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## Tying the Knot: Applications of Topology to Chemistry

Tarini S. Hardikar

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# **Tying the Knot: Applications of Topology to Chemistry**

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Colby College, Waterville, ME

In Partial Fulfillment of the Requirements for Graduation

With Honors in Mathematics

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# Tying the Knot: Applications of Topology to Chemistry

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Approved:

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“YOU HAVE TO SPEND SOME ENERGY AND EFFORT TO SEE THE BEAUTY OF  
MATH”

- Maryam Mirzakhani

“I WISH THE FIGURE EIGHT KNOT WAS THE EIGHTH FIGURE, BUT IT IS KNOT. ”

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# Preface

Chirality (or handedness) is the property that a structure is “different” from its mirror image. Topology can be used to provide a rigorous framework for the notion of chirality. This project examines various types of chirality and discusses tools to detect chirality in graphs and knots. Notable theorems that are discussed in this work include ones that identify chirality using properties of link polynomials (HOMFLY polynomials), rigid vertex graphs, and knot linking numbers. Various other issues of chirality are explored, and some specially unique structures are discussed. This paper is borne out of reading Dr. Erica Flapan’s book, *When Topology Meets Chemistry*. It follows the structure of the book closely, and in a sense, tells the same story, but as a modern adaptation. Every uncited theorem and definition and fact is from this book.

The second part of this work focuses on using graph theory to better span molecular graphs. This part is significantly less explored, but nevertheless, presents some interesting prospects.

I hope you enjoy reading this work and are left with an appreciation for why chirality is not a trivial problem.

# Introduction

## 1.1 A Brief History and Motivation

Topology and chemistry have an interesting shared past. The field of knot theory began when Lord Kelvin, in the 1880s, proposed that atoms were made from vortex rings in space, composed of ether. To better understand atoms, Peter Tait categorized knots into classes that could not be deformed into one another. This was the first creation of a table of knots, and the field took off from there [Flapan, 2000]. While ether clearly does not make up the space in our universe, chemistry and topology have borrowed ideas from each other since then.



Figure 1.1: The simplest link is two unknots (or unit circles) coiled through each other.

The field of molecular (or chemical) topology began with the synthesis of a class of topologically interesting molecules called nonplanar molecules. These molecules cannot be deformed into a plane even if all possible motion is allowed. One of the simplest examples of such a molecule is a catenane (see Figure 1.1). First synthesized in 1961 by

Frisch and Wasserman, the molecule was a Hopf link (two interlocked rings) [Frisch and Wasserman, 1961]. In 1982,

David Walba and others synthesized a Möbius ladder with three rungs. This is similar to a Möbius strip where the sides are replaced by a ladder, and additional rungs are added that connect the two sides (see Figure 1.2) [Walba et al., 1982].

Walba tried to extend the Möbius ladder synthesis to a trefoil, by forcing the molecule to twist two more times in space [Walba, 1987]. However, the method failed, and it was only in 1989 that Dietrich-Buchecker and Sauvage synthesized the first molecular knot, a trefoil (Figure 1.3) [Dietrich-Buchecker and Sauvage, 1989]. Since then, more knots have been synthesized, including an 8-crossing knot earlier this year. The 8-crossing knot is the tightest knot yet, and provides applications for new materials in the future [Danon et al., 2017]. There are many more molecules that have a non-

planar molecular graph, leading to interesting properties. The 2016 Nobel Prize in Chemistry was awarded to Sauvage, Frasier, and Stoddart for their work on developing molecular machines. These molecules in fact, are topologically complex, and derive their motion from their non-planarity. These molecules were categorized as rotaxanes, catenanes, and knotanes. While catenanes were introduced earlier as links, rotaxanes may take more forms, and are categorized by their ability to create some internal rotations. Knotanes are knotted molecules that also move along their strands.

In addition to synthetic applications and elegant advances in molecular machinery, molecular topology has many other applications. DNA's twisted helical nature has led to interesting notions of knottiness on biologically relevant molecules [Flapan, 2000].

However, the existence of topologically non-trivial molecules doesn't warrant a new field of mathematics. So, why are nonplanar molecular graphs topologically interesting, and why are topologists and chemists invested in this field?

David Walba, in the 1980s, developed the notion of **stereochemical topology** or **topological stereochemistry** as the study of topologically interesting molecules and their interaction in space. He stated that the field had a two-fold purpose: (1) to synthesize and develop new molecules that present stereochemical novelties (2) to build a framework for using topology to analyze these molecules. [Walba, 1987].<sup>1</sup>

Until the synthesis of topologically complex molecules, like the ones mentioned above, the stereochemical properties of molecules were quite straightforward to analyze, at least mathematically. However, these new molecules necessitate new ideas to examine how they interact in space, and with their mirror images. For instance, it is known that there are two trefoils: a right-handed twist, and a left-handed twist. Are the molecular trefoils similarly distinct? Does the presence of rings in the molecule affect the chirality or the movement of the molecule? Given some molecule, can we develop mathematically sound tests for its chirality?

It is important to note that there are different "levels" of chirality. In other words, a molecule's chirality is dependent on what space it is embedded in, and what movements can be performed on it. For instance, topologically valid motion involves all continuous movement, while chemically, it might be more appropriate to restrict motion to physically accessible movement. Additionally, there



Figure 1.2: A schematic representation of the 3-rung Möbius ladder.

<sup>1</sup>**Stereochemistry** refers to the study of a molecule's structure and orientation in three-space. **Chirality**, from the Greek word for handedness, refers to a structure being distinct from its mirror image.

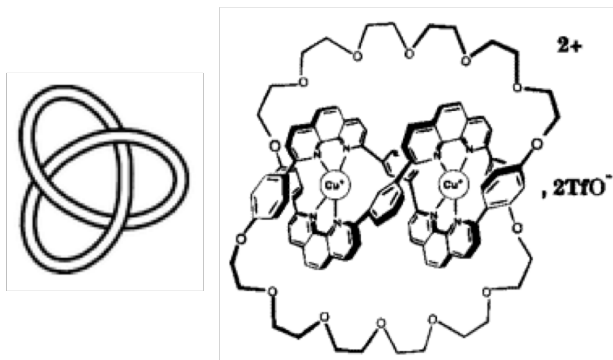


Figure 1.3: (left) Standard representation of the trefoil knot; (right) Molecular trefoil knot synthesized by Sauvage and Dietrich-Buchecker.  
Image from the Knot Table and [Dietrich-Buchecker and Sauvage, 1989]

are different stereochemical relationships molecules can have: they can be enantiomers, diastereomers, etc. Some of them are explored here, while more rigorous definitions will be provided later as required.

## 1.2 Molecular Graphs and Stereoisomers

A **graph** is a pair  $(V, E)$ , where  $V$  refers to a collection of points called vertices, connected by edges, denoted  $E$ . A molecule can be represented as a graph by considering atoms to be vertices and bonds to represent edges. Connectivity in the molecule is transferred directly as adjacency in the graph. Different types of bonds are represented as various kinds of edges that cannot be interchanged and have different properties. Such a graph is called a **molecular bond graph** [Flapan, 2000].

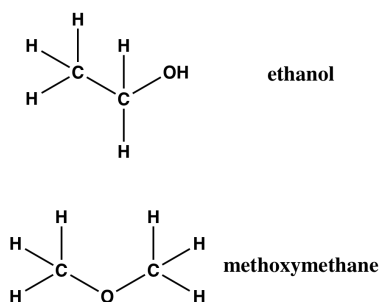


Figure 1.4: An example of structural isomers. Both molecules have the same formula, but different structures.

Chemically, **isomers** are structures that have the same formula, but different connectivity. Correspondingly, these molecular graphs have the same number of edges and vertices, but have a different adjacency matrix. This difference in connection could be structural, stereochemical, or even tautomeric. For instance, Figure 1.4 shows two molecules that have the same chemical formula, C<sub>2</sub>H<sub>6</sub>O, but are connected differently.

On the other hand, **stereoisomers** are molecules that have the same molecular graph, but in the given embedding, cannot be rigidly (or Euclidean-ly) transformed to each other. For instance, consider the molecule shown in Figure 1.5 on the left. It cannot be deformed to its mirror image shown on the right through any chemically accessible manner. This graph is a rigid stereoisomer. Chemists call these

two molecules to be **enantiomers** of each other. There is, in fact, an experimental difference between these two molecules. When each of these molecules is hit with plane polarized light, the molecule causes the light to rotate. An isomer that causes counterclockwise rotation is the (L) isomer, while the right rotation is the (D) isomer. This system of naming isomers is entirely experimentally determined, and so we will not be using it here.

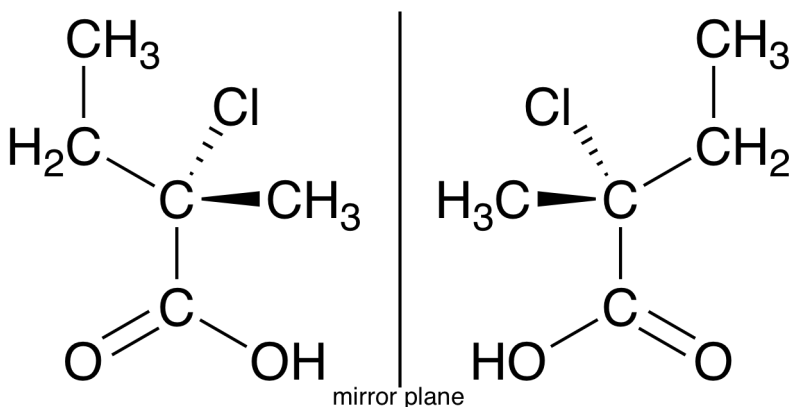


Figure 1.5: An example of enantiomers. The mirror image is taken across the given plane.

