects which can be attributed to the presence of an average knot size $\langle m_\tau \rangle$. By simulating off-lattice chains with n (the number of beads) up to 750, Farago *et al.* found, in the swollen regime, the power-law behavior (59) with $t = 0.4 \pm 0.1$. This result agrees with the one of Marcone *et al.* (2005) in showing that knotted polymers in the extended phase are weakly localized although the estimate of t is slightly smaller.

C. Flat knots

A simplified model, which has played an important role in the development of ideas concerning localization and delocalization properties of real knots in equilibrium, is that of *flat knots* (Guitter and Orlandini, 1999; Metzler *et al.*, 2002b). These are closed curves in the plane, e.g., in the square lattice, that can be seen as quasi-two-dimensional projections of the three-dimensional (3D) knots. Physically they can be realized by adsorbing 3D polymer rings on a strongly attractive planar surface or membrane or by confining the polymer between two close parallel walls (see the model by Michels and Wiegel in Sec. III.A.4). In these cases the flat polymer knot can still equilibrate in two dimensions. Macroscopic realization of flat knotted polymer rings comes also from experiments in which macroscopic knotted chains are flattened by gravity onto a vibrating plane (Ben-Naim *et al.*, 2001). Flat knots have the advantage of being easy to image by microscopy and more amenable to numerical studies, for example, on the entropy and dimension of knotted rings, than their 3D counterparts. In this respect a first numerical study on flat knots was by Guitter and Orlandini (1999). As a model of a flat knot they considered a configuration in the square lattice which has edges which are lattice edges but also crossings between pairs of edges which cross a unit square; see Fig. 19. The initial configuration corresponds to a projection of a knotted curve in three-space. They used BFACF plus some additional moves corresponding to lattice versions of Reidemeister moves I and II (see Fig. 2). They showed that the connective constant is independent of knot type, to numerical accuracy, and that

$$\alpha(\tau) = \alpha(\emptyset) + N_\tau, \tag{60}$$

where N_τ is the number of prime components in the knot τ. They also showed that the critical exponent ν is independent of knot type. Although they did not carry out a detailed study of tightness, they observed that the knotted regions were typically very small. See Fig. 20 for a typical configuration of the composite knot $3_1 \# 3_1$. The two prime components are separated and localized. If

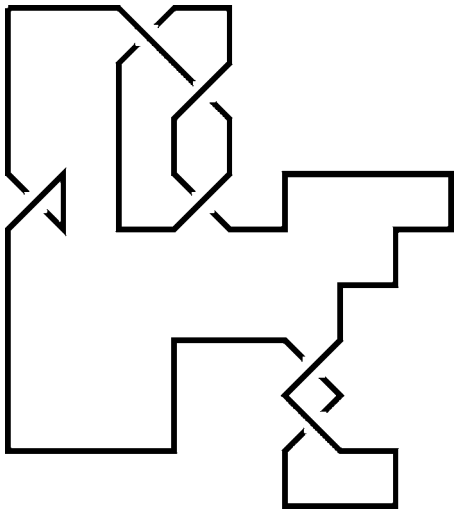

FIG. 19. An example of a flat knot configuration on the square diagonal lattice with six crossings and the topology of a trefoil knot.

the number of overlaps of the polymer ring with itself is restricted to the minimum compatible with the topology (e.g., 3 for a 3_1 knot), the flat knot model enjoys a drastic simplification and an analytic approach to the problem of the size of a knot within a flat knot is possible (Metzler *et al.*, 2002b). Indeed the overlaps of the chain can be interpreted as vertices of a two-dimensional polymer network, for which a well-developed theory exists (Ohno and Binder, 1988; Duplantier, 1989). By exploiting results coming from this theory Metzler *et al.* (2002b) were able to predict that prime flat knots would be strongly localized in the good solvent regime. They confirmed this prediction by a Monte Carlo simulation.

