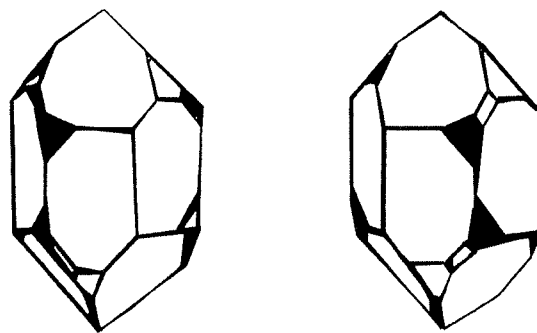


III. RIGHT HAND, LEFT HAND

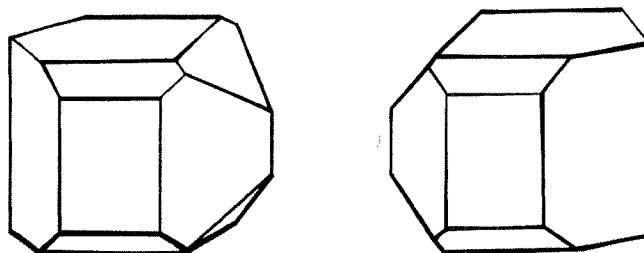
Molecular Chirality

Crystals and molecules can also be either right-handed or left-handed (such as quartz crystals), although many crystals and molecules have no handedness. The discovery of chirality itself is related to crystals. In his famous experiments in 1848, Louis Pasteur recrystallized a salt of tartaric acid and obtained two kinds of small crystals; their shapes were mirror images of each other.



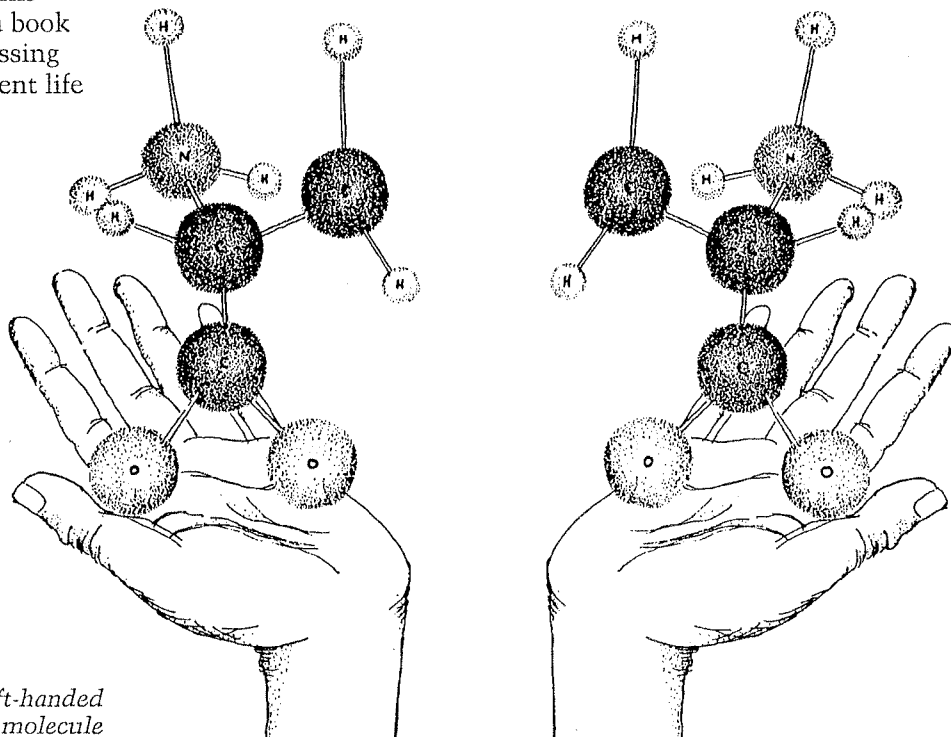
Quartz crystals

Molecules of many substances can also be right-handed or left-handed. Living organisms contain a large number of such molecules. All naturally occurring amino acids are chiral (except one of them: glycine).