Instead, there is another way of labeling stereoisomers. This method labels a molecule as either (R) or (S), for *rectus* and *sinister* which is Latin for right and left respectively. The labeling process is as follows:

1. Identify the stereocenters of the molecule. A **stereocenter** is any atom in the molecule that has distinct substituents leading to distinct orientations in space. For instance, in the example shown in Figure 1.5, the carbon atom connected to chlorine is a stereocenter since it is connected to four unique things that are oriented specifically in space.
2. Then, assign a number to each substituent based on priority, where the lowest number implies lowest priority. The priority is a function of atomic number. If substituents have the same atom (and so the same atomic number), then the next adjacent atom's priority is considered.
3. Once priorities have been assigned, the molecule is reoriented so that the substituent marked "1" is placed back in the plane of the paper. Then, the path of the numbers is traced.
4. If this path is clockwise, the molecule is labeled (R). If anticlockwise, then it is labeled (S).

Based on this nomenclature, it is seen that the molecule on the left in Figure 1.5 is (S), while the one on the right is (R).

Note that there are more kinds of stereoisomeric relationships than enantiomerism that are chemically relevant. However, for the purpose of this thesis we are going to examine relationships between molecules and their mirror images.

### 1.3 Must We Care About Chirality?

It is natural, and in fact, important to ask: why should we develop all this structure to understand chirality? How much does chirality matter? Why does it matter?

Most chemicals we interact with on a daily basis: drugs, soap, shampoo, fabrics, etc, are chiral. In many instances, only one of the enantiomers has the properties we need. For example, the common pain relieving drug, ibuprofen, has two isomers, as shown in Fig 1.6. The (S)-enantiomer is the biologically active one, while the (R) enantiomer is not. Interestingly, commercially sold ibuprofen is not stereospecific —both forms are sold. This is because the stomach's acidic conditions convert the (S) to the (R), and so there is no advantage to eating enatio-specific ibuprofen.

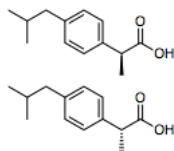


Figure 1.6: (top) (S)-ibuprofen is biologically active while (bottom) the (R)-enantiomer has no pain relieving properties.

While the nonactive stereomer is harmless in the case of ibuprofen, that has not always been the case. Thalidomide is a famous example where the left stereoisomer treated morning sickness while the right stereoisomer caused birth defects.

Thankfully, the consequences are not always so drastic. But thalidomide presents a dark example of the importance of understanding stereospecificity of the chemicals we use.

## 1.4 A Note on Convention

For drawing molecular bond graphs, this thesis retains chemistry convention. This means that an unlabeled vertex refers to a carbon atom. A carbon vertex can only have order four. Hydrogens will not explicitly be shown on molecular bond graphs. Therefore, if a vertex has an order less than four, it is implied that there are hydrogens connected to the carbon, fulfilling the four-valence rule.

A wedged bond ( $A \blacktriangleright B$ ) denotes an edge coming out of the plane of the paper. A dashed edge ( $A \dashv\dashv B$ ) denotes an edge going into the plane of the paper, while regular edges ( $A \text{ --- } B$ ) simply denote edges in the plane of the paper.

A molecule has fairly restricted “legal” motion. For instance, the length of an edge (a bond) cannot be arbitrarily altered. Embeddings of a molecular graph not only indicate connectivity, but also describe the lengths, angles, and orientations of the edges. These can be altered freely only under topological consideration. Under Euclidean (or physically accesible) motion, there are more restrictions, but these unfortunately, cannot be rigorously defined. This is because there are multiple factors that are involved in determining whether an atom can rotate around another, or if a bond can rotate, or if it can be extended. These restrictions will be discussed further and denoted by different edge types as needed.



# Chirality

## 2.1 Chemical Chirality

As briefly discussed earlier, chirality refers to a molecule’s ability to transform to its mirror image. We add the word “chemical” here to denote that the transformation must be physically valid, or accessible. Unfortunately, there is no rigorous way to categorize this motion. However, Walba provides a very useful way of thinking about these transformations in [Walba, 1987]. Consider the total space of all possible transformations. Now, within this space, add axes for time and energy. If the transformation is favorable on the energy scale, that is, if the transformation can lead to a more favorable position for the molecule, then it could occur. Furthermore, if this transformation can occur on some timescale that allows its detection, then we can actually track the movement. If it is too fast, it is impossible to tell if it actually occurred. If it is too slow, then it is difficult for the transformation to occur with any significant statistical likelihood. And so, we now have a picture of chemically valid transformations as a subspace of topological transformations, where this subset is constructed on the basis of energy and time favorability.

Despite there being no rigorous definition of legal chemical movement for molecular bond graphs, there is a rigorous condition to check for chemical chirality. This requires a bit of detour into the world of symmetry and group theory.

### 2.1.1 Molecular Symmetry

Molecular symmetry uses a set of operations to precisely describe the structure and geometrical orientation of a molecule. These operations are defined as actions on a molecule that leave the molecule “unchanged.” These operations generate or identify elements of symmetry, such as a plane, or a point. There are five symmetry operations that describe all permutations of a molecule in three-space. They are as follows:

1. **Identity:** As the name suggests, this operation doesn't alter the molecule, and sends every point to itself. It is denoted by the letter  $E$ .
2. **Rotation:** This operation defines an axis of rotation on the molecule, and specifies an angle of rotation. Then, the molecule is left unaltered by the rotation along the prescribed axis at the prescribed angle. It is denoted by  $C_n$ , where  $360/n$  is the angle of rotation in degrees.
3. **Inversion:** This operation identifies the center of mass of the molecule, and pushes every point equivalently through this point. It is denoted by  $i$ .
4. **Reflection:** This operation reflects every point through some specified plane. It is denoted by  $\sigma$ . Subscripts are used to denote the orientation of the mirror plane with respect to the axis of rotation.
5. **Rotation-reflection:** This operation is a composition of rotation followed by a reflection perpendicular to the axis of rotation. The axis of rotation is referred to as the improper axis. This operation is denoted as  $S_n$  where the  $360/n$  is the angle of rotation.

For a given molecule, one can assign symmetry groups, also called point groups. These sets are actually groups, following the group axioms. The fact that the identity axiom is fulfilled is made obvious by the existence of the identity element that sends every point in the molecule to itself. Since each action leaves the molecule unchanged, the composition of multiple operations also leaves the molecule unchanged, fulfilling the closure axiom. Associativity is similarly fulfilled. The inverse axiom is fulfilled once we consider that every operation can be reversed —rotating in the opposite direction, reflecting it twice and inverting it twice can undo every action. Therefore, each symmetry assignments actually creates groups.

Additionally, note that technically, the inversion, reflection, and identity operations can be described using  $C_n$  and  $S_n$ . This is because the identity operation can be thought of as  $C_1$ , while the mirror is  $S_1$  and inversion is  $S_2$ .

We can now use this structure to develop a rigorous test for chemical chirality It is stated as follows:

**Theorem 1** (Chemical Chirality). *For a given molecular graph,  $G$ , in  $\mathbb{R}^3$ ,  $G$  has an improper axis of rotation if and only if  $G$  is achiral.*

*Proof.* This proof is from [Cotton, 1990]. To prove this theorem, let us begin by showing that if an improper axis of rotation does exist, then the molecule is achiral. So, suppose that a given molecular graph,  $G$ , has some axis of rotation  $S_n$ . Now, since this is a reflection-rotation operation, we can rewrite it as  $S_n = \sigma \cdot C_n$ . Let's consider two cases here:

Case 1:  $n$  is odd

In this case, performing the  $S_n$  operation is equivalent to performing a rotation and only 1 reflection (since reflections have order 2). Then,  $G$  also has a  $\sigma$  symmetry operation under which it is equivalent to, since the operations are closed under composition. If a molecule has a mirror plane of symmetry, it definitely is superimposable on its mirror image since it is equivalent to it.

Case 2:  $n$  is even

Now, in this case, performing the  $S_n$  operation is equivalent to performing just the rotation, since the reflection might not exist independently. Then, we have a molecule that undergoes a rotation by  $2\pi/n$  and comes into coincidence with the starting orientation ( $G$ ). And so, the molecule can be superimposed on its mirror image.

Conversely, if  $G$  is achiral, then it is superimposable on its mirror image. And, so there is some operation in the symmetry group that will produce the mirror image, since it is coincident with  $G$ . Clearly, this will hold for any point group with an improper axis of rotation since  $S_n$  implies the existence of a  $\sigma$  operation for the molecule. ■

## 2.2 Topological Chirality

### 2.2.1 Definitions

In this section, I will introduce some definitions that are necessary to provide a rigorous framework for chirality. These definitions are from [Flapan, 2000].

**Definition. Homeomorphism:** Let  $A$  be a subset of  $\mathbb{R}^n$  and let  $B$  be a subset of  $\mathbb{R}^m$ . Let  $h : A \rightarrow B$  be a function. We say that  $h$  is a homeomorphism if  $h$  is continuous and has a continuous inverse. In this case, we say that  $A$  and  $B$  are homeomorphic. If there is a homeomorphism  $h : \mathbb{R}^n \rightarrow \mathbb{R}^m$  such that  $h(A) = B$ , then we write  $h : (\mathbb{R}^n, A) \rightarrow (\mathbb{R}^m, B)$ .

