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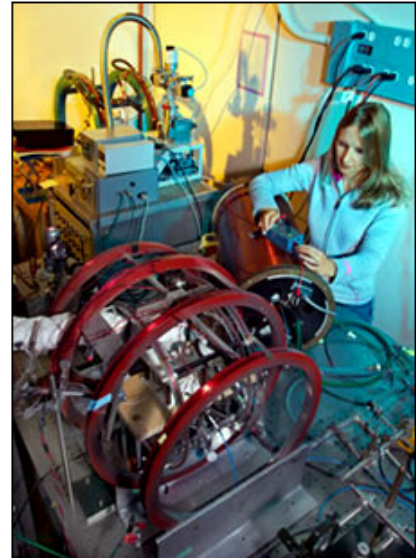
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Detection at a Distance for Better NMR/MRI

BERKELEY, Calif., March 19 -- A remarkable new way to improve the versatility and sensitivity of magnetic resonance imaging (MRI) and the technology upon which it is based, nuclear magnetic resonance (NMR), has been discovered by Alexander Pines, a scientist in the Materials Sciences Division at Lawrence Berkeley National Laboratory, and Glenn T. Seaborg, professor of chemistry at the University of California at Berkeley. The latest details of the new technique, known as remote detection, are reported by Pines, postdoctoral fellow Song-I Han and doctoral candidate Juliette A. Seeley in the *Journal of Magnetic Resonance*.

HIGHLY SENSITIVE: Juliette Seeley works with a remote-detection assembly that can encode images in a low magnetic field and detect them with non-NMR detectors. A xenon polarizer provides a continuous flow of sensor gas to the low-field MRI encoding probe and then to the remote detector, a highly sensitive, gas spin-exchange, optical detection apparatus.

Remote detection depends on physically separating the two basic steps of NMR, signal encoding and detection -- normally carried out in the same instrument -- in order to customize each step for the best results. Using laser-polarized xenon gas as the medium for "remembering" the encoded information and carrying it to the remote detection site, Pines and his group said they have achieved orders-of-magnitude improvement in MRI image resolution and manifold increases in NMR sensitivity.



"NMR encoding is exceptional at recovering chemical, biological, and physical information from samples, including living organisms, without disrupting them," said Pines, noting that MRI, a closely related technology, is equally adept at nondestructively picturing the insides of things. "The problem with this versatile technique is low sensitivity."

"However," said Han, "by separating the encoding and detection phases of NMR/MRI, we can gain data about physical, chemical and biological properties of samples that we simply could not have gotten previously."

The conceptual foundation and feasibility of remote detection were earlier established in Pines's laboratory by Adam Moule, Megan Spence, Kimberly Pierce and Sunil Saxena, in addition to Han and Seeley. The group reported their results in the August 5 *Proceedings of the National Academy of Sciences*. Saxena, now an assistant professor of chemistry at the University of Pittsburgh, said that while using two distinct pieces of apparatus might seem counterintuitive at first glance, but "in many circumstances the use of one set-up in NMR leads to an uneasy balance between effective signal

encoding and sensitive signal detection. By separating the two, not only can the signal fidelity be vastly improved, but also many new schemes that use much more powerful and sensitive detection and coding methods and principles can be envisaged."

The basic steps

NMR and MRI work because many atomic nuclei have magnetic moments, acting like toy bar magnets with north and south poles. In a magnetic field, these spinning nuclei orient themselves along the field lines, with spins up or down. Slightly more energy is required to maintain the spin-down state.

In the encoding phase, a radiofrequency (RF) pulse matched to the energy difference between the two states knocks the target nuclei atilt, causing their spin axes to precess around the field lines like off-center toy gyroscopes. The exact precession rate is characteristic of each chemical species -- ubiquitous hydrogen is the most commonly used species in NMR and MRI -- and is also affected by the chemical and physical surroundings.

For MRI, an extra step encodes additional data. In addition to the uniform magnetic field, additional magnets are turned on briefly to superimpose fields that are stronger in one direction than the other. When the target nuclei are subjected to RF pulses, the differences in field strength are reflected in changed angles and speeds of precession. Together with the timing of the pulses, the gradient fields give each spinning nucleus a unique set of coordinates corresponding to its position.

