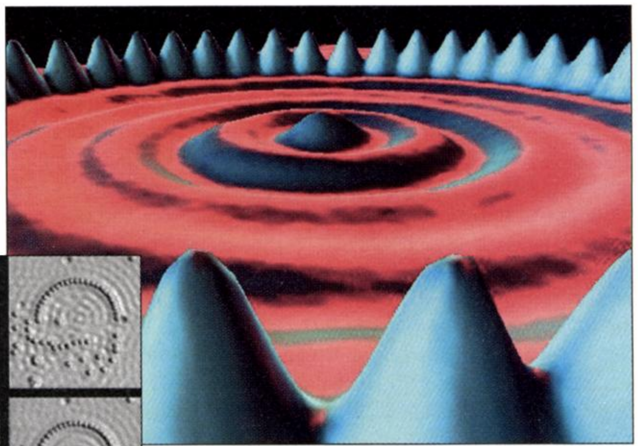
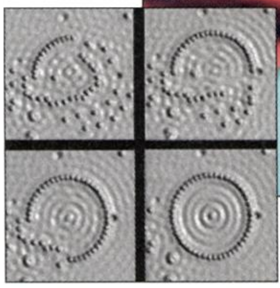
Atom-Scale Research Gets Real

Nanotechnology has spawned useful new materials and impressive technical feats. But the field's most grandiose dreams, and nightmares, remain the stuff of fiction

In September, speaking to an audience of prominent researchers and government leaders at a meeting on the future impacts of nanotechnology, Michael Crow crossed a familiar line. "How many of you have read *The Diamond Age*?" the science policy expert and vice provost of Columbia University in New York City asked his listeners. The book, by science-fiction novelist Neal Stephenson, depicts a near-future world in which advances in nanotechnology make it possible to build essentially anything from scratch, atom by atom, leaving society to sift through the cultural ramifications of limitless choices. In response to Crow's question, a few hands fluttered in the air and quickly dropped. These people, after all, were nanotechnology's practitioners—not wide-eyed dreamers.





Atomic Stonehenge. In an early nanocoup, IBM researchers rounded up 48 iron atoms to make a "quantum corral."

Crow wasn't promoting the book as a prophecy. He mentioned it, he says, to encourage researchers to think about their unique position at the dawn of a field that most in the room agreed will be a force in the coming century. But clearly his question touched a nerve. Since its inception, nanotechnology has been dominated by fiction, both unabashed hype and better grounded hope. Science-fiction writers have dreamt up lush scenarios of life with nanosized robots that do everything from building gleaming cities to reaming out clogged coronary arteries. Meanwhile, some researchers have been hard at work drawing impressive but equally fictional blueprints for arrays of tiny gears and pistons that could form the foundation of nanomachines—if anyone ever figures out how to assemble the thousands of atoms needed to build them.

This year, dystopian fiction came on the scene, as nanotech prophets of doom made bold new pronouncements of nanotechnology's potential to destroy humanity and called for either an end to research in the area or new guidelines to ensure that researchers don't accidentally wipe out life on the planet (see sidebar, p. 1526). "Nanotechnology seems to have this wonderful property of having the most extravagant favorable and unfavorable predictions," says Edward Tenner, a historian of science at Princeton University in New Jersey.

In response, many researchers at the cutting edge of dealing with matter on the near-atomic scale have become aggressively matter-of-fact, squirming at the suggestion of cornucopian nanofactories or even humbler mass-produced nanodevices. The nearby hurdles, they say, are challenge enough. "Nanotechnology is a vision, a hope to manufacture on the length scale of a few atoms," says Don Eigler of IBM's Almaden Research Center in the hills above San Jose, California. For now, he says, "nanotechnology doesn't exist."

Yet even the most hard-headed nanoscientists must admit that their minute world, by whatever name, is on the move. Advances in manipulating nanosized materials have already led to improvements in computer data storage, solar cells, and rechargeable batteries. Computer disk

NANOPROFILES

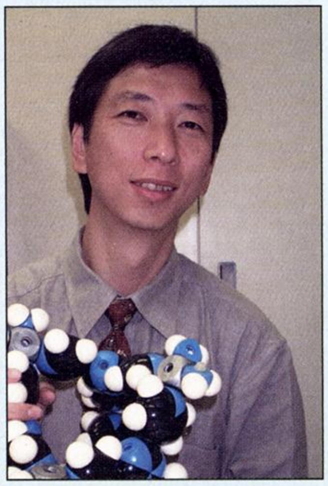
Coaxing Molecular Devices to Build Themselves

NAGOYA—When Nagoya University chemist Makoto Fujita thinks about how to store data in tiny spaces, he thinks big—about how nature handles the problem. Then he tries to emulate the answer. "A living cell is incomparably smaller than a compact disc, but its DNA carries far more information," he says. "Handling data at the DNA's molecular scale could lead to handheld supercomputers. But to do that we need more efficient ways to manipulate molecules."

Fujita and others are doing exactly that through a technique called directed self-assembly. By adroitly exploiting the chemical and electrical bonds that hold natural molecules together, they can get molecules to form desired nanometer-scale structures. This could lead to computer logic and memory devices up to 100 times smaller than their current counterparts. Self-assembled molecules might also serve as cages to hold and deliver unstable medical compounds, and as crucibles for chemical reactions.

The technique builds upon two properties of matter. One is the bonding between hydrogen atoms, which holds the two strands of DNA in its double helix. The other is the electrical attraction between positively charged organic ions and negatively charged metal ions. The organic ions are strategically placed on organic molecules, or ligands, which are like the rods of Tinkertoy sets. The metal ions are like the socketed disks that hold the rods together. Unlike Tinkertoys, however, these metal ions and ligands assemble themselves if mixed together in solution in the right proportions and under the right thermodynamic conditions.

Fujita was among those who pioneered the metal-ion technique in the early 1990s. His first



Spontaneous. Makoto Fujita shows off a self-constructing molecule.