We will be considering graphs in  $\mathbb{R}^3$  and examine how they map to themselves. When talking about homeomorphisms on graphs, we want vertices to map to vertices, and edges to edges. Next, we must formalize what we mean by a deformation of our graphs in space:

**Definition. Ambient Isotopy:** Let  $A$  and  $B$  be contained in a set  $M$  which is a subset of  $\mathbb{R}^n$ . We say that  $A$  is ambient isotopic to  $B$  in  $M$  if there is a continuous function  $F : M \times I \rightarrow M$  such that for each fixed  $t \in I$  the function  $F(x, t)$  is a homeomorphism,  $F(x, 0) = x, \forall x \in M$  and  $F(A \times \{1\}) = B$ . The function  $F$  is said to be an ambient isotopy.

A more intuitive picture for an ambient isotopy is to think of the parameter  $t$  in terms of the time. And so, we have a function that at time  $t = 0$  maps every point to itself, and then slowly over time, takes  $A$  to  $B$ , such that at  $t = 1, F(A \times \{1\}) = B$ . By making  $F$  a homeomorphism, we are requiring that at every point in this transformation,  $F$  has a continuous inverse. This prevents  $A$  from wrapping over itself.

As an example, observe that the unknot,  $S^1$  is homeomorphic to the trefoil knot,  $K$ . The location on the curve can be parametrized by  $[0, 2\pi]$ . However,  $S^1$  and  $K$  are not ambient isotopic to each other. This is because there is no way you can form the unknot from a trefoil without two points crashing through each other. This prevents the mapping from being injective, and therefore, an ambient isotopy cannot be constructed. However, note that every ambient isotopy is a homeomorphism, simply consider the function created at  $F(A \times \{1\})$ . And so, we will be using a deformation to refer to an ambient isotopy. Next, let's consider an isotopy, which is a bit different from ambient isotopy.

**Definition. Isotopy:** Let  $A$  and  $B$  be subsets of  $\mathbb{R}^3$ , and let  $h : A \rightarrow B$  and  $g : A \rightarrow B$  be homeomorphisms. We say that  $h$  and  $g$  are isotopic if there exists a continuous function  $F : A \times I \rightarrow B$  such that  $F(x, 0) = h(x), F(x, 1) = g(x)$ , and for every fixed  $t \in I$ , the function  $F(x, t)$  is a homeomorphism.

Intuitively, the difference between an isotopy and an ambient isotopy is that an isotopy matches functions to functions, while an ambient isotopy takes functions and their **neighboring spaces** to functions. So visualize a knot made with thin string. An isotopy matches this string to another thin string. However, an ambient isotopy would take a thick rope knot and map it to another knot.

Now, using these definitions, we can now construct our first rigorous definition of topological chirality:

**Definition.** A graph  $G$  in  $\mathbb{R}^3$  is topologically chiral if it is not ambient isotopic to its mirror image.

Basically, this definition formalizes the notion that if a graph cannot be “deformed” to its mirror image, it is chiral. Next, let us extend the space we are working in. Up until this point, we have been examining structures in  $\mathbb{R}^3$ . Now let’s consider the three dimensional sphere,  $\mathbb{S}^3$ . So, the one dimensional sphere is simply the unit circle in  $\mathbb{R}^2$ . Next, the two-dimensional sphere is a unit ball in  $\mathbb{R}^3$ . So, now the equivalent notion of a three dimensional sphere would be considering a unit hyperball in  $\mathbb{R}^4$ . An alternative way of constructing this space is by adding a single point at infinity to  $\mathbb{R}^3$ . Conversely, given  $\mathbb{S}^3$ , we can construct three-space by removing the point at infinity.

So why are we doing this? If we are mapping physical reality (like atoms and molecules), why are we looking at four dimensional space and points at infinity? This is because there is more topological machinery in  $\mathbb{S}^3$ , and we will use it to prove various theorems. Note that for most theorems, we will be able to move between the two spaces.

**Theorem 2.** *A graph,  $G$  is ambient isotopic to its mirror image in  $\mathbb{R}^3$  iff it is ambient isotopic to its mirror image in  $\mathbb{S}^3$ .*

*Proof.* Let  $A$  and  $B$  be two graphs in  $\mathbb{R}^3$ . First, suppose that we have our ambient isotopy  $F : A \times I \rightarrow B$  in  $\mathbb{R}^3$  is a homeomorphism. Then, we can add a point at infinity to this space and define  $F$  to be such that  $F(\infty, I) = \infty$ . This extends the homeomorphism to  $\mathbb{S}^3$ .

Conversely, suppose that we have a homeomorphism  $F : A \times I \rightarrow B$  in  $\mathbb{S}^3$  for  $A, B \subset \mathbb{S}^3$ . Then,  $F(A \times I)$  will not include all of  $\mathbb{S}^3$ , an assertion we will not be proving. We can modify the homeomorphism so that it misses a single fixed point every time. This point is now the fixed point at infinity. Removing this point preserves the rest of the homeomorphism which is now on  $\mathbb{R}^3$ . ■

Now, armed with a basic definition of chirality and isotopies, let us consider on developing a more useful definition of chirality. Let us begin by defining orientations.

**Definition.** Every homeomorphism is isotopic to either the identity map or a reflection map, but not to both. If it is isotopic to the identity, it is called an orientation preserving. Else, it is called orientation reversing.

Another way of thinking about orientation preserving functions is that these functions maintain the orientation of axes. So, a right handed axis system stays right handed if the function preserves orientation. If the function maps it to a left handed axis system, then it is orientation reversing.

Now, since when considering chirality, we are considering how a graph interacts with its mirror image, we are looking to see if a homeomorphism on a graph is isotopic to its mirror image. And so:

**Definition.** A graph  $G$  in  $\mathbb{R}^3$  is topologically achiral if there exists an orientation reversing homeomorphism on  $(\mathbb{R}^3, G)$ . Else, it is chiral.

This definition of chirality agrees very well with our intuitive picture of chirality. If you can continuously deform a graph to its mirror image, then the graph cannot be chiral. Therefore, if you can map your homeomorphism as an orientation reversing one, the graph cannot be chiral.

## 2.2.2 Knots and Knot Theory

Armed with the basic definitions that we need, let us now take a quick detour into the world of knot theory. A knot is, very simply put, an embedding of the unit circle in  $\mathbb{R}^3$ . A link is defined as the union of multiple knots.

**Definition. Equivalence of knots:** Two knots are said to be equivalent if they are ambient isotopic to each other. Then, the two knots are said to have the same knot type.

There are many different projections of any given knot. To see if two given projections are the same, there are series of “legal” moves that can be performed, under which they must remain constant. These are called the Reidemeister moves (see Figure 2.1):

1. A twist can be added or removed in a knot.
2. A strand can be slid over or under another.
3. A strand can be slid over or under a crossing.

## Link Polynomials

Polynomials are useful tools in categorizing links and knots. If two links are ambient isotopic to each other, and the “algebraic expression” associated with the link is the same, then it is called

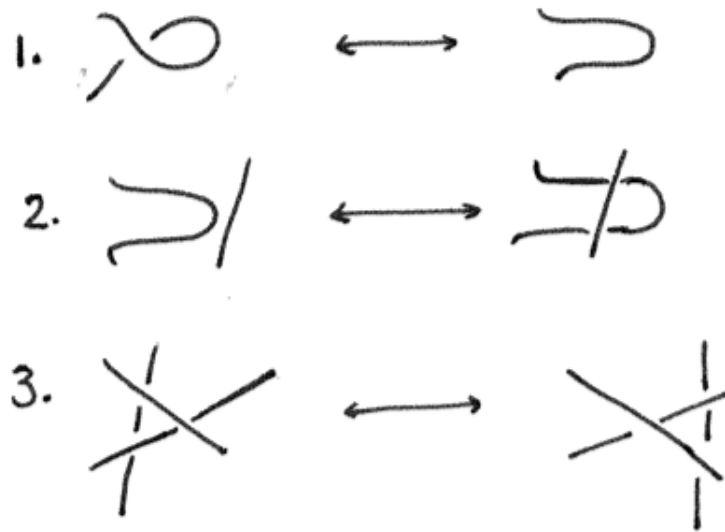


Figure 2.1: The three Reidemeister moves are shown here. Image adapted from Wolfram Mathworld.

a topological invariant. This is very convenient for us while categorizing chirality. Given a link  $L$ , we can construct a topological invariant for it. If the mirror image of  $L$ ,  $L'$  has the same topological invariant, we know that  $L, L'$  are ambient isotopic to each other and hence achiral. So now, whether or not a graph and its mirror image are ambient isotopic to each other can be reduced to if they have the same polynomial expression for a well chosen invariant. It is important to note that to construct a polynomial expression for a link, the link must have an orientation.

Let us now consider the HOMFLY polynomial, named after the six mathematicians involved in its construction: Hoste, Ocneanu, Millett, Freyd, Lickorish, and Yetter. It is often also described as the HOMFLY-PT polynomial to account that Przytycki and Traczyk discovered it independently. First, we must define oriented crossings:

**Definition.** Given two strands crossing each other with an orientation defined on both strands, the crossing is called positive if it corresponds to a right handed twist, and negative if otherwise. (Figure 2.2).

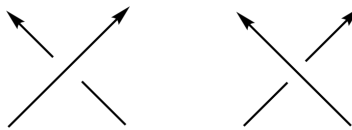


Figure 2.2: (left) Positive crossing. (right) Negative crossing.

