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Advanced School and Conference on Knot Theory and its Applications to Physics and Biology

11 - 29 May 2009

Topological Chirality and Symmetries of Non-rigid Molecules

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Proceedings of Symposia in Applied Mathematics

Topological Chirality and Symmetries of Non-rigid Molecules

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Abstract. We discuss the topology of non-rigid molecules. In particular, we introduce techniques which can be used to show that a molecule is topologically distinct from its mirror image, and we present the concept of the topological symmetry group of non-rigid molecules.

1. Introduction

Most chemists take a geometric approach to understanding the 3-dimensional structure of molecules. While this approach works well for rigid molecules, it does not always tell the whole story for flexible or even partially flexible molecules. In this chapter, we present a topological approach to the study of complex molecular structures.

In Section 2, we begin with an introduction to the concept of chemical chirality and its importance in chemistry. While chirality can be defined according to the behavior of a molecule in the laboratory, characterizing this concept mathematically can be subtle. The standard approach relies on the concept of *geometric chirality*, which treats all molecules as rigid objects. We present this approach in Section 3 together with examples of molecules where a geometric approach does not correspond to the chemical behavior of the molecules. In Section 4, we contrast chemical chirality and geometric chirality with the concept of *topological chirality*, which treats all molecules as completely flexible. Then in Section 5, we present four techniques for proving that a molecule is topologically chiral, and examples are given of when each technique can be applied. Finally, in Section 6, we discuss geometric and topological approaches to the study of molecular symmetry groups. In analogy with our study of chirality, we see that for complex molecules, the geometric approach given by using the *point group* does not always reflect molecular behavior as well as the topological approach given by the *topological symmetry group*.

2. Chemical Chirality

Molecules can be modeled as graphs in space, where vertices represent atoms or groups of atoms, and edges represent bonds. For example, the molecule L–alanine can be illustrated by the graph in Figure 1. The dark triangular segment in the

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2000 *Mathematics Subject Classification.* 57M25, 92E10.

figure indicates an edge which comes out of the plane of the paper towards the reader, the dashed segment indicates an edge which goes back behind the plane of the paper, and the ordinary line segments indicate edges which lie in the plane of the paper. In 3–dimensional space, the vertices of this graph lie at the corners of a regular tetrahedron.

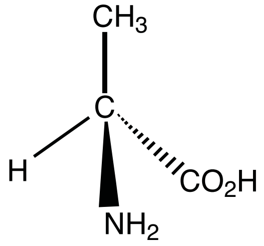


Figure 1. This molecule has the form of a tetrahedron

The geometry of a rigid molecule determines many of its properties. However, large molecules may be flexible. For a flexible molecule, topology rather than geometry determines many of its properties. An example of a topologically interesting flexible molecule is the molecular Möbius ladder, which was *synthesized* (i.e. made in the laboratory) by David Walba [**24**] in 1982. This molecule (illustrated in Figure 2) has the form of a Möbius strip that is made of a 3-rung ladder. The rungs of the ladder are carbon-carbon double bonds and the sides of the ladder are chains of carbon atoms (indicated in the figure with a corner) and oxygen atoms.

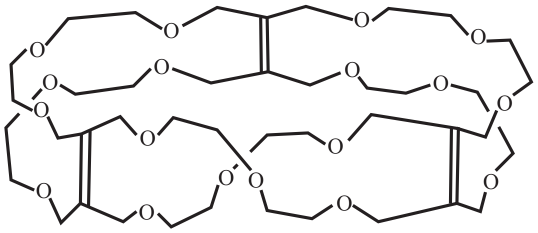


Figure 2. A molecular Möbius ladder

While a molecular Möbius ladder has not resulted in new pharmaceutical products or other practical applications, synthesizing this molecule was an important chemical acheivement. Chemists create “targets of synthesis” such as a Möbius ladder, a knot, or a link in order to force the profession to develop new techniques of synthesis. Knotted and linked molecules were targets of synthesis since the early 1900’s. Both have now been achieved. Dietrich-Buchecker and Sauvage [**7**] synthesized the first knotted molecule in 1989. This molecule is illustrated in Figure 3.

The molecular Möbius ladder was synthesized by forcing the ends of a ladder to join. Some of the ladders were joined without a half-twist and others were joined with a half-twist. Figure 4 illustrates a closed circular ladder without a half-twist.

These molecules are too small to see in a microscope, so it was not obvious that any of the closed ladders had the form of a Möbius ladder. In order to show that at least some contained a half-twist, Walba showed experimentally that some of the molecules were chemically different from their mirror image. Since a closed circular

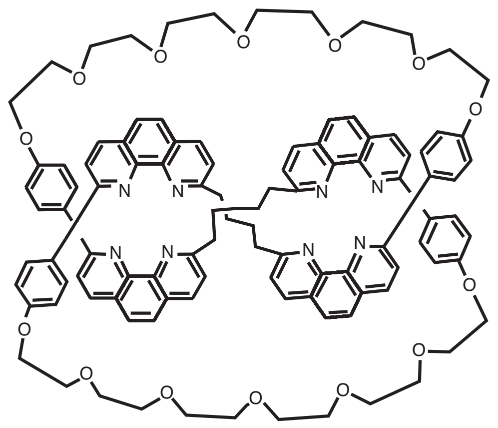


Figure 3. The first knotted molecule

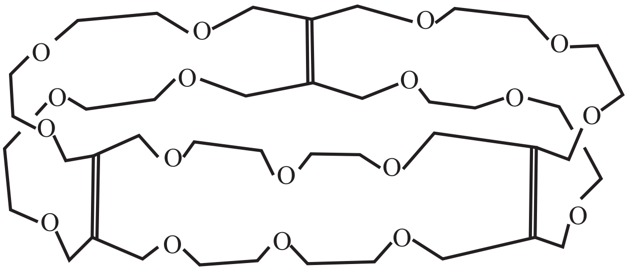
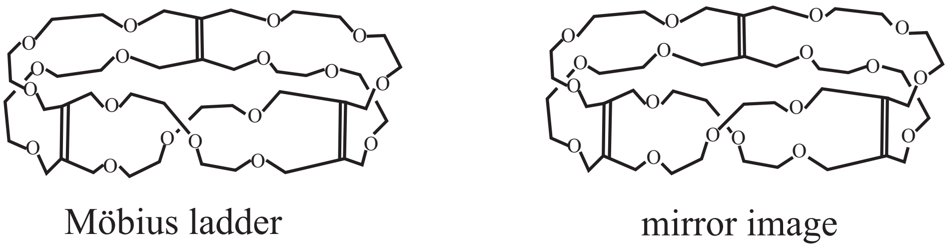


Figure 4. A closed ladder without any twists

ladder with no twists is the same as its mirror image, not all of the molecules could be such circular ladders. However, Walba did not know whether a molecular Möbius ladder was actually different from its mirror image. We illustrate a molecular Möbius ladder and its mirror image in Figure 5. A Möbius strip with a left-handed twist cannot be isotoped to a Möbius strip with a right-handed twist. But a Möbius ladder has isotopys that a Möbius strip does not have. So perhaps a Möbius ladder could be isotoped to its mirror image, in which case perhaps a molecular Möbius ladder could convert itself to its mirror form.



Möbius ladder

mirror image

Figure 5. A molecular Möbius ladder and its mirror image

In fact, it is possible to isotop a Möbius ladder to its mirror image. We illustrate such an isotopy in Figure 6. For simplicity we represent the Möbius ladder as a graph without indicating the different types of atoms. We number the atoms just to help us keep track of the isotopy. The first step of the isotopy is to rotate the graph by 90°. Next, we slide the edges $\overline{25}$ and $\overline{36}$ forward. Then we slide vertex 5 up and pull the edge $\overline{34}$ to the left. Then we shorten the edge $\overline{16}$. Next we make the loop $\overline{1456321}$ into a figure eight. Finally, we fold the top and bottom of the figure eight back, and shorten the edges $\overline{43}$, $\overline{25}$, and $\overline{16}$. If we ignore the numbers, the final illustration is identical to the original illustration except the crossing in the center has been reversed. Thus this isotopy takes the Möbius ladder to its mirror image.

