Knotty Problems—and Real-World Solutions

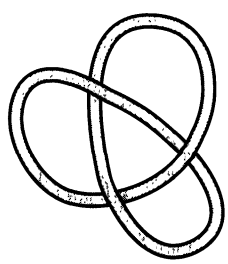
Knot theory, once a math backwater, turns out to have applications that extend all the way to clinical medicine

We all know what a knot is—if we didn't, our shoes would fall off. But for mathematicians, a knot is something a little different from what we picture—more like an electrical extension cord that's been tangled up and plugged back into itself. How the cord winds through space, crossing over itself before finding the right opening to plug into again is what makes all the difference to mathematicians—and also, increasingly, to researchers with practical things in mind.

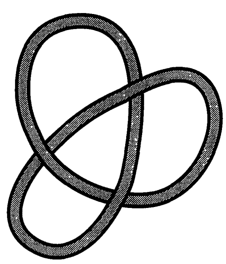
Ten years ago knot theory was a backwater in low-dimensional topology and virtually unknown in the pragmatic realms of applied science. Today it is becoming a chic topic in mathematical circles as well as big business elsewhere, with theoretical ramifications stretching from molecular biology to theoretical physics. Reflecting this burgeoning interest, knot theory was the subject of several of the hottest talks at the recent annual mathematics meetings in Baltimore.*

One of knot theory's biggest growth areas is molecular biology. The short, circular pieces of DNA that biologists work with often come all knotted up. Electron microscopy has revealed a whole taxonomy of trefoil knots, square knots, and granny knots, as well as catenanes, which are two or more circular strands of DNA linked together. Enzymes called Type II topoisomerases act as molecular fingers, changing the knots from one form to another by cutting one strand, passing a strand through the opening, then resplicing the cut. Other enzymes, called Type I topoisomerases, play a role in DNA supercoiling, a molecular version of the coiled telephone cord that winds itself into a larger coil.

In his presentation at Baltimore, Nicholas Cozzarelli of the University of California at Berkeley argued that studying knot theory is important to understanding how topoisomerases tie and untie DNA, changing its topology as they do so. And that study isn't of mere theoretical significance, he said, because the changes in topology are intimately connected with the crucial biological processes of gene expression and cell division. The vital importance of these topological processes is shown by the fact that drugs that inhibit topoisomerase activity quickly cause the cells to die. Says Cozzarelli, "They are lethal because they stop DNA replication within a fraction of a second." That makes topoisomerases particularly tempting targets for anticancer drugs or antibiotics, he concluded.



Three-ring circus. *A trefoil knot and its mirror image. Mathematicians have hit on intriguing new ways to tell them apart.*



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Working with Paul Englund of Johns Hopkins, Cozzarelli's Berkeley team has recently teased apart the topology of a particularly tangled form of DNA found in the clinically important one-celled parasites called trypanosomes. A membrane-bound organelle called a kinetoplast contains a catenane made up of thousands of tiny rings of DNA spread out in a two-dimensional network. Combining a mathematical analysis by James White at the University of California, Los Angeles, with experimental work by Jung-Huei Chen at Berkeley, Cozzarelli's group determined that in the kinetoplast DNA, each small circle is linked with precisely three of its neighbors. Now the mathematician-biologists are trying to find out how the tangle replicates itself to produce exactly that structure.

Knots in DNA and other large natural polymers have been known for more than a decade, but chemists have only recently begun to invent knots of their own in synthesized molecules. The first one was tied in 1989 by Christiane O. Dietrich-Buchecker and Jean-Pierre Sauvage of the Institut de Chemie in Strasbourg, France; they reported twisting a synthetic molecule with 124 atoms into a trefoil knot. The motivation for producing such knotty specimens is partly aesthetic, but it also provides a way of testing the limits of chemistry's synthetic capabilities, says Jonathan Simon, a mathematician at the University of Iowa who works on applications of topology to chemistry. Along the way, the mathematicians and the chemists have gotten more intricately involved—the chemists raising theoretical questions that the mathematicians hadn't thought of, and the mathematicians reciprocating by pointing out further novel properties that chemists could replicate at the lab bench.

Some of the progress that the mathematicians themselves have made in straightening out the theory of knots was also on view in Baltimore. The fundamental theoretical problem in the subject is to tell whether two knots are the same or different topologically. The criterion knot theorists apply is: Given two knots, no matter how different they look initially, can they be deformed so as to look the same? One way mathematicians try to answer the question is by computing invariants—numerical or algebraic expressions assigned to each knot that remain the same no matter how much the knots are deformed.

Until fairly recently, mathematicians made do with an invariant called the Alexander polynomial. Unfortunately, this invariant cannot distinguish between a knot and its mirror image; it assigns the same polynomial to each, even if they are known on other grounds to be different. In 1984, however, Vaughn Jones of the University of California at Berkeley discovered a new, more powerful polynomial invariant that can separate a knot and its mirror image. The Jones polynomial, as it's called, led to a slew of other invariants as well as to some unexpected connections with statistical mechanics and quantum-field theory.

Now comes Russian mathematician Victor Vassiliev with a novel and intriguing approach that is radically different from previous invariants. Rather than being defined in terms of the properties of individual knots in ordinary three-dimensional space, Vassiliev's invariants are based on topological properties of an abstract "space" whose "points" are knots. At first glance, Vassiliev's invariants seemed to have no connection to more familiar invariants, but that isn't the case. At Baltimore, Joan Birman of Columbia University gave a talk describing work she did recently with her colleague Xiao-Song Lin. They proved that substituting the power series of the familiar exponential function e^x, that is $(1+x+x^2/2+x^3/6\ldots)$, for the variable in the Jones polynomial yields a power series whose coefficients are Vassiliev's invariants. That remarkable connection suggests that many more tangles remain to be profitably combed out of the burgeoning theory of knots. ■ **Barry Cipra**

*Joint meetings of the American Mathematical Society and the Mathematical Association of America, held 6-11 January 1992.