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## Tiny Is Beautiful: Translating 'Nano' Into Practical

By KENNETH CHANG

In the hip science of ultrasmall nanotechnology, fantastical future possibilities like rampaging nanorobots capture the most attention, but the first fruits of the field have been more mundane: tiny bits of mostly ordinary stuff that just sit there.

Yet these bits - nanoparticles - gain wondrous new capabilities simply because they are so small.

Nanoparticles of various sorts are already found in products like sunscreen, paint and inkjet paper. More exotic varieties offer promise in medicine for sensitive diagnostic tests and novel treatments: the detection of Alzheimer's disease by finding a protein in spinal fluid, for instance, or nanoparticles that heat up and kill cancer cells.

Some nanoparticles are not even on the cutting edge.

Medieval artisans unknowingly became nanotechnologists when they made red stained glass by mixing gold chloride into molten glass. That created tiny gold spheres, which absorbed and reflected sunlight in a way that produces a rich ruby color.

Nanotechnology, nanoparticles and all of the other nano words derive from nanometer, a billionth of a meter, or about one 25-millionth of an inch. That is far smaller than the world of everyday objects described by Newton's laws of motion, but bigger than an atom or a simple molecule, particles ruled by quantum mechanics.

A nanoparticle, an object with a width of a few nanometers to a few hundred, contains tens to thousands of atoms and exists in a realm that straddles the quantum and the Newtonian.

At those sizes, said Dr. Chad A. Mirkin, a director of Northwestern University's Institute for Nanotechnology, "everything, regardless of what it is, has new properties." And that, he added, is "where a lot of the scientific interest is."

This in-between realm gives rise to an unusual physics where the properties of a material change depending on its size. At the quantum level, one gold atom acts like any other gold atom, and a nugget of gold large enough to hold has the same chemical and electrical properties as another nugget. But two nanoparticles, both made of pure gold, can exhibit markedly different behavior - different melting temperature, different electrical conductivity, different color - if one is larger than the other.

"That creates a new way to control the properties of materials," said Dr. A. Paul Alivisatos, a professor of chemistry at University of California, Berkeley. "Instead of changing composition, you can change size."

Dr. Alivisatos works with nanoparticles known as quantum dots, made of semiconductors like silicon and gallium arsenide. The edges of the small particles influence the motion of electrons in the semiconductor, and the shape and size of quantum dots can be tailored to fluoresce specific colors. Current dyes used for lighting up protein and DNA fade quickly, but quantum dots could allow tracking of biological reactions in living cells for days or longer.

"They're just little rocks," Dr. Alivisatos said. He is a founding scientist of Quantum Dot Corporation, in Hayward, Calif., which is trying to turn the science into a business.

Other applications of nanoparticles take advantage of the fact that more surface area is exposed when material is broken down to smaller sizes. For magnetic nanoparticles, the lack of blemishes produces magnetic fields remarkably strong considering the size of the particles. Nanoparticles are also so small that in most of them, the atoms line up in perfect crystals without a single blemish.

Dr. David F. Kelley, a professor at the University of California, Merced, is making tiny disks exactly four atoms thick out of exotic semiconductors, which he hopes to stack together into solar cells. The disk shape reduces the space between particles, which should allow electrons to hop more easily between them. Because nanoparticles almost always contain flawless crystal structure, Dr. Kelley hopes that his nano solar cell will be more efficient at capturing light and turning it into electricity.

He plans more work on the basic properties of the disks before trying to connect everything together. "We will have a very good idea whether we can make this in the next year or two," he said.

For the medieval stained glass, the gold nanoparticles are simple spheres about 25 nanometers in diameter.

At those small sizes, gold no longer glitters gold. Electrons at the surface of the nanoparticles slosh back and forth in unison, absorbing blue and yellow light. But longer-wavelength red light reflects off the particles and passes through the window. Similarly, nanoparticles of silver in stained glass give a bright yellow hue.

With much more sophisticated tools, scientists today can make nanoparticles of many more different shapes and sizes. Larger gold spheres appear green or orange; smaller silver ones are blue. Dr. Mirkin has also made triangular pieces of silver 100 nanometers across that look like little Doritos; those are red. "You can get every color of the spectrum," he said.

Dr. Yi Lu, a chemistry professor at the University of Illinois, takes advantage of the color of nanoparticles for a test for detecting hazardous levels of lead. He attaches DNA molecules to gold nanoparticles, which tangle with other specially designed pieces of DNA into clumps that appear blue.

The presence of lead causes the connecting DNA to fall apart. That cuts loose the individual gold nanoparticles and changes the color from blue to red.

