



## How Far Can We Push Chemical Self-Assembly?

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Most physical scientists nowadays focus on uncovering nature's mysteries; chemists build things. There is no synthetic astronomy or synthetic physics, at least for now. But chemists thrive on finding creative new ways to assemble molecules. For the last 100 years, they have done that mostly by making and breaking the strong covalent bonds that form when atoms share electrons. Using that trick, they have learned to combine as many as 1000 atoms into essentially any molecular configuration they please.

Impressive as it is, this level of complexity pales in comparison to what nature flaunts all around us. Everything from cells to cedar trees is knit together using a myriad of weaker links between small molecules. These weak interactions, such as hydrogen bonds, van der Waals forces, and  $\pi$ - $\pi$  interactions, govern the assembly of everything from DNA in its famous double helix to the bonding of  $H_2O$  molecules in liquid water. More than just riding herd on molecules, such subtle forces make it possible for structures to assemble themselves into an ever more complex hierarchy. Lipids coalesce to form cell membranes. Cells organize to form tissues. Tissues combine to create organisms. Today, chemists can't approach the complexity of what nature makes look routine. Will they ever learn to make complex structures that self-assemble?

Well, they've made a start. Over the past 3 decades, chemists have made key strides in learning the fundamental rules of noncovalent bonding. Among these rules: *Like prefers like*. We see this in hydrophobic and hydrophilic interactions that propel lipid molecules in water to corral together to form the

two-layer membranes that serve as the coatings surrounding cells. They bunch their oily tails together to avoid any interaction with water and leave their more polar head groups facing out into the liquid. Another rule: *Self-assembly is governed by energetically favorable reactions*. Leave the right component molecules alone, and they will assemble themselves



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into complex ordered structures.

Chemists have learned to take advantage of these and other rules to design self-assembling systems with a modest degree of complexity. Drug-carrying liposomes, made with lipid bilayers resembling those in cells, are used commercially to ferry drugs to cancerous tissues in patients. And self-assembled molecules called rotaxanes, which can act as molecular switches that oscillate back and forth between two stable states, hold promise as switches in future molecular-based computers.

But the need for increased complexity is growing, driven by the miniaturization of computer circuitry and the rise of nanotechnology. As features on computer chips continue to shrink, the cost of manufacturing these ever-smaller components is skyrocketing. Right now, companies make them by whittling materials down to the desired size. At some point, however, it will become cheaper to design and build them chemically from the bottom up.

Self-assembly is also the only practical approach for building a wide variety of nanostructures. Making sure the components assemble themselves correctly, however, is not an easy task. Because the forces at work are so small, self-assembling molecules can get trapped in undesirable conformations, making defects all but impossible to avoid. Any new system that relies on self-assembly must be able either to tolerate those defects or repair them. Again, biology offers an example in DNA. When enzymes copy DNA strands dur-

ing cell division, they invariably make mistakes—occasionally inserting an A when they should have inserted a T, for example. Some of those mistakes get by, but most are caught by DNA-repair enzymes that scan the newly synthesized strands and correct copying errors.

Strategies like that won't be easy for chemists to emulate. But if they want to make complex, ordered structures from the ground up, they'll have to get used to thinking a bit more like nature.

—ROBERT F. SERVICE

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