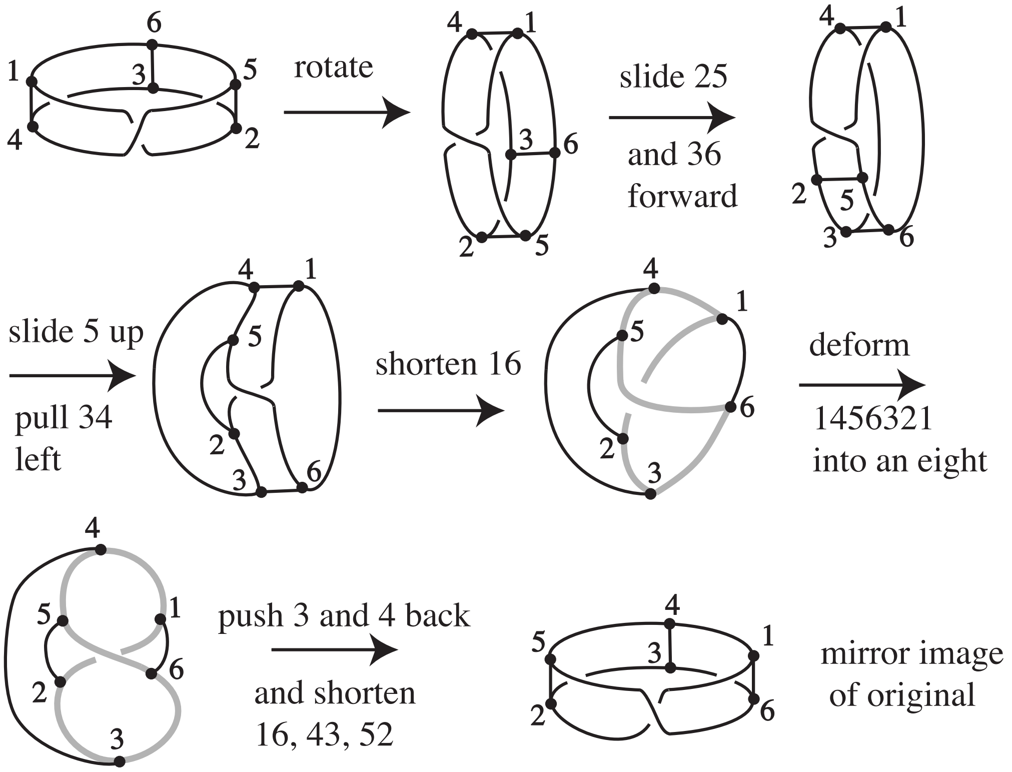


Figure 6. An isotopy from a Möbius ladder to its mirror image.

Observe that the isotopy illustrated in Figure 6 takes the rungs $\overline{14}$ and $\overline{36}$ to sides of the ladder. While this makes sense mathematically, from a chemical point of view such a transformation is impossible. The rungs of the ladder are carbon-carbon double bonds and the sides of the ladder are chains of carbons and oxygens. A carbon-carbon double bond cannot be changed into a chain of carbons and oxygens. In 1986, Jon Simon [**19**] used topology to prove that a molecular Möbius ladder cannot chemically change into its mirror image. To do this, he used colors to distinguish the sides from the rungs of a Möbius ladder (see Figure 7). Then he proved that this colored graph cannot be isotoped to its mirror image.

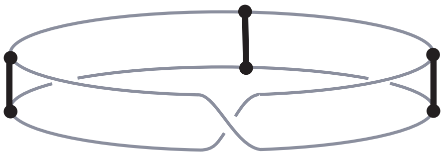


Figure 7. We represent a Möbius ladder and as a colored graph in order to distinguish sides from rungs.

Knowing whether or not a molecule is different from its mirror image is important in predicting its chemical behavior. Thus it is useful to introduce the following terminology.

Definition 2.1. We say a molecule is **chemically achiral** if it can change into its mirror image. Otherwise, we say it is **chemically chiral**.

Chemists omit the word "chemically" and just say *chiral* and *achiral*. We include the word *chemically* to make it clear that this is an experimental rather than a mathematical definition. The word "chiral" comes from the ancient Greek word for hand because a hand cannot change into its mirror image. Thus the word "achiral" means not like a hand.

Living organisms generally have a preferred handedness on both a large and a small scale. For example, the human heart is normally on a person's left side, and the amino acids in the human body are chemically chiral. Your right hand reacts differently to a right glove and a left glove. Similarly, organisms react differently to the two forms of a chiral molecule. For example, one form of the molecule carvone smells like spearmint and the other form smells like caraway. Generally, one form of a medication is more effective and the mirror form has more side effects. Occasionally the two mirror forms of a pharmaceutical product have different uses. For example the medication Darvon is a painkiller, while its mirror form, Novrad, is a cough medicine.

If a pharmaceutical product is known to be chiral, then the pharmaceutical company that produces it may choose to manufacture only the preferred form in order to minimize side effects and maximize effectiveness.

3. Geometric Chirality

The concept of chirality is so important that we will spend much of this article discussing how chirality can be characterized and recognized mathematically. Such a characterization is useful because it enables chemists to know whether or not a molecule will be chiral even before it is synthesized. However, there is no mathematical definition of chirality that perfectly corresponds to chemical chirality, since whether or not a molecule is chemically chiral often depends on how flexible the molecule is. In the next few sections we will introduce and compare two different approaches to this problem: a *geometric* approach which treats all molecules as rigid objects, and a *topological* approach which treats all molecules as completely flexible. In order to see the subtleties of characterizing chirality we will consider some molecules which are partially flexible.

We begin by discussing the geometric approach to chirality that was first introduced by Lord Kelvin in 1884. In particular, Lord Kelvin wrote:

> "I call any geometrical figure or group of points *chiral*, and say it has *chirality*, if its image in a plane mirror, ideally realized, cannot be brought to coincide with itself."

According to this definition, an achiral object is one which is identical to its mirror image. For example, a person is chiral because a person is not identical to its mirror image. The molecule and its mirror image, illustrated in Figure 8, each have the form of a tetrahedron. Since the groups of atoms at the four corners of the tetrahedron are all distinct, this molecule is different from its mirror image. Hence it is chiral according to Lord Kelvin's definition.

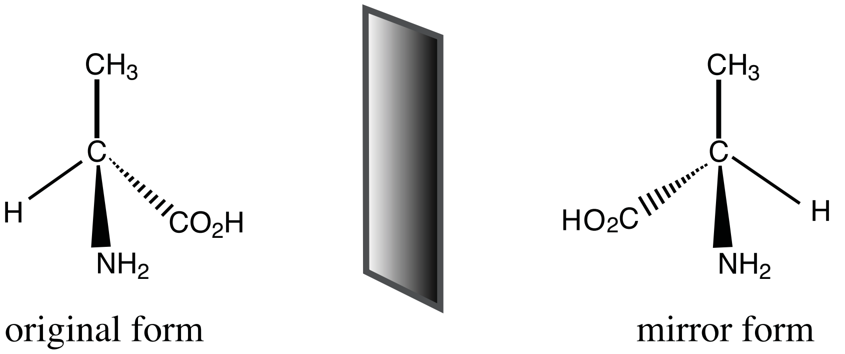


FIGURE 8. A chiral molecule and its mirror image.

Most modern organic chemistry textbooks reword Lord Kelvin's original definition only slightly. Here is the definition given in a standard organic chemistry textbook.

DEFINITION 3.1. An **achiral** molecule is one which is "superposable" with its mirror image. Otherwise, it is **chiral**.

We restate this mathematically as follows.

DEFINITION 3.2. A molecule is **geometrically achiral** if, as a rigid object, it can be superimposed on its mirror image. Otherwise it is **geometrically chiral**

We add the word "geometrically" here to distinguish this definition from our earlier experimental definition, and to make it clear that this type of chirality comes from the geometry of a rigid molecule.

Many chemists consider geometric chirality and chemical chirality as synonyms. However there are examples of molecules where these two concepts do not coincide. In order to illustrate the distinction between these concepts, in 1954, Kurt Mislow [**17**] synthesized the molecule illustrated in Figure 9.

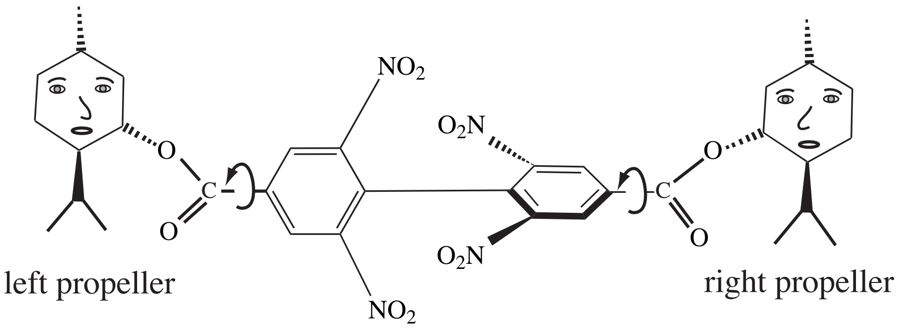


FIGURE 9. A molecule which is chemically achiral but geometrically chiral.

