New vibes in magnetic resonance detection

By using the technology that made possible both the scanning tunneling microscope and the atomic force microscope, researchers have now devised an extremely sensitive method for detecting magnetic resonance. This detection technique — which relies on the vibration of a tiny sliver of silicon nitride rather than the activation of an electromagnetic circuit — represents a potentially important step toward attaining significantly higher resolution than that achievable using conventional magnetic resonance imaging (MRI).

"This is a new way of doing magnetic resonance, and it seems to be very sensitive and very amenable to high spatial resolution," says Daniel Rugar of the IBM Almaden Research Center in San Jose, Calif. "We're very excited about the prospects for the future."

The ultimate goal of this research is the development of a technique that would enable investigators to obtain images showing the full three-dimensional structure of individual proteins and other biological molecules in their natural settings. "We want to give molecular biologists access to a 'microscope' working at the molecular level," says John A. Sidles of the orthopedics department at the University of Washington School of Medicine in Seattle.

Rugar and Sidles described progress toward this goal in separate presentations at this week's American Physical Society meeting, held in Seattle.

The idea for developing this technique initially came from Sidles, who last year proposed an ingenious scheme for detecting and locating single protons deposited on a surface (SN: 3/7/92, p.150). Sidles then persuaded Rugar and his coworkers to try to build such a device based on the kind of technology they had already used to measure tiny variations in magnetic forces across a surface.

Rugar realized that current technology wasn't yet good enough to permit detection of the tiny magnetic effect due to a proton or a single atomic nucleus. But it was probably good enough to detect a magnetic resonance effect involving electron spins in a microscopic grain of a suitable material. "We had to come up with an experiment to get us started — something that demonstrated the basic principle," Rugar says.

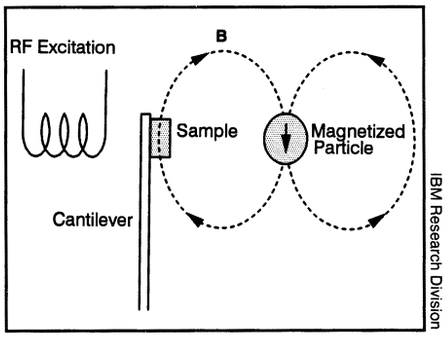
The key element in the device fashioned by Rugar and his co-workers was a cantilever — a strip of silicon nitride about 0.2 millimeter long, which could vibrate back and forth like a miniature, vertically mounted diving board (see diagram). The magnetic sample itself was glued to the tip of the cantilever. As the researchers changed the sample's magnetization by sending in radio waves of a particular frequency to flip the spins of electrons in the sample, they could monitor the minuscule vibrations of the loaded cantilever, looking for increases in vibration amplitude because of magnetic force interactions between the sample and a nearby magnetized particle.

Even though the cantilever had not been designed for this particular purpose, the researchers managed to detect a resonance effect. They confirmed that an oscillating cantilever could do at least as well as a conventional electromagnetic device for detecting magnetic resonance.

Rugar and his team are now looking into the possibility of generating two-dimensional images from such measurements. Sidles and his group are starting to explore ways of improving the basic device to get closer to detecting nuclear magnetic effects rather than those caused by electron spins. "There's a lot of room to improve these oscillators," Sidles says. "We're interested in using much smaller cantilevers at much lower temperatures."

"We're still a long way from what we would ultimately like to do, which is to do [nuclear magnetic resonance] imaging with single spins," Rugar notes. Nonetheless, "I believe that it may be achievable."

— I. Peterson



Basic configuration used to detect magnetic resonance by measuring the small, oscillating magnetic force acting between electron spins in a sample and a nearby magnetic particle.

Custom antibody cracks cocaine molecule

The behavior of a laboratory rat addicted to cocaine soon shrinks to a single action: pushing a metal lever to flood its central nervous system with molecules of pleasure. But for all cocaine's initial narcotic fury, the pleasure soon trickles away, as natural enzymes begin to break down the drug. To compensate, the rat pushes the lever again and again. "The animal will neglect food and sex. It will perform the task necessary to get the cocaine — even if it triggers electric shocks," explains organic chemist Donald W. Landry. "The reinforcing tendency of the drug is almost overwhelming."

Now Landry and others at the Columbia University College of Physicians and Surgeons in New York City have created a unique catalytic antibody — a kind of fast-acting, artificial enzyme — that may someday help humans beat cocaine addiction. The antibody rapidly cleaves cocaine molecules into two inert fragments, neither of which has any narcotic effect.

Unlike a natural antibody, a catalytic antibody can disarm more than one cocaine molecule, possibly offering a long-lasting immunity against the drug, researchers report in the March 26 SCIENCE. Scientists invented the burgeoning field of catalytic antibody synthesis in 1986 (SN: 9/2/89, p.152).

Cocaine users often seek treatment voluntarily. After a few days, however, drug cravings can overwhelm their desire to abstain, Landry explains. A series of attempts at sobriety and subsequent relapses may follow. "One clear way to break this cycle is to ensure that using the drug either doesn't give any high, or gives such a blunted high that the sort of maniacal behavior to obtain more drugs is not reinforced," Landry says.

Indeed, a 1970s study of heroin addiction in rhesus monkeys, which used the animals' own antibodies to build immunity, indicates that cravings may subside when attempts at intoxication end in failure, Landry notes. In humans, immunization with fast, long-lived cocaine antibodies may keep users sober long enough for conventional forms of treatment, including psychotherapy and antidepressant drugs, to take effect.

But there's a catch, says neuroscientist and cocaine researcher Bertha K. Madras of Harvard Medical School in Boston: A person could simply take enough cocaine to overwhelm his or her immunity to the drug.

This is why any habit-breaking drug based on catalytic antibodies would have to defang cocaine molecules 1,000 times faster than the body's own enzymes can, a rate other catalytic antibodies already have far exceeded, says Landry. This level of immunity could shield the brain from even large doses of cocaine, making it prohibitively expensive for people in treatment to satisfy their craving for the drug.

Next, the researchers will begin animal studies to learn if the antibody can provide immunity against typical doses of cocaine without serious toxic effects. Success may clear the way for tests of the antibody in humans, Landry says.

— D. Pendick