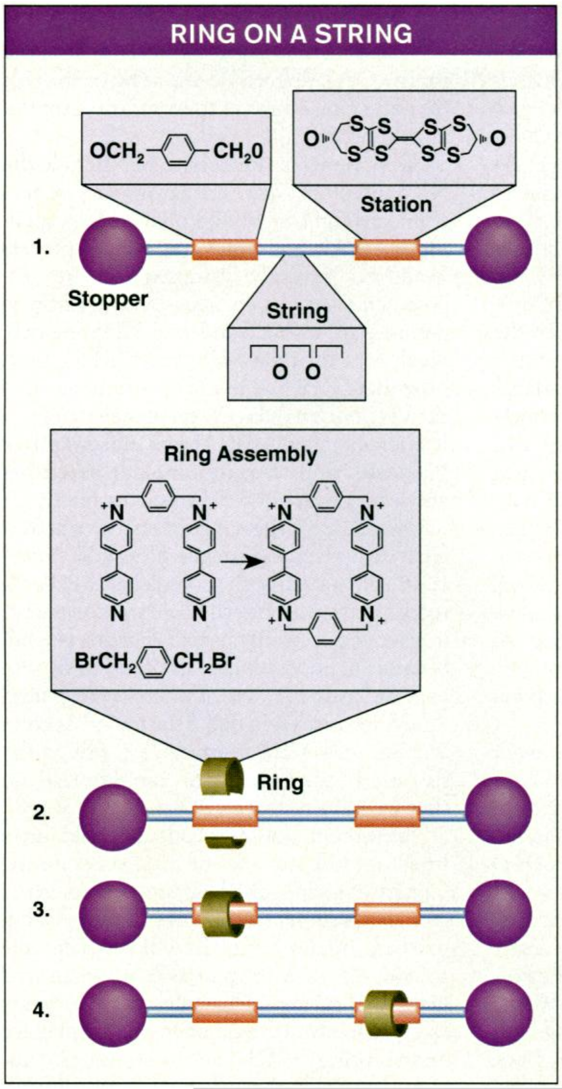
Will Future Computers Be All Wet?

Could be–if visionaries in the growing field of supramolecular chemistry continue to have their way with molecules that self-assemble in solution

Consider the molecule known as a 12-crown-4 ether. This ring of 4 oxygen and 8 carbon atoms may seem simple, but its straightforward design conceals acrobatic talents worthy of the circus. When a lithium ion comes floating by, for example, the crown ether will pull it in and trap it in the ether's central cavity. But because the cavity has just the right charge and shape to recognize only a narrowly defined set of atoms, other ions—even closely related ones such as sodium or potassium—go right on by. And that doesn't exhaust the molecule's repertoire of tricks. Remarkably, if the components of the ring are mixed with a solution containing lithium ions, the parts spontaneously assemble around the metal ion, forming the complete ring.



L. OWENS

Closing the deal. The formation of a supramolecular switch (1) depends on the self-assembly of two paraquat units into a ring on a polyether "string" (2). The ring can then shuttle back and forth between two different "stations" on the ring (3 and 4).

These two qualities—recognition and self-assembly—are providing the basis for a very hot field called supramolecular chemistry. Researchers around the world are working on a growing menagerie of self-assembling chemical structures like crown ethers, turning them into highly selective sensors and sieves (see box on next page), synthetic enzymes, and light-harvesting and energy-transfer units for use in artificial photosynthesis. And the list of potential applications goes on. Chemists are beginning to exploit the properties of these supermolecules to make tiny devices: molecular switches, diodes, and transistors, as well as molecular wires to join them together. And the most fantastic promise embodied in that work is that, if all these diminutive devices could be packaged into "wetware," it might one day be possible to construct an entire computer based on supermolecules interacting on thin film supports.

The field is growing very rapidly now, but its roots go back to the 1970s, when Jean-Marie Lehn of the University Louis Pasteur in Strasbourg, France, began probing the properties of supermolecules—work for which he shared the Nobel Prize in chemistry in 1987. Lehn points out that while most ordinary chemistry involves the making and breaking of covalent (electron-sharing) bonds within molecules, supramolecular chemistry goes beyond that arena to manipulate interactions of entire molecules. He calls supramolecular chemistry "the designed chemistry of intermolecular bonds."

As the example of the 12-crown-4 ether suggests, the principles of supramolecular chemistry are present in many natural systems. Every time an enzyme or an antibody binds to its unique substrate, for instance, molecular recognition is on display. Similarly, the construction of the geometrically ornate tobacco mosaic virus from its constituent parts shows self-assembly at its most intricate. And this leads Fraser Stoddart of Birmingham University in England, a leader in the effort to design supermolecules, to argue that the essential requirement for the supramolecular chemist is to follow nature's lead. "Structurally large and highly ordered supramolecular arrays [can be built] from relatively small subunits often without the need for an apparent internal influence," says Stoddart.