The two ends of the molecule, which we call "propellers", rotate simultaneously as indicated by the arrows. Of course the actual molecule does not have faces on it. The faces are drawn there to help illustrate the difference between the two propellers. The left propeller can be thought of as a person facing you with her left hand forward, as indicated by the dashed bond connecting the hexagon face to the oxygen. The right propeller can be thought of as a person facing you with her right hand forward. Because of the rigidity of the structure of the propellers, the notion of "forward" is unambiguous. The faces help us remember that forward is the direction the hands are pointing in. As rigid structures, a right propeller can never become a left propeller. If they were not rigid, we could flatten them out, and then they would be interchangeable. The hexagon next to the left propeller is vertical, while the hexagon next to the right propeller is horizontal.

We illustrate the mirror image of Figure 9 in Figure 10. Observe that the mirror form is identical to the original form except that the horizontal and vertical hexagons in the middle have been switched.

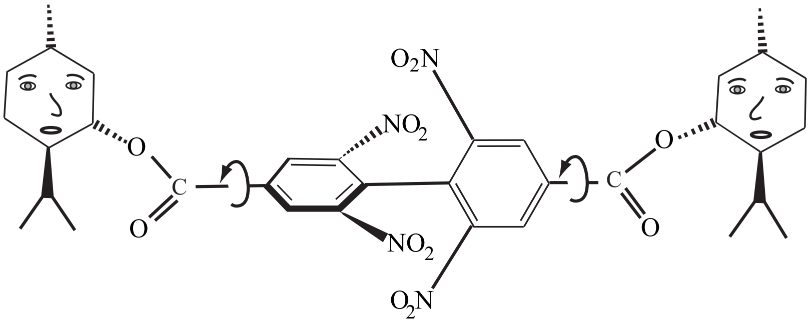


Figure 10. The mirror image of Figure 9.

We see as follows that the molecule illustrated in Figure 9 is chemically achiral. First we rotate the molecule about a horizontal axis which goes from left to right. This rotation takes the vertical hexagon in the middle to a horizontal hexagon, and takes the horizontal hexagon in the middle to a vertical hexagon. The propellers become horizontal as a result of this rotation. However, we can let the propellers rotate back to their original vertical positions. This gives us the mirror form illustrated in Figure 10. The motions we have just described can occur chemically, hence the molecule is chemically achiral.

On the other hand, we can see that the molecule in Figure 9 is geometrically chiral as follows. If we consider the molecule as a rigid object, then the propellers cannot rotate. In the original form, the left propeller is parallel to the adjacent hexagon. In the mirror form, the left propeller is perpendicular to the adjacent hexagon. As rigid objects, a left propeller cannot change into a right propeller. Hence as rigid objects, the original form and the mirror form are distinct. Thus the molecule is geometrically chiral.

Observe that as the propellers simultaneously rotate, they never get into identical positions relative to their adjacent hexagons. For example, if the left propeller is 45° behind its adjacent hexagon, then the right propeller is 45° in front of its adjacent hexagon. Thus, no matter what angle the propellers are at, the above argument shows that the molecule cannot be rigidly superimposed on its mirror image. Hence allowing the propellers to rotate will not enable the molecule to become geometrically achiral.

We see as follows that in the above sense this molecule and its mirror image are similar to a pair of rubber gloves. A right handed rubber glove is the mirror image of a left handed rubber glove. Also a left handed rubber glove can become a right handed rubber glove if it is turned inside out. However, at no stage of the turning inside out process is the rubber glove rigidly superimposable on its mirror image. So at no stage does it become geometrically achiral. These characteristics of a rubber glove motivated the chemist, Van Gulick [**23**] to introduce the following definition.

DEFINITION 3.3. A molecule is said to be a **Euclidean rubber glove** if it is chemically achiral, but it cannot attain a position which can be rigidly superimposed on its mirror image.

The word *Euclidean* indicates that geometric (i.e., physical or chemical) constraints are keeping the molecule from attaining a position which could be rigidly superimposed on its mirror image. The molecule illustrated in Figure 9 and a real rubber glove are both examples of Euclidean rubber gloves. We have seen that each can be transformed into its mirror image. If the molecule in Figure 9 were completely flexible, it could lie in the plane and become rigidly superimposable on its mirror image. However, the rigidity of the chemical bonds prevents it from lying in a plane. Similarly, if a rubber glove were 100% flexible, it could be stretched out flat like a pancake, and then it too would be rigidly superimposable on its mirror image. However, the physical limitations of a rubber glove do not allow enough stretchiness to completely flatten it out (try it!). Thus in both cases it is the physical limitations of the object which prevent it from attaining a position which is rigidly superimposable on its mirror image.

Walba introduced the following definition in order to see what happens if we ignore all of these types of physical limitations.

DEFINITION 3.4. A molecule is said to be a **topological rubber glove** if it is chemically achiral, but it cannot be isotoped to a position which can be rigidly superimposed on its mirror image (even if it is completely flexible).

The molecule illustrated in Figure 9 is not a topological rubber glove, because if it were completely flexible it could be isotoped to a position which could be rigidly superimposed on its mirror image. At first glance it might seem like a topological rubber glove would be impossible. If a molecule can be isotoped to its mirror image should not it be possible to isotop it to a position which can be rigidly superimposed on its mirror image? In fact, a topological rubber glove is possible. The first topological rubber glove was synthesized by Chambron, Sauvage, and Mislow [**5**] in 1997. This molecule is a pair of linked rings, where the pair of adjoined hexagons at the top can rotate. We illustrate the molecule and its mirror image in Figure 11.

We see as follows that this molecule is chemically achiral. The bottom ring of the original molecule can turn over, in which case it looks like the bottom ring in the mirror form. When the ring is turned over we write the H_3C as CH_3 to indicate that the tail is still attached at the C. When the pair of adjoined hexagons at the top of the original form rotates, it gets into the position of the two hexagons illustrated in the mirror form. In this way, we see that the original form can change into the mirror form. Since these motions are chemically possible, the molecule is chemically achiral.

On the other hand, it can be shown that even if the molecule in Figure 11 were completely flexible it could not be isotoped to a position which could be rigidly

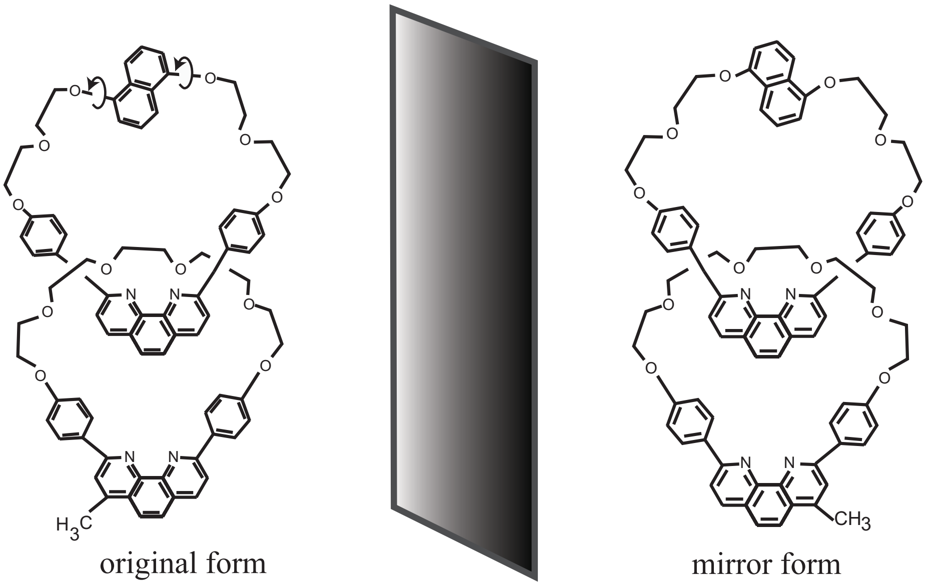


Figure 11. A topological rubber glove and its mirror image.

superimposed on its mirror image. We give a vague idea of the proof here (for a detailed proof see [**8**]). The H_3C in the original form gives the bottom ring an orientation. If the molecule were rigid, then the hexagons at the top cannot rotate, and hence they give the top ring an orientation. Thus we can model this molecule as a pair of oriented linked circles (as shown in Figure 12) with arrows to indicate an orientation on each circle. It can be shown that there is no isotopy from this oriented link to its mirror image. It follows that there is no isotopy from the molecule in Figure 11 to a position which can be rigidly superimposed on its mirror image. Hence the molecule in Figure 11 is a topological rubber glove.

Figure 12. This oriented link cannot be isotoped to it mirror form.

We summarize the relationship between geometric and chemical chirality as follows. If a structure can be rigidly superimposed on its mirror image, then it is physically the same as its mirror image. Hence it must be chemically the same as its mirror image. Thus geometric achirality implies chemical achirality. Taking the contrapositive of this statement, we see that chemical chirality implies geometric chirality. On the other hand, Euclidean and topological rubber gloves are examples of molecules which are geometrically chiral but not chemically chiral. Hence geometric chirality does not imply chemical chirality.