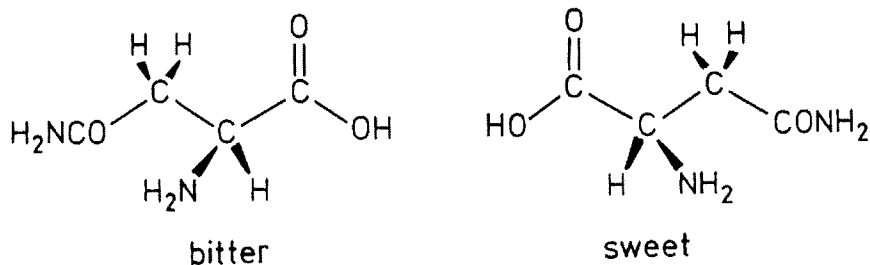


Tartaric acid crystals

Here is an illustration showing a pair of hands with a pair of right-handed and left-handed amino acid molecules. This illustration appeared in a book by R. N. Bracewell discussing the possibility of intelligent life in outer space.



*Right- and left-handed
amino acid molecule*



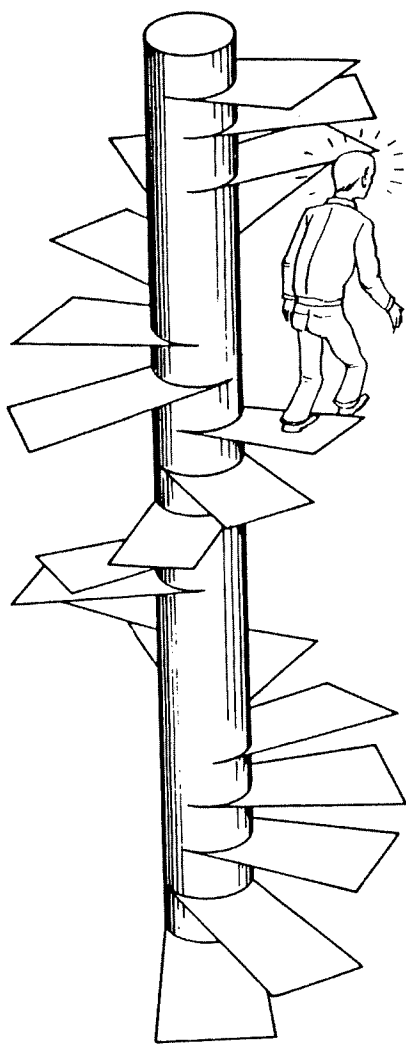
Bitter/sweet structural formulas for asparagin

Many biologically important chemical compounds exist in left-handed and right-handed forms, and the biological activity of the two forms may be very different. The left-handed form, for example, may be a cure, and the right-handed one may be indifferent, or even a poison. You may remember Lewis Carroll's *Through the Looking Glass* in which Alice is wondering: "Perhaps Looking-glass milk isn't good to drink." As a milder example, humans metabolize only right-handed glucose. Left-handed glucose, although still sweet, passes through the system untouched. Chiral separation thus opens up new frontiers in what synthetic chemistry can do for feeding and curing people, and perhaps keeping them slim as well. An example of a chiral pair with differing characteristics is the organic acid asparagin.

Chirality and Life

There is a unique situation in that all amino acids in living organisms occur as left-handed, but never right-handed. Other substances important for life, such as nucleotides in nucleic acids, appear in right-handed versions only. That some substances occur always left-handed and others always right-handed is characteristic for all life processes, and is the same in humans, animals, plants, and microorganisms. Why this happens is a great puzzle, one that can't be solved satisfactorily at this time. (Nobel Laureate V. Prelog has suggested that this phenomenon is a problem of molecular theology!)

It seems easier to answer the question as to why one substance consistently occurs as left-handed and another as right-handed. Imagine a spiral staircase. Spiral staircases are chiral, and either right-handed or left-handed, depending upon their direction. (We'll discuss spirals in more detail later.) Let's say this is a left-handed spiral staircase that suddenly switches to right-handed. What happens? The continuity of the staircase is interrupted and you bump your head on the stairs. This example demonstrates why once a system starts out left-handed, it should remain consistently left-handed, and vice-versa. If only some components of a complex molecular system are replaced by their mirror images, a chaotic system emerges, such as this spiral staircase.