The polynomial is defined in variables  $m, l$  and is constructed as follows ([Flapan, 2000]):

1. The unknot,  $K_u$  has polynomial,  $P$  defined as  $P(K_u) = 1$ .
2. Given a link projection, make three copies of the link. Keep the copies exactly the same except for one point of difference at the orientation of a crossing (as shown in Figure 2.3). Label the positive crossing as  $L_+$ , the negative crossing as  $L_-$ , and the no-crossing as  $L_0$ . Then,  $lP(L_+) + l^{-1}P(L_-) + mP(L_0) = 0$ .
3.  $P(L)$  is invariant under ambient isotopy of  $L$ .

The HOMFLY polynomial is calculated by identifying smaller links within the given link recursively, until the unknot is reached. It is quite clear that this process is quite tedious and time-consuming. However, there are many computer programs that calculate the polynomial for a given oriented link. It is important to note that the actual orientation of the link affects the polynomial. Using this polynomial, we can now construct a new theorem for chirality that is more easily implementable.

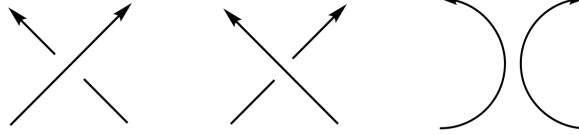


Figure 2.3: Three copies of a crossing are made, and each crossing type is replicated. Image adapted from [Flapan, 2000].

**Theorem 3.** *Given an oriented link  $L$  with HOMFLY polynomial  $P(L)$ , where an oriented link is one where every component of the link has a defined orientation. Let  $\bar{P}(L)$  refer to the polynomial obtained by interchanging the variables  $l$  and  $l^{-1}$  in  $P(L)$ . If  $P(L) \neq \bar{P}(L)$ , then  $L$  is topologically chiral as an oriented link. If  $L$  is a knot, then the same conclusion can be made independent of orientation.*

*Proof.* From [Flapan, 2000]. For the given oriented link  $L$ , let the mirror image be called  $L^*$ . Since  $L^*$  is the mirror image, it will have all the opposite crossings from  $L$ . Then, the  $L_+$  crossings in  $L$  will correspond to  $L_-$  in  $L^*$  and vice versa. And so, in the equation that defines the HOMFLY polynomial, the  $l$  and the  $l^{-1}$  variables will be swapped. So:

$$lP(L_+) + l^{-1}P(L_-) + mP(L_0) = 0$$

$$lP(L^*_-) + l^{-1}P(L^*_+) + mP(L_0) = 0$$

Then,  $P(L^*) = \bar{P}(L)$ . So, if  $P(L) = \bar{P}(L)$ , then  $P(L) = P(L^*)$ , and since the polynomial is invariant



under ambient isotopy, there exists an ambient isotopy between  $L$  and  $L^*$ . Therefore,  $L$  is achiral with the given orientation.

Similarly, if the two polynomials aren't equal, then there is no ambient isotopy between  $L$  and  $L^*$ , and so the link is achiral. ■

As an example, consider the Hopf link, the simplest non-trivial link, with the orientation give in Figure 2.4. The HOMFLY polynomial for this link is  $l^3m^{-1} + lm^{-1} - lm$ . Clearly, this polynomial is not symmetric in  $l$  and  $l^{-1}$ , and so the oriented Hopf link is chiral. However, if there was no orientation, then the mirror image could just be rotated to get the original Hopf link, and so the unoriented link is achiral.

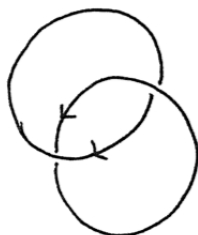


Figure 2.4: A Hopf link with a fixed orientation.

### 2.2.3 Constructing Graphs with Restrictions

Chemical structures often have limited motion because of energy constraints and atomic properties. Additionally, carbon typically forms four bonds, leading to four-valence graphs. To better model these properties, we can place restrictions on our graphs:

**Definition. Rigid vertex graph:** A rigid vertex graph is one in which each vertex is replaced by a two-dimensional disk with the edges attached to the boundary of the disk.

The order of edges around the disk is very important, and it must be maintained under ambient isotopy of the graph. Next, let us define an invariant created by Louis Kauffman on these graphs.

**Definition.  $C(G)$ .** For a given four-valent rigid vertex graph  $G$ , the set  $C(G)$  is constructed by taking every rigid vertex and replacing it with the all possible attachments of the four strands coming out of it. (Figure 2.5)

This set leads to a very powerful theorem by Kauffman, which simplifies the process of recognizing the chirality of a graph.

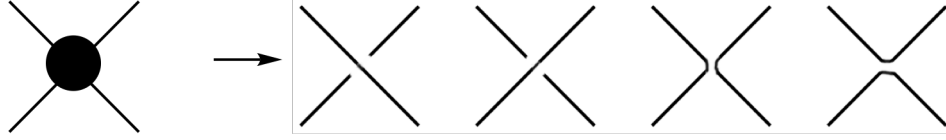


Figure 2.5: The construction of the set  $C(G)$  for the given rigid vertex on the left. Image adapted from [Flapan, 2000].

**Theorem 4.** *Let  $G$  be a four-valent rigid vertex graph embedded in  $\mathbb{R}^d$ . If there is an element of  $C(G)$  that is topologically chiral and that cannot be deformed to the mirror image of any other element of  $C(G)$ , then  $G$  is topologically chiral as a rigid vertex graph.*

As an example, consider Figure 2.6, which shows a modified trefoil knot with a rigid vertex. When  $C(G)$  is examined, it is seen that it contains a trefoil, without its mirror image. The trefoil is chiral, and the mirror image is not in the set. Therefore, the graph is chiral.



Figure 2.6: An example of how Kauffman's theorem can be used. Image adapted from [Flapan, 2000].

So let's prove this theorem now.

*Proof.* This proof is from [Kauffman, 1989]. First, let us add two new moves to the existing three Reidemeister moves. The first additional move is a straightforward sliding of vertices over and under strands (call Move 4). The second move is slightly trickier: it maintains the knot through knot braidings as shown in Figure 2.7.

First, note that the  $C(G)$  stays invariant under all of these moves for a given graph  $G$ . The original three Reidemeister moves definitely hold. In the case of the two new moves, observe that they just modify the orientation of the vertex with respect to the emergent strands.

Now, since  $C(G)$  is invariant under ambient isotopy for  $G$ , it can be used to predict other ambient isotopy invariant properties of  $G$ .

And so the proof follows immediately: for a given  $G$ , if  $C(G)$  is chiral, then since  $C(G)$  is invariant under ambient isotopy,  $G$  is chiral. ■

Kauffman however extended this theorem to construct a more powerful theorem that is not restricted to four valence vertices. First, let us define the set  $T(G)$  for a given graph  $G$ . This set is

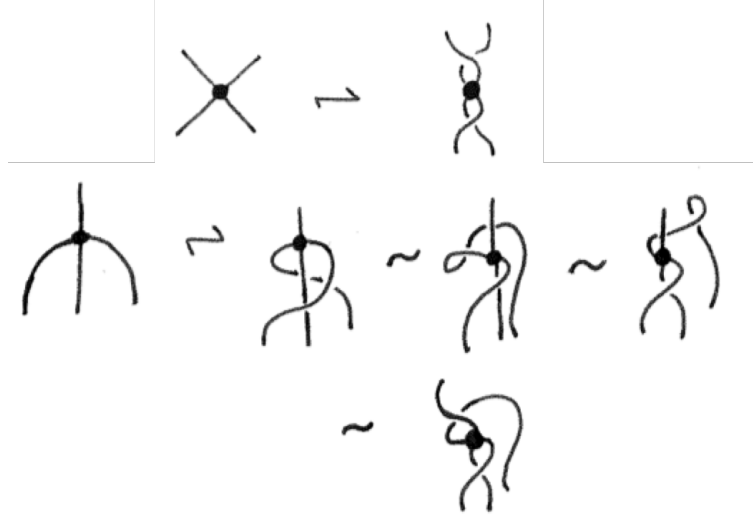


Figure 2.7: The second knot move added by Kauffman for rigid vertex graphs shows how the strands move around the vertex. Image adapted from [Kauffman, 1989].

constructed by disconnecting one strand from the rigid vertex and maintaining the connectivity of the rest. Then, we have the following theorem:

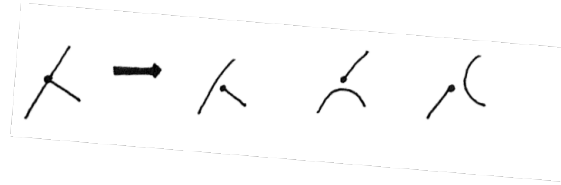


Figure 2.8: The construction of the set  $T(G)$ , given a rigid vertex in graph  $G$ .

**Theorem 5.** *Let  $G$  be a graph embedded in  $\mathbb{R}^3$ . If there is an element of  $T(G)$  that is topologically chiral and that cannot be deformed to the mirror image of any other element of  $T(G)$ , then  $G$  is topologically chiral.*

*Proof.* This proof is very similar to the proof for the first Kauffman theorem. Let us begin adding knot moves to the original Reidemeister moves. First, let us add Move 4, which was described earlier. Next, let us add another vertex move, a simple vertex braiding move (see Figure 2.9).

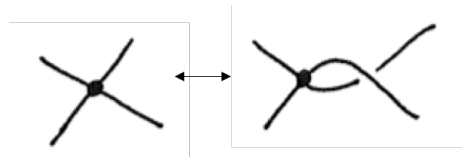


Figure 2.9: The knot move added by Kauffman for rigid vertex graphs shows how the strands braid around the vertex. Image adapted from [Kauffman, 1989].