CREDIT: (BOTTOM) D. NORMILE

drives alone—which rely on controlling the thickness of various layers of material on the nanometer scale—account for a multibillion-dollar market. The field's promise has prompted the creation of about a dozen nanotech research centers in U.S. universities alone. The European Community runs several programs in nanotechnology, including the Nano Network, which contains 18 member research centers working in nanomaterials synthesis. Japan, Singapore, China, Australia, Canada, Germany, the United Kingdom, and Russia all support nanotechnology efforts.

And there is more to come. Last month Congress approved the bulk of the Clinton Administration's request for money to launch a new National Nanotechnology Initiative. Next year the initiative will spend some $423 million on nanoscience, with more sure to follow. In Japan, nanotechnology funding is slated to jump 41% next year to $396 million. Several European countries are ramping up efforts as well.

Some U.S. experts hope that the surge in funding will carry over to bolster American research in the physical sciences as a whole. Whereas Congress is 3 years into a 5-year effort to double biomedical research funding at the National Institutes of Health, "support for physical sciences and engineering has been stagnant," says Tom Kalil, a White House specialist on the economics of technology. "We see [nanotechnology] as a way [of] increasing support for physical sciences and engineering."

Richard Smalley, a Nobel Prize–winning chemist, thinks the emerging field may even reverse the long slide in the number of new students choosing careers in science, just as the space race inspired an earlier generation. "It was Sputnik that got me into science," Smalley says. "Of all the impacts of [nanotechnology's rise], the most important impact—and one that I dearly hope will happen—will to be to get more American girls and boys interested in science."

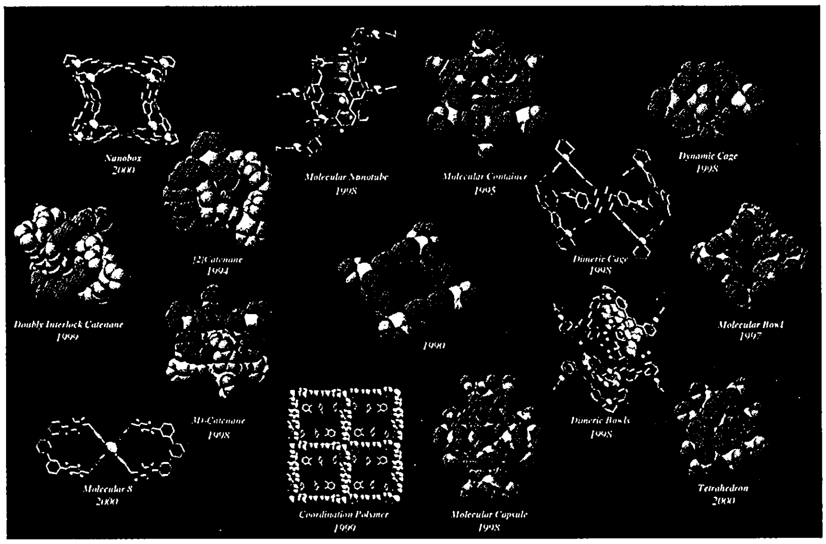
All of this activity is leading to some rather grandiose pronouncements. "This is an area that can have a huge potential payoff that can be as significant as the development of electricity or the transistor," says Kalil. And at a 1998 congressional hearing, Neal Lane, the president's adviser for science and technology and former National Science Foundation (NSF) director, stated, "If I were asked for an area of science and engineering that will most likely produce the breakthroughs of tomorrow, I would point to nanoscale science and engineering."

But however promising nanotech's future may be, transforming it from the world of fiction to reality will mean overcoming some daunting obstacles. Beyond manipulating atoms, nanoscientists must perfect ways to mass-produce nanosized objects and integrate them with the larger, human-scale systems around them. And they must do it while working in an interdisciplinary field that requires new levels of cooperation among different specialties, raising familiar challenges of herding academic cats and coaxing them to march in lockstep.

A new hammer

Of course, nanotechnology—in the guise of nanoscale materials—has already been around for a long time. For the last 100 years, tire companies have reinforced the rubber in car tires by adding nanosized carbon particles, called carbon black. And living organisms from bacteria to beetles rely on nanosized protein-based machines that do everything from whipping flagella to flexing muscles.

Today, the term "nanotechnology" refers most broadly to the use of materials with nanoscale dimensions, a size range from 1 to 100 billionths of



Zoo story. Exotic nanostructures may serve as "molecular cages" or even computers.

CREDIT: COURTESY OF M. FUJITA

construction used four simple linear ligands and four metal ions to produce square macromolecules. More recently, his group has built an eight-sided, three-dimensional structure made up of two pyramids joined at their bases. The molecule is 3 nanometers across, and the cavity is big enough to hold a C_{60} molecule, the so-called buckyball. Fujita and other researchers have also created a variety of grids, tubes, cages, and catenanes, which are rings interlocked like links of a chain. "Such structures cannot be synthesized by conventional chemical reactions, but we can very easily construct them using directed self-assembly," Fujita says.

J. P. Sauvage, a chemist at Louis Pasteur University in Strasbourg, France, has proposed using catenanes as computing devices. One ring would be mechanically fixed, allowing the second ring to rotate. If the second ring has an additional ion, it could be rotated 180 degrees back and forth in response to an adjacent electrical charge. The position of the ring would indicate the 1 and 0 of digital data.

The molecular cages can be constructed to have small openings through which atoms can enter and react with other atoms, forming molecules that are too big to escape. This arrangement, which can capture and stabilize molecules that otherwise rapidly react and disappear if free in solution, could be the basis for a drug-delivery system.

Donald Cram, a Nobel laureate in chemistry who is now retired from the University of California, Los Angeles, used such a cage to capture cyclobutadiene, a compound that briefly appears at intermediate stages of some chemical reactions but which until then had been too unstable for chemists to isolate. Julius Rebek, director of the Skaggs Institute for Chemical Biology of the Scripps Research Institute in La Jolla, California, who works on self-assembly using hydrogen atoms, explains that the characteristics of cyclobutadiene had been theoretically predicted but never confirmed. "By encapsulating the molecule, [Cram kept it] stable long enough to be characterized by nuclear magnetic resonance," he says. Aside from its value to basic research, this trick could be used to deliver drugs that are hard to stabilize.