A spiral staircase that changes its chirality

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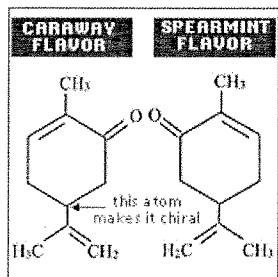
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**Your Nose Knows!**

Would you like spearmint or caraway flavor? That's a strange choice, but believe it or not, they are the same thing. Well, almost. Spearmint and caraway both contain a molecule called carvone with the empirical formula $C_{10}H_{14}O$, or rather 10 carbon atoms, 14 hydrogen atoms, and 1 oxygen atom. The thing that makes them taste different is that one is left-handed and the other is right-handed. In order for something to have a left or right-handedness, it must

be chiral.

Chiral molecules contain the same atoms arranged as mirror images that are non-superimposable. Examples of chiral objects are your hands. Your left hand is the same as your right hand, but they are not interchangeable. Your right hand cannot be replaced by your left hand just as you cannot put your left glove on your right hand. In fact, if you look at your right hand in the mirror, the image you would see would be a left hand. They are mirror images of each other that are non-superimposable; therefore they are 'chiral'. Superimposable objects are things such as balls, cubes, and baseball bats. They are not chiral. When you look at their reflection in a mirror, it looks just like the actual object.

Chiral things only exhibit differences between right and left-handedness when tested with other chiral things. There is no advantage to picking up a chicken egg with the left hand as opposed to the right, because the egg is not chiral. Similarly, a non-chiral piece of test equipment can't distinguish between caraway or spearmint flavoring. The molecules have the same melting point, molecular weight, density, optical absorption, etc. In order to differentiate them, you need a chiral probe. So how can you tell the difference between them when expensive equipment can't? Your nose is a chiral probe!

About the Author**Willa Larsen, MS**

Willa Larsen writes on a wide array of topics for ScienceIQ. Willa received a BS in physics from University of Colorado and a MS in materials science and engineering from UCLA. She previously worked making infrared detectors for the Hubble, missiles and surveillance equipment. Willa is the publisher of WillasArk.com which helps fund animal rescue.

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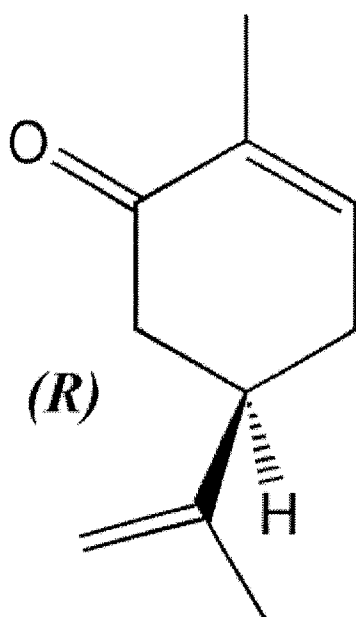
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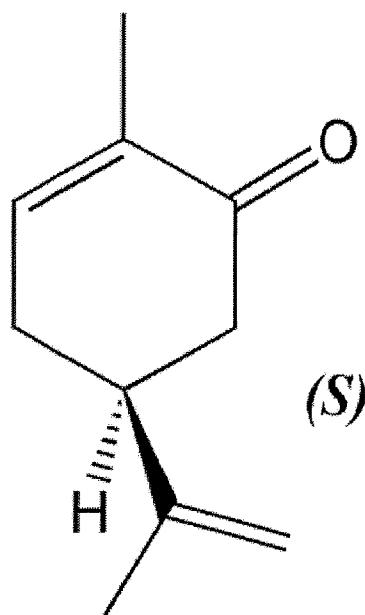
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Spearmint



Caraway



Carvone.png (20KB, MIME type: image/png)



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Structure of R- and S- carvone. Drawn in ChemDraw by User:Walkerma, November 2005.