During the detection phase, the net magnetic moment of the spinning nuclei is measured and analyzed for information about the chemical environment. In MRI, the magnetization of each batch of spins formed by a train of RF pulses is measured, which yields the spatial characteristics of the sample.

Many factors determine the best ways to encode and detect information about a particular sample, whether it's a living organism, a sample of tissue on a slide, a gas, liquid or mineral sample, or even a solid surface. During encoding, the RF coil has to be of the same dimension as the sample and often surrounds it; in addition, the main magnet has to be big enough to bathe the sample in a magnetic field that is typically very strong. In hospitals, for example, MRI equipment big enough to examine the head or lungs is bulky and expensive.

For both encoding and detection, the proportion of target nuclei in the sample is another important consideration. If the sample is large but the proportion of target nuclei is small, this small "filling factor" makes for a weak signal.

Polarization -- the difference in the number of spin-up versus spin-down nuclei -- is also vital. Even in a strong magnetic field, the excess of spin-up hydrogen is at best 1 in 100,000.

Xenon-129, unlike hydrogen, can be optically "hyperpolarized" before it is introduced into the sample, where its nuclei interact with the surroundings to encode NMR and MRI information. Because xenon is a noble gas, chemically inert and nontoxic, it is ideal for many biological applications. In hyperpolarized xenon, some 20 percent of nuclei are spin-up -- "so we don't waste all those spins," Han said.

For optimum signal encoding, then, an NMR/MRI set-up may include a big RF coil and a strong magnetic field, while the best detection setup for the same sample might require a more sensitive magnetic field and a smaller RF coil -- or even a supersensitive, non-MRI detector like a superconducting quantum interference device or a laser magnetometer.

Conversely, weak magnetic fields might be an advantage for encoding some subjects, for example patients with pacemakers or metal implants. Signals encoded in a weak field can only be recovered by a high-field detector.

"Remote detection allows us to combine the ability to obtain rich information about a variety of interesting samples with sensitive detection," Seeley said. "This is possible because nuclear spins have the ability to retain memory of their prior surroundings. They remember the information that was encoded in an environment not optimized for detection, and later they can be detected more sensitively."

Fantastic Notion

Saxena described the successful first attempt to prove the remote-detection principle: "We were able to demonstrate the rather fantastic notion that a picture of a sample cell could be obtained by saturating it with xenon gas in one spectrometer and then moving the gas -- by as much as 15 feet -- to another spectrometer for signal detection. Despite the long separation and travel time, the xenon gas faithfully remembered the shape of the sample cell."

Recently, Seeley, Han and Pines have demonstrated remote detection of MRI of porous samples at higher resolution, again using xenon gas to carry the signal to a detector of optimum design. The xenon is optically hyperpolarized, then introduced into the encoding chamber, where it flows through the voids in the sample. Because the sample is surrounded by a large radiofrequency coil, the filling factor is poor. Bearing the encoded information, the gas flows on to the detection chamber. Since xenon has a long spin-relaxation time, no spin-polarization or pulse-timing information is lost during transport.

In the recent experiment, the different encoding and detection coils were near each other but physically separated, and both were subjected to virtually the same strong magnetic field. With a much smaller detector coil the filling factor was greatly enhanced: the coil surrounds only the target nuclei, not the entire sample.

Encoding and detecting NMR/MRI signals separately makes many otherwise difficult or impossible applications possible. For example, xenon can be dissolved in chemical solutions or in the metabolic pathways of biological systems, then concentrated for more sensitive detection. Since xenon is not normally present in biological or geological samples, its signal stands out clearly against a noiseless background.

Other signal carriers can also be used for remote detection, including hyperpolarized helium gas for medical imaging or liquid oil or water for geological analysis. Since only the carrier reaches the detector, alternate detection methods, incompatible with the sample because they may be intrusive or require transparency, can also be used -- for example, optical methods that can detect the miniscule NMR signals from living cells.

By freeing the detection phase from the confines of the sample chamber, remote detection liberates NMR/MRI technology from its restraints and opens a new realm of possibilities -- from targets as big as geological core samples and human bodies down to microstructures and single cells. No other spectroscopic or imaging tool has such a rich combination of capabilities.

For more information, visit: www.lbl.gov

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