To see how the above results can be affected by the quality of the solvent, Orlandini *et al.* (2003, 2004) extended the model introduced by Guitter and Orlandini (1999) to incorporate an attractive vertex-vertex interaction as a pseudopotential to mimic poor solvent conditions. Due to the presence of both excluded volume and attractive interactions, the model undergoes a θ transition. Orlandini *et al.* (2003, 2004) showed that, while in the good solvent regime the knots are strongly localized [in agreement with the results of Metzler *et al.* (2002b)], in the poor solvent regime (where the polymer is relatively compact) they are delocalized. At the right θ temperature weak localization prevails with $t=0.44\pm0.02$. This last result can be explained by extending the scaling theory of polymer networks of fixed topology at the θ point and assuming that the configurations having the shape of a figure-eight dominate the statistics in that regime. This assumption, confirmed by the numerical data, gives $t=3/7$ as the conjectured exact value (Orlandini *et al.*, 2003, 2004), in good agreement with the numerical estimate. If, on the other hand, the above assumption is discarded, one finds that knots are loose also at the θ point, i.e., $t=1$ (Hanke *et al.*, 2003).

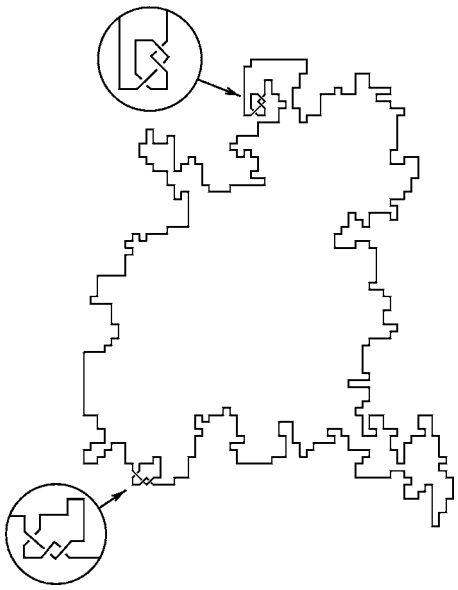

FIG. 20. A typical configuration for the composite knot $3_1\#3_1$. We have indicated the location of the two prime knots.

D. Some open problems

(i) Are there better ways to estimate the size of a knot within a knotted polymer ring? (ii) To what extent are the methods that have been proposed mutually consistent? (iii) Can flat knots be regarded as a good model of adsorbed polymers in the low-temperature limit (i.e., when the polymer is strongly adsorbed)? (iv) Are flat knots a good model of polymers confined in thin slabs?

VII. IDEAL KNOTS

Any embedding in R^3 of a particular knot (say, 3_1 to be specific) is equally good, from the topological point of view, since they can all be interconverted by an ambient isotopy. However, these embeddings differ in their geometry and it is clear that geometry, as well as topology, is important in determining the properties of ring polymers. Katrich *et al.* (1996) asked if a particular embedding was in some way preferable, in that its properties characterized at least some properties of all embeddings. They coined the term *ideal knots* for such embeddings.

The idea that one embedding is *better* than others is connected to the notion of *knot energies*. The idea is to attach a potential to the embedding and to minimize the energy over all embeddings. There is no particular potential which is obviously the correct potential since this potential does not come from the physics of the problem. Nevertheless, many different potentials have been proposed and there are some reasons for preferring one over another (Diao *et al.*, 1997a). One hopes to be able to use such potentials as discriminators between different knot types. If two knots have different minimum energies for a given potential then they must be topologically distinct and must be different knot types.

The scheme used by Katrich *et al.* (1996) was to ask how long a piece of rope was needed to tie a particular

knot. For a particular knot type consider all possible embeddings in R^3 where the knot is the center line of a tube of uniform unit diameter. This curve has some length. Now minimize this length over all embeddings of this knot, subject to the tube not intersecting itself. Call this the *length* of the knot. The minimizing conformation is called the *ideal* representation of the knot. This is a nice idea but there are some difficulties to be faced. The conformation which minimizes the length may not be unique in which case there is not a unique ideal representation. At a more practical level, it is hard to know if one has found the global minimum in the space of embeddings. One also has to worry about what properties the tube, or the center line, should have. Should the center line have continuous first derivative or continuous first and second derivatives? Should it be smooth? These questions have been examined by several groups. The background and further references can be found in papers by Diao and co-workers (Diao *et al.*, 1997a, 1997b, 1999). As mentioned in Sec. III.A.6, polymers can have different degrees of flexibility and in this respect it is interesting to explore the notion of ideal representation of the knot for tubes with different flexibilities. For example, it is reasonable to expect that the more flexible the tube is the tighter the knot can be. Buck and Rawdon (2004) have shown that this is, however, not always true since there a value of flexibility beyond which more flexibility adds very little entanglement.