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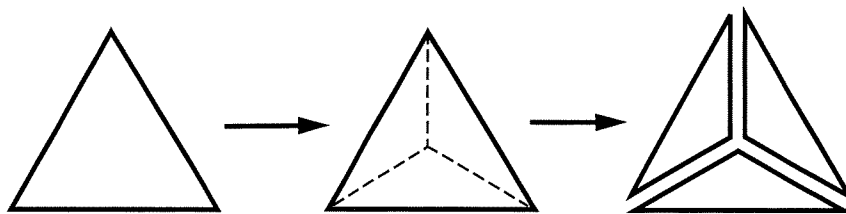
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III. RIGHT HAND, LEFT HAND

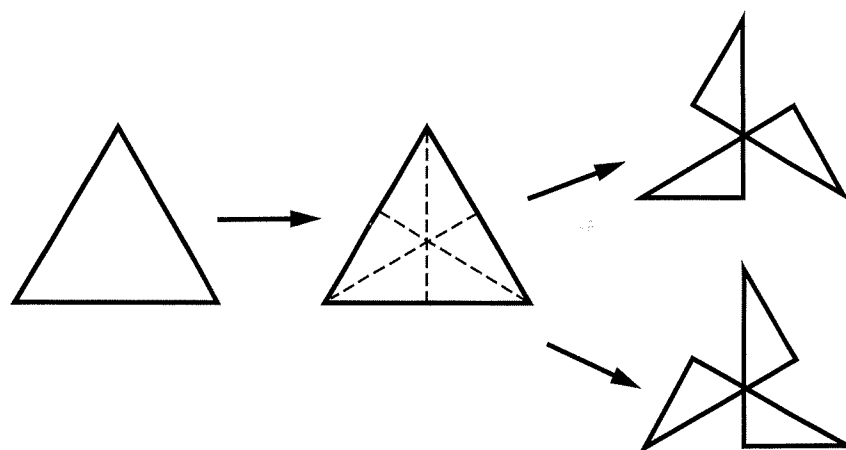
Creating Chiral Shapes by Dissection

Let's talk about some simpler aspects of chirality. First, let's dissect an equilateral triangle into parts which themselves also possess mirror symmetry. Here, the dissected parts are not chiral. (They can be superimposed one over the other.)

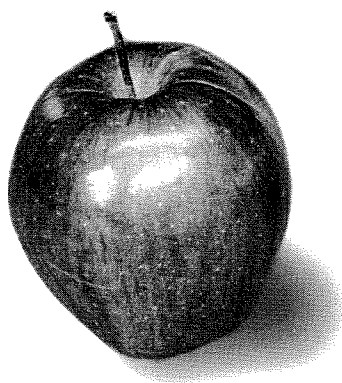
Then dissect another equilateral triangle into left-handed and right-handed parts. Here, the dissected parts are chiral. (They cannot be superimposed one over the other.)



The products of this dissection are not left-handed or right-handed; they have no handedness (they can be superimposed)

