RESEARCH NEWS
BERKELEY LAB

October 10, 2005 news releases | receive our news releases by email | science@berkeley lab

NMR Technology Comes to the Lab on a Chip

Remote Detection Makes NMR Compatible with Microfluidics

Contact: Lynn Yarris, lcyarris@lbl.gov

BERKELEY, CA – A breakthrough in the technology of nuclear magnetic resonance (NMR), one of the most powerful analytic tools known to science, is opening the door to new applications in microfluidic chips, devices for studying super-tiny amounts of fluids. A team of scientists with Lawrence Berkeley National Laboratory (Berkeley Lab) and the University of California, Berkeley, has demonstrated a means by which NMR can be made compatible with microfluidic "lab-on-a-chip" devices. This demonstration holds great promise for biomedical research, the detection of biohazards and toxic chemicals, and other endeavors in which the chemical composition of a fluid must be determined.

Christian Hilty is a member of the Alexander Pines research group and principal author of a paper in which it was demonstrated that Nuclear Magnetic Resonance or NMR spectroscopy can be used with microfluidic "lab-on-a-chip" devices.

"Our novel methodology bypasses the long-standing problem of optimizing the two basic steps of NMR, signal encoding and detection, by physically separating them, and, at the same time, adds an important dimension to the study of fluid flow dynamics with the possibility of time-of-flight measurements," said Alexander Pines, one of the world's leading authorities on NMR technology. Pines holds a joint appointment as a chemist with Berkeley Lab's Materials Sciences Division and with UC Berkeley, where he is the Glenn T. Seaborg Professor of Chemistry.

The technique in which NMR signal encoding and detection are carried out independently (in a conventional NMR setup, the two actions take place within a single device) is called remote NMR detection. In a paper published in the online edition of the Proceedings of the National Academy of Sciences (PNAS), for the week of October 3, Pines and his collaborators describe the use of remote NMR to study the flow of gases through microfluidic devices.

"Remote detection of the NMR signal overcomes the sensitivity limitation of NMR and enables spatially resolved imaging in addition to time-of-flight measurements," said chemist Christian Hilty, a member of

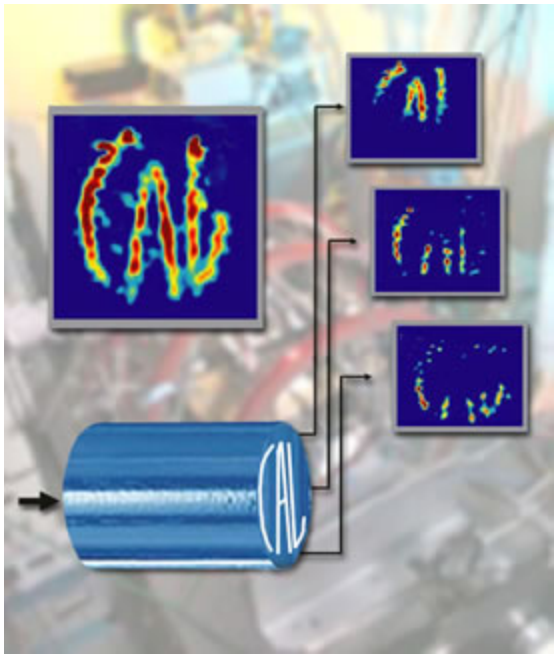
Pines' research group and the principal author of the PNAS paper. "Our approach also offers the unique advantage of being non-invasive. We can use it to measure microfluidic flow without the introduction of foreign tracer particles. This is important for the design and the operation of microfluidic devices."

Co-authoring the PNAS paper with Hilty and Pines were Erin McDonnell, Josef Granwehr, Kimberly Pierce and Song-I Han , all of whom at the time of the study held joint appointments with Berkeley Lab and UC Berkeley. The work is supported by the U.S. Department of Energy's Basic Energy Sciences program in the Office of Science.

NMR is a phenomenon involving a property found in the atomic nuclei of almost all molecules called "spin," which gives rise to a magnetic moment, meaning the nuclei act as if they were bar magnets with a north and south pole. When a sample is exposed to a strong external magnetic field, these "bar magnets" attempt to align their axes along the lines of magnetic force. The alignment is not exact, resulting in a wobbly rotation about the magnetic field lines that is unique for each type of nuclei.

