The Application of Knot Theory to Models in Biology and Physics

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Abstract

In this paper, we begin by explaining some basic knot theory terminology by walking through a few problems. We then discuss the applications of knot theory to biology, specifically in examining and modeling the effects of enzymes on cyclic DNA. We also introduce new terminology, writhe, to model this type of cyclic DNA. Next, we explore the use of Ising models to represent interactions between particles in statistical mechanics, an important field of physics. Specifically, we examine the Yang-Baxter equation, also known as the star-triangle relation.

1 Introduction

As a heavily theoretical subject, the more concrete implications of knot theory may escape those who do not study the field. However, knot theory was in fact first created and used by chemists and physicists like William Thomson, 1st Baron Kelvin, who (incorrectly) hypothesized that atoms of different elements were defined by different knots within each [3]. Though Thomson's theory was later proved incorrect, his work inspired Peter Tait, who developed many concepts that are used today in applications of knot theory to biology, chemistry, and physics [3]. Due to these origins in science, it is unsurprising that knot theory has many wide uses in different branches thereof.

Specifically, because of its theoretical nature, knot theory is often used to create mathematical models of more tangible concepts in these branches. For instance, knot theory is used when modeling DNA and the effects of enzymes on it, as well as in statistical mechanics, when examining the interactions between particles in a system. By using more theoretical models, scientists and mathematicians can make these concrete concepts more abstract and therefore easier to manipulate and work with.

In this paper, we will explore these two specific examples of models using knot theory. Before we delve into the applications of knots to these branches of science, however, we must first define a few key ideas used today in knot theory.

1.1 Knot Theory Concepts to Know

One concept vital to understanding knot theory is the definition of a knot.

Definition 1.1. Knot: A *knot* is a closed loop of "string," where the string has no thickness at all. It must not intersect itself, since that would cause branches in the "string," but may cross over itself.



Figure 1: Three common knots. From left to right: the unknot (trivial knot), the trefoil knot, and the figure-eight knot.

Links, too, form a large part of the foundation of knot theory.

Definition 1.2. Link: A link is a group of one or more knots. Those knots do not necessarily need to be connected to each other as the name suggests. The only requirement is that the link consist of more than one discrete piece of string.

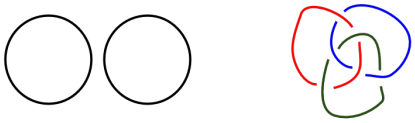


Figure 2: Two common links: the unlink (left) and the Borromean rings (right).

Both knots and links share certain features. One of the most obvious of these features is crossings.

Definition 1.3. Crossing: A crossing is a location on a projection of a knot where two strands appear to cross. The strand that can be seen completely in the crossing is called the overstrand and the one that is obscured by the overstrand is called the understrand.

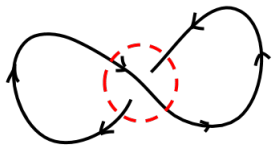


Figure 3: A crossing in which the overstrand passes from left to right and the understrand goes from right to left.

Crossings in links help us define a measure known as the linking number.

Definition 1.4. Linking number: The *linking number* is a measure of how intertwined two components of a link are. To calculate it, we first give each of the two components an orientation - in other words, we pick a direction to trace along for each component. Then, we assign every crossing either a +1 or a -1, according to the direction of the overstrand and understrand as seen in Figure 4. Finally, we add all these values and divide by two. The linking number is constant across all projections.