Fujita predicts that the number of self-assembled molecules and their uses will rise rapidly in the years to come. Whereas a decade ago there were only a handful of groups working on self-assembly using metal ions, he says, "now there are dozens. The field is advancing very rapidly." —DENNIS NORMILE

Is Nanotechnology Dangerous?

The only realistic alternative I see is relinquishment: to limit development of the technologies that are too dangerous, by limiting our pursuit of certain kinds of knowledge.

Bill Joy, co-founder of Sun Microsystems, in the April issue of *Wired*.

Bill Joy is nobody's Luddite. As co-founder and chief scientist of Sun Microsystems in Palo Alto, California, he can match technophile credentials with anybody on the planet. So when he argued that research into nanotechnology and other fields should be stopped before it wipes out humanity, humanity took notice.

To the legion of chemists, physicists, and materials scientists who spend their lives trying to understand and manipulate matter at the nanoscale, Joy's warning—published in the April issue of *Wired* magazine—felt like a bucket of ice water poured over their heads. Others had raised similar concerns for decades. But Joy's status among the digerati lent his allegations new heft. His fears of nanotechnology, genetic engineering, and robotics research were broadcast worldwide by news organizations including the *Los Angeles Times* and CNN.

Other voices joined the chorus of woe. In June, a group of nanotechnology aficionados released what they called the Foresight guidelines. Like Joy, they raised the specter of nanotechnology out of control. But rather than simply calling for a halt to research, they outlined measures they said would encourage governmental oversight of nanotech's development. Such supervision, they argued, could help prevent accidental catastrophe, much as the National Institutes of Health's guidelines on recombinant DNA technology helped the emerging biotech industry avoid accidental releases of genetically modified organisms.

At first, stunned nanoscience researchers quietly shrugged off the concerns. But more recently, they've begun to fight back, arguing vehemently at meetings that what Joy and others fear is at best implausible and more likely plain wrong. "The research community needs to divorce itself from the lunatic fringe," says Steven Block, a biophysicist at Stanford University in Palo Alto.

These fears date back to the 1986 book *Engines of Creation*, by K. Eric Drexler. In it, Drexler, a theoretician and chair of a nanotech think tank called the Foresight Institute, paints a picture of utopia that will result from the coming age of nanotechnology, a time when miniature "assemblers" will run atomic-scale assembly lines, fabricating virtually any imaginable product from the ground up, be it a car, a carpet, or the steak for your grill. But Drexler also applies his vivid imagination to nanotechnology's potential downside. Of particular concern is something he dubs the "grey goo" problem, in which assemblers replicate themselves ad infinitum, consuming everything in their path, including plants, pets, and people.

In his *Wired* article, Joy admits that on the advice of scientist friends, he initially dismissed Drexler's prophesies of nanoboom and nanodoom. But last summer, he says, he learned that hypothetical pieces of futuristic tiny machines were falling into place. One component of such assemblers—molecule-sized electronic devices—was "now practical," Joy writes. Furthermore, he learned that self-replication—a feared component of nanomachines running amok—has already gone beyond biological systems: Researchers had shown that simple peptide molecules can catalyze their own reproduction. Although perhaps not around the next bend, self-reproducing nanomachines were becoming all too plausible, Joy concluded. And that spelled danger.

Horror show. Most researchers downplay fears that rampaging "nanobots" might devour the world ...

But all it really spells, Block and others say, is a flawed extrapolation of current capabilities into the future. "This has all the depth of a parking lot puddle," says Block. It's simply incorrect to make the logical leap that, just because simple molecules can reproduce, scientists and engineers will be able to construct complex nanomachines that do the same thing. "Nobody has a clue how to build a nanoassembler, much less get one to reproduce," Block says. Biological systems, of course, reproduce. But they are both far larger

a meter, or nanometers. Because this range includes everything from collections of a few atoms to those protein-based motors, researchers in chemistry, physics, materials science, and molecular biology all lay stake to some territory in the field. That tends to make nanotechnology a scientific Rorschach blot: What it includes depends on whom you ask.

"Nanotechnology is a wonderful umbrella term that takes into account many things that we were doing before some very helpful tools came along," says William Tolles, a nanotechnology consultant for the U.S. Department of Defense. "To a 5-year-old with a hammer, the world looks like a nail," adds Lester Lave, an economist at Carnegie Mellon University in Pittsburgh, who studies the development of technology. "Nanotechnology is a hammer, and nanotechnologists are looking around to see what they can hit with it."

The development of that hammer was launched by a breakthrough in manipulating atoms back in the early 1980s. In 1982, physicists Heinrich Rohrer and Gerd Binnig of IBM's Zurich Research Laboratory in Switzerland created a new type of microscope, called a scanning tunneling microscope (STM), that is capable of imaging individual atoms. By tracking the changes in a tiny electrical current from an ultrasharp tip to atoms on a surface, Binnig and Rohrer's STM enabled researchers, essentially, to feel their way along a surface at the atomic level and create a computerized image of it atom by atom.

Other imaging tools followed close behind. In 1985, Binnig teamed up with Calvin Quate, an electrical engineer at Stanford University in Palo Alto, California, to make an atomic force microscope, which enabled them to image surfaces that do not conduct electricity. And since then, versions of these microscopes have been developed to pinpoint atoms' magnetic and chemical signatures.

It wasn't long before researchers used their new tools to jump from imaging atoms to manipulating them. In 1990, Eigler and Erhard Schweizer, also of IBM's

CREDITS: (LEFT TO RIGHT) DEREK LEA; THE KOBAL COLLECTION than the nanoscale and fantastically complex, with separate systems to store and copy genetic information, produce energy, assemble proteins, transport nutrients, and so on. Viruses, by contrast, are nanosized, points out Viola Vogel, a nanoscientist at the University of Washington, Seattle. But they can reproduce only by co-opting the machinery of living cells. "Even nature did not make a nanoscale structure that can self-replicate," she says.