If, while exposed to the magnetic field, the nuclei in a sample are also subjected to a sequence of radiofrequency (rf) pulses, they will absorb and re-emit energy at characteristic frequencies. This is called the signal "encoding" phase of NMR. In the detection phase, the frequencies of these encoded signals are measured to obtain an NMR spectrum. This spectrum will feature distinct peaks of varying height that, like a set of fingerprints, can be used to identify the sample's chemical structure.

While NMR has long been a powerful tool for studying the chemical composition of macroscopic samples, its application to microfluidic chip devices has been hampered by low sensitivity. When atomic nuclei align their axes along the lines of a magnetic field, the nuclear spin of some will point "up" while that of others will point "down." Obtaining an NMR signal depends upon an excess of nuclei in a sample with spins pointing in one direction or the other, but the natural population difference in a typical fluid sample, even under a powerful magnetic field, is usually no more than one in 100,000 at room temperature.



In a demonstration of remote NMR detection, the letters CAL, carved through the end of a plastic tube placed in an NMR encoding coil, were reconstructed from 10 batches of spin-polarized xenon carried to a detection coil at a separate location. Although the batches arrived at different times, the spatial arrangement of the letters was accurately reproduced.

To overcome this low spin polarization so they can measure gas flow, Pines and his research group have been injecting their samples with xenon whose atomic nuclei have been hyperpolarized by laser light. Hyperpolarized xenon boosts the NMR sensitivity of a sample by at least four orders of magnitude, and, xenon being inert, does not interfere with the other sample constituents as it is carried along in the flow.

When working with microfludic samples of gas, Pines and his collaborators apply their NMR encoding technique to the hyperpolarized xenon. With its long spin-relaxation time (several minutes), hyperpolarized xenon is well-suited for transporting the encoded NMR information to a separate site for detection. By staging the encoding and detection phases at separate sites, each site can be customized to obtain optimal results.

"Xenon's long spin-relaxation time (several minutes), make it an ideal carrier of an NMR signal for remote measurements of gas flow," said Hilty.

Microfluidic devices are essentially miniaturized chemistry laboratories, featuring a series of micrometer-sized channels etched into a chip in which nanoliter-sized samples of fluids can be analyzed. Such analyses can provide a wealth of information for biomedical and analytical chemistry studies. Because of their incredibly small sample sizes — thousands of times smaller in volume than a typical droplet – microfluidic "labs on a chip" are highly prized for providing rapid analysis at relatively low costs.

Currently, the most common way to analyze gas flow in a microfluidic device is to inject it with marker particles that will fluoresce under optical illumination, or that are of sufficient size to be viewed under a microscope. Using remote NMR instead offers several advantages.

"With remote detection of NMR, we don't need the addition of markers that perturb the flow because we can use the spins of the hyperpolarized xenon nuclei," said Hilty. "Also, when we apply the hyperpolarized xenon for the encoding step of remote detection, we can individually tag a fluid sample in any and all points within the device, whereas we can inject a fluorescent marker only at a device's inlet."

According to Hilty and Pines, their NMR remote detection technology is ready to be applied to any existing microfluidic device, so long as the fluid is transported to the detection site within the spin relaxation time of encoded NMR information.

"In our PNAS paper, we describe an application in which we measure gas flow in microfluidic devices by remote detection of NMR," said Hilty. "However, the same principles are applicable without hyperpolarization to the less challenging case of liquids, which have a much higher spin-density."

Another limiting factor for the widespread use of NMR with microfluidic devices is the relatively high cost of an NMR spectrometer. Pines and his research group are working on the development of alternative, less expensive means of detecting encoded NMR signals — for example, a magnetometer. According to Hilty, preliminary results on this line of research have been promising.

Berkeley Lab is a U.S. Department of Energy national laboratory located in Berkeley, California. It conducts unclassified scientific research and is managed by the University of California. Visit our Website at www.lbl.gov.

Additional Information

- To read the PNAS paper by Hilty, Pines and their collaborators, visit http://www.pnas.org/papbyrecent.shtml
- For more information about the Pines Laboratory click here.

Top