Now, the proof follows exactly as before. First, observe that the set  $T(G)$  is invariant upto ambient isotopy under these five knot moves.

Then the theorem follows immediately: the set maintains the chirality of the original graph  $G$ , and so it can be compared to the set  $T(G')$ , where  $G'$  is the mirror image, to recognize the chirality of  $G$ . ■

As an example, consider the graph shown in Figure 2.10. We see that most elements of  $T(G)$  are just links or strands. However, the trefoil is there, without its mirror image, making  $G$  chiral.

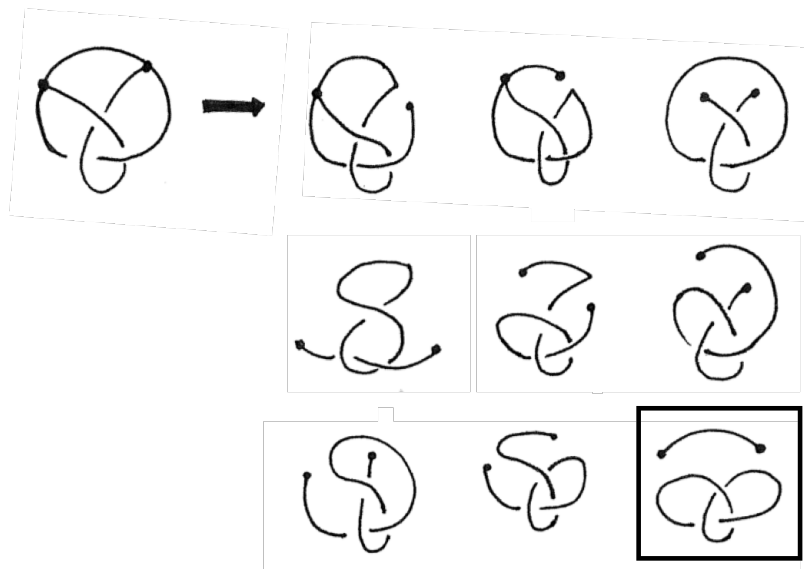


Figure 2.10: An example of the theorem can be used to identify if a molecule is chiral. Here, since  $T(G)$  contains a trefoil without its mirror image,  $G$  is chiral. Image adapted from [Flapan, 2000].

### Do We Really Need This Machinery?

Over the last few sections, we have developed some definitions and proven some powerful tools to understand topological chirality. Practically, do we need these tools? Why do we need this machinery?

Let us consider an example. Recall that one of the earlier chemical structures of topological interest was a trefoil knot (Figure 2.11). This trefoil is composed of various hexagonal rings (benzenes and phenanthrolines), and if we consider these to be straight edges, we have a regular trefoil. However, can we make that assumption? Unfortunately, we cannot, since the rings are not topologically equivalent to edges, and the edges coming off the rings cannot move freely. However, each of the hexagons could be a rigid vertex, and then  $T(G)$  can be constructed. However, since we started with one orientation of the trefoil, every knotted element of  $T(G)$  will inherit the same orientation. And so,  $T(G)$  is chiral, making the molecular trefoil knot chiral. It might be that to use Kauffman's theorem, the original graph might have to be modified to ensure no information is lost. For instance, it might be crucial to

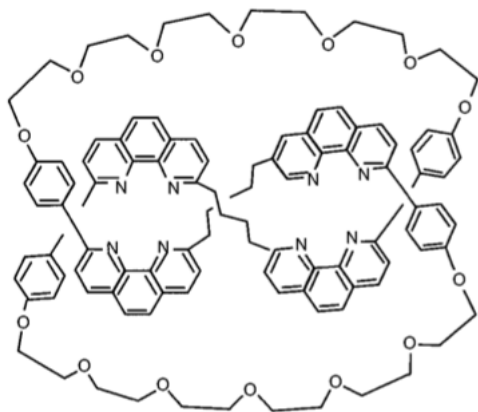


Figure 2.11: The right-handed molecular trefoil knot. Image taken from [Flapan, 2000].

label vertices with the actual atom label (Nitrogen/Oxygen) and use these labels to create orientations. In the absence of this, Kauffman's method can lose orientation information [Flapan, 2000].

In his 1989 paper, Kauffman wondered how thorough his theorem was for four valence graphs. Was there a graph that needed some other tools to identify its chirality?

Kauffman's theorem is definitely not sufficient for some kinds of molecular embedded graphs. Consider any system with only one crossing (such as a Möbius ladder). Then, the sets  $C(G), T(G)$  will only contain the unknot and loose links. In this case, Kauffman's method is not sufficient, and we need the HOMFLY polynomial to identify chirality. However, these ladders are quite unique in their chiral properties, and these will be discussed in coming chapters.

First, let us consider some other tools that can be used for some special classes of knots.

## 2.2.4 More Definitions

So going back to knots: we have some tools for identifying the chirality of knots and links, such as the HOMFLY polynomial. However, for *nicer* classes of knots, we can develop some more theorems. We need more definitions for this though (from [Flapan, 2000]):

**Definition. Alternating.** A projection of a link is alternating if the crossings alternate between going over and under.

**Definition. Reduced:** A link projection is said to be reduced if it doesn't contain crossings that can be removed by Reidemeister I moves.

In 1987, Murasugi and Thistlethwaite independently proved a theorem that connects the minimal number of crossings of a knot to alternating projections:

**Theorem 6.** (*Murasugi, Thistlethwaite*): *If a link has a reduced alternating projection, then that projection has the minimal number of crossings of any projection for the link.*

We will not prove this theorem: it requires constructing spanning trees and Jones polynomials of knots, which is not our main focus. This theorem is very powerful, even outside of chirality considerations. It allows knot theorists to identify the lowest crossing number of a knot, which is surprisingly difficult and naturally, very useful.

**Definition. Writhe.** For a given projection of a link, assign a +1 to every positive crossing, and a -1 to every negative crossing. The total sum is the writhe of the projection.

Writhe is not an invariant, since they are very projection-dependent. Simply adding a loop to a knot projection creates a crossing, and changes the writhe by  $\pm 1$ . But, Thistlethwaite was able to prove a remarkable theorem about writhe for alternating links.

**Theorem 7.** *All reduced alternating projections of an alternating oriented link have the same writhe.*

This theorem is extremely useful for us! Consider an alternating reduced topologically achiral knot,  $K$  and its mirror image,  $K^*$ . Both these knots have to have the same writhe since they are ambient isotopic to each other, and so are equivalent links. Next, note that every positive crossing gets switched to a negative crossing and vice versa while taking a mirror image. So, if  $K$  has writhe  $w$ ,  $K^*$  has writhe  $-w$  since every crossing got swapped. But the writhe has to be equal, and so,

$$w = -w \Rightarrow w = 0$$

And so, we get a pretty useful corollary. Note that a “(a)chiral” projection means that the underlying link is (a)chiral.

**Corollary.** *If an alternating reduced projection of a link is topologically achiral, then the projection has writhe 0.*

This is useful in recognizing chirality, since if we have a reduced alternating projection of a link with nonzero writhe, it is chiral! Of course, the converse doesn’t hold: any knot with an equal number of positive and negative crossings has writhe 0. Also, a chiral projection of an alternating knot can have nonzero writhe (consider the trefoil). However, we can develop more machinery with the writhe.

**Definition. Linking number.** Let  $K_1$  and  $K_2$  be two oriented knot projections. The linking number,  $Lk(K_1, K_2)$  is one-half the sum of +1 for every positive, and -1 for every negative crossing between the two knots.

The linking number is always an integer (since components must cross an even number of times to form closed loops). It is an invariant on the link constructed from the components, and so it is actually an invariant on two-component links independent of projection. Finally, one more definition:

**Definition.**  $i(Q)$ . Let  $Q$  denote a projection of an oriented link. Then,  $i(Q)$  is the sum of  $+1$  for every positive crossing between two strands of a single component of  $Q$  and  $-1$  for every negative crossing, where the sum is taken over all components.

And so, we have the machinery for a new theorem!!

## 2.2.5 Chirality of Alternating Links

**Theorem 8.** *Let  $L$  be an unoriented alternating link, and let  $L_1$  and  $L_2$  each be an oriented reduced alternating projection of  $L$ . Then  $i(L_1) = i(L_2)$ . Furthermore, if the unoriented link  $L$  is topologically achiral, then  $i(L_1) = 0$  and  $L_1$  has an even writhe.*

*Proof.* This proof is from [Flapan, 2000]. Let us begin by defining one more concept:

$$j(L_1) = \sum_{K_i, K_j \in L_1} 2Lk(K_i, K_j)$$

Then, by definition, we have:

$$i(L_1) = \text{writhe}(L_1) - j(L_1)$$

All this equation states is that (weighed) number of crossings within components of this link is equal to the total number of crossings, without the crossings between components.

Now, we know that the linking number is invariant, and so  $j$  is an invariant for two orientations of the link. But, we know from the Thislethwaite theorem that the writhe stays the same for different projections of reduced alternating links. Then, for these two projections, it follows that  $i$  is constant. And since the writhe is unaffected by orientation, the orientation doesn't affect  $i$ . And so, for the two projections of  $L$  we have,  $i(L_1) = i(L_2)$ .