Richard Smalley, a Nobel Prize–winning chemist at Rice University in Houston, Texas, says that there are several good reasons to believe that nanomachines of the sort imagined by Drexler and company can never be made. "To put it bluntly, I think it's impossible," Smalley says. As he sees it, the idea of little machines that grab atoms and assemble them into desired arrangements suffers from three faults. First, he says, it's wrong to think you can just manipulate an individual atom without handling the ones around it as well. "The essence of chemistry is missing here. Chemistry is not just sticking one atom in one place and then going and grabbing another. Chemistry is the concerted motion of at least 10 atoms." That means to move that one atom where you want it, you'll need 10 nanosized appendages to handle it along with all of its neighbors.

... but Bill Joy says it's no laughing matter.

Which raises the second problem—what Smalley calls the "fat fingers" problem. A nanometer is just the width of eight oxygen atoms. So even if you're trying to build something hundreds of nanometers in size, "there's just not enough room" in that space to fit those 10 fingers along with everything they are trying to manipulate. Finally, there's the "sticky fingers" problem: Even if you could wedge all those little claspers in there with their atomic cargo, you'd have to get them to release those atoms on command. "My advice is, don't worry about self-replicating nanobots," says Smalley. "It's not real now and will never be in the future."

In an e-mail exchange, Joy replies that he agrees that at the moment the task of making nanobots seems implausible. "No one denies it's beyond the state of the art today, but many people see that this isn't sufficient, in an era of such rapid progress, to allay our concerns." Twenty or 30 years in the future, he argues, some combination of a chemical self-assembly process and a bit of directed placement of other atoms could create synthetic organisms that prey on cells just as viruses do. And although researchers may raise objections to specific schemes for making nanobots, "where is the reasoned argument that says this is impossible?" Joy asks. "Must we have a demonstration of the danger—a grey goo accident—before we act?"

But this focus on what is possible is beside the point, says Irwin Feller, who directs the Institute for Policy Research and Evaluation at Pennsylvania State University, University Park. "All things may be possible," Feller says. "But society will not place equal value on all things." Or equal concern, for that matter, if the things are considered wildly improbable.

Which is not to say there are not reasons to be concerned about nanotechnology. At a meeting sponsored by the National Science Foundation in September, representatives from the research community, think tanks, and government funding agencies huddled to discuss emerging concerns for the field. Rather than nanobots, the greatest issues were social: Is the educational system up to the task of training enough nanotech workers? Could nanoscience's progress in areas such as electronics undermine traditional businesses on which thousands of jobs depend? Could the decreasing cost of tools for doing nanoscience and molecular biology make it easier for terrorists or other small groups to engineer dangerous microbes? Such concerns, the researchers concluded, are very real indeed.

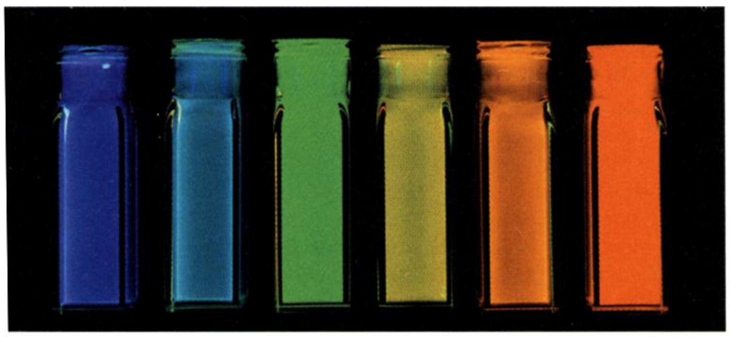
But that wasn't all. The biggest problem nanotechnology could face down the road is public acceptance, said Richard Klausner, head of the National Cancer Institute. Klausner wasn't worried about nanobots. Rather, he argued that nanoscience is exploring numerous revolutionary medical applications, such as creating implantable sensors to watch for the signature molecules of cancer. But unless patients are aware of the development of such tools beforehand, many of them may balk at having their bodies invaded by technology.

To better understand such concerns ahead of time, researchers need to involve outsiders in the development process, much as AIDS activists helped set priorities for research on AIDS drugs, says Klausner. "I think that didn't happen very effectively over the last 10 years with genetically modified organisms," he adds. And that's a danger that nanotechnology developers would like to avoid.

–R.F.S.

CREDITS: (TOP TO BOTTOM) OLIVER LAUDE/LIAISON AGENCY; FELICE FRANKEL

Almaden Research Center, used an STM to spell out "IBM" with 35 xenon atoms atop a nickel surface. It was the first time scientists had built something by manipulating individual atoms. Since then, Eigler and colleagues have gone on to build a series of atomic-scale corrals that reveal the wavelike nature of atoms and their electrons for all to see. "Seeing the electrons in their quantum state seems to have had a larger psychological effect than the bare bones of the research itself," Eigler says.



Bright idea. Fluorescent dyes made from nanoscale semiconductors show promise as biological tracers.

Part of that psychological effect lay in convincing researchers that they could build structures an atom at a time. It's an idea that continues to spread. Last year, Wilson Ho, a chemist and physicist at the University of California, Irvine, showed that he could use an STM to help forge chemical bonds between iron atoms and carbon monoxide molecules. Other researchers have used similar techniques to alter the chemistry of silicon atoms on a surface, transforming them into a key component of a transistor.

Early advances have gone beyond manipulating atoms. Groundbreaking work in materials synthesis has given researchers the ability to control the size and shape of a wide variety of materials at the nanoscale. Along the way, researchers discovered that in many cases the large surface-to-volume ratio of nanoscale materials gives them unique characteristics not shared by their bulk-sized cousins. Nanosized crystallites made from semiconductors such as cadmium selenide, for example, fluoresce in different colors of light as they change sizes. That's already made them a hot property for use as fluorescent "dyes" in biology experiments, and several companies are now racing to commercialize the technology.

The large surface area of nanoparticles also makes them ideal catalysts, whose surface atoms orchestrate chemical reactions. Whereas bulk gold, for example, is unreactive at room temperature, 3- to 5-nanometer gold particles can promote a number of common reactions and have already been developed commercially by a Japanese company as bathroom "odor eaters."