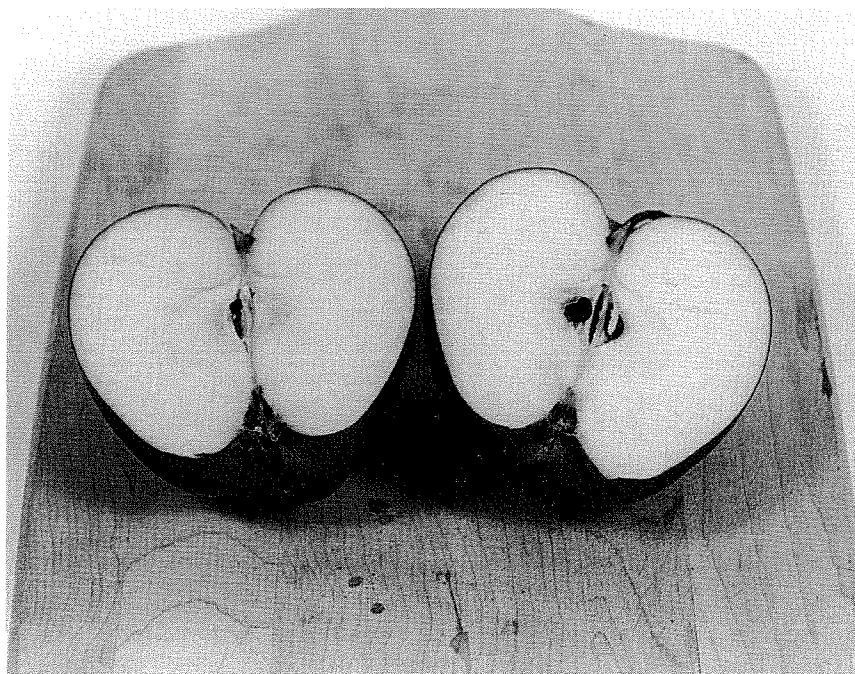


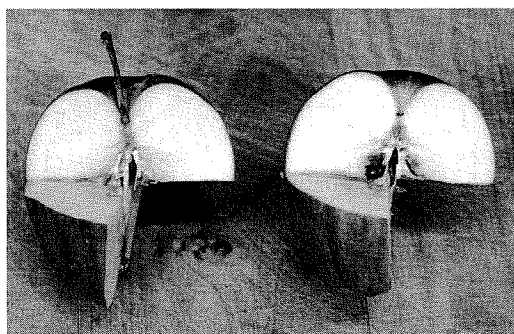
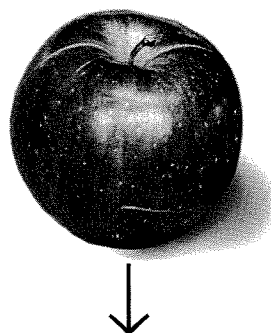
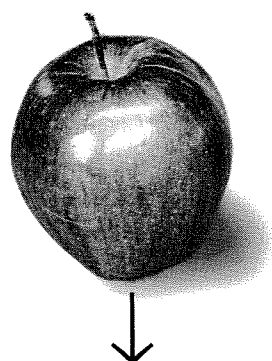
The products of this dissection are left-handed and right-handed (they cannot be superimposed)



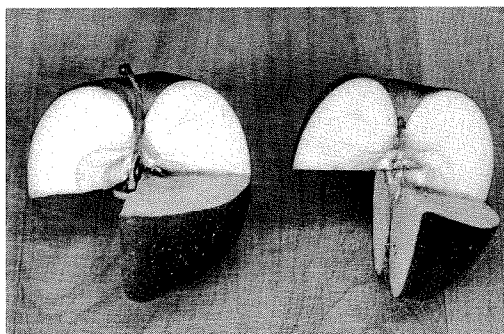
Let's now dissect an apple.

Cutting an apple in the usual way gives us two halves that are not left-handed or right-handed. Each half is mirror-symmetric.





Apple cut into pair of left-handed halves

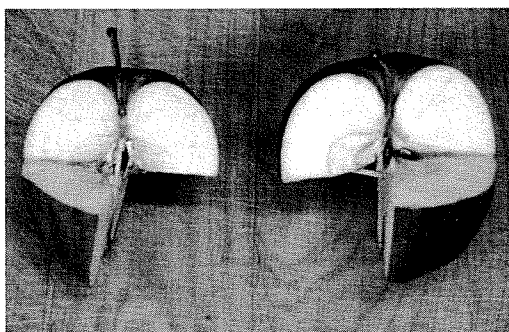


Apple cut into pair of right-handed halves

We may also ask, Can an apple be dissected (like the triangle) into left-handed and right-handed halves? No. However we try, it proves impossible. It is possible, though, to dissect it into a pair of two left-handed or a pair of two right-handed halves.

In fact, from two different apples you can produce a pair of opposites: a pair of right-handed and left-handed halves—but they cannot be combined into one apple.

The French call this parlor trick “La Coupe du Roi” (“The Royal Cut”).



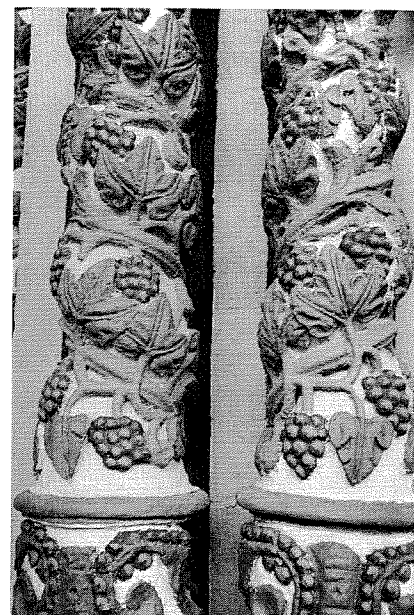
One of the two left-handed and one of the two right-handed halves will not combine into a whole apple.