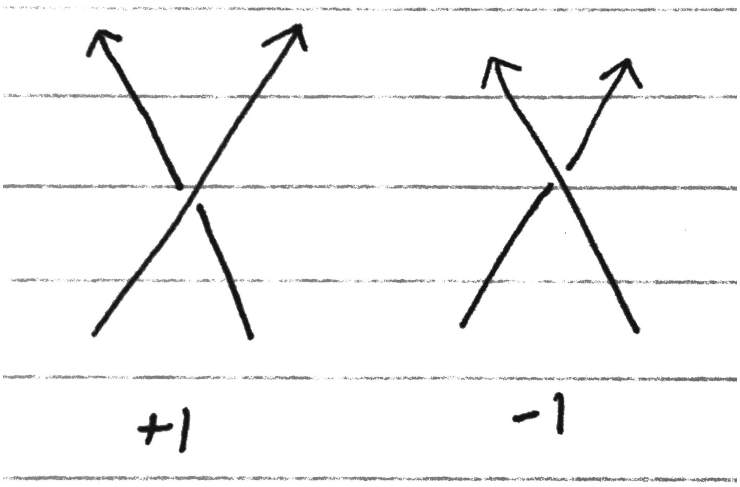


Figure 4: +1 and -1 crossings used for determining the twist of a ribbon.

The calculation for linking number appears when calculating other values for knots and links as well, as we will see later.

Nontrivial knots (i.e. not the unknot) must have more than one crossing in a projection. This makes sense, because a knot with no crossings is simply a circular loop, the simplest projection of the unknot. But we can also easily show that knots with exactly one crossing are trivial as well. All one-crossing knots can be simplified to one of the four shown in Figure 5.

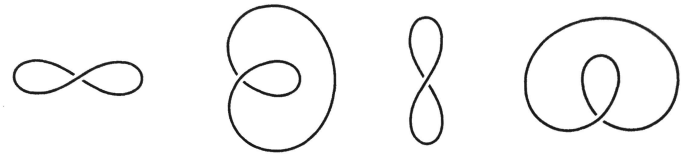


Figure 5: The four simplest one-crossing knots. [1]

It is clear that for each of these four knots, the single crossing can be untwisted to form the zero-crossing image of the unknot seen in Figure 1.

Through this, we see that there are several different ways to draw the same knot: the unknot can be shown as a circular loop with no crossings, or we can add a twist and draw it as a knot with only one crossing, and we could surely add as many more twists as we like to change its appearance even more. Still, its identity as the unknot remains the same. All of these different ways of drawing the same knot are called projections of that knot.

Definition 1.5. Projection: A knot has different projections, which are different expressions of the same knot. They appear different but can actually be twisted and pulled to become the same knot.

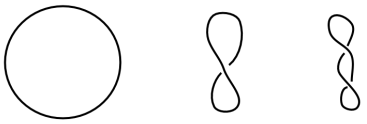


Figure 6: Three projections of the unknot.

Twisting and pulling is a very vague term, however. There are a few specific actions we can take on one projection of a knot to transform it into another called Reidemeister moves.

Definition 1.6. Reidemeister moves: These moves preserve the identity of a knot, and all projections of a single knot can be made into each other using some sequence of these three moves. In Figure 7, the three Reidemeister moves are shown.

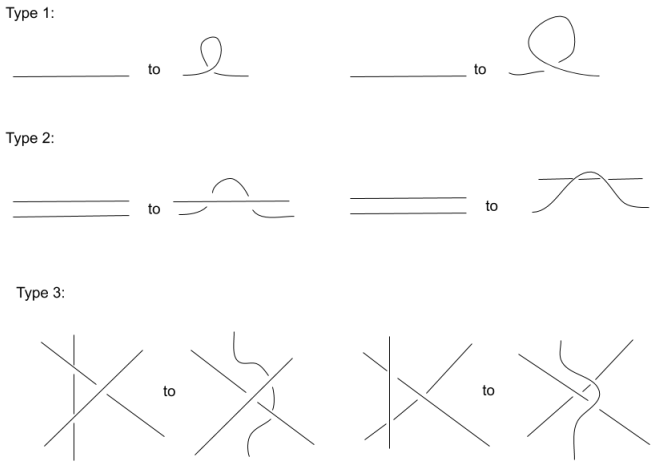


Figure 7: The Reidemeister moves in their various forms. The reverse of the moves also preserves the identity of the knot.

When moving between different projections of the unknot as shown in Figure 5 and Figure 6, we used only Type I Reidemeister moves by adding and removing twists. More complex knot projections, however, will require more complex series of Reidemeister moves to be transformed.