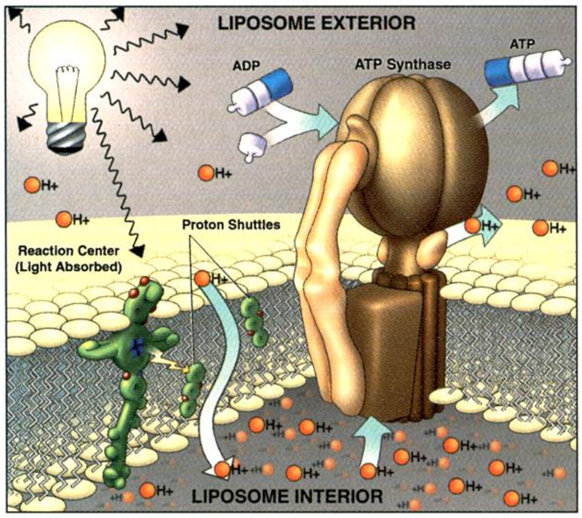
Enhanced properties on the nanoscale continue to be discovered. A number of companies are experimenting with spiking common plastics with nanosized particles in order to bolster properties such as strength and impact resistance. Nanosized probes are being developed to detect biological weapons such as anthrax. And carbon nanotubes—

Powering the Nanoworld

Whereas most scientists who long to produce nanoscale machines might look to Henry Ford for inspiration, Devens Gust seems to have his sights set on John D. Rockefeller. Today, researchers are making rudimentary nanomachines by harnessing biological motor proteins—such as those involved in muscle contraction—and plunking them down on surfaces in hopes of getting them to do some new types of work. That work takes energy. "If you're going to do this, you will need fuel," says Gust, a chemist at Arizona State University in Tempe. And like Rockefeller, whose Standard Oil provided the juice that launched Ford's automotive revolution, Gust is ready to prime the pumps.

Gust and a handful of colleagues have built tiny refineries that convert the energy in sunlight to chemical fuel. The fuel in this case is adenosine triphosphate (ATP), the same energy-rich molecule that powers chemical reactions inside cells. At last August's meeting of the American Chemical Society (ACS) in Washington, D.C., Gust reported that he and his colleagues had collaborated with other groups to run their protein-based molecular machines on little more than sunlight. "They're like GM [General Motors] and Ford, and we're like Exxon," Gust says.

Gust didn't start out to make the world's smallest gas stations. For much of the past 15 years, he has worked with Arizona State colleagues Thomas and Ana Moore and numerous students to mimic nature's ability to harvest light energy—an ability on which nearly all life depends either directly or indirectly. In 1997, Gust and the Moores reported in *Nature* that they had developed a unique photosynthesis mimic inside the protected confines of liposomes, spherical membranes made from two layers of fatty lipid molecules. Spanning those lipid membranes are three-part molecules called artificial reaction centers, after the apparatus in chlorophyll that allows plants to absorb sunlight and put that energy to work. In this case, a square-shaped porphyrin group absorbs light, which kicks an electron out of its normal ground state and into a higher energy level, leaving behind a positively charged electron vacancy called a hole. The electron and hole are then snapped up by a pair of chemical groups in the reaction centers, separating the charges and creating a chemical potential. In a multistep process, the electron-grabbing molecule then uses this charge separation to shuttle protons from the outside to the inside of the liposome.



Power plant. Molecules embedded in a membrane use light to generate energy-rich ATP.

Light-harvesting bacteria and plants use a similar buildup of protons and a protein called ATP synthase to generate ATP. And following nature's lead, in another *Nature* paper in 1998, the Arizona State researchers showed that they could incorporate ATP synthase proteins inside their liposomes and generate ATP. As the protons pass through the ATP synthase molecule to the outside of the liposome, they cause the protein to spin, a mechanical motion that helps create ATP, which is dumped outside the liposome.

That set the stage for powering nanotech devices. One such set of devices—nanopropellers—is being developed by Carlo Montemagno of Cornell University in Ithaca, New York, and is reported on page 1555 of this issue. Montemagno and his colleagues also use ATP synthase, which harbors a tiny shaft that spins inside a cylinder. But in this case they anchor copies of the protein rotor on surfaces. They then fuse tiny metal bars to the top of the shaft, creating what looks like a nanoscale version of a helicopter blade that rotates when it's fed ATP.

To set these minichoppers spinning, Montemagno and his colleagues normally just spike a solution by covering them with ATP. But if nanomachines are ever to have a more independent future, researchers will need simpler ways of providing them with energy. So Gust recently teamed up with Montemagno to supply the ATP-generating liposomes. By merely adding them to the nanocopter solution and then shining light on them, the researchers showed that they could set the blades spinning. Michael Therien, a chemist at the University of Pennsylvania in Philadelphia, says he's impressed with the work. "It's a first step to a purely engineered system" of nanomachines that can work without human intervention, he says.

Gust has also begun teaming up with Viola Vogel and colleagues at the University of Washington, Seattle, to help power a series of nanoshuttles that also make use of ATP-driven biological motors to do the work. Finally, Gust's team has adapted its artificial photosynthesis scheme to do what plants do best: convert CO_2 into more complex molecules. At the ACS meeting, Gust reported that his team can start with a compound called pyruvate and add the carbon from a CO_2 molecule to make oxaloacetate. Gust believes he and his team may eventually be able to coax their tiny refineries to regenerate complex hydrocarbons such as those found in gasoline from simple sunlight and CO_2. If so, nanorefineries may one day be the key to powering both the nanoworld and the world at large.

–R.F.S.

CREDIT: D. GUST/C. SLAYDEN

tiny, straw-shaped molecules a mere nanometer or so across—have been shown to conduct either like metals or semiconductors depending on their precise geometry, and they have already been incorporated into a range of electrical components such as transistors and diodes.