Recipe for “La Coupe du Roi”

Make two vertical half-cuts through the apple; one from its top to its equator, and the other, perpendicular to the first, from its bottom to its equator. Then make two nonadjacent quarter cuts along the equator of the apple. Following these cuts the apple should split into two homochiral halves. This recipe can be followed in two senses and thus produce two left-handed halves in one case and two right-handed ones in the other.

XII. HELIX & SPIRAL



Grape decorations around columns at an Eastern Orthodox monastery in Zagorsk, Russia

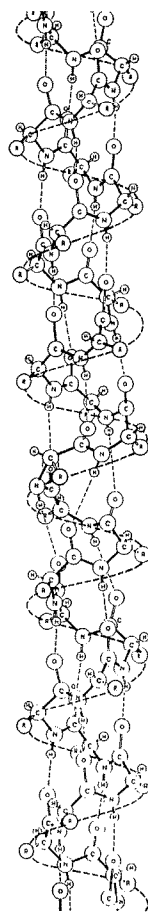
The columns in a monastery in Zagorsk, Russia (above), are decorated with grapevines displaying helical symmetry.

The directions of the two helices, however, are different, with mirror symmetry between the two. Thus, helices, as well as spirals, may be left-handed or right-handed—they may be chiral.

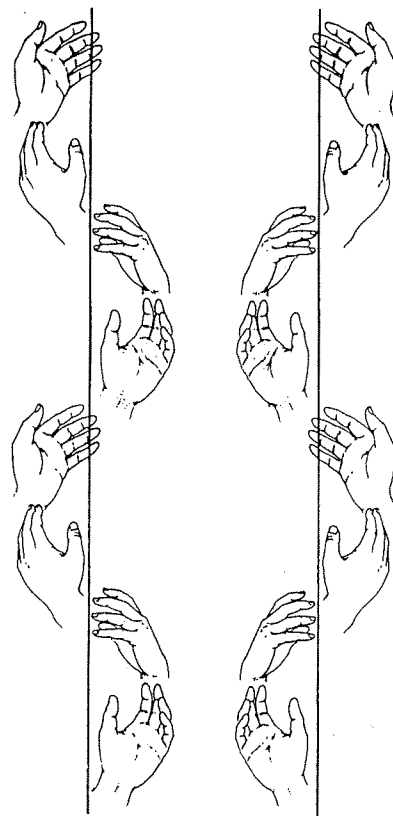
On an entirely different scale, many biologically important macromolecules have helical structures, as shown at right.

Spirals

The helix may also be considered a special case of a spiral in which the amount of rotation and translation remains constant. While a helix always extends in three dimensions, a spiral can also be drawn on a piece of paper, that is, in two dimensions.



Helical biological macromolecule



Left-handed and right-handed helices from a textbook on biochemistry

Chiral:

Describes an object that cannot be superimposed on its mirror image

ISBN 0-471-29657-1

message AAA would remain unchanged. We can imagine further losses of symmetry that would lead, step by step, to the code that is enshrined in cryptographic history, with ... for S, --- for O, and so on.

Now think about the genetic code. We have already observed a key feature: The genetic code is redundant. That is, different triplets often code for the same amino acid. There is no great regularity to this lack of uniqueness, but a definite degree of symmetry—albeit imperfect—is clearly visible in the genetic code. Often, just the first two bases in a triplet let determine the corresponding amino acid. For example GA? is always leucine, CG? always arginine. In short, the code for these amino acids is symmetric under changes of the third base. If this symmetry were perfect, then the 64 triplets would break up into 16 quartet triplets, such as GAC, GAG, GAA, GAT, with each triplet of the quartet coding for the same amino acid (but a different amino acid for each quartet). However, there are more than 16 amino acids, so sometimes the third base matters. Indeed sometimes the *second* base matters. Either way, the symmetry of the arrangement into quartets is broken.