Following nature's lead

Stoddart's team is following that strategy in its race to build molecular devices that could act as switches in the imagined molecular computers of the future. And they've already made considerable progress in that direction, building supermolecules that include catenanes (two or more cyclic molecules joined like links in a chain) and rotaxanes (each of which is a molecular "ring on a string"). In constructing these chemical Tinker-Toy sets, the aim of Stoddart's group was to find cheap, readily available starting materials that could be built molecule-by-molecule via recognition and self-assembly into complex structures with novel functions.

Quite early on in their work, they decided that one promising path was to build up chemical components into ring systems with functional groups attached. One such system is turning out to be an intriguing supramolecular switch that has the form of a movable ring on a string. The researchers knew that the positive ion of one of the simplest bipyridinium salts (more commonly known as the pesticide paraquat) could identify and bind electron-rich, and hence residually negative, aromatic units in a molecule. If the right starting materials were used, for example a molecule composed of two paraquat subunits and a molecule that can react with it, they might assemble to form a ring under the templating effect of an aromatic unit, such as the hydroquinol chemical group on a molecular string (see illustration).

The researchers mixed the components of the ring—bis(pyridinium) bis(hexafluorophosphate), which is the paraquat part of the ring, and 1,4-bis (bromomethyl) benzene, the reactive molecule—with a polyether "string" in a suitable solvent at room temperature. Under those conditions, the molecule self-assembles: The ring components wrap around one of the hydroquinol recognition sites,

Chemists Work Their Way From Pores to Riches

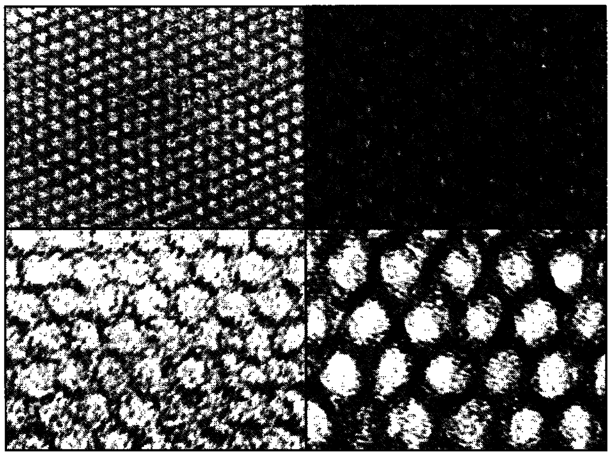
Molecular sieves don't make it into a whole lot of dinner conversations. Yet the labyrinthine interiors of these natural and synthetic materials can play host to so much important chemistry that they are among the hottest industrial materials around. Now, a team of scientists from the Mobil Research and Development Corp. in New Jersey hopes to marry two hot fields by using molecular self-assembly (key to the rapidly emerging field of supramolecular chemistry) to enter the big-bucks molecular sieve market.

That market already includes oil companies, which use tons of zeolites—the most commercially successful class of molecular sieves—to "crack" larger petroleum molecules into gasoline and make petrochemicals for paints and polymers. Detergent manufacturers use piles of the stuff as water softening and lathering agents. Molecular sieves are also used to clean up hazardous nuclear sites, including Chernobyl and Three Mile Island.

The key to this variety is that molecular sieves are highly selective. By choosing a sieve with the right pore size, investigators can target their chemistry to a specific substance. Most commmercially available sieves—whether from naturally occurring clays or from chemical engineers' vats—have pore sizes of less than 10 angstroms—enough for several water molecules to squeeze through. But the Mobil team is exploiting self-assembly to come up with a strategy for making "mesoporous" molecular sieves with pores ranging from 15 angstroms to 100 angstroms or more. "It is the first time I am aware of where we have materials in which we can continuously tune the pore diameter over wide ranges," remarks David Olson, a group leader at Mobil's Central Research Laboratory in Princeton. He and his Mobil colleagues aren't willing to say much about specific uses of the new materials, but other researchers say the more capacious pores should enable these materials to play host to biological molecules, broadening the molecular sieve market even further.

Others are impressed. A poster from the Mobil team was the talk of the International Zeolite Conference in Montreal last summer. The researchers went on to publish a brief account of the work last October in *Nature* and a more extended write-up in the 30 December *Journal of the American Chemical Society*. Because the Mobil researchers can tune both the size and geometry of the pores, their work is "a tour de force," says molecular sieve chemist Galen Stucky of the University of California, Santa Barbara.