Reality gap

For most nanobased applications, the key to progress is straightforward: Find ways to make very fine particles or layers of material of a precise size, which, when incorporated directly into a final plastic or solar cell, all share the same electronic, optical, and mechanical properties. These simple products are already finding their way into the marketplace, and their relative ease of production might always ensure them the biggest share of the business.

Most of the buzz about nanotechnology, however, involves more sophisticated applications of nanomaterials, such as electronic devices and tiny chemical sensors. The holdup, so far, is that in most cases there's no obvious way to transform single demonstration devices into a working technology. "Nanotechnology is an area that is profoundly reductionist," says Harvard University chemist George Whitesides. "We can pick matter apart at its basic level of the atom and reassemble it." But researchers, he warns, mustn't take that ability too seriously. "We want to be sure we don't fall completely over that cliff."

Whitesides's point is that although it is possible to manipulate individual atoms, it's much harder to do it on a grand scale. In 1998, for example, researchers led by Cees Dekker at the Delft University of Technology in the Netherlands reported making the first transistor using a carbon nanotube as a key component of the device. Work since has shown that the electronic performance of such transistors can approach or even surpass that of conventional silicon transistors. "But there is a problem here," says Tom Theis, who heads physical sciences research at IBM's Thomas J. Watson Research Laboratory in Yorktown Heights, New York. When it comes to making computer chips containing millions of such devices, "it's completely unmanufacturable."

The problem of manufacturability remains nanotechnology's Achilles' heel, particularly for the much-hyped possibility of creating nanosized machines. "The technology is still almost

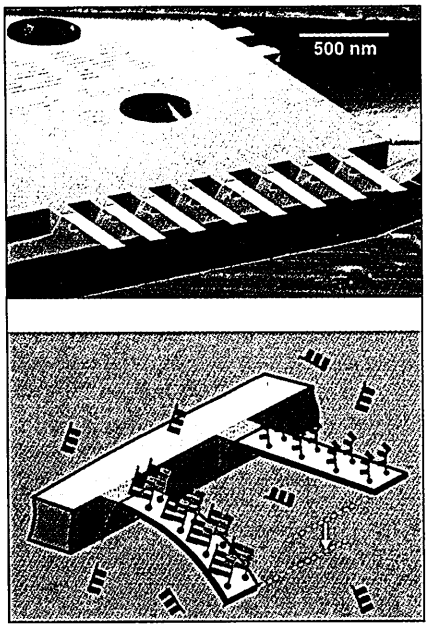
CREDIT: IBM ZURICH RESEARCH LABORATORY

Cantilever Tales

Building even the simplest nanomachines is a daunting challenge, but working models serve as springboards to grander designs. A classic example is the cantilever, an indispensable cog in the nanoworld that ushered in the scanning probe microscopy revolution. Today cantilevers, which resemble tiny diving boards, are the operating principle behind a host of experimental devices that could debut in the next decade.

Nanosized cantilevers earned their claim to fame in the mid-1980s with the invention of atomic force microscopes (AFMs). To chart the surfaces of molecules, AFMs run the tip of a cantilever across an object under investigation; intermolecular forces between probe and object tug the cantilever tip up and down over the surface, like the stylus of a record player. A reflected laser beam records this motion, and the signal can be converted into an image of the surface.

Cantilevers are proving to be more versatile than anyone imagined. Perhaps it's no surprise that a pioneering center for manipulating these tiny tools is the IBM Zurich Research Laboratory in Switzerland, the birthplace of scanning probe microscopy. "The whole field was started right there," says Naomi Halas, a specialist in applying nanotechnology to chemistry at Rice University in Houston. One master cantilever builder at IBM Zurich is James Gimzewski, leader of the Nanoscale Science group. He and his team set the pace for the rest of the field, Halas says: "When they publish something, it is usually the first and best for a long time."



Flexitime. DNA-coated cantilevers bend as strands bind with their complements.

The key to the next generation of cantilever devices is being able to make the miniature planks bend on demand. One approach is to coat the top surface of an AFM cantilever, a blade of silicon about 500 nanometers long and 100 nanometers wide, with short DNA chains called oligonucleotides. The researchers next expose these coated cantilevers, which are in solution, to oligonucleotides with a complementary sequence of base pairs. When the matched pairs bind, they exert an intermolecular force that expands the coating, bending the cantilever downward much as the bimetallic strip in a thermostat curls in response to temperature changes.

A scanning laser can measure the extent to which the oligonucleotide pairs bend the cantilever; the more base pairs that match, the more the cantilever bends. Thus coated, cantilevers might serve as sensitive probes for specific DNA sequences. "We were able to detect a single [base-pair] mismatch," says Gimzewski, whose team described its advance in *Science* (14 April, p. 316). This proof of principle has attracted attention from biotech companies, which view cantilever setups as potential rivals to DNA arrays for searching for genetic sequences of interest, including disease genes. "We are now trying to make [coated cantilevers] into a general-purpose diagnostic technique," Gimzewski says. "This is a new area. There aren't many sensitive tools around."

But cantilever-based devices need not be constrained to having the action—or molecules—come to them. They might be used as smart gates that release drugs or other chemicals in response to precise molecular signals. For instance, an anticancer pill equipped with cantilever gates might unleash a powerful drug at the site of a tumor only when a tumor-specific protein gloms onto a specially tailored molecular adhesive coating the cantilevers. Or a chemical for cleaning up a hazardous spill might be stored in pellets and released only when the target pollutant tugs at a cantilever gate, "rather than putting chemicals all over the place," Gimzewski says.

Closer to reaching the market, however, are cantilevers for computer data storage. In a project called "Millipede" spanning several labs at IBM Zurich, scientists are testing an array of about 1000 cantilevers as a new way of building nanoscale memory devices. Piezoelectric signals would tell the cantilevers when to jab their hot tips at a polymer film. The impressions in the film would record the data in a much denser format than current media do. "That has the potential to displace magnetic technologies," Gimzewski says. That bold prediction, no doubt, will be heeded in the nano community: Gimzewski's group has a track record for coming through. "I always aim very high and fail a lot of the time," he says, "but the few things in which I succeed make an impact and are extremely enjoyable."