How? The precise pattern of redundancy in the genetic code is messy. Instead of a tidy 16 quartets, there are three sextets (amino acids corresponding to six different codes), five quartets, two trios, nine duos, and two singles. The Hornoses assume that these numbers are determined by a chain of broken symmetries. The mathematical machinery reveals just eight possible chains; exactly one comes close to the correct numerical pattern. A final breakage of symmetry is needed to reproduce the precise pattern of redundancy found in the genetic code. This final breakage is somewhat empirical, and it suggests that the code may be a frozen version of one that ideally would have had 27 amino acids. The first broken symmetry—where the 64 triplets would code for just 6 amino acids—may represent a primordial version of the genetic code, the first step in its evolution. If the Hornoses are right, the genetic code is no accident. Pretty much the same code would arise again if we reran the origins of life.

Earlier, I said that the copying of DNA strands is quite a complex business. In fact, there are geometric reasons why it can't be simple. If you pull the two DNA strands apart in order to attach complementary ones, the strands wind around each other and get tangled up. Therefore, something else has to happen—such as special molecules, known as “enzymes,” cutting the strands apart and rejoining them later. This aspect of DNA is currently being studied using some surprisingly sophisticated and very new mathematics: topology. *Topology* is often called “rubber

sheet geometry,” because it studies those features of a geometric shape that are unchanged if the shape is stretched, compressed, bent, or twisted—but not cut or torn. It is what geometry would be like if you drew the diagrams on a sheet of rubber: no fixed angles, no parallels, no straight lines. If this description makes the topic sound frivolous, here is a more sober description: the geometry of continuous transformations. *Symmetry transformations* keep objects the same shape—and the same size, unless we're talking about dilations. *Continuous transformations* can distort the shape and change the size; the only constraint is that the object has to remain in one piece. Because continuity is one of the deep properties of nature, topology is a fundamental mathematical tool.

Topology deals with geometrical features such as holes, knots, links, and boundaries. I now briefly describe two typical uses: a classical approach to DNA supercoiling and a modern attack on the role of enzymes in DNA chemistry. Supercoiling is just one of the ways in which the textbook double-helix model of DNA fails to represent the true complexity of that molecule. To experience supercoiling for yourself, take an elastic band and loop it loosely *between* the thumb and forefinger of each hand, pulling your hands slightly apart to keep the band taut. Now rub your right thumb against your finger to rotate one section of the band several times. This introduces a number of clockwise turns along one section of the band, and an equal number of counterclockwise turns along the other (Figure 23a). Now, pressing thumbs against fingers to prevent the band from twisting, bring your hands closer together. The two stretches of elastic twine around themselves like the tangles you often find in a stretchable telephone cord (Figure 23b). When this kind of thing happens in a DNA molecule, it is known as *supercoiling* because the standard helical form is already coiled (around itself). A supercoil is a coiled coil, and it is merely one of the simpler ways for DNA topology to make life difficult for the biologist. Supercoiling particularly occurs in *plasmids*, closed loops of DNA purified from bacteria, and it causes the loops to tangle up when viewed in an electron microscope (Figure 24).

The topology here is governed by two simple quantities known as the “linking number” and the “writhing number.” A *link* is one turn in an elastic band after being twisted but before it is allowed to supercoil, and the *linking number* is the number of links that occur in the molecule. A *writhe* is the kind of tangle that occurs when the molecule supercoils, and the *writhing number* is the number of such tangles. These two types of twists in DNA may seem very different, but topology tells us that they