Next, let's consider a reduced alternating oriented projection  $L_1$  and its mirror image, call  $L_1^*$ . Assuming  $L_1$  is achiral, it follows that it is ambient isotopic to  $L_1$ . Then,  $L_1$  and  $L_1^*$  are just equivalent projections of  $L$ , and from what we just proved, it follows that  $i(L_1) = i(L_1^*)$ . However, since the two projections are mirror images, the positive and negative crossings swap, and so  $i(L_1) = -i(L_1^*)$ . Then, it follows that

$$i(L_1^*) = -i(L_1^*) \Rightarrow i(L_1^*) = i(L_1) = 0$$

Now, since  $i(L_1)$  is zero, it follows from above that  $\text{writhe}(L_1) = j(L_1)$ . And since  $j$  was defined to be twice another integer, it follows that the writhe is even for the achiral oriented projection  $L_1$ . ■

Note that it is important to not get confused between when the writhe is zero and when it is even. According to the corollary presented earlier, the writhe is zero for achiral oriented reduced alternating links. However, the writhe is even when we are considering oriented alternating projections of inherently unoriented (not necessarily reduced) links.

So we can now present a few corollaries of this work:

**Corollary.** *Given a reduced, achiral, alternating, oriented projection of an alternating oriented link, the invariants  $i$ ,  $j$ , in addition to the writhe are all zero.*

So, for oriented links, if  $j$  is nonzero, the link is chiral as an oriented link.

**Corollary.** *Any topologically achiral alternating unoriented link has an even minimal crossing number.*

*Proof.* Given an achiral alternating unoriented link, we can find a reduced projection. We have already shown that any reduced alternating projection of a link has minimal crossing number. Now, we also know that the writhe of this projection must be even. That means that it has an even number of positive and negative crossings or an odd number of positive and negative crossings. But then, it follows that the minimal crossing number is even. ■

Since alternating and reduced links are easy to recognize, we now have a variety of methods to detect chirality by inspection for a special class of knots.

## 2.2.6 Tait's Conjecture and a Summary

Over 100 years ago, Tait conjectured that every topologically achiral knot or link had to have even minimal crossing number. In the last section, we showed that Tait's conjecture holds for alternating knots and links. Does it hold for nonalternating links?

In the last three decades, researchers have shown that the conjecture doesn't hold for nonalternating links or knots, with examples of a 11 crossing link and a 15 crossing knot that are topologically achiral. So, can we use minimal crossing number to learn something about chirality?

In 1997, Corinne Cerf proved that every alternating oriented link with even number of components is topologically chiral. This is a remarkably powerful result. Consider for example, the oriented Hopf link. It is a two component alternating link, and this theorem immediately classifies this as chiral!



Note that the orientation is important; we know that the unoriented Hopf link is achiral. Additionally, there are also oriented links with odd number of components that are chiral [Flapan, 2000].

Unfortunately, there is no one conclusive method to identify whether or not a molecule, a graph, a link is chiral or not. However, in this chapter, we have developed some powerful tools that can be used. If the reader is hoping this work concludes in one iff statement about a topological property and topological chirality, similar to the one about chemical chirality, that doesn't happen. But, there are some fascinating conclusions that can still be made about various structures that will be explored.

# Types and Levels of Chirality

In the previous chapter, we discussed different notions of chirality. A molecule was chemically chiral if it could not transform to its mirror image via physically accessible motion. Similarly, a molecule was topologically chiral if it could not transform to its mirror image via continuous deformation. So, how do chemical and topological chirality relate to each other? Figure 3.1 shows how the two ideas interact. Let us examine each quadrant individually. First, consider the quadrant that is topological chiral but chemically achiral. Since the set of all continuously possible motion is a superset of all physically accessible motion, it follows that topological chirality is strictly stronger than chemical chirality. If a molecule cannot get to its mirror image despite being allowed all possible motion, then, the molecule can clearly not get to its mirror image when allowed lesser motion. And so, such structures don't exist. Next, consider the top right quadrant: structures that are topologically achiral but chemically chiral. This is a large class of molecules! These molecules cannot rotate or otherwise physically deform to their mirror image, but allowed all continuous motion, the chirality is lost [Flapan, 2000].

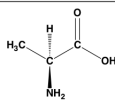
	Topologically Chiral	Topologically Achiral
Chemically Chiral	Molecular Mobius Ladder	
Chemically Achiral	⊗	Topological Rubber Glove

Figure 3.1: A summary of the relationship between different types of chirality.

For the other two quadrants of the table, we need to develop some more ideas. These two concepts, in a sense, are intermediates between topological and chemical notions. So how can we capture some of the rigidity of physical motion into the idea of topological chirality? Let us begin by developing some more definitions!

### 3.1 Definitions

First, let us define a symmetry presentation, which is a special embedding of a graph. The definitions are from [Flapan, 2000].

**Definition. Symmetry Presentation.** A symmetry presentation is an embedding of a graph that can be superimposed on its mirror image.

David Walba, of the Möbius ladder, used this idea to develop the notion of rubber gloves.

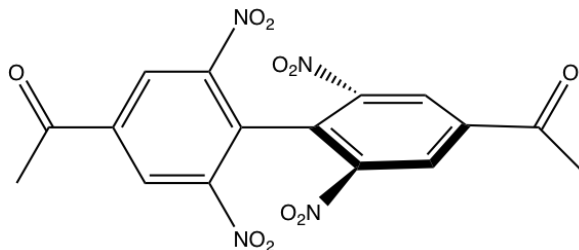


Figure 3.2: Kurt Mislow’s molecule is a “biphenyl” derivative and is an example of an Euclidean rubber glove [Flapan, 2000].

**Definition. Rubber Gloves.** A molecule is an Euclidean rubber glove if it can chemically change itself to its mirror image but can’t chemically be deformed to a symmetry presentation.

This definition of rubber gloves is confusing, and is difficult to encode into more topological rigorous ideas. So, let’s introduce a new kind of chirality: *rigid chirality*.

**Definition. Rigid Achirality.** An embedded graph,  $G$  in  $\mathbb{R}^3$  is rigidly achiral if there is an orientation-reversing finite-order homeomorphism of the pair  $(\mathbb{R}^3, G)$ .

To see why this definition is useful, let us prove that the concept of rigid achirality is equivalent to that of rubber gloves [Flapan, 2000].

First, consider a finite graph,  $G$  in  $\mathbb{R}^3$  that can be deformed to a symmetry presentation. That is, there exists an ambient isotopy  $F : \mathbb{R}^3 \times I \rightarrow \mathbb{R}^3$  such that for all  $t \in I$ , the function  $F(x, t)$  is a homeomorphism such that  $F(x, 0) = x$  for all  $x \in \mathbb{R}$  and  $F(G \times \{1\}) = G'$ , where  $G'$  is a symmetry presentation. And since  $G'$  is a symmetry presentation, there is some rotation, call  $r$ , that can deform  $G'$  to the mirror image,  $G^*$ . Since this is a finite graph, the rotation has to have finite order. Let’s create a homeomorphism,  $h$ , by composing  $r$  with some reflection.  $h$  is a finite-order orientation-reversing homeomorphism on  $(\mathbb{R}^3, G')$ . Let us construct a function  $f : \mathbb{R}^3 \rightarrow \mathbb{R}^3$  such that  $f(x) = F(x, 1)$ . Then,  $f(G) = F(G \times \{1\}) = G'$ . Next, let’s conjugate  $h$  with  $f$ , and since both functions are homeomorphisms,

we will construct a new homeomorphism,  $f^{-1} \circ h \circ f$ . Let the order of  $h$  be  $n$ , and let us examine  $(f^{-1} \circ h \circ f)^n$ .

$$(f^{-1} \circ h \circ f)^n = (f^{-1} \circ h \circ f) \circ (f^{-1} \circ h \circ f) \dots (f^{-1} \circ h \circ f) = (f^{-1} \circ h^n \circ f) = (f^{-1} \circ f) = E$$

where  $E$  is the identity. And so,  $(f^{-1} \circ h \circ f)$  is a finite order orientation reversing homeomorphism. And so, there's a finite order orientation reversing homeomorphism on  $G'$ , making  $G$  rigidly achiral.

Next, consider a rigidly achiral embedded graph  $G$  in  $\mathbb{R}^3$ . That is, by definition, there exists an orientation-reversing finite-order homeomorphism on  $(\mathbb{R}^3, G)$ . To prove that this is equivalent to a symmetry presentation, we will use a theorem without proving it:

**Theorem 9.** *Any orientation-reversing finite-order homeomorphism on  $\mathbb{R}^3$  is conjugate, by an orientation-preserving homeomorphism to a reflection or to a rotation composed with a reflection.*

So, given an orientation-preserving homeomorphism  $f$  and a reflection or rotation-reflection  $r$ , we have  $h = f^{-1} \circ r \circ f$ . Since  $f$  is orientation-preserving, it is isotopic to the identity, and so there exists a function  $F : \mathbb{R}^3 \times I \rightarrow \mathbb{R}^3$  such that  $F(x, 0) = I$ ,  $F(x, 1) = f(x)$  and  $\forall t \in I$ ,  $F(x, t)$  is a homeomorphism. Define  $A$  as  $F(G \times \{1\})$ . Then, by definition,  $A$  is ambient isotopic to  $G$ . Then,  $f(G) = A$  and  $f^{-1}(A) = G$  since  $f$  is a orientation-preserving homeomorphism. Now, since  $G$  is rigidly achiral, and we have the homeomorphism  $h$  on it, we have  $h(G) = G$ . So:

$$h(G) = (f^{-1} \circ r \circ f)(G) = (f^{-1} \circ r)(A) = G \Rightarrow r(A) = f(G) = A$$

And so,  $A$  is ambient isotopic to  $G$ , but with a reflection or rotation-reflection,  $A$  is taken to itself. And so, by definition,  $A$  is a symmetry presentation of  $G$ .