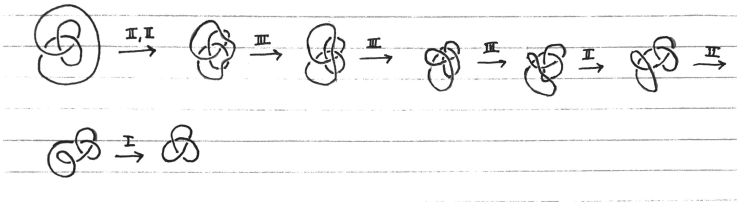


Figure 8: A more complicated series of Reidemeister moves to simplify a projection of the trefoil knot.

Because these concepts are so fundamental in knot theory, they appear frequently in knot theory's applications to other areas of science. Now that we have a solid foundation, we can move on to examine how these ideas are used to model DNA in biology and particle interactions in statistical mechanics.

2 Applications in Biology

One of the most significant applications of knot theory to biology is as it pertains to DNA, the molecule that contains the genetic code for all living organisms.

2.1 A Background of DNA

DNA has a very particular structure illustrated in Figure 9: a DNA molecule is composed of two molecular strands twisted together in a double helix held together by pairs of nitrogenous bases bonded together in between them. There are four possible bases: adenine (A), thymine (T), guanine (G), or cytosine (C). However, there are only four specific pairings - AT, TA, CG, and GC - as adenine only bonds with thymine and guanine only with cytosine.

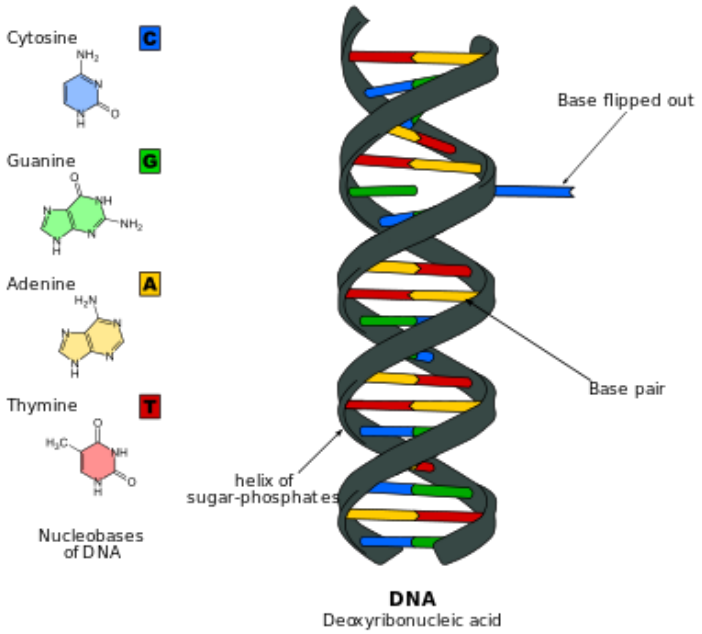


Figure 9: The structure of DNA. [2]

Because of the small number of possible pairings, each DNA molecule must contain millions of pairs to hold all the genetic information necessary for life. To make matters worse, this genetic material is usually very tangled, which makes it very difficult to replicate, copy, or modify the DNA when the cell's biological mechanisms require it.

2.2 Topoisomerases and DNA Manipulation

In order to make these disorganized tangles of DNA easier to work with, cells use enzymes called topoisomerases to manipulate the DNA topologically. Specific enzymes can perform very sophisticated manipulations on DNA, but topoisomerases can also perform several more general actions, as pictured in Figure 10.

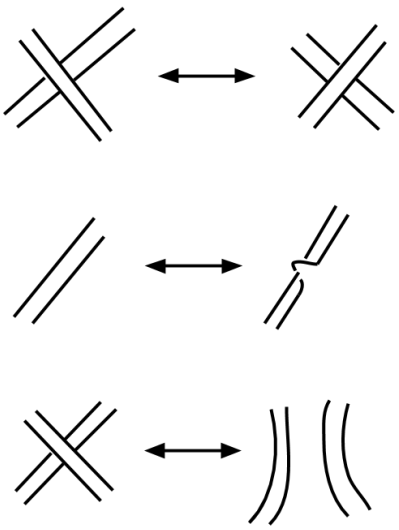


Figure 10: Three actions that topoisomerases can perform on DNA.