4. Topological Chirality

When we defined geometric chirality, we were treating all molecules as if they were completely rigid. There is no mathematical definition of chirality that corresponds to chemical chirality for all molecules, since some molecules are more or less rigid than others. Now we will take the opposite point of view and treat all molecules as if they were completely flexible.

Definition 4.1. A molecule is said to be **topologically achiral** if, assuming complete flexibility, there is an isotopy which takes it to its mirror image. If there is no such isotopy, the molecule is said to be **topologically chiral**.

If there is no isotopy from a molecule it to its mirror image, then there is no way for it to chemically transform itself into its mirror image. Thus every topologically chiral molecule is chemically chiral. For example, in order to prove that the molecular Möbius ladder is chemically chiral, Jon Simon [**19**] actually proved that it was topologically chiral.

The molecule illustrated in Figure 13 is chemically chiral because it has the form of a rigid tetrahedron. On the other hand, if the molecule were completely flexible we could twist around the edge with the H on the end and the edge with the HO_2C on the end. This would transform the original form of the molecule to the mirror form. Thus this molecule is topologically achiral. However, such a transformation is chemically impossible. This example, illustrates that topological achirality does not imply chemical achirality.

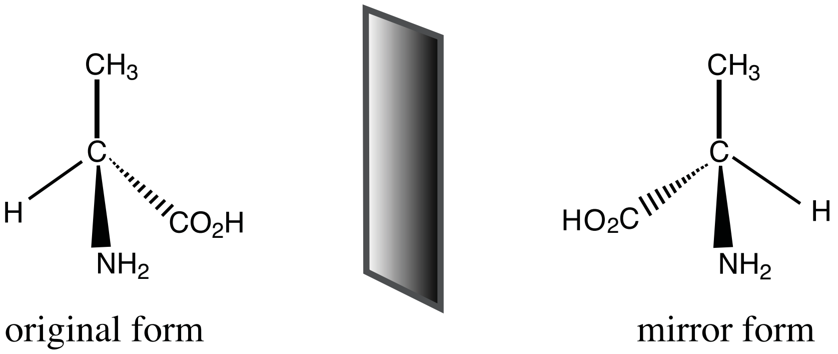


Figure 13. This molecule is chemically chiral because it has the form of a rigid tetrahedron.

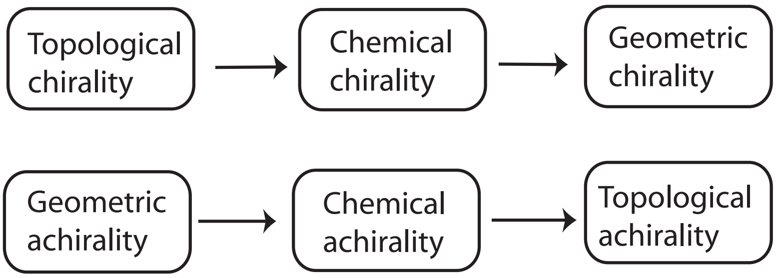


Figure 14. The relationship between the different types of chirality and achirality.

Figure 14 summarizes the relationships between the different types of chirality and achirality that we have been discussing. As we have seen in this and the previous section, none of the reverse implications hold.

If we heat a geometrically chiral molecule enough, it will change into its mirror form. By contrast, in order for a topologically chiral molecule to change into its mirror form, bonds would have to pass through one another. Even if we heat such a molecule, this will not occur. In this sense, topological chirality is a deeper and more enduring property than geometric chirality. This is one of the reasons that topological chirality is a meaningful concept for chemists.

5. Techniques to Prove Topological Chirality

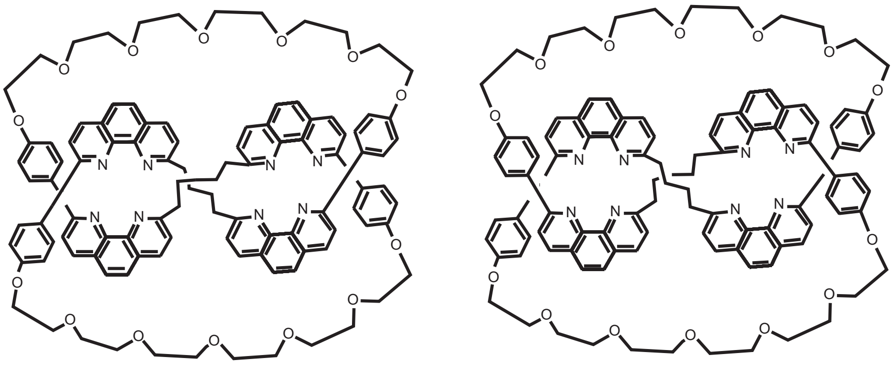
Now that we understand topological chirality and why it is chemically useful, we will introduce four different mathematical techniques for proving that a molecule is topologically chiral. Different techniques can be used for different molecules. There is no single technique that works for all molecules.

5.1. Knot Polynomials. The first technique that we introduce involves using knot polynomials to show that a knotted or linked molecule is topologically chiral. As mentioned at the beginning of this paper, knotted molecules have been synthesized since 1989 (see Figure 3). The idea is that there is a method of assigning a polynomial to a knot and link such that if two knots or links have different polynomials, then one cannot be isotoped into the other. In particular, if the polynomial assigned to a knotted molecule is different from the one assigned to its mirror image, then we know that the molecule is topologically chiral.

We present a very brief history of knot polynomials before we give an example. J. W. Alexander [**1**] developed the first knot polynomial in 1928. Alexander's polynomial played a major role in enabling topologists to distinguish one knot from another. In 1967, John H. Conway [**6**] discovered a recursive method for computing a related polynomial, in terms of the polynomials of simpler knots and links. While the Alexander polynomial and Conway polynomial are very important topological tools, they cannot help us detect topological chirality because the polynomials of a knot and its mirror image are the same.

In 1985, Vaughan Jones [**15**] developed a new polynomial which uses a recursive method similar to Conway's for its computation. In contrast with the Alexander and Conway polynomials, the Jones polynomial of a knot or link is often different from that of its mirror image. For example, Figure 15 illustrates a molecular knot and its mirror image together with their Jones polynomials. Observe that the picture of the mirror form of the molecule is identical to that of the original form except that the three crossings between bonds have been reversed. The Jones polynomial of the original form is $t+t^3-t^4$ and the Jones polynomial of the mirror form is $t^{-1}+t^{-3}-t^{-4}$. Since these polynomials are different, we conclude that there is no isotopy taking the original form its mirror form. Thus this molecular knot is topologically chiral. You may have noticed that the Jones polynomial is not technically a polynomial, since the exponents are negative as well as positive integers. However, it is standard to abusive terminology and refer to this as a polynomial.

Observe that for the knotted molecules illustrated in Figure 15, the Jones polynomial of the mirror form is identical to the Jones polynomial of the original form



$t + t^3 - t^4$ $\qquad$ $t^{-1} + t^{-3} - t^{-4}$

Figure 15. The Jones polynomial of a molecular knot and its mirror image.

except that the signs of the exponents have been reversed. This is not a coincidence. If K is any knot and K^* is its mirror image, then the Jones polynomial of the knot K^* will always be equal to the Jones polynomial of the knot K except that the signs of the exponents will be changed from positive to negative and from negative to positive. So if the Jones polynomial of a knot is not symmetric with respect to the signs of the exponents, then we can conclude that the knot is topologically chiral. Note however, that if the Jones polynomial of a knot is symmetric with respect to the signs of the exponents, it does not necessarily mean that the knot is topologically achiral. In particular, the Jones polynomial is useful for proving topological chirality, but not for proving topological achirality.

Using the Jones polynomial is a very effective way to prove that certain molecular knots and links are topologically chiral. However, this method will not help us establish chirality if a molecule does not contain any knots or links. For example, the molecular Möbius ladder (illustrated in Figure 16) does not contain any knots or links. Thus the Jones polynomial will not help us prove that it is topologically chiral. We will use the next method to prove that the molecular Möbius ladder is topologically chiral.

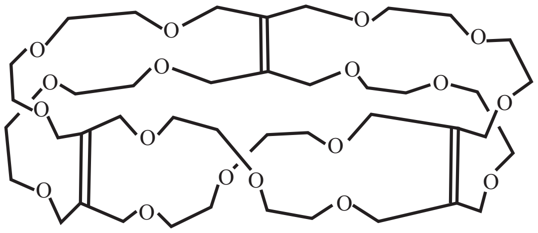


Figure 16. We cannot use polynomials to prove that the molecular Möbius ladder is topologically chiral.

5.2. 2-fold branched covers. The next method we introduce, involves using 2-fold covers to translate the question of whether a graph in 3-space is topologically chiral into the question of whether a particular link is topologically chiral. Covering spaces and branched covers have been a useful tool in topology for over 100 years.

However, Jon Simon [**19**] was the first to use this idea to prove that a molecule was topologically chiral.

