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Key Concepts

- Scientists have for decades used nuclear magnetic resonance (NMR) systems to investigate the chemical composition of materials without damaging them. And physicians have employed essentially the same technique, using magnetic resonance imaging (MRI) machines to view inside the human body.
- NMR and MRI machines are large. But researchers have now developed portable versions. A good example is the NMR-MOUSE, which has found applications in the control of manufacturing processes, the nondestructive testing of materials, archaeology and art conservation.
- Ongoing research could lead to improved, specialized versions, including perhaps a football-helmetlike brain scanner that could operate in a speeding ambulance.

--The Editors

The Incredible Shrinking Scanner: MRI-like Machine Becomes Portable

By Bernhard Blümich

A portable version of a room-size nuclear magnetic resonance machine can probe the chemistry and structure of objects ranging from mummies to tires

You or someone you know has probably had an internal malady examined with a magnetic resonance imaging (MRI) machine. Lying in the claustrophobic confines of the room-size magnetic doughnuts that make MRI possible can be stressful, but the diagnostic value of the resulting high-contrast pictures of the various soft tissues inside the body makes up for any angst. A more generalized version of the technique, nuclear magnetic resonance (NMR), also offers enormous benefits, enabling scientists to characterize the chemical compositions of materials as well as the structures of proteins and other important biomolecules without having to penetrate the objects under study physically.

But doctors and scientists have long yearned for portable NMR devices that could be used outside the laboratory. They have envisioned, for example, paramedics using a helmetlike MRI scanner to pinpoint blood clots in the brain of a stroke victim while still inside a speeding ambulance. And they have imagined a handheld NMR spectroscope that could discern the chemical makeup of pigments, thus permitting art experts to distinguish old-master paintings hanging in museums and galleries from modern fakes.

Researchers are nowhere near producing the all-purpose "tricorder" of television's *Star Trek* fame, but Peter Blümler -- a former doctoral student of mine -- and I took some of the first baby steps toward a portable NMR device in 1993, when we were both at the Max Planck Institute for Polymer Research in Mainz, Germany. Our effort eventually resulted in a small materials-testing tool that provides useful findings to investigators out in the field. Since then, other workers in the now budding discipline of "mobile NMR" have been building on our initial approach and those of others to develop a wide range of related technologies that pack increasingly powerful analytical and imaging capabilities.

The Simplest NMR

Fifteen years ago, when Blümler and I first began to speculate half-jokingly on the simplest setup that could produce a practical NMR signal, the entire notion was indeed rather laughable. Most researchers were moving in the opposite direction -- designing ever more complex NMR measurement protocols to provide ever finer details about the structure of objects and matter. But our earlier efforts to develop MRI techniques for polymer materials had taught us that the costly and bulky magnets -- and the uniform, or homogeneous, fields they create -- are not always needed for successful imaging.

We realized that the weaker and nonuniform, or inhomogeneous, magnetic fields of cheap permanent magnets (though some 20 to 50 times stronger than those that adorn refrigerators) could likewise produce data that could clearly distinguish among regions of different varieties of soft matter. Blümler soon came up with a design for a device that would yield the basic information contained in a single pixel of a conventional magnetic resonance image. Thinking that we could shift it around like a computer mouse to scan sizable objects, we named it NMR-MOUSE, for *n*uclear *m*agnetic *r*esonance *mo*bile *u*niversal *s*urface *e*xplorer.

The most intriguing aspect of our invention was that it promised to be potentially as small as a coffee cup, which would make it easy to move around. And unlike conventional NMR, which limits the maximum size of samples to something smaller than the big bore diameters of the toroidal magnets it uses, our system could be positioned on the surface of arbitrarily large objects to look inside them.

Examining A Painting with the NMR-MOUSE, a portable materials analyzer *(inside a positioning frame)*, allows Eleonora Del Federico of Pratt Institute to discriminate among the layers of varnishes, paints, gesso and the canvas backing to determine the work's state of conservation.
GRANT DELIN (photograph); NEW DOMESTIC DAYDREAMING, BY KENNETH BROWNE, 2007 (painting)

But the NMR-MOUSE's highly inhomogeneous magnetic field was a problem. According to the textbook knowledge of the time, it would eliminate the possibility that the tool would be able to provide chemical analyses of materials.