Scientists use circular (cyclic) DNA, or DNA molecules whose ends are joined, to examine the effects of these enzymes. On linear DNA, any knots caused by the enzyme would slip off the end, while they would be captured in a circular molecule. Both single-stranded and duplex (double-stranded) forms of cyclic DNA are common not only in bacteria and viruses but also in human mitochondria. However, although they appear naturally, scientists often apply enzymes to artificially created, synthetic cyclic DNA to determine their effects.

To create this cyclic DNA, scientists attach the tail ends of a strand of linear duplex DNA to the head ends. However, a wrinkle appears when we consider that DNA has a set orientation. Each strand contains sugar molecules, and depending on the orientation of the sugar molecules at either end, one end is defined as 3' and the other as 5'. Further, the structure of linear duplex DNA is antiparallel, so one strand's 3' end will correspond to the other's 5' end, and vice versa (Figure 11).

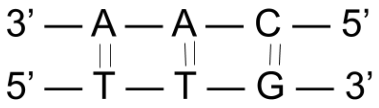


Figure 11: Linear duplex DNA is antiparallel.

When attaching the heads to the tails, we must attach a 3’ end to a 5’ end, as illustrated in Figure 12. Therefore, each strand’s head gets attached to its own tail, and the strands form a link rather than a knot.

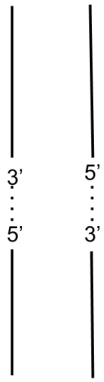


Figure 12: Because the 3’ end of DNA must be attached to a 5’ end, each strand’s head gets attached to its own tail.

We keep the fundamental structure of cyclic DNA in mind when we examine the effects of enzymes on these molecules. One particular action an enzyme may take is site-specific recombination, where the enzyme attaches to two specific sites on two strands of DNA (recombination sites), cuts the strands connecting these sites, and reconnects the ends in a new order. One possible example of a site-specific recombination is shown in Figure 13.

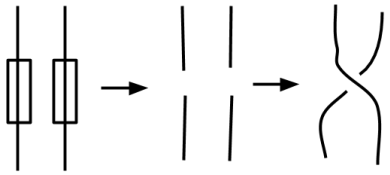


Figure 13: An example of a site-specific recombination. Here, the enzymes recombine the two strands such that they form a new crossing.

To study these site-specific recombinations more closely, scientists create single-stranded circular DNA molecules that contain copies of the recombination sites. They can then examine the DNA after introducing the enzyme to see how the molecule's structure has changed.

When creating these circular molecules, scientists also choose an orientation for each recombination site. This is possible because each recombination site is defined as a nonpalindromic sequence of base pairs that can be read differently either forwards or backwards. There are two possibilities for this circular DNA: either we have direct repeats, where both recombination sites face the same direction, or inverted repeats, where they face opposite directions (Figure 14.

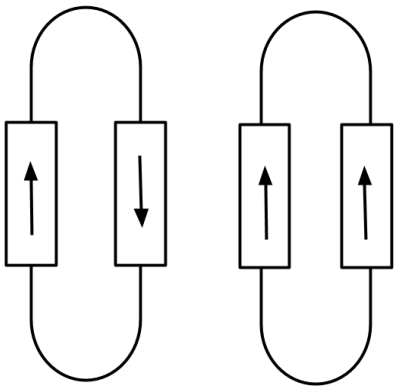


Figure 14: Direct repeats (left) and inverted repeats (right) on a piece of cyclic DNA.

The goal is to choose orientations that will match when the enzyme pulls the sites together. When the sites are pulled together, the resulting molecule, called a product, can take on several forms, as shown in Figure 15.