In order to avoid getting too technical, we will not formally define a 2-fold branched cover (chapter 3 of [**8**] provides the definition of a 2-fold branched and gives a detailed exposition of Simon's proof). Instead, we present an intuitive picture of what a 2-fold branched cover is and how Simon used this idea to prove that the molecular Möbius ladder is topologically chiral.

We begin by representing the molecular Möbius ladder as a colored graph with different colors for each rung (see the illustration on the left side of Figure 17). We are not assuming that the rungs are chemically different from one another. We are only assuming that the rungs are chemically different from the sides of the ladder. The colors just help us keep track of each rung, but otherwise have no meaning. Observe that the sides of the Möbius ladder have the form of a folded over figure eight. We assume the molecule is completely flexible, and we isotop the sides of the ladder to a planar circle. The result of this isotopy is illustrated on the right side of Figure 17. This gives us a nice picture of the Möbius ladder as a circle with three arcs attached at different levels.

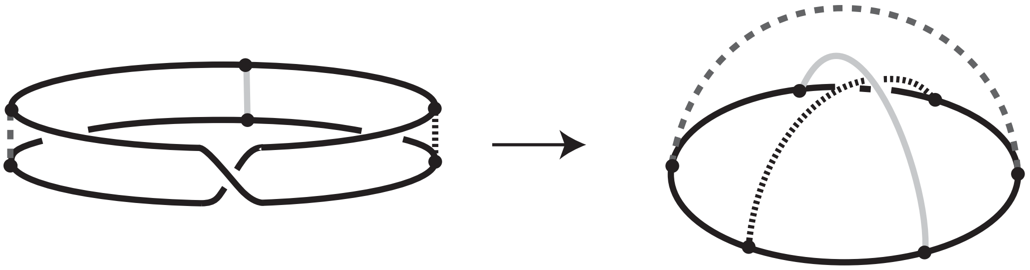


FIGURE 17. We color the rungs of a Möbius ladder and then isotop the sides of the ladder into a planar circle.

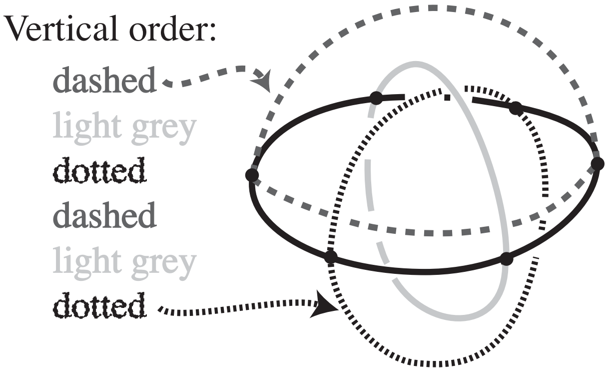


FIGURE 18. The 2-fold branched cover of a Möbius ladder, branched over the sides of the ladder. The vertical descending order of the rungs is: dashed, light grey, dotted, dashed, light grey, dotted.

The intuitive idea of the 2-fold cover of the Möbius ladder branched over the black circle in Figure 17, is illustrated by gluing two copies of the Möbius ladder together along the black circle. This gives us only one black circle, but two sets of rungs stacked one on top of the other. We illustrate this branched cover in Figure 18. In Figure 17, there is a grey dashed rung at the top, a light grey rung in the middle, and a dotted rung at the bottom. In the branched cover this pattern repeats with the endpoints of a rung of a given color attached to the endpoints of the second rung of that same color to create a circle of that color.

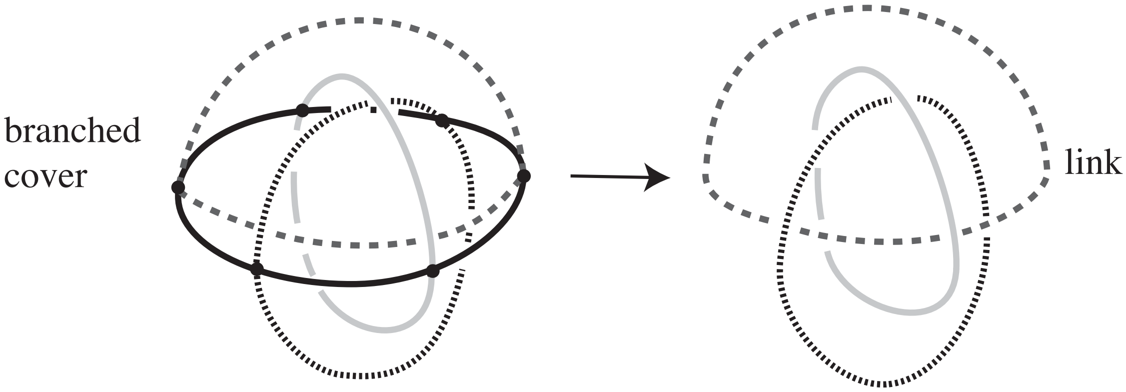


FIGURE 19. If we remove the black circle, we obtain a link.

If we remove the black circle, then we obtain a link (illustrated in Figure 19). It can be shown using the *linking number* (see for example, [**8**]) that the link in Figure 19 is topologically chiral (without distinguishing the different colors). It follows that the branched cover of the Möbius ladder is topologically chiral, distinguishing the link from the black circle. From this, it can be shown that the molecular Möbius ladder is topologically chiral, distinguishing the rungs from the sides.

This is a powerful method to use when a molecule has a special circle (like the sides of the Möbius ladder) which, for chemical reasons, must be invariant under any isotopy.

5.3. Using a known topologically chiral molecule. The idea of this method is that if we know a given molecule is topologically chiral, then we use that molecule to show that other molecules which contain it are also topologically chiral. In particular, this method is useful for molecules which contain a Möbius ladder within them. This method was first introduced by Liang and Mislow [**16**] in 1994, in order to prove that the triple layered naphthalenophane molecule is topologically chiral. We illustrate this molecule in Figure 20. A naphthalene molecule consists of a pair of hexagons, and is the primary ingredient in mothballs. This molecule has three layers of naphthalenes, like a triple layered fudge cake made of mothballs.

We consider this molecule as a graph where each corner is a vertex. It is not hard to show that this graph contains a unique longest cycle C, which we highlight in Figure 21. Any isotopy of triple layered naphthalenophane to its mirror image would take the cycle C to the corresponding unique longest cycle in the mirror image molecule. Now observe that there are exactly three edges in the graph which have both of their endpoints on C. These edges are indicated as dotted segments in Figure 22. Any isotopy of triple layered naphthalenophane to its mirror image would take these three dotted edges to three corresponding edges in the mirror image. Thus if triple layered naphthalenophane could be isotoped to its mirror image, then so could the colored graph illustrated in Figure 23. However, the graph illustrated in Figure 23 can be isotoped to the colored Möbius ladder which is illustrated in

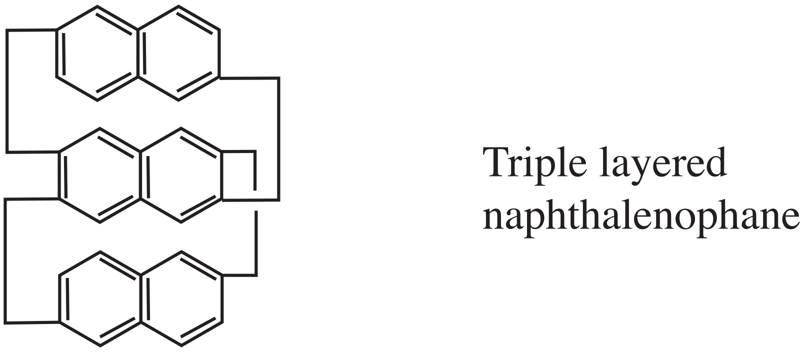


Figure 20. This molecule has three levels, each consisting of a pair of hexagons known as a *naphthalene*.

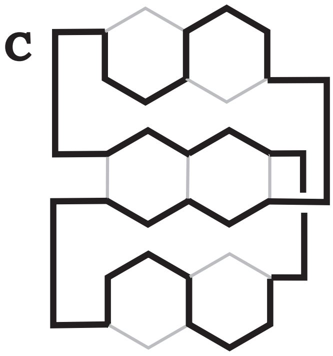


Figure 21. Triple layered naphthalenophane contains a unique longest cycle C.

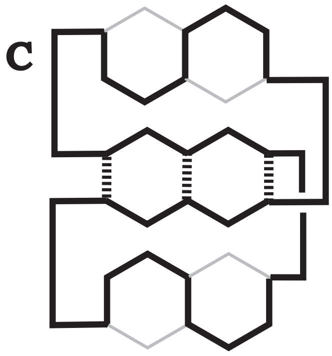


Figure 22. The three dotted edges are the only edges in this graph which have both of their endpoints on C.