Having proved the equivalence of rigid achirality and symmetry presentations, it is important to note that rigid chirality is not equivalent in  $\mathbb{R}^3$  and  $\mathbb{S}^3$ . This is because when moving from  $\mathbb{S}^3$  to  $\mathbb{R}^3$ , the point at infinity that needs to be removed might not necessarily be off the graph, and so the graph and the homeomorphism might not be constructed in three-space.

So now, let's us return to rubber gloves:

**Definition. Topological Rubber Gloves.** A topological rubber glove is an embedded graph that is topologically achiral but not rigidly achiral.

Now, we are ready to discuss topological rubber gloves, and how they present some very weird properties of structures. Before we proceed, we need two more definitions.

**Definition. Möbius Ladder.** A Möbius Ladder,  $M_n$  is the graph consisting of a simple closed curve  $K$  with  $2n$  vertices together with  $n$  additional edges  $\alpha_1 \dots \alpha_n$  such that if the vertices on  $K$  are consecutively labeled  $1, 2, 3, \dots, 2n$  then the vertices of each edge  $\alpha_i$  are  $i$  and  $i + n$ . (Figure 3.3)

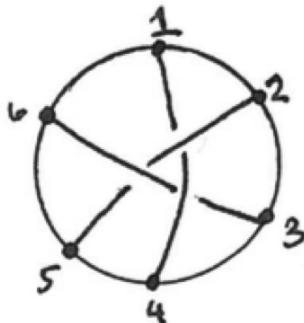


Figure 3.3: The Möbius ladder with three rungs, constructed as defined in the definition. Since there are 6 vertices, vertex 1 and 4 connect, as do 2 and 5 and 3 and 6 [Flapan, 2000].

**Definition. Intrinsic Chirality.** A graph is said to be intrinsically chiral (chemically or topologically) if all embeddings of the graph are chiral.

## 3.2 Topological Rubber Gloves

To rigorously prove whether a structure is a rubber glove requires a lot of machinery, with more types of chirality, and an expansive knowledge of math beyond the scope of this thesis. [Flapan, 2000] provides partial proofs for these ideas. Instead, we will just be considering and discussing some examples of rubber gloves. An example of a rubber glove is the knot  $8_{17}$ . This knot can be rotated to its mirror image, but doesn't have any symmetry presentation, making it a rubber glove (Figure 3.4). However, this knot has not been synthesized chemically, and while a 8 crossing knot has been synthesized, this knot is quite complicated for a chemical synthesis. But, some chemical structures have been synthesized that have been proven to be topological rubber gloves. One example is a single-stranded DNA molecule that was knotted to a figure eight. While the molecule was globally a figure eight, locally, it was composed on subunits of DNA that added to the structure's complexity (Figure 3.5), [Flapan, 2000].

In 1997, a molecule was synthesized that was not only a topological rubber glove, but was the first glove with confirmed chemical achirality. This molecule was a link, with the global structure of the Hopf link, but with many intricacies locally. Since we have not developed theorems to prove if a structure is a chemical presentation, we will not venture further into this proof. It is seen that these



Figure 3.4: The knot  $8_{17}$  is a topological rubber glove. From the first image, the knot can be rotated  $180^\circ$ , and then the outer loop can be pulled upwards to create the mirror image knot on the right. Image adapted from [Flapan, 2000].

local intricacies cannot be treated trivially, and require attention when applying topological principles [Flapan, 2000].

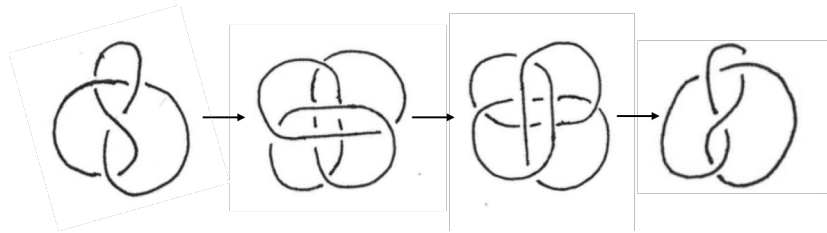


Figure 3.5: The DNA molecule is a figure eight knot globally. It is a topological rubber glove. From the first image, the knot can be redrawn to form the second image, then rotate  $90^\circ$ , and then deformed again to create the mirror image knot on the right. Image adapted from [Flapan, 2000].

### 3.3 Möbius Ladders

As mentioned earlier, the first Möbius ladder was synthesized by David Walba and his group. The chirality of this structure was difficult to ascertain, since the chains were large and wobbly enough that some rotation would allow mirror-image accessibility. These ladders caught the attention of topologist Jon Simon, who proved some remarkable theorems regarding them:

**Theorem 10.** *The embedded graph of a molecular Möbius ladder with three or more rungs cannot be deformed to its mirror image in such a way that rungs go to rungs and sides go to sides. In terms of the definition earlier, this means that  $K$  maps to  $K$  and  $\alpha_i$  maps to  $\alpha_j$  for  $\forall i, j \in 1, 2, \dots, 2n$ .*

Erica Flapan extended this theorem to the following stronger statement:

**Theorem 11.** *No embedding of a Möbius ladder with an odd number of rungs greater than 1 can be deformed to its mirror image such that rungs go to rungs and sides go to sides.*

Additionally, if the ladder has an even number of rungs, then, there will always exist an embedding that can be rotated to its mirror image, i.e., a symmetry presentation will always exist. Unfortunately, the proofs for all three statements are beyond the scope of this thesis, but are in [Flapan, 2000]. However, examples are shown.

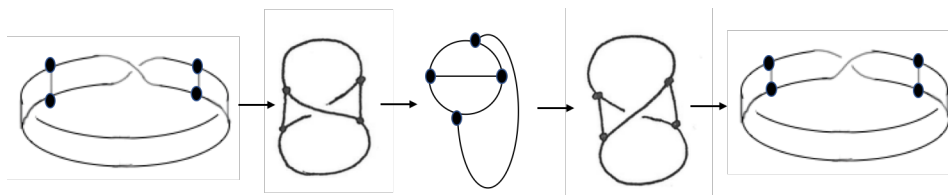


Figure 3.6: The two rung Möbius ladder is achiral. Image adapted from [Flapan, 2000].

Then, we have now explored every quadrant from Figure 3.1 and discussed how their structures affect their chirality. Finally, let us turn our attention to hierarchies within these classes of chiralities.

### 3.4 Hierarchies

We have already established topological chirality is strictly stronger than chemical chirality. But what about all the kinds of chirality developed in this chapter? How do they relate to each other? Let us consider intrinsic chirality, rigid achirality and topological achirality in  $\mathbb{R}^3$ .

It is clear that intrinsic chirality is the strongest property, since it holds for *all* embeddings of a given graph. As an example, consider a Möbius ladder with an odd number of rungs greater than 1.

Next in this hierarchy are graphs that embedded to be topologically achiral, but cannot be embedded to be rigidly achiral. And finally, we have graphs that are rigidly achiral, which is every graph with a planar embedding [Flapan, 2000].

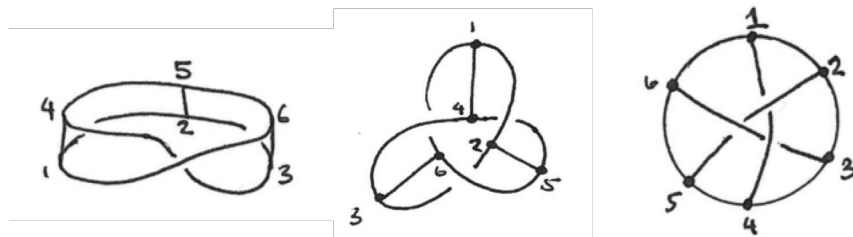


Figure 3.7: Different representations of the three-rung Möbius ladder. This ladder is intrinsically chiral. However, the removal of just one rung will make this ladder topogically achiral. Image adapted from [Flapan, 2000].

And so now, based on this hierarchy in topology, we can evaluate if a graph has a shot at being chemically chiral. For instance, it is obvious that intrinsically chiral graphs will not be chemically achiral. However, graphs without a rigidly achiral embedding could be chemically achiral, and in this manner, we could eliminate classes of structures when identifying chirality.



# Graph Theoretical Applications

As we have seen, graphs are a very useful method of describing molecules since bonds can be mapped to edges and atoms to vertices. Therefore, molecular graphs are a very convenient way of storing information about a molecule. Consequently, a lot of work has been done to develop better algorithms and functions to sort, identify, and categorize molecular graphs. This chapter briefly discusses some work on molecular graph algorithms and introduces some topological tools for these algorithms.

Before we go any further, let us discuss why and how we got here. There are two main kinds of interactions that atoms in a molecule experience:

1. Through Bond: These interactions are more commonly seen. Atoms are affected by what other atoms they are directly bonded to. For instance, if there is a carbon atom connected to an oxygen atom, it will behave differently than when it is connected to a hydrogen atom. These differences are caused by the fundamental differences in electronegativity and size for different atoms.
2. Through Space: These interactions are seen when atoms behave differently because they are influenced by atoms they are not connected to. For instance, the magnetic behavior of a molecule could be affected by whether an atom was being shielding electronically.