—ALEXANDER HELLEMANS

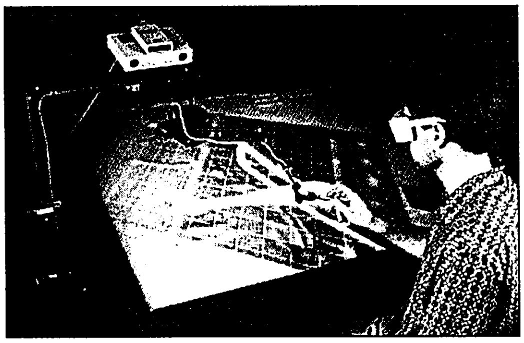
Alexander Hellemans writes from Naples, Italy.

NanoManipulator Lets Chemists Go Mano a Mano With Molecules

Interacting with the nanoworld is like shadowboxing in the dark. Because objects only a few molecules across are too small to be seen or touched directly, scientists approach them essentially blind and numb. Now a team of physicists, chemists, biologists, and computer scientists at the University of North Carolina (UNC), Chapel Hill, has developed a tool that restores their eyes and fingers. It's called the nanoManipulator.

"It is like the movie *Honey, I Shrunk the Kids*, except you don't really get smaller," says UNC computer scientist Warren Robinett. "We reconstruct your perception so that you see and feel exactly what you would if you were the size of a virus." Robinett created the nanoManipulator with chemist Stan Williams, who is now the director of basic research in the physical sciences at Hewlett-Packard. The device "puts humans in the loop in a very nice way," says Ari Requicha, an electrical engineer who works on virtual reality interfaces at the University of Southern California in Los Angeles.

Robinett and Williams, who have been friends since their undergraduate days in the early 1970s, came up with the idea for the nanoManipulator during a 1991 phone call. At the time, Williams was trying to string single silicon atoms into a nanoscale wire, but he was frustrated by his inability to touch the atoms. "Chemists want to get their hands on stuff," he says. For his part, Robinett was looking for a safer application of his expertise in programming people-sized robots that mimic the motions of their human operator. When working with big machines, Robinett explains, "a bug in your program can turn a robot into an eggbeater, and it can punch a hole in your skull."



Tiny fingers. Postdoc Martin Guthold uses the nanoManipulator to probe carbon nanotubes.

To Robinett, the scanning probe microscope (SPM) that Williams used to view his surfaces looked like a small and safe robot. Instead of the robot's TV camera eyes, the SPM has a computer-controlled probe that "looks like an upside-down pyramid at the end of a flexible diving board," says UNC computer scientist Russell Taylor. The probe skates across the silicon surface, and a computer interface converts the probe's wiggles into an electric signal, a bit like the way a phonograph needle creates sounds from the bumps in a vinyl record.

The probe can also be programmed to push against the surface like a robotic finger. In the push mode, scanning tunneling microscopes (STMs) are commonly used to photograph products of chemical reactions, measure the mechanical properties of various materials, and rearrange atoms and bend carbon nanotubes. But there's a problem. To point the tip in the correct direction, researchers first scan the surface and find the target in the resulting three-dimensional (3D) image. Then, they must switch from visualization mode to manipulation mode, program the STM tip to move to the right spot, and finally press it against the surface. In the meantime, thermal vibrations of the surface might have bounced the atom away from the tip's preprogrammed target. It is like trying to play blindfolded billiards during an earthquake.

But even in the push mode, the changing separation between the flexing tip and its fixed mount creates an electric current that is proportional to the pressure exerted on the tip. By transmitting that current to the proper computer interface, Robinett and Williams realized that a human could locate the target object by touch at the same time they were pushing gently against it. All Robinett had to do was revamp his human-sized robot control programs to link the microscopic "robot" to a human. And the nanoManipulator was born.

In its current form, the nanoManipulator is a computer program that fuses an STM with a real-time 3D graphics rendering program and a haptic interface that fits over one finger like a high-tech thimble. The scientist's fingertip gets a little push each time the probe hits a bump. And when the scientist pushes back with his finger, a nanoscale finger presses against the surface.

"The key to the manipulator is that it immerses users in the environment so they develop a good feel for what they are doing," says electrical engineer Joe Lyding, an expert in molecular computing and visualization at the University of Illinois, Urbana-Champaign. For example, a user can tell the difference between signal noise and real texture by simply running a "finger" over the surface, says Williams, who has also used the nanoManipulator to "nanoweld" atoms into a wire strand.

Garrett Matthews, a graduate student in physics at UNC, is using the nanoManipulator to figure out if a virus feels more like a cue ball, a tennis ball, or a rotten tomato. The results are inconclusive. "Right now it feels like a cue ball, but we have other measurements that indicate it should be soft and sticky," says Matthews. Versions of the nanoManipulator are also being used by chemists and materials scientists at Catholic University of Leuven in Belgium, the University of Toronto, the National Institute of Standards and Technology, and Arizona State University in Tempe.

Williams is not surprised at the device's increasing popularity. "We used to have to stare for hours at a black-and-white picture of a surface just to tell what was up and what was down," he says. "The nanoManipulator has untied our hands and opened our senses."

–MARK SINCELL

Mark Sincell is a science writer in Houston.

wholly on the drawing board," John Seely Brown writes in a research paper submitted to the September NSF meeting. Brown, who heads the famed Xerox Palo Alto Research Center in California, points out that two of the main proponents of nanomachines, Ralph Merkle and K. Eric Drexler, built powerful nano-CAD tools and then ran simulations of the resulting designs. "The simulations showed definitively that nano devices are theoretically feasible," Brown writes. "But theoretically feasible and practically feasible are two different things. And as yet, no-one has laid out in any detail a route from lab-based simulation or the extremely elementary nanodevices that have been chemically constructed to practical development."