Figure 24. Since we know that this colored Möbius ladder is topologically chiral, triple layered napthalenophane must be topologically chiral as well.

This method can sometimes be used even if the molecular graph contains more than one Möbius ladder. For example, consider the graph illustrated in Figure 25. It contains three hexagons at the top and two hexagons at each of the other levels. Thus it contains two equal length longest cycles, and hence two equivalent Möbius ladders, as illustrated in Figure 25. In this case, a similar argument can be used to show that the graph is topologically chiral.

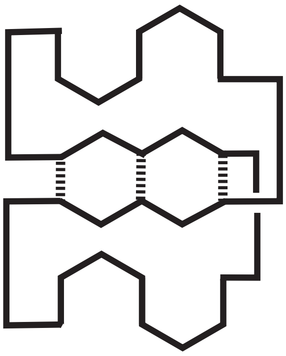


Figure 23. If triple layered naphthalenophane could be isotoped to its mirror image, then so could this colored graph.

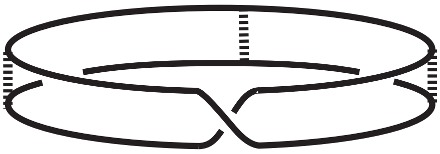


Figure 24. The graph illustrated in Figure 23 can be isotoped to this colored Möbius ladder.

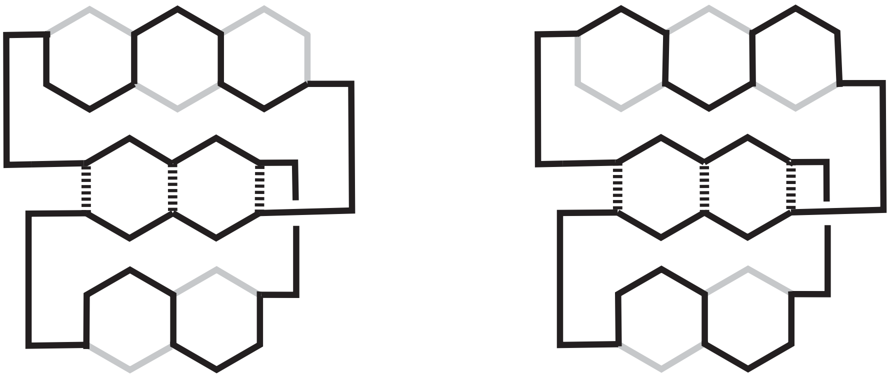


Figure 25. This graph contains two equal length longest cycles, and hence two equivalent Möbius ladders, as indicated.

5.4. A combinatorial approach. The idea of this method is to translate the question of showing that a molecular graph is topologically chiral into an easier question about an abstract graph. We begin with several definitions.

Definition 5.1. An **automorphism** of a graph is a permutation of the vertices of the graph that takes adjacent vertices to adjacent vertices. For a molecular graph, we also require that an automorphism take atoms of a given type to atoms of the same type.

Consider the molecular Möbius ladder illustrated in Figure 16. An automorphism must take oxygens to oxygens and carbons to carbons. Thus an automorphism takes rungs to rungs and sides to sides.

Now consider the Möbius ladder with numbered vertices illustrated in Figure 26. The numbers are to help us keep track of what happens to the vertices during a particular permutation. Observe that the permutation (26)(35) (which interchanges

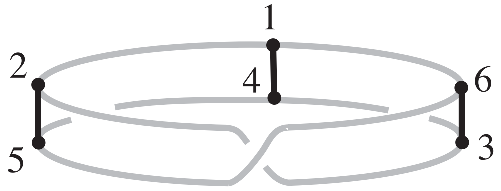


Figure 26. The premutation (26)(35) is an automorphism, but the permutation (12) is not an automorphism.

vertices 2 and 6 and interchanges vertices 3 and 5) is an automorphism of the Möbius ladder because it preserves adjacency of vertices. By contrast, the permutation (12) is not an automorphism, since vertex 2 is adjacent to vertex 5, but vertex 1 is not adjacent to vertex 5.

Definition 5.2. The **order** of an automorphism is the smallest number of times you must to perform the automorphism to get every vertex back to its original position.

For example, the order of the automorphism (26)(35) in Figure 26 is 2.

Definition 5.3. The **valence** of a vertex in a graph is the number of edges that contain it.

All of the vertices in the Möbius ladder in Figure 26 have valence 3. By contrast, if we look at the graph of the molecular Möbius ladder in Figure 16 the oxygen atoms have valence 2.

Definition 5.4. The **distance** between two vertices in a graph is the fewest number of edges contained in a path from one to the other.

It is not hard to prove the following two properties of automorphisms that we will use in our subsequent examples.

- An automorphism takes vertices of a particular valence to vertices of the same valence.
- An automorphism takes a pair of vertices which are a certain distance apart in the graph, to a pair of vertices which are that same distance apart.

Finally, we will need to refer to the two special graphs that are illustrated in Figure 27. The complete graph on five vertices, K_5, has an edge between every pair of vertices. The complete bipartite graph on two sets of three vertices, $K_{3,3}$, has an edge joining every vertex in one set to every vertex in the other set, and no edges joining a vertex in one set to another vertex in that same set. The graphs K_5 and $K_{3,3}$ are important because a graph can be embedded in the plane if and only if it does not contain one of these two graphs.

Theorem 5.5 (Flapan). [**9**] *If a graph contains either K_5 or $K_{3,3}$ and has no order 2 automorphism, then any embedding of the graph in $\mathbb{R}^3$ is topologically chiral.*

Theorem 5.5 translates a problem about the topology of how graphs are embedded in $\mathbb{R}^3$ into a problem about abstract graphs. All of the topology of Theorem 5.5

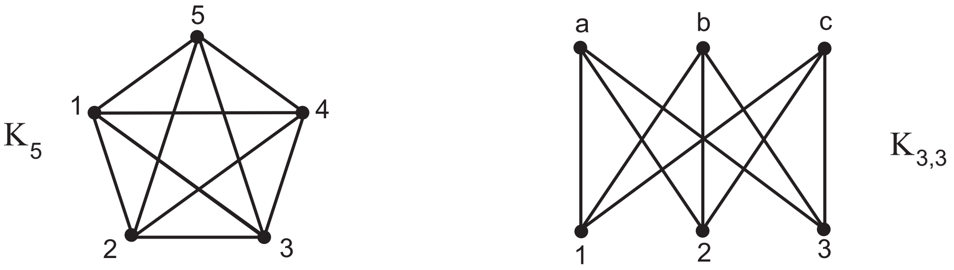


Figure 27. A graph has a planar embedding if and only if it does not contain one of these two graphs.

is contained its proof, which uses a lot of topological machinery, including: Jaco-Shalen [**13**] and Johannson's [**14**] Characteristic Submanifold Theorem, Thurston's Hyperbolization Theorem [**22**], and Mostow's Rigidity Theorem [**18**].

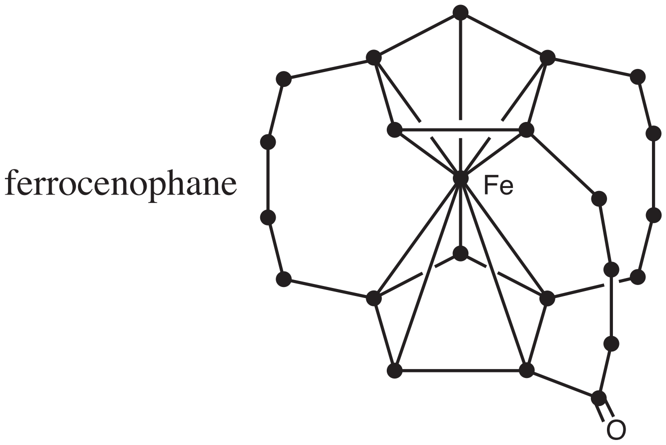


Figure 28. We consider the valence of adjacent vertices to argue that Ferrocenophane has no non-trivial automorphisms.

We can use Theorem 5.5 to prove that various molecules are topologically chiral. For example, we consider the molecule ferrocenophane, which is illustrated in Figure 28. All of the atoms in this molecule are carbons except for the iron atom in the center and the oxygen at the bottom. Since an automorphism must take atoms of a given type to atoms of the same type, any automorphism of this graph fixes the single oxygen atom and the single iron atom. Since the oxygen is fixed, the carbon atom attached to the oxygen must also be fixed by any automorphism. Now adjacent atoms must remain adjacent and valence must be preserved. It follows that the two atoms which are adjacent to this carbon are also each fixed by any automorphism. By progressively using the valence of adjacent vertices, we see that any automorphism of ferrocenophane fixes every single atom. Thus ferrocenophane has no non-trivial automorphisms.