A graph representation of a molecule clearly encodes the through bond effects, since each bond is preserved. When we are detecting chirality, we are looking for some through space effects, as well as some through bond effects. For instance, if a carbon atom is bonded to four hydrogens, the molecule is achiral since it is equivalent to its mirror image (Figure 4.1). However, whether or not the molecule can physically bend and twist to its mirror image depends on both its connectivity and its spatial interactions. So, whether it is to study chirality or study some other graph properties, we need some way to encapsulate both connectivity and spatial information about a molecule. Of course, having a full 3D model of the molecule is an option, but it is very inefficient and requires too much space. And so, let us begin by considering a popular algorithm that is used to encode information about a molecule.

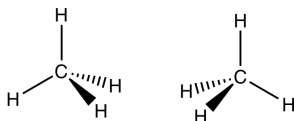


Figure 4.1: This molecule, methane, is not chiral since it is equivalent to its mirror image since carbon is connected to the same atoms.

## 4.1 The SMILES Algorithm

The most obvious way to store connectivity information of a graph is via a connectivity matrix. For a graph with  $n$  vertices, a  $n \times n$  matrix is created. Entries are either 1 or 0, depending on whether the two vertices are connected or not. However, this is an expensive method of storing information, and it would be more efficient for the connection matrix to be read linearly.

A popular algorithm that does this is the Simplified Molecular-Input Line-Entry System (SMILES) algorithm. This is a simple language that has notation for atoms and bond types and gives a linear expression for a molecule. This algorithm first computes the graph invariants, and then labels them. The invariants take various parameters into account (taken directly from [Faulon and Bender, 2010]):

1. The valence of each vertex
2. The number of non-hydrogen bonds
3. The number of attached hydrogens
4. Atom number
5. Charge (sign and value) on atoms

To uniquely label every atom, this process first doubles the invariants. Then, one of the atoms with the smallest label is chosen, and its label is reduced by one, and then the doubling is repeated. This is continued until every atom has a unique label [Faulon and Bender, 2010]. Assuming the first set of invariants is assigned, a summary of the algorithm is provided below (again, taken directly from [Faulon and Bender, 2010]):

```
function: canonical-SMILES (G, inv)
input:  - G: a molecular graph
        - inv: a set of initial invariants
output : - printout of a canonical SMILES string of graph G
1. inv = compute-invariant (G, inv)
```

```

2. Let lab be the set of atom labels assigned in increasing
   invariants order
3. if |lab| = |G| then print-SMILES (G, lab), end if
4. lab = new set of labels doubling each label value
5. let L = set of atoms with smallest label such that
   |L| > 1
6. For all atom x in L do:
7.   lab(x) = lab(x) - 1,
       canonical-SMILES(G, lab),
       lab(x) = lab(x) + 1
8. done

```

There are quite a few things that this recursive algorithm is doing. However, let us focus on some parts. Note that the algorithm assigns a unique label to each atom, which gives a canonical ordering of vertices of the molecular graph. This ordering provides a linear string that describes the molecule, and can reconstruct the graph by spanning the string. This is very useful, because we have now condensed the connectivity information of the graph down to a string from a matrix [Faulon and Bender, 2010].

By extending the grammar of the language, it can also include chirality information about the molecule. However, there is no spatial information about the molecule, about distances in space, or other through space effects. So, a concept from topology could be added to these algorithms to provide more structural information about the molecule, without having to construct the molecule in full.

## 4.2 Distortion

So, let us consider the concept of distortion. Distortion is a topological and geometrical idea. It provides information about distances in a graph or knot that go beyond connectivity. Let us begin with the formal definition.

**Definition. Distortion.** For a graph or knot  $G$  with points  $P, Q$ , the distortion,  $U(K)$  is given by:

$$U(K) = \max_{P, Q \in K} \frac{|P, Q|_G}{|P, Q|}$$

where  $| \cdot |_G$  is the graph/knot metric. [Gromov, 1983]

The graph/knot metric is a method of measuring distance on the graph/knot. This measurement takes into account how you would travel on the graph/knot. So, distortion is the maximum measure

of how far two points on the graph are versus how far they are in space. This is very useful because it is a relatively well-established quantization of how through space and through bond effects relate to each other. In [Denne and Sullivan, 2007], it was shown that the distortion for any closed curve (like all knots) had to at least be 5.2. However, it has also been shown that distortion is unbounded [Pardon, 2011].

The goal, then, would be to incorporate the distortion of a molecule into a new algorithm. One potential way to do this would be to place atoms closer together and adjust the distance between them until it reached some ideal value. Then, this distance could be included in the distortion value and used in the molecule string description. And so, when building the molecule back from the descriptor, there would be the additional parameter that quantifies through space relationships between atoms [Shattuck and Taylor, 2017]. However, this is just a preliminary idea and has not been implemented in the form of a new algorithm. Clearly, there are issues of space and time efficiency with incorporating distortion to a molecular descriptor, but with more work, something might be constructed.

## Modern Work and Future Directions

So we have now discussed chirality and how it can be detected, and its different types. We have discussed how molecules can be efficiently described and how distortion might be a really useful tool in developing new algorithms. We have seen examples of molecular Möbius ladders, knots, and links. Where does this field of molecular topology stand currently and what are researchers working on?

The Nobel Prize in Chemistry in 2016 was awarded to three chemists, Fraser Stoddart, Jean-Pierre Sauvage, Ben Feringa, “for the design and synthesis of molecular machines” [2016, 1]. We have already met some of these scientists before: they were involved in synthesizing the first molecular knot and other interesting structures we have seen so far. The reason this Prize and their work is relevant is because they use fundamental ideas from molecular topology to develop these molecules. The molecular machines they have built are broadly classified into three categories: knotanes, rotaxanes, and catenanes [Sauvage, 2016]

Catenane is the chemical term for links. Rotaxanes are molecules that derive their motion from their ability to rotate. Knotanes are molecules with some knottiness that contributes to their properties and movement. These molecular machines, though in their preliminary stages, have incredible potential. They have important biological function, could be used to develop artificial muscles, and can be developed to actually perform machine tasks [Sauvage, 2016]. Molecular machines have already been used to develop cars for nanocar racing [Davenport, 2017]! Chemically, the drive for these machines is through a broad range of sources: mechanical, electrical, photochemical, thermal are some of the possibilities [Sauvage, 1998]. Physically though, the drive for strands of the molecule to rotate come from topological properties. The knotanes move by shimmying across strands, the rotaxanes move between circular lobes and rotate, generating their motion. And catenanes can also shim through the interlinked loops to move. The inspiration for all these molecules stems from Frisch and Wassermann’s first synthesis in 1961, and the field of molecular topology. Basically, the motor of these machines comes from the principle that these class of molecules needs topology to describe their structure [Sauvage, 2016].

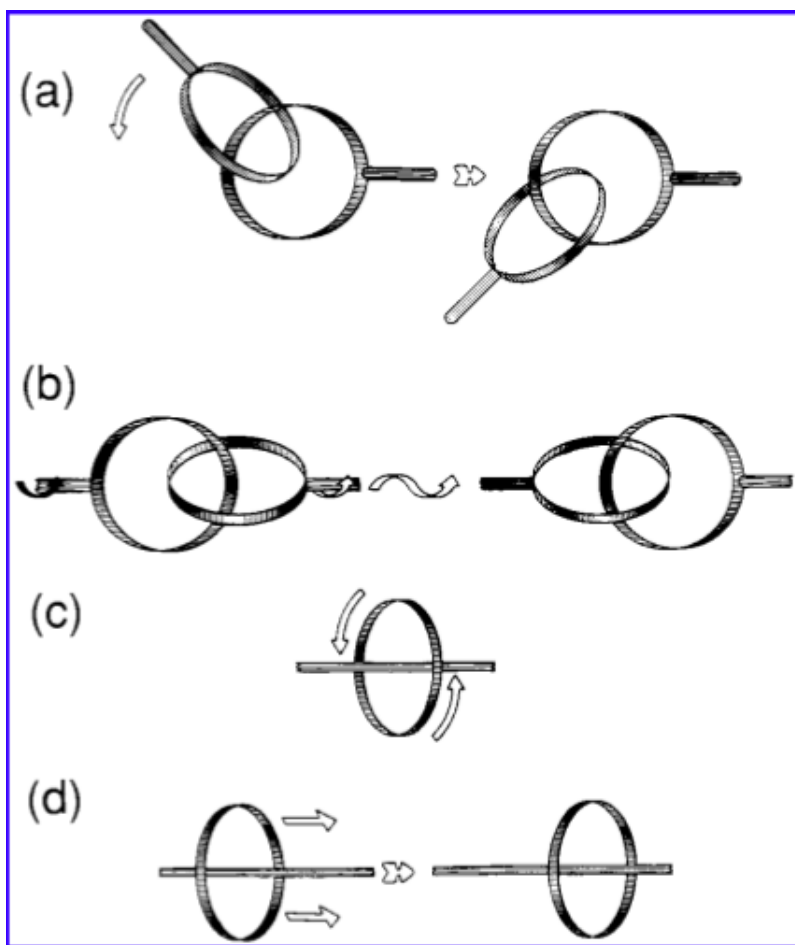


Figure 5.1: Four different types of motion that can be generated from some kinds of molecular machines. Image from [Sauvage, 1998].

In addition to the remarkable work in the field of molecular machines, there have also been synthetic developments — larger and more complex knots and links are being synthesized. The drive and inspiration for this work comes from knot theory. On the other hand, physical restrictions provided by chemical systems are providing interesting new challenges to build different topological structures, in addition to potential for algorithmic development. The field of molecular topology truly presents some remarkable opportunities.

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