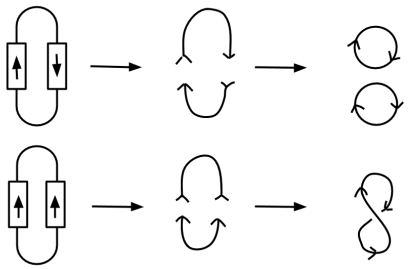


Figure 15: Direct repeats (top) produce a two-component link, while inverted repeats (bottom) produce a projection of the unknot.

In this setting, we can examine the effects of enzymes by using tangles. The substrate molecule (the molecule before the enzyme acts): the site tangle T, where the enzyme acts, and the substrate tangle S, the rest of the molecule that the enzyme does not affect. After the enzyme acts, the site tangle is replaced by the recombination tangle, denoted by R (Figure 16), in the product molecule.

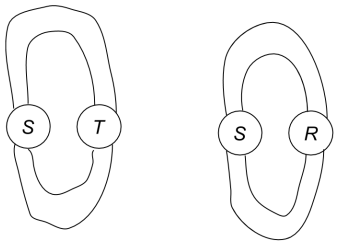


Figure 16: The enzyme replaces the site tangle T with the recombination tangle R while leaving the substrate tangle S the same.

To represent the molecules formed by these tangles, we use the notation $N(Q)$, which denotes the knot or link formed when we connect the top two and bottom two strands of a knot Q to each other. We also let $Q + V$ denote the tangle we get when we add the tangles Q and V. Therefore, we can write the substrate molecule as $N(S + T)$ and the product molecule as $N(S + R)$.

Studies of this type have been done on many enzymes, including Tn3 resolvase, which acts on cyclic DNA with direct repeats. Usually, this enzyme acts in the same way that we describe above - by replacing the T tangle with an R tangle - but occasionally, it will add in extra R tangles. Adding these extra tangles produces more complicated product molecules: adding two R tangles instead of one produces the figure-eight knot, while adding three produces the

Whitehead link (Figure 17).

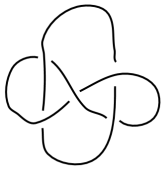


Figure 17: The Whitehead link. For an image of the figure-eight knot, see Figure 1

Using this information on the behavior of Tn3 resolvase, De Witt Sumners and Claus Ernst, from Florida State University and Western Kentucky University respectively, were able to prove that for this particular enzyme, S = (-3, 0) and R = (1).

2.3 Writhe and Supercoiling

As we have seen, enzymes usually act on DNA molecules by adding and subtracting tangles at the recombination sites. However, the term "site" is a little misleading - in fact, though the enzyme attaches to a particular location on the DNA, its actions affect the shape of the entire molecule. In order to describe these broader-reaching effects, we must define some new terminology relating to cyclic duplex DNA.

Because duplex DNA is made of two antiparallel strands (Figure 11), we can model it as a flat ribbon, with the strands on each edge of the flat side, as seen in Figure 18. Because it is cyclic, we can make this ribbon a continuous loop.

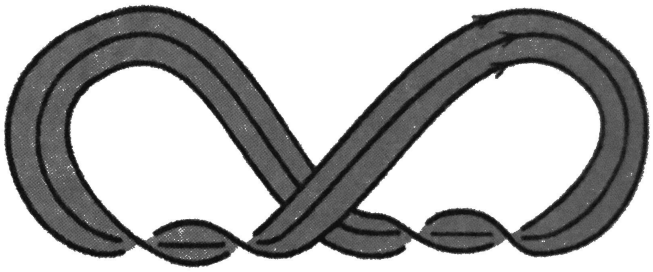


Figure 18: A ribbon modeling cyclic duplex DNA. [1]

We now define several characteristics of this ribbon that will allow us to examine it in greater detail:

Definition 2.1. Twist: The *twist* of a ribbon R is given as $Tw(R)$. It is, as the name suggests, a measured of how twisted around its own axis a ribbon is. We calculate twist by taking half of the sum of the +1s and -1s occurring at crossings of the ribbon's axis and one of its two edges. The +1s and -1s are determined in the same manner as linking number (see Figure 4).