It is not apparent at first glance that ferrocenophane contains one of our special graphs, K_5 or $K_{3,3}$. However, Figure 29 illustrates a K_5 that is contained in ferrocenophane. Thus we can apply Theorem 5.5 to conclude that the molecule ferrocenophane is topologically chiral.

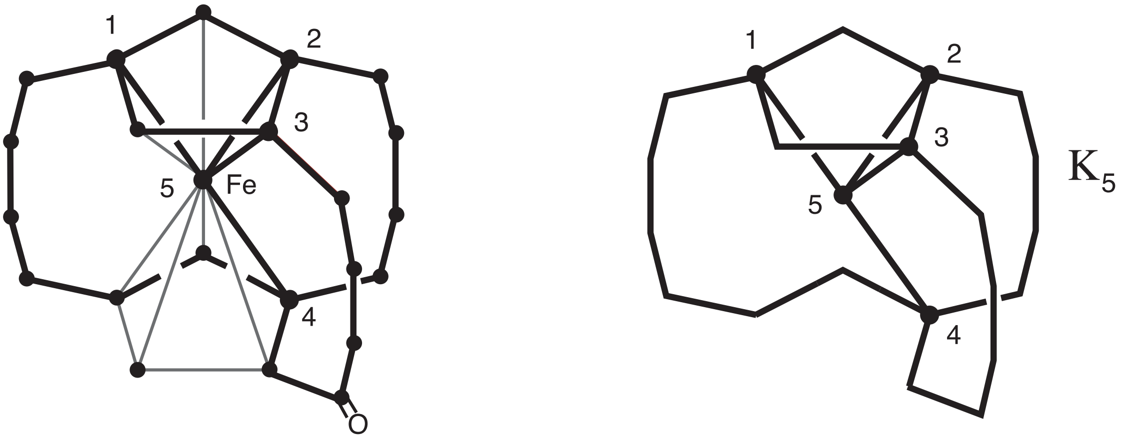


FIGURE 29. Ferrocenophane contains the graph K_5. We illustrate this K_5 without the rest of the graph on the right.

Next consider the Simmons-Paquette molecule, which is illustrated in Figure 30. In this case, we can see that the molecule contains the graph K_5 by simply omitting the vertices of valence two.

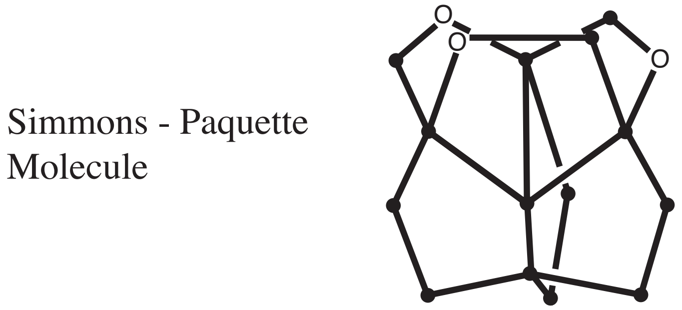


FIGURE 30. To see that the Simmons-Paquette molecule contains K_5 we omit the vertices of valence two.

To prove that the Simmons-Paquette molecule has no automorphisms of order two, we first observe that there is a unique cycle in the graph containing all three oxygen atoms. We label this unique cycle as C in Figure 31. Assume the Simmons-Paquette molecule has an automorphism ϕ of order two. Then ϕ must take the cycle C to itself. Since C has three oxygen atoms and ϕ has order two, one oxygen atom must be fixed by ϕ. Since ϕ preserves valence and adjacency, it now follows that every vertex on C is fixed by ϕ. Starting with the vertices on C, we progressively see that ϕ actually fixes every vertex on the Simmons-Paquette molecule. This contradicts our assumption that ϕ had order two. Thus the Simmons-Paquette molecule cannot have an automorphism of order two. We can now apply Theorem 5.5 to conclude that the Simmons-Paquette molecule is topologically chiral.

Observe that when we use Theorem 5.5 to show that a graph is topologically chiral, then any other embedding of the graph is also topologically chiral. For example, since Theorem 5.5 applies to the Simmons-Paquette molecule, we know that no matter how we embed the graph of the Simmons-Paquette molecule in $\mathbb{R}^3$, it will still be topologically chiral. So we could twist together the edges, or even

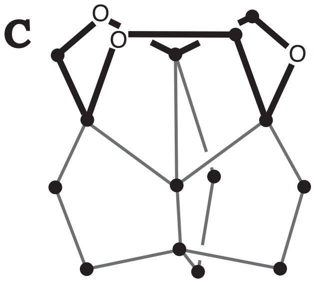


FIGURE 31. C is the unique cycle containing all three oxygens.

tie little knots in some edges, and the embedded graph would still be topologically chiral. Of course, not every embedding of a graph in $\mathbb{R}^3$ represents an actual molecule. In particular, an edge of the Simmons-Paquette molecule represents a bond, and hence is too short to contain a little knot in it. The fact that Theorem 5.5 can be applied to any embedding of a graph motivates us to make the following definition.

DEFINITION 5.6. A graph G is said to be **intrinsically chiral**, if every embedding of G in $\mathbb{R}^3$ is topologically chiral.

This terminology indicates that the topological chirality of the graph is *intrinsic* to the graph itself, rather than depending on how the graph is embedded in $\mathbb{R}^3$. Different embeddings of the same molecule in $\mathbb{R}^3$ are called *stereoisomers.* For example, the two molecules illustrated in Figure 32 are stereoisomers.

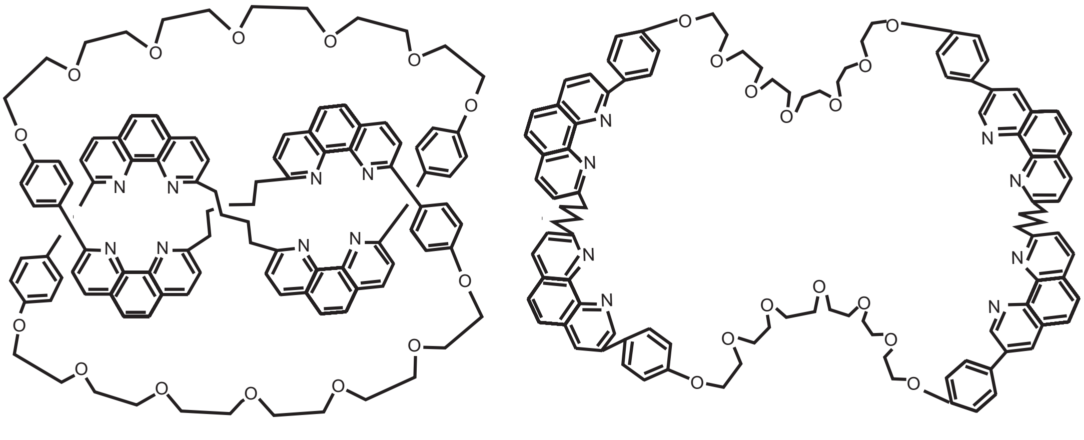


FIGURE 32. The molecule on the left is topologically chiral. The molecule on the right is a stereoisomer that is topologically achiral.

If a molecule is known to be intrinsically chiral, then it and all of its stereoisomers are topologically chiral. Thus we know that all of the stereoisomers of ferrocenophane and the Simmons-Paquette molecule are topologically chiral. Not every topologically chiral molecule is intrinsically chiral. For example, the molecules illustrated in Figure 32 are stereoisomers, but the one on the left is topologically chiral and the one on the right is topologically achiral.

6. Molecular symmetry groups

A molecule which is chemically achiral can be said to have *mirror image symmetry.* In order to predict molecular behavior it is important to understand all of the symmetries of a molecule, not just mirror image symmetry. If we consider only rigid molecular symmetries, then the possible symmetries of a molecule are rotations, reflections, and combinations of rotations and reflections. In more mathematical language we would refer to these rigid symmetries as *isometries* of $\mathbb{R}^3$ which take the molecule to itself. If a molecule is geometrically chiral, then its only rigid symmetries are rotations. The rigid symmetries of a molecule form a group. (We warn the reader that in this section we assume that the reader has some familiarity with group theory.)

Definition 6.1. The **point group** of a molecule is the group of rigid symmetries of the molecule.

This group is called the *point* group because it leaves the *point* at the center of the figure fixed. The point group of the Simmons-Paquette molecule (see Figure 30) is the cyclic group of order three, $\mathbb{Z}_3$, because its symmetries consist of the identity element (i.e., a rotation by 0°), and rotations by 120°, and 240°.

We can also consider the symmetries of an abstract graph independent of any embedding of it in space. The *symmetries* of an abstract graph are just the automorphisms of the graph (which we defined in the last section). As with the rigid symmetries, the automorphisms of a graph form a group.

Definition 6.2. Let Γ be a graph. The **automorphism group of** Γ is the group of automorphisms of Γ.