Dr. Mirkin also uses gold nanoparticles as a connecting point, to build sensors of a different sort, for disease. A common technique for a diagnostic test consists of an antibody attached to a fluorescent molecule. When the antibody attaches to a protein associated with the disease, the fluorescent molecule lights up under ultraviolet light.

Instead of a fluorescent molecule, Dr. Mirkin attaches a gold nanoparticle to the antibody. To the nanoparticle, he adds other molecules, typically snippets of DNA that act as bar codes. Because many copies of the antibodies and DNA can be attached to a single nanoparticle, this approach is much more sensitive and accurate than the fluorescent-molecule tests used today, he said.

Dr. Mirkin and his colleagues reported this month in *The Proceedings of the National Academy of Science* that this approach had produced a test to detect the onset of Alzheimer's by measuring minuscule amounts of a protein in spinal fluid associated with the disease.

"To me, that's just a beautiful example of the power of this particular approach," Dr. Mirkin said. He has started a company, Nanosphere Inc., to bring his techniques to market.

Nanoparticles may help cure disease as well as detect it.

Dr. Naomi J. Halas, a professor of electrical and computer engineering at Rice University, invented a type of particle she calls nanoshells - hollow gold or silver spheres wrapped around a filling of silica.

The hollow shape makes sloshing electrons in the gold particularly efficient at absorbing energy from light, and changing the thickness of the shell changes the frequency of light absorbed. That makes it a promising treatment for killing cancer tumors. Inject nanoshells into a tumor, shine infrared light on them, and they heat up, killing the tumor.

In demonstrations, researchers in Dr. Halas's lab squirt nanoshells into uncooked chicken parts and then shine a near infrared laser on the chicken. Water does not absorb much infrared light, so the laser light passes through most of the chicken meat without effect. But the nanoshells absorb the energy and heat up. The spot they were injected starts smoking and catches fire. (In actual treatments, a much lower intensity of light would be used, killing the cancer cells but not cooking flesh.)

Dr. Halas and a colleague, Dr. Jennifer West, a Rice bioengineering professor, founded Nanospectra Biosciences Inc.

Shrinking some medicines to nanoparticle size could improve effectiveness.

As a possible drug for kidney patients, Altair Nanotechnologies of Reno, Nev., has developed nanoparticles of lanthanum dioxycarbonate. The chemical - the planned brand name is RenaZorb - binds to phosphate, a waste product that builds up because failing kidneys no longer remove it. The binding prevents it from entering tissues in the first place.

Here, the advantage of small is the surface area. For the same amount of material, small particles have more surface, allowing a small amount of the drug to absorb large amounts of phosphate. Patients would only need one tablet of RenaZorb a meal, compared with the two or three per meal required by competing drugs, said Dr. Alan J. Gotcher, Altair's chief executive.

Greater surface area also makes nanoparticles well suited for certain types of environmental cleanup. Dr. Weixian Zhang, a professor of civil and environmental engineering at Lehigh University, has been working with nanoparticles of iron for almost a decade. That is longer than the term nanoparticles has been in wide use. Dr. Zhang remembers calling them "clusters" of atoms in an early scientific paper. The editors did not find that descriptive enough, so he changed the wording to "nanoscale particles."

Iron is effective at breaking down contaminants like trichloroethylene, TCE for short, a cancer-causing chemical solvent that has found its way into drinking water. When iron rusts into iron oxide, it lets loose an electron. If the electron hops to a molecule of TCE, it starts a chemical reaction that breaks TCE into harmless pieces.

The current method is to dig a trench and dump a ton or more of iron powder into it. But in small-scale tests of the new technique at contaminated sites in Trenton and North Carolina, TCE levels were reduced by more than 90 percent in the water. Dr. Zhang said one pound of nanoparticles could cleanse 10,000 to 30,000 pounds of water.

But nanoparticles may have potential dangers that are still not well understood. The fear is that because they are so small, they could slip past the body's immune systems and into cells. A study last year reported that exotic soccer-ball-shaped carbon molecules known as buckyballs in water caused brain damage in fish.

But not all nanoparticles are considered equally harmful. Zinc oxide has long been an ingredient in cosmetic products, and so the smaller particles of zinc oxide now used to eliminate the white pasty appearance in sunscreens are not thought to pose danger.

Dr. Zhang says iron nanoparticles will eventually rust into iron oxide nanoparticles, which occur naturally. "I am fairly confident that it will have no impact," he said. "Most of the particles will attach to soil, slowly oxidize and become part of the background."

Still, he said experiments were needed to document that supposition before the iron nanoparticles went into wide use.

Nanoparticles will also be the building blocks for complex structures like nanowires and molecule electronic devices. Some of the pieces will be built into moving parts, and perhaps, one day, scientists will get around to the rampaging nanorobots.