Definition 2.2. Writhe: The *writhe* of a ribbon R is given as $Wr(R)$. It measures how contorted the axis of the ribbon is. The writhe of a ribbon is the average signed crossover number over all possible projections of the ribbon in space.

Definition 2.3. Signed crossover number: The *signed crossover number* is the sum of +1s and -1s occurring at crossings of the axis with itself. The signs of these crossings are determined in the same manner as linking number (see Figure 4).

Our final term is, in fact, an old term being applied to a new situation: linking number.

Definition 2.4. Linking number (of a ribbon): To calculate the *linking number of a ribbon* R, denoted as $Lk(R)$, we first treat the two edges of the ribbon as components of a link. The linking number of the ribbon is equal to the linking number of this link, which is defined in Definition 1.4.

To summarize, we now have three new measures: twist, writhe, and linking number. Twist measures how twisted an axis and an edge are, writhe measures how twisted the axis is about itself, and linking number measures how twisted the two edges are with each other.

Individually, each of these values gives us an interesting piece of information about a ribbon. Together, however, they have an even more interesting relation discovered independently by James White of UCLA, Brock Fuller of Caltech, and Czech mathematician G. Calugareanu:

$$Lk(R) = Tw(R) + Wr(R): \tag{1}$$

In words, this equation tells us that changes in twist and changes in writhe must balance each other exactly regardless of how we change the position of a ribbon, since the linking number stays constant.

In the context of a physical piece of cyclic duplex DNA, we also take into account the number of base pairs in the molecule. DNA naturally twists at a rate of 10.5 base pairs per twist, and twisting any more frequently than this will overwind the DNA.

Now suppose an enzyme doubles the number of tangles in a cyclic duplex DNA molecule. This will double the twist, because each edge crosses over the axis twice as many times, and the linking number, because the edges cross over each other twice as many times. However, doubling the number of twists means there are fewer base pairs per twist - half as many, to be exact. To return to its natural twist rate, the DNA will decrease its twist - but according to Equation

Equation 1, a decrease in twist means an increase in writhe. As writhe increases, the axis of the ribbon will become more twisted around itself and will become contorted in space in an effect known as *supercoiling*.

Thus when an enzyme adds too many more tangles to a cyclic duplex DNA molecule, though it performs this action at a specific site, it can change the shape and position of the entire molecule. Biochemists today use electrophoresis in gels to detect these changes and further study the effects of enzymes on DNA.

3 Applications in Physics

3.1 Physics Concepts to Know

Statistical mechanics is an topic in physics where the overall state of a system is studied rather than that of the individual particles. A simple example might be how temperature describes average kinetic energy of a set of particles, rather than the kinetic energy of a specific particle. Statistical mechanics is useful in describing things like phase transition (which does not occur for a single molecule), or the effects of magnetization on a conductor.

It can be difficult to model a large system. One simple model for that purpose is the Ising model, which models situations in which only particles that are near to each other interact. To visually describe an Ising model, we can use a graph in which the vertices represent particles and the edges represent interactions. Because metals are often shaped in regular, repeating patterns, this allows Ising models to be particularly simple when modeling them.

Ising models of 3D states have been very difficult to solve mathematically, but the study of 2D lattices provides a foundation for later study of them. In Ising models, vertices receive a positive or negative 1 value. In magnetization, this value would denote spin.

Each edge of the graph has energy based on the states of the vertices on either side of the edge. We can say that in general the energy of an edge that has vertices of the same value is $E_{=}$, and if the vertices have different values the energy of the edge between them is $E_{6=}$. The energy of the system, $E(s)$, is then the sum of energies of all the edges. We can define the following:

$$!\,(s_i; s_j) = \exp\left(\frac{E(s_i; s_j)}{kT}\right): \tag{2}$$

This allows us to take the partition equation over all the possible states of the vertices:

$$P = \sum_s \exp\left(\frac{E(s)}{kT}\right) = \sum_s \prod !\,(s_i; s_j): \tag{3}$$

Essentially, what this equation states is that the partition function simply equals to the product of the $!$ function for all edges in a state, summed across all possible states.