Every rigid symmetry of a molecule induces an automorphism of its graph. The point group can be associated with this induced subgroup of the automorphism group of the graph. In general, this subgroup is not equal to the entire automorphism group of the graph.

For example, consider the colored Möbius ladder with numbered vertices (illustrated in Figure 26) which represents the molecular Möbius ladder. We have seen that any automorphism of this graph must take rungs to rungs and sides to sides. Observe that the only non-trivial rigid symmetry of this graph is the order two automorphism (23)(56)(14) that is induced by turning the entire graph over left to right. Hence the point group of the molecular Möbius ladder is the cyclic group of order two, $\mathbb{Z}_2$. However, the abstract graph also has an order six automorphism (123456) which is not induced by a rigid symmetry. It follows that the automorphism group is the dihedral group with 12 elements denoted by D_6. Thus, in this case, the point group is associated with a proper subgroup of the automorphism group of the graph.

Next we consider the molecule illustrated in Figure 33. The only non-trivial rigid symmetry of this molecule is a reflection through the plane containing the three hexagons. Thus the point group of the molecule is the cyclic group $\mathbb{Z}_2$. However, the molecule in Figure 33 has a propeller at the top that rotates by 120°. The motion of the propeller is not a rotation of the entire graph; and hence it is not a rigid symmetry of the graph. Thus the point group does not include this symmetry. On the other hand, this motion of the propeller does correspond to an order three automorphism of the graph. Observe that the order two automorphism induced by the reflection does not commute with the order three automorphism induced by the motion of the propeller. Thus, the automorphism group of the graph is D_3, the dihedral group with six elements.

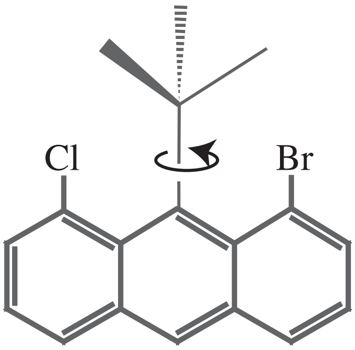


FIGURE 33. The point group of this molecule is $\mathbb{Z}_2$.

Recall from our discussion of rubber gloves that by treating all molecules as rigid, we do not detect that certain flexible, or even partially flexible, molecules are chemically achiral. Examples of this type motivated us to introduce the definition of topological chirality, which treats all molecules as flexible. While there is no mathematical definition of chirality that precisely corresponds to chemical chirality, we saw that chemical chirality falls somewhere between the notions of geometric chirality and topological chirality, depending on the rigidity of the particular molecule involved. Our situation in studying molecular symmetries is analogous. Treating all molecules as rigid, ignores symmetries of a propeller (like that of Figure 33), as well as symmetries which may require even greater flexibility of the molecule. We would like to consider what we would mean be a molecular symmetry group if we treated all molecules as flexible.

DEFINITION 6.3. Let Γ be a graph embedded in $\mathbb{R}^3$. The **topological symmetry group** of Γ is the subgroup of the automorphism group which is induced by isotopys and/or reflections of $\mathbb{R}^3$ which take Γ to itself.

The notion of the topological symmetry group of a molecule was first introduced by Jon Simon [**20**] in 1987. Since any rigid symmetry of a graph in $\mathbb{R}^3$ is induced by isotopys and/or reflections, the group of automorphisms induced by the point group is a subgroup of the topological symmetry group.

As examples, we determine the topological symmetry groups of some molecules that we have already seen. First we consider the Simmons-Paquette molecule, illustrated in Figure 30. Observe that the only automorphisms of the Simmons-Paquette molecule are induced by rotations of 120° and 240°. Thus the topological symmetry group, the point group, and the automorphism group of the Simmons-Paquette molecule are all equal to $\mathbb{Z}_3$.

Now, we consider the molecular graph illustrated in Figure 33. The topological symmetries of this graph are induced by a rotation of the propeller by 120° and a reflection through the plane containing the hexagons. Both of these symmetries are induced by isotopys and/or reflections. Thus, the topological symmetry group is equal to the automorphism group, which we saw above was D_3, the dihedral group with six elements.

Next, we consider the colored Möbius ladder with numbered vertices (illustrated in Figure 26). We saw above that the automorphism group of this graph is D_6, generated by the order two automorphism (23)(56)(14) together with the order six automorphism (123456). The automorphism (23)(56)(14) is induced by turning the graph over left to right, and the automorphism (123456) is induced by rotating the graph by 120° around a central axis, while bringing the half-twist back to its original position. Thus again the topological symmetry group is equal to the automorphism group.

In general, the topological symmetry group of an embedded graph does not have to equal the automorphism group of the graph. Consider the embedded graph illustrated in Figure 34. The automorphism group of this graph is generated by the three involutions (24), (68), and (15)(26)(37)(48). Since these involutions commute, the automorphism group is $\mathbb{Z}_2 \times \mathbb{Z}_2 \times \mathbb{Z}_2$. The involution (24) is induced by turning the left side of the graph over, and the involution (68) is induced by turning the right side of the graph over. However, since it is impossible to isotop an unknotted circle into a knotted circle, there is no isotopy and/or reflection which induces the involution (15)(26)(37)(48). Thus the topological symmetry group of this embedded graph is $\mathbb{Z}_2 \times \mathbb{Z}_2$, which is a proper subgroup of the automorphism group of the graph.

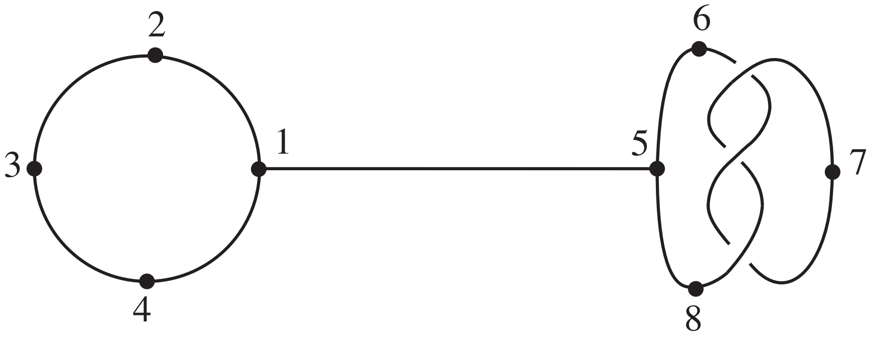


Figure 34. The topological symmetry group of this embedded graph is not equal to the automorphism group.

In 1938, Frucht [**12**] proved that every finite group is equal to the automorphism group of some graph. It is natural to wonder whether every finite group is equal to the topological symmetry group of some embedded graph. In 2005, we answered this question in the negative by proving Theorem 6.4.

Theorem 6.4 (Flapan, Naimi, Pommersheim, Tamvakis). [**10**] *There is no graph Γ embedded in $\mathbb{R}^3$ such that the topological symmetry group of Γ is equal to an alternating group A_n with $n > 5$.*

In order to compare the different approaches to understanding symmetries of molecules, we identify the point group with the subgroup of the automorphism group of its graph, and we make the following final definition.

Definition 6.5. The **chemical symmetry group** of a molecule is the subgroup of the automorphism group which is induced by chemically achievable motions taking the molecule to itself or to its mirror image.

A rotation of a molecule is a chemically achievable motion. If an automorphism is induced by a reflection of the molecule, then the molecule and its mirror image are identical as rigid objects. Hence there is a chemically achievable motion taking the molecule to its mirror image. Thus the point group is a subgroup of the chemical symmetry group. Every chemically achievable motion is an isotopy. If a chemically achievable motion takes the molecule to its mirror image, then this motion followed by a reflection takes the molecule to itself. Thus every automorphism which is the result of a chemically achievable motion taking the molecule to itself or to its mirror image is also the result of an isotopy and/or a reflection. So the chemical symmetry group is a subgroup of the topological symmetry group. Finally, every automorphism which is induced by an isotopy and/or a reflection is certainly an element of the automorphism group of the graph. Thus the topological symmetry group is a subgroup of the automorphism group of a graph. The relationship between the different symmetry groups is illustrated in Figure 35. As we have seen above, these subgroups may or may not be proper subgroups depending on the specific example involved.

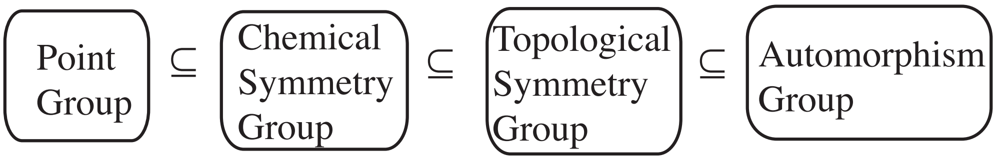


Figure 35. The relationship between the different types of symmetry groups.

For a more detailed presentation of topological chirality and symmetries of non-rigid molecules, the interested reader should see [**8**].

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