Conventional NMR

We overcame that roadblock by taking advantage of a specific metric used in standard NMR procedures known as the T_2 time constant. Classic, high-resolution NMR spectroscopy is typically conducted today by placing a sample inside a huge, stationary magnet that produces a powerful, homogeneous magnetic field. The technique exploits the fact that the atomic nuclei (bundles of positively charged protons and neutral neutrons) in certain atoms spin on their axes like miniature tops, which makes them behave like tiny bar magnets with north and south poles [*see box below:* How Magnetic Resonance Works]. In a strong magnetic field these spinning "bar magnets" try to line up with the magnetic field lines. Their alignment is not exact, however, and so the spinning nuclei, or spins, wobble (precess) about the field force lines in a way that resembles the dancing motion of a spinning top when a sideways force is applied to it.

If these nuclei are then hit with a pulse of radio-frequency (RF) energy, they will absorb and later reemit energy at specific frequencies according to their individual rates of rotation. These frequencies give rise to an NMR spectrum as distinct peaks of varying height that, like a set of fingerprints, can be used to identify the sample's constituent chemical groups. The data can also be manipulated to yield images that distinguish different materials.

More specifically, NMR spectroscopy relies on measuring the precession frequencies of the spins when they respond to the applied magnetic field and RF pulses. When a nonmagnetized sample is first exposed to a magnetic field, the spins roughly align with the field. After the sample is subjected to an RF pulse (from an RF coil), the spins first precess in synchrony, eventually fall out of sync, then return to their original states. Their return to equilibrium takes a characteristic time T_1 during which they release the energy they absorbed from the RF pulse. (A characteristic time or time constant is something like a radioactive half-life, which is the time it takes for the level of nuclear-decay emissions from a sample to drop by half.)

The synchronous precession of magnetic spins induces an oscillating voltage in the coil that decays with a characteristic T_2 time constant for each spin type as the spins fall out of synchrony. To create NMR spectra that indicate the chemistry of a substance and to produce images, the T_1, T_2 and precession data results are massaged with various complex mathematical formulas that, for example, derive the density of the spins in a volume of a sample, from which the contrast of an image of an object can be derived.

Riding the Echo Train

The key to our device was the realization that T_2 could be measured in nonuniform magnetic fields. Back in 1949, Erwin L. Hahn, a noted physicist then at the University of Illinois, had shown that responses to NMR stimuli can be detected even when one employs inhomogeneous magnetic fields because of certain signals called echoes that arise. In these nonuniform fields the coil voltage caused by the excitation of an RF pulse rapidly decays to zero, but it can be recovered some time later by applying a second pulse. Adding further pulses generates a series of echoes that form what scientists call an echo train. The amplitudes of the echoes in a train decay with the T_2 relaxation time that varies characteristically for different materials.

The T_2 value reflects the mobility of the molecules under investigation: soft matter (in which molecules can move easily) has a long T_2, whereas hard matter (in which there is less molecular mobility) has a short T_2. Whenever a chemical reaction or a phase transition occurs, the molecular mobility of the constituents also changes. The different T_2 values thus provide information about the physics and chemistry of a material as well as contrast data that can be used to help differentiate regions of dissimilar tissues in medical images.

When Blümler and I moved to RWTH Aachen University in Germany in 1994, we started to build the first version of the NMR-MOUSE. Two years later we observed the first signal from the device and were amazed to find that our invention was capable of producing responses from nearly any proton-containing material, including wood, rubber and chocolate. For some materials, the echo trains were long; for others, they were short. We then began to systematically investigate how the associated T_2 values correlate with the properties of the materials we probed.

After several years of refinement and with key contributions from Federico Casanova and Juan Perlo, researchers who had since joined the RWTH group, we ended up with the purse-size configuration of the NMR-MOUSE that we currently use. It has a single-sided design, in which the magnetic field extends outward away from the magnet, and it consumes little power, about the same amount needed to run an incandescent lightbulb. Some 40 to 50 such units are now operating worldwide.

Using the NMR-MOUSE

Rubber was one of the first materials we studied because it is commercially important for products such as tires and is soft like the body tissues for which MRI works so well. Rubber consists of long, spaghettilike polymer molecules that are tied together into a three-dimensional network by random cross-links. For many applications, the density of the cross-links is the most important characteristic in determining overall stiffness. The performance of a tire, which is composed of multiple layers of rubber compounds with different chemistries and cross-link densities, depends on the interplay of all these components. Tests on the track are typically needed to determine how a new design will perform. It turned out, however, that the NMR-MOUSE could analyze the cross-link density of the layers in the finished product individually without having to destroy the tire. This capability also eliminated the need for some tests on the racetrack.

