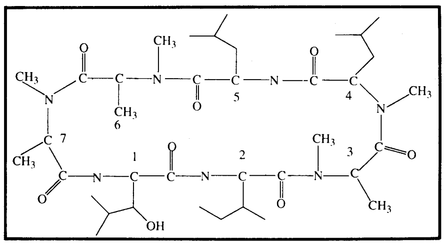
To make the scheme workable, computer scientist Russ Miller of SUNY-Buffalo and his co-workers developed algorithms specially designed to run efficiently on computers consisting of large numbers of parallel processors, which operate simultaneously while working on different pieces of a problem.

The result was a "shake-and-bake" strategy, which starts with "trial" molecules consisting of random arrangements of atoms, subject only to chemical constraints. "You essentially toss the atoms in a shoebox with enough chemical knowledge to make sure the arrangement makes chemical sense," Miller says.

The computer calculates the phases associated with these atomic positions. Then it randomly perturbs the resulting phases in such a way as to provide a slightly lower value for Hauptman's formula, and computes the new positions of the atoms. The atoms, in turn, move slightly, leading to another calculation of the phases, and so on. The computer may go through as many as 200 such phase-position cycles for each initial arrangement of atoms.

In April, the researchers used this technique to solve the structure of the antibiotic gramicidin-A, which contains 317 atoms, excluding hydrogen. They accomplished in a matter of weeks what had originally taken David Langs, a senior research scientist at the Medical Foundation of Buffalo, 10 years to work out using other methods.



Medical Foundation of Buffalo

Positions of 52 atoms (excluding hydrogen) in one of a pair of molecules having the same formula but two different conformations in a crystal.

Last month, having a few days of free time between projects, Miller came to Langs asking for crystallographic data on which to test his newly refined version of the structure-determination algorithm. Langs, highly skeptical that anything would come of it, suggested finding the structure of a molecule that had long stymied Russian scientists. Over two years, Langs himself had tried half a million possibilities with no success.

"I put the data into the program before I went to bed at night, and the next morning I looked through the results," Miller says. One of the 64 random arrangements of atoms with which he had started gave a value for Hauptman's formula that was significantly lower than the others, indicating the right answer.

This particular trial result provided sufficient information for Langs to work out the details of the molecule's structure in only a few hours (see diagram). Out of the millions of possible atomic arrangements, Miller's algorithm had converged on the correct structure with remarkable efficiency. It was like looking for a needle in a haystack with the advantage of having a magnet on hand.

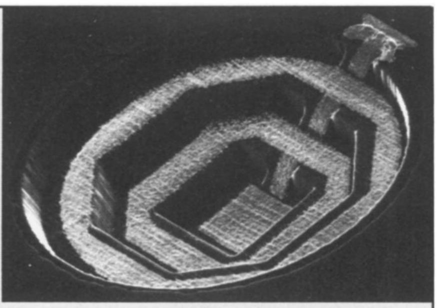
Subsequent tests involving 640 random atomic arrangements produced two additional results that converged to the same, correct molecular structure. "I had been lucky," Miller says. "The first one happened to come out in the first batch of 64." Each set of 64 trials took about 1.5 hours on a multiprocessor computer known as the CM-5 Connection Machine.

After this initial success, Langs provided Miller with a second unknown structure related to the first but deemed more difficult to solve. "We gave it a shot, and the answer emerged just as rapidly," Miller says.

"It was quite remarkable to us. It made believers out of a lot of people," says Jane Griffin, head of molecular biophysics at the Medical Foundation of Buffalo. "But we still have a lot of research to do in extending [the method], seeing how high the resolution of the data has to be, and solving a variety of other problems."

– I. Peterson

Laser process shapes microscopic parts



Bloomstein, Ehrlich/MIT

Laser-induced chemistry first shaped the micron dimensions of this multilevel silicon "hot tub," then deposited a pattern of metal (white) inside it.

By combining advances in lasers, chemistry, and computer-aided design and manufacturing techniques, scientists have scaled machining down to microscopic proportions.

This new technology makes possible machined pieces one or two orders of magnitude tinier than the finest parts crafted by watchmakers, says Daniel J. Ehrlich, a physicist at the MIT Lincoln Laboratory in Lexington, Mass. Ehrlich and Theodore M. Bloomstein, a graduate student in electrical engineering at MIT, describe their three-dimensional micromachining process in the Aug. 10 Applied Physics Letters.

Using this process, "you can do almost anything and make any shape both along the [surface] and the depth," comments Howard R. Schlossberg, a physicist with the Air Force Office of Scientific Research in Washington, D.C.

To make their three-dimensional designs, Ehrlich and Bloomstein rely on a computer to guide a laser as it scans a piece of silicon. First they use computer-aided design and manufacturing (CAD/CAM) software to draw and scale a part. A second program slices that computer blueprint into many parallel planes. The computer notes the coordinates of the part in a given plane and then directs the laser to etch plane by plane, leaving silicon only at those coordinates.

For shaping, Ehrlich and Bloomstein place a newly cleaned silicon crystal into a vacuum chamber and blow chlorine through the chamber. The instant the laser hits the silicon surface, it heats that spot to about silicon's melting point. The heated silicon combines with chlorine atoms hitting it and escapes as a silicon chloride gas. "Among reactions that occur on a surface, it's among the very fastest," Ehrlich says. The researchers then pump out this gas.

The computer can direct the laser to any 1-micron location on a square surface 256 microns wide. The laser then etches down in 1-micron steps. It can hit up to 20,000 spots per second and moves at a rate of 20 millimeters per second. The longer the laser dwells at a spot, the more deeply it etches the silicon, enabling the researchers to shape the part in the third dimension. Higher pressures of chlorine also speed etching, Ehrlich says. In addition, varying the chlorine pressure lets the researchers control the part's final texture.

The MIT group got the idea for this process in part from recent advances in stereolithography, in which a computer-directed laser causes liquid plastic to solidify into a particular shape. "We also have begun to build [up] three-dimensional things," says Ehrlich. For example, they have used the laser and a technique called chemical vapor deposition to lay down patterns of platinum or cobalt in the newly shaped silicon.

Ehrlich expects manufacturers to use the micromachining technique to make microscopic prototype parts, molds, and stamping tools. The MIT researchers have produced plastic parts from these micromolds, and they hope to use those parts to make valves and pumps for implantable medical devices. They are also refining the technique for micromachining metals and ceramics.

– E. Pennisi