The new design-to-order sieves have been designated MCM-41, with MCM standing for Mobil Composition of Matter. The crucial strategy for making MCM-41 sieves—as in supramolecular chemistry generally—is finding molecular subunits that will construct the desired form without much external intervention. A typical MCM-41 synthesis starts with a solution containing alumina and silicate molecules (which network into the sieves' hard skeleton) and surfactant molecules (which the researchers believe serve as an organic scaffolding).


Holy ground. Electron micrographs showing MCM-41 sieves with pore sizes of *(beginning at upper left and going clockwise)* 20, 40, 65, and 100 angstroms.

Frequently in supramolecular chemistry, it's easier to see the result than to understand the process that led there. But the Mobil team has gathered evidence leading them to the following scenario: The surfactant molecules, with their long, water-avoiding hydrocarbon tails and polar, water-soluble heads, huddle into rosette-like assemblies with the polar heads on the outside. The rosettes then stack up like coins to form rods, which arrange in hexagonal honeycombs.

And that isn't the end of the self-construction. The honeycomb-like organic structures serve as templates on which the inorganic silicate and/or alumina adhere and bond into sieves. A final heating step burns off the surfactant, leaving hard, three-dimensional frameworks. The Mobil researchers can easily tailor the pore sizes and overall sieve structures since changes in the solution temperature, surfactant concentration, additives, and other factors influence the architecture of the templates. In addition to the honeycomb structures, the researchers have also made cubic sieves and lamellar ones made up of sheets that pile up like paper.

In spite of the Mobil researchers' tight lips about applications, Stucky predicts: "The main theme will be doing biotechnology in these pores." MCM-41 has spaces large enough to host enzymes that could do chemistry on other biomolecules, perhaps drug precursors. MCM-41 sieves might also serve as selective filters that let through or exclude only specific molecules, such as those found in blood and other biological fluids. It took a while for Stucky to finish his litany of possibilities. But his summation was short and sweet: "This is a major breakthrough."

–Ivan Amato

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forming a rotaxane ring on a polyether string. Completing the picture are two bulky groups attached to the ends of the string, which function to prevent the system from falling apart. "That these molecules self-assemble is quite amazing," enthuses team member Neil Spencer. Indeed it is. But, in fact, the components of the rotaxane molecule are chosen so that they have no choice: They cannot fit together any other way.

The self-assembly of the rotaxane ring on the polyether string inspires a kind of awe at the natural world—and the ingenuity of Stoddart's team. But that isn't the property that endows the system with its potential use. The possible utility of the supermolecule stems from the fact that the positively charged ring has equal affinity for the two negatively charged hydroquinol groups on the string and shuttles back and forth between these "stations" several hundred times per second at room temperature.

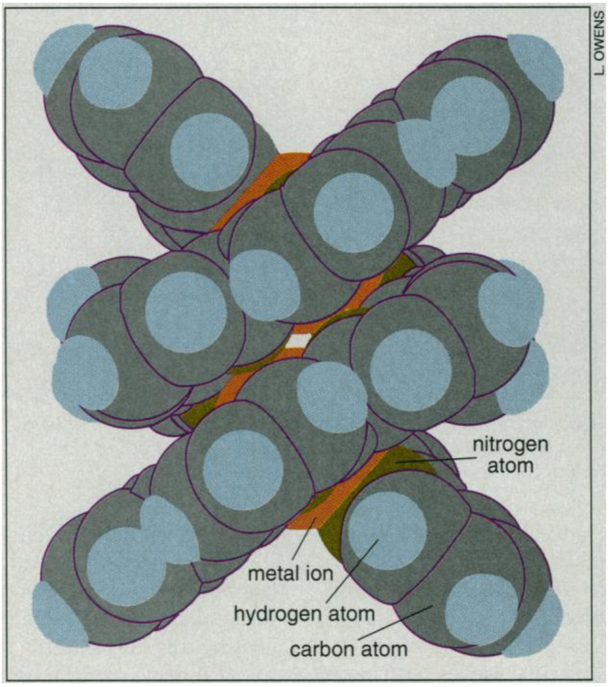
Stoddart's team reasoned that if the shuttling could be controlled using an external input, such as a light source or an applied voltage, then the rotaxane structure could be used to store information—with each position of the ring corresponding to a unique information state. Furthermore, if there were two chemically different stations on the thread, the affinity of the ring for each station might be induced to change under varying conditions. And if the conditions could be manipulated efficiently, the ring would then be forced to shuttle between stations on command, making the informationstoring properties of the ring useful in just the way that the "on" and "off" states of a transistor are.