The NMR-MOUSE can access layers at different depths -- up to a few centimeters deep. Its magnetic field generates an NMR signal only at a certain distance from the device, so investigators shift this sensitive region through the different layers of a tire to obtain T_2 readings (and thus cross-link densities) for each layer. Other similar uses for the NMR-MOUSE include analysis of the degree of environmental degradation inflicted on polymers (including rubber and polyethylene) and of the chemical makeup of tempera paint binders in old-master paintings.

Another key application revolves around the production of internal profiles of materials under the surface of, say, human skin or the layers of dirt, varnish and touch-up paints on old paintings. A few years ago, for instance, we applied our probe technology to Ötzi the Iceman, the well-preserved Neolithic mummy that climbers found in 1991 when the glaciers at the border between Austria and Italy melted enough to reveal the body. The device successfully produced a clear-cut depth profile that shows a layer of ice, a layer corresponding to Ötzi's freeze-dried skin and subcutaneous tissue, and a layer corresponding to the underlying bone structure of dense and spongy material. Such a nondestructive visualization of bones could prove to be of great value to archaeologists searching for intact but buried caches of prehistoric DNA.

The uses for portable NMR machines are meanwhile starting to expand elsewhere as the principles of the technique become more widely known. One notable example is the work by Magritek, a Wellington, New Zealand-based firm co-founded by Paul Callaghan, a pioneering NMR researcher. Among other endeavors, Magritek is using a technology that is related to ours to analyze how the mechanical properties of Antarctic ice cores change as the glaciers there encounter the effects of global warming.

Progress in Mobile NMR

Casanova and Perlo have recently increased the homogeneity of the magnetic field generated by the system's permanent magnet to improve its resolution. As a result, the improved NMR-MOUSE can now reveal the chemistry of a solution in a beaker that has been placed on top of the device. This surprising capability has opened the door to chemists to use the NMR-MOUSE for molecular analysis. Today researchers are studying various arrangements of magnets that could allow for coffee cup-size NMR systems that could perform chemical assays.

And because the current hardware is essentially that of a cell phone combined with a small magnet, the cost of the device should drop as demand grows. At some point in the future, portable NMR machines may even be sold in department stores for personal use. Someone suffering from a skin condition, for example, may one day monitor a problem with a home NMR device and then adjust a skin care program according its findings. Perhaps something like the Star Trek tricorder is not so far off after all.

ABOUT THE AUTHOR
Bernhard Blümich, a professor of macromolecular chemistry at RWTH Aachen University in Germany, studies the methodology and use of NMR spectroscopy and imaging in materials science and chemical engineering. He received his doctoral degree from the Technical University of Berlin in 1981. More information on his chief development, the mobile NMR-MOUSE materials probe, can be found at www.nmr-mouse.de

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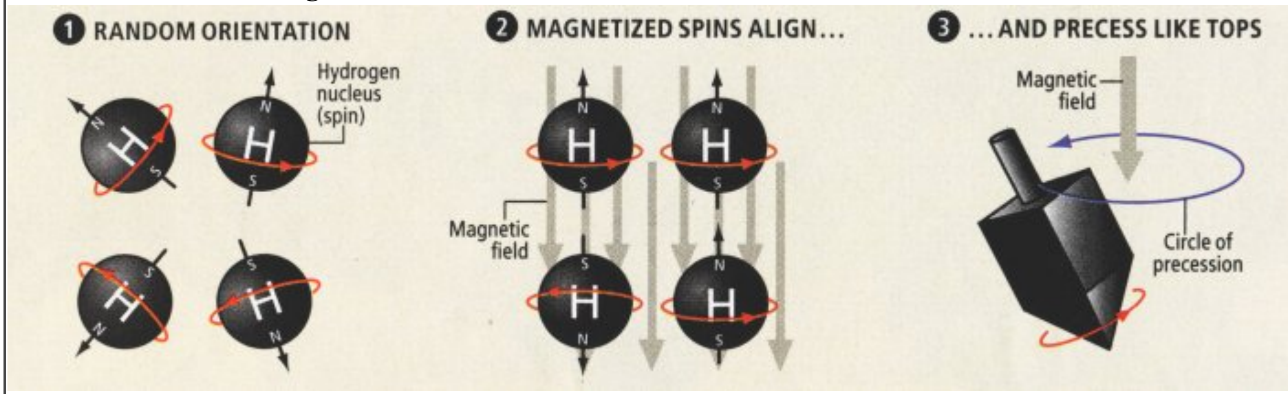
How Nuclear Magnetic Resonance Works

Nuclear magnetic resonance (NMR) technology exposes objects to a magnetic field and pulses of radio-frequency (RF) energy. Analysis of a material's response to those inputs can reveal both the constituent molecules and such properties as the substance's strength or hardness. Huge magnetic resonance imaging (MRI) machines common in hospitals are a form of NMR device.