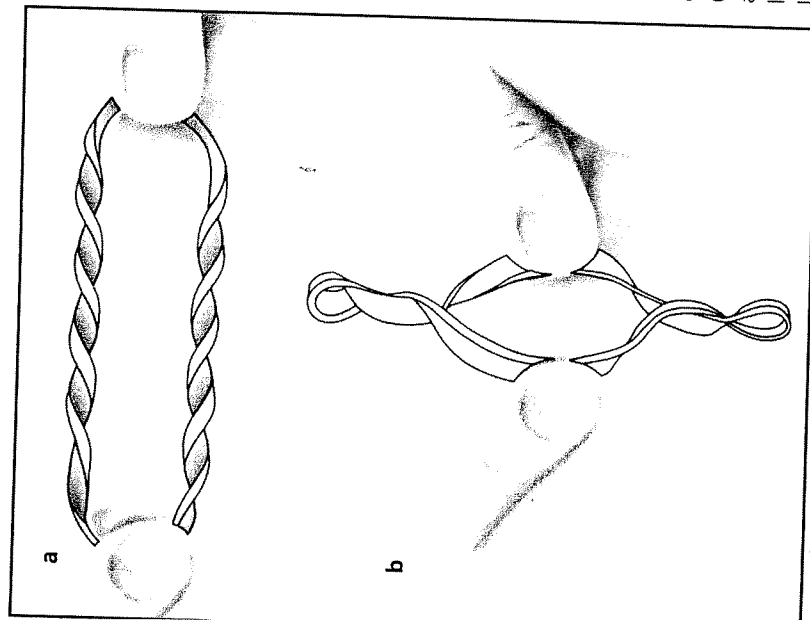


Figure 23
Supercoiling in an elastic band:
(a) creating clockwise and counterclockwise links; (b) trading the links for writhes.

are actually closely related: In fact, the linking number is the sum of the writhing number and the number of helical turns in the DNA. This means that by making continuous deformations of the DNA, links can be traded for an equal number of writhes, or for extra turns in the helical structure itself. All three quantities can be computed rather simply by counting how the DNA strands cross each other, and the three together provide the-ists with a powerful grip on the geometry of the DNA molecule.

The application to enzymes requires much deeper topological quantities, which capture not just the coarse overall geometry, but also the fine details of knotting and linking. Since 1928 or so, mathematicians have been startled to find how rich and difficult the classification and analysis of knots has proved to be. Apparently simple problems, such as distinguishing a reef knot from a granny knot, succumbed only to 3D-powered machinery and deep and complicated theories. Then, in 1984, a New Zealander named Vaughan Jones opened up a new chapter of

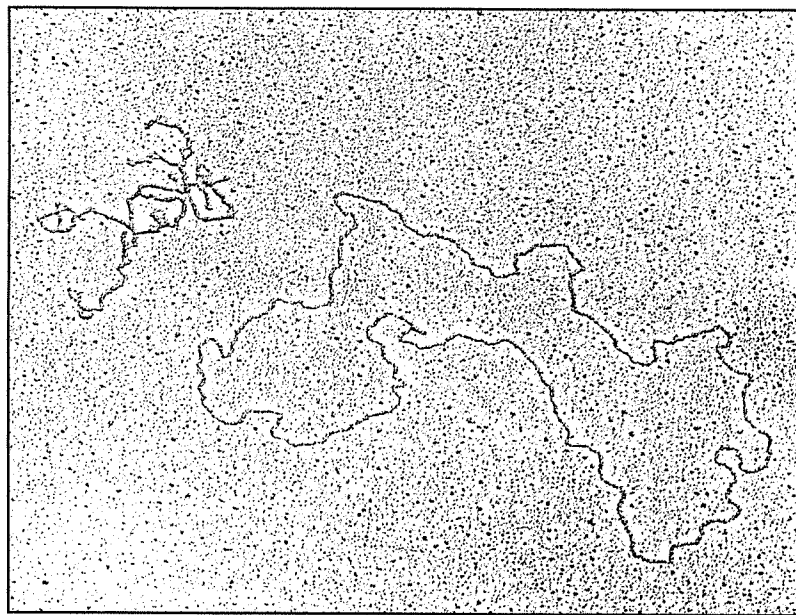


Figure 24
Electron micrograph of supercoiled DNA (top) and relaxed DNA plasmids (bottom). Each plasmid contains about 9,000 base pairs.

knot theory by inventing a totally new way to detect which knot is which—computable quantities that can distinguish many different knots from each other. These quantities, now called “Jones polynomials,”⁷ were the tip of an iceberg, and generalizations and new discoveries are still flooding in.

Since the mid-1990s, this new machinery, together with some of the old machinery, has been harnessed to problems in DNA biochemistry, addressing the important problem of finding out the shape of strands of DNA *when in solution*. The traditional apparatus of X-ray diffraction requires the DNA to be in crystalline form, which doesn’t help here; instead, biochemists inspect the actual molecule, squashed flat on a surface, and revealed in a high-powered electron microscope. As we know, the DNA double helix comprises two intertwined strands. When enzymes cut and then rejoin the molecule, the resulting strands form tangled knots and links. A fundamental problem is to work out which knot or link you