But others argue that visionary research serves a purpose, too. Even if nanogears and pistons cannot be built yet, says Deepak Srivastava, who heads the computer nanotechnology design group at NASA's Ames Research Center in Moffett Field, California, the computer designs still help focus experimentalists on what's worth looking for: "If the ideas are based on real

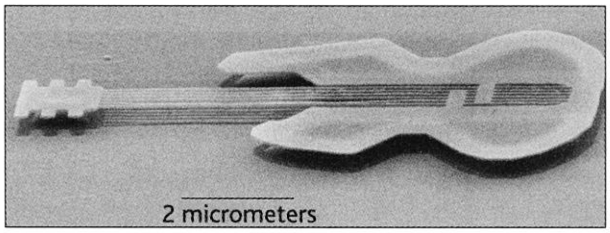
CREDIT: LARRY KETCHUM

physics and chemistry, one has to know the real possibilities."

And of course, experimental science is constantly expanding the scope of what is feasible. Whitesides and Stephen Chou of Princeton University have recently pioneered a new rubber stamping method for patterning surfaces with features as small as 10 nanometers. That is well below the current size limit of about 200 nanometers faced by photolithography, the primary patterning tool used by the computer chip industry. Still, the stamping technique has its own drawbacks: It has trouble patterning multiple materials in three dimensions, as is needed for making computer chips, and ensuring proper alignment of all the various layers of material.

Another patterning alternative making headway is a burgeoning subfield of chemistry known as self-assembly, in which researchers design materials to assemble themselves into desired finished structures. For example, last year IBM researchers led by chemist Christopher Murray came up with a way to make metallic particles as small as 3 nanometers and then assemble them into a three-dimensional array. Such structures could lead to material for future computer disks in which each nanoparticle stores a bit of data. Still, for now such successes tend to be the exception rather than the rule.

Future nanoapplications face other grand challenges as well. Even if particular nanocomponents can be mass-produced, researchers will still need to figure out how to position them on surfaces or other structures so they can be used as components in electronic devices, sensors, and the like. For tiny electronic components, researchers will then face the major stumbling block of wiring them up to the macro world.



Nanocaster. World's smallest guitar, with strings 100 silicon atoms wide, is huge by the latest nanostandards.

They will also confront the more mundane challenge of connecting with one another. By all accounts, nanotechnology will require an extraordinary range of expertise. Researchers have long embraced the concept of interdisciplinary research. And organizations such as the NSF make it a point to finance interdisciplinary centers. Still, academia remains largely hidebound in disciplines, making it difficult to pursue research that falls between traditional fields. "There still exist many elements in the culture of our research universities that discourage multidisciplinary research," says James Merz, the vice president for graduate studies and research at the University of Notre Dame in Indiana.

Among the chief culprits Merz points to are the administrative autonomy given to separate departments and the fact that faculty members must obtain tenure from specific departments. Furthermore, Theis points out, essentially no curricula have been developed to train future researchers in the field, let alone degree programs to turn out new nanotech Ph.D.s. Although those impediments aren't necessarily fatal, they can easily hamper the field's development, Merz says.

Beset by such challenges, nanoreality is bound to fall short of nanohype. The danger is that disenchantment with the gap could dampen financial support for the field, says Mihail Roco of NSF, who heads the U.S. National Nanotechnology Initiative. That's a scenario well known to researchers in high-temperature superconductivity, an enterprise that has struggled to live up to the fanfare that greeted it in the mid-1980s. Still, unlike superconductivity—a narrow field whose impact is limited to a comparatively small sphere of applications—nanotechnology is likely to benefit from its breadth, says Srivastava. "Since the net is much wider," he says, "the chance is bigger that you will catch some fish."

—ROBERT F. SERVICE

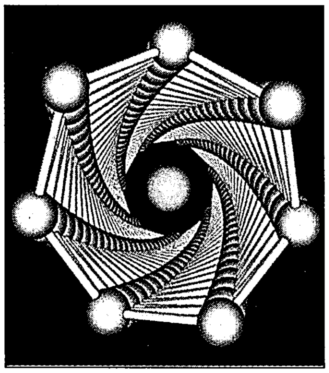
NANOPROFILES

Strange Behavior At One Dimension

TOKYO—For Kunio Takayanagi, a physicist at the Tokyo Institute of Technology, thinner is better. Takayanagi has calculated that electrons should pass through the 1-nanometer gold wires he has crafted at speeds several orders of magnitude faster than those at which they pass through larger wires. If such wires could be fashioned into circuits, they could set the stage for even faster supercomputers. "In electronic device technology," he says, "the speed of the electron is the most important thing."

Such high speeds are made possible by the internal structure of the nanowires through which the electrons pass. "At larger scales, materials form crystals," explains Erio Tosatti, a theorist at the Institute for Theoretical Physics in Trieste, Italy. "In the nanowires, the material is not a crystal. It is very different, electrically and mechanically."

Takayanagi was the first to determine this structure by putting a miniaturized scanning tunneling microscope (STM) within an ultrahigh-vacuum, high-resolution transmission electron microscope (TEM). By irradiating a thin gold film with an electron beam, he reduced it to a wire. Imaging with the TEM and the STM revealed that when the wire was thinned to a diameter of roughly 1 nanometer, atoms organized themselves into nested tubes, with the atoms in each tube arranged in a helix coiled around the wire axis. The structure is akin to that of carbon nanotubes.



Twister. Spirals of gold, 1 nm across, may rev electrical currents up to record speeds.

Takayanagi's prediction of the speed of electron transport is based on some preliminary conductance measurements and theory. Theory suggests that the electrons would move so efficiently that no heat would be generated. Groups at Nagoya and Osaka universities in Japan and at Leiden University in the Netherlands have produced similar wires and plan to measure some of their mechanical and electrical properties.

In addition to the obvious advantages for the electronics industry, the work has important implications for basic science. Pointing to the helical structure of carbon nanotubes and the double helix of DNA, Takayanagi says it's possible that "all material will take on a stable helical structure if it is one-dimensional like a nanowire." Tosatti is equally excited. "I think this work could lead to an understanding of how matter spontaneously organizes itself at the nanoscale," he says.

—DENNIS NORMILE

CREDITS: (TOP TO BOTTOM) DUSTIN W. CARR AND HAROLD W. CRAIGHEAD/CORNELL UNIV.; K. TAKAYANAGI