There is an equivalent scheme in which one fixes the length of the knot and asks for the maximum diameter of a tube around the center line. This intrinsic property of the knot is sometimes called the *thickness* of the knot and the curve itself provides an *ideal shape* or representation of the knot type (Buck and Simon, 1997, 1999; Litherland *et al.*, 1999). Approximations of ideal shapes in this sense have been found via a series of computer experiments (Katrich *et al.*, 1996, 1997). A simple characterization of curve thickness is the notion of *global radius of curvature* for a curve (Gonzalez and Maddocks, 1999). This can be seen as a suitable three-body interaction among triplets of points along the curve that leads to a family of integral knot energies that do not require explicit regularization and that can be more easily implemented in models of polymers with a given thickness (Maritan *et al.*, 2000; Marenduzzo *et al.*, 2005).

The idea of an ideal knot has proved quite fruitful (Stasiak *et al.*, 1998). We introduced the writhe of a closed curve in Sec. III.A.8 when discussing ribbon models of duplex polymers. Since writhe is a property of a curve, one can also ask for the writhe of an embedding of a knot. If we fix the length of the embedding of a knot of type τ and average over all embeddings of τ with this length then $\langle Wr(\tau)\rangle$ will depend on the knot type τ. If τ is an achiral knot then $\langle Wr(\tau)\rangle=0$. For chiral knots it has been observed that $\langle Wr(\tau)\rangle$ is either independent of the length of the curve or, at least, depends only weakly on the length, going to a constant as the length increases (Janse van Rensburg *et al.*, 1997; Stasiak *et al.*, 1998). There are strong positive correlations between the writhe of an ideal knot, the average writhe of a knot on the simple cubic lattice, and the writhe of a model of circular DNA (Janse van Rensburg *et al.*, 1998; Stasiak *et al.*, 1998).

Another interesting feature of ideal knots is the so-called *quasiquantization of writhe*. If one computes the values of the writhe of the tightest conformations of prime knots, their distribution turns out to be concentrated around multiples of 4/7 (Pieranski, 1998; Cerf and Stasiak, 2000, 2003; Pieranski and Przybyl, 2001). Interestingly enough the quasiquantization phenomenon seems to appear not only in the ideal representation but also in random knots when the single writhe value is replaced by its average value (Janse van Rensburg *et al.*, 1993, 1998).

Finally, there is also a strong correlation between the speed with which a knotted circular DNA molecule moves through a gel under the influence of an applied electric field and properties of the ideal representative of a knot (Stasiak *et al.*, 1996, 1998).

VIII. DISCUSSION

In this review we have discussed how entanglements in long linear and ring polymers can be investigated both rigorously and numerically. These entanglements can occur in DNA and can have serious consequences for cellular processes such as replication. There can be no doubt that long synthetic polymers are also entangled and that these entanglements affect crystallization and rheological properties.

In order to make any useful statements about the problem one must choose a suitable model of the polymer and we have discussed several possibilities. For some of these models it is possible to prove that most sufficiently long ring polymers are knotted and what is meant by "most" can be made precise. What is meant by "sufficiently long" is more difficult and this question can only be answered numerically. One can also ask how badly knotted a ring polymer will be. There are various measures of this topological entanglement complexity and, using many of these measures, sufficiently long ring polymers are very badly knotted.

We have also looked at the effects of geometrical constraints, adsorption, and flexibility on the knot probability. In each case it is possible to make statements rigorously about the asymptotic behavior but not about smaller systems.

We have discussed numerical methods which are useful in investigating models of knotting and described some of the main results which come from these approaches. Extensions to linking and to ribbon models have also been briefly considered.

It is much more difficult to address the question of the dimensions of knotted polymers and we have reviewed the numerical work in this area, focusing on the question of whether knots are "tight" or "loose."

The field has undergone a rapid development since the late 1980s and we understand many features of knotting and linking. Many questions remain to be answered

and we have discussed some open problems which we regard as being particularly interesting.

Our focus has been on equilibrium properties but knotting and other entanglements can play an important role in dynamics. An obvious example is in gel electrophoresis where the effect of knotting on the dynamics can be used to identify the knot type. For linear polymers there are interesting questions about the creation and removal of entanglements (i.e., the knotting and unknotting of the linear chain) as a function of time. Another intriguing problem is the effect of topological constraints on the kinetics of the collapse of a polymer in bad solvent (Nechaev, 1990; Grosberg and Nechaev, 1991). These are interesting issues but they are beyond the scope of this review.

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