Writing in the November issue of the organic chemistry journal *Synlett*, Stoddart's group describes how they have recently taken one additional step toward this tantalizing goal. To the original string, they have added another station, a derivative of the electron-rich, sulfur-containing molecule known as tetrathiafulvalene, TTF. Their hope was that the ring would preferentially occupy this station depending on the solvent. And, in fact, the researchers found that in acetone (Me_2CO) the hydroquinol sites were occupied, while in dimethyl sulfoxide (Me_2SO) the TTF derivative site is occupied. According to Stoddart, this is just the sort of affinity change that bodes well for controlling the shuttle's position by electrochemical means: "We want to package the shuttles together and introduce them into an air/water interface so that perhaps hundreds of thousands would be present and not just randomly saying their own thing" as is the case with a single shuttle.

Impressive though these developments are, Stoddart's supermolecules are still a long way from being turned into commercially useful switching devices. How long will it take? Stoddart emphasizes that the field is so new, and the continuing research so basic, that it is not possible to pinpoint a date. "We are walking blindfolded," he says, although he hopes his team will be in "a very strong position" for total control of the shuttle by the end of 1993. Once they have reached that goal, the next step will be to investigate the behavior of large numbers of these molecules and then build interconnected arrays that might one day be used in molecular information storage, processing, and retrieval devices.

Before such a goal could be attained, however, it would be necessary to interconnect all the supramolecular transistors, capacitors, and diodes with the wetware equivalent of wires. That is a need that Lehn's team at the University Louis Pasteur is hoping to fill. They are working on possible precursors of molecular wires called caroviologens: long, chain-like conducting polymers with charged pyridinium groups acting as terminals at each end.

Incorporating the caroviologens across the membrane of a lipid vesicle (analogous to a cell membrane in solution), the researchers have been able to study how easy it is for electrons to flow between the terminals of their "molecular wire." According to Lehn, measurements made using a reducing phase outside the vesicle and an oxidizing phase inside indicate that electron conduction is indeed possible in this supramolecular-scale system. He adds that varying the length of the "wire" might influence the efficiency of the electron transfer. He also believes that using an alternative molecule such as a carotenoid might result in "one-way" electron transfer, which would enable the wires to act as molecular diodes.



L. OWENS

DNA Not! Around the templates provided by metal ions, organic molecules called oligopyridines form a double helix that is reminiscent of DNA.

Going beyond nature

Most of the workers who are toiling in the vineyard of supramolecular chemistry are heeding Stoddart's axiom of following the leads provided by nature. But some researchers are beginning to suspect that in the future it will be essential to go beyond that approach and understand how to design supermolecules from scratch—molecules that even nature hasn't yet come up with. One way to get a handle on that way of doing things is to understand the topology of supermolecules, and that is the subject that lately has preoccupied Edwin Constable of Cambridge University. Constable is puzzling out the three-dimensional shapes of supramolecular components and the relations among them, which may yield important clues to the processes behind recognition and self assembly, clues that will later be taken up by chemists solving specific practical problems.

Recently, Constable and his colleagues used metal ions as templates to construct helical organic molecules. Lehn and Jean-Pierre Sauvage at the Institute Le Bel in Strasbourg have also studied related compounds with similar aims. Constable's helical structures, known by such convoluted names as 2,2:6',2'':6'',2''':6''',2''''-quinquepyridine complexes, with five pyridine units and the related sexipyridines (six pyridines) help to demonstrate how design can influence molecular topology. Constable argues that "relying on statistics and chance for molecular threads to adopt the correct conformations [to form molecular] trefoil knots would not be a fruitful approach."

Instead of relying on chance, Constable argues that making supermolecules has to be approached at the level of the molecular units involved. Careful choice of components, he thinks, will make possible self-assembly into predictable structures. As an example, the Constable group's so-called oligopyridines will adopt interesting conformations depending on the number of pyridines that are incorporated into the design under the templating influence of metal ions. Around nickel ions, for instance, sexipyridine will form a double helical structure reminiscent of DNA. Each pyridine donates its spare electron pair to the positively charged nickels resulting in a stable arrangement. Thus choosing the components leads to predictable topology of the supermolecule. This can then provide insights into how more complex and useful structures might be constructed.

Constable's work is not immediately intended to produce commercially viable techniques. Instead, he is working out general principles that might later be used by others to formulate useful commodities. And even the work of Stoddart and Lehn, which is inherently more practical, is not yet yielding the kinds of switches and wires that supramolecular chemists dream of. Nonetheless, the results already obtained in this rapidly expanding field are very encouraging to its practitioners. Encouraging enough, in fact, that the dream of a molecular computer seems more likely with each passing day.

–David Bradley

David Bradley is a science writer based in Cambridge, England.

Additional Readings

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