Creation of Nuclear Magnetization

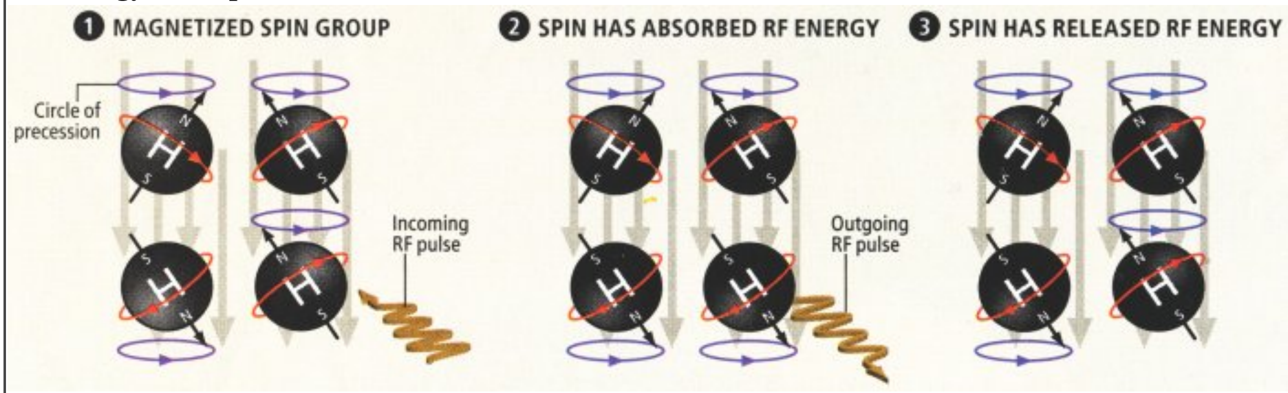


Single, unpaired protons (here, hydrogen nuclei) spin on their axes along random orientations. The motion of the positively charged protons (known as spins) makes them act as if they are tiny bar magnets.

When the NMR machine applies a strong magnetic field to the sample, the spins (on average) tend to align their axes along the field lines.

The alignment is inexact, though, resulting in precession -- the axes rotate around the field lines -- at a frequency that is unique for each type of nucleus and chemical group in a molecule.

RF Energy Absorption and Release



Magnetized spins precess along random orientations in the magnetic field. When a coil

Absorption causes the spin to flip 180 degrees. All nuclei that interact with the RF pulse in the same

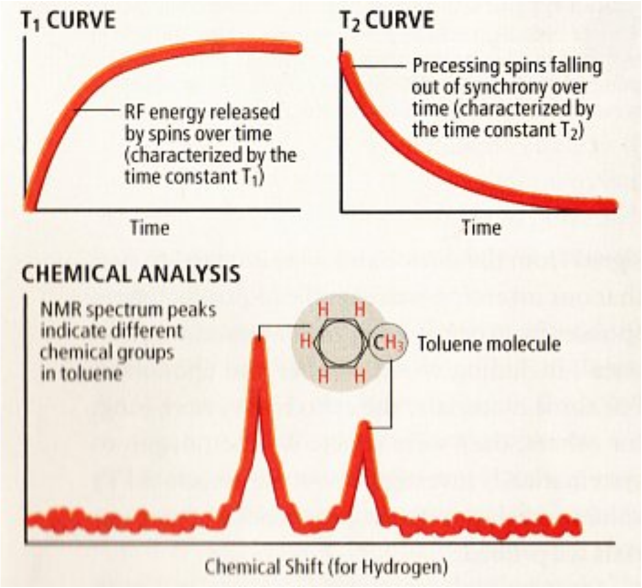
At random intervals, flipped spins release the in the NMR machine sends an RF pulse toward the group, only a spin that precesses at a rate and phase that matches the pulse's frequency can absorb its energy.

way absorb its energy and flip 180 degrees. The machine's coil picks up the signal induced by the magnetization caused by these changes in spin precession and feeds it to a computer.

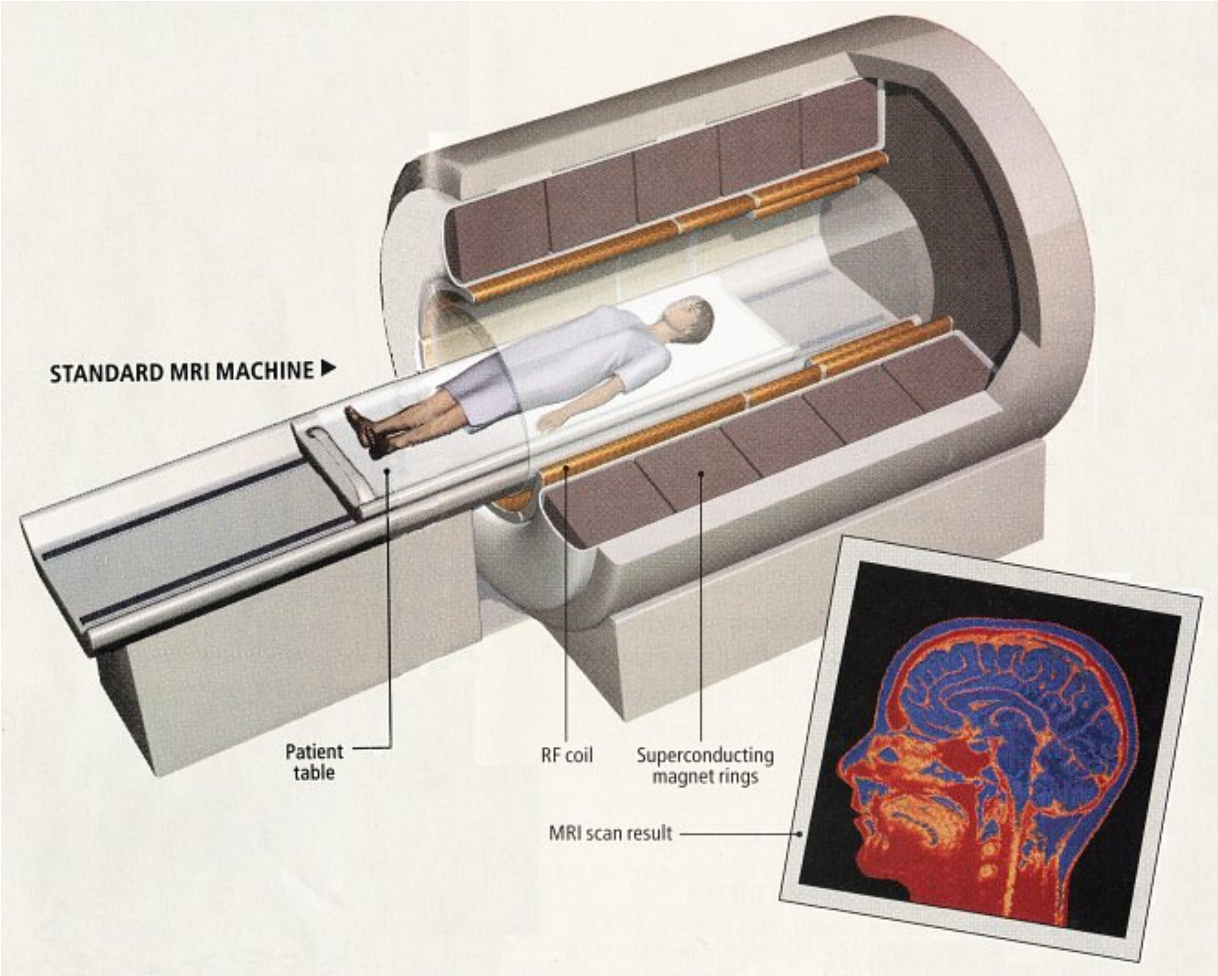
absorbed RF energy and return to their original (prepulse) orientations.

Results

The computer registers the time it takes for each type of spin to release the absorbed radio energy (*T_1 graph*). The system can also monitor the precessing spins as they fall randomly out of sync (*T_2 graph*). At the same time, it records the precession frequency of the spins of different chemical groups, which are summarized by a value called the chemical shift. The shift forms the basis of NMR spectra plots that identify constituent chemical groups in a sample, such as those in the hydrocarbon molecule toluene (*chemical analysis graph*). MRI machines combine all these NMR data to produce views of internal body tissues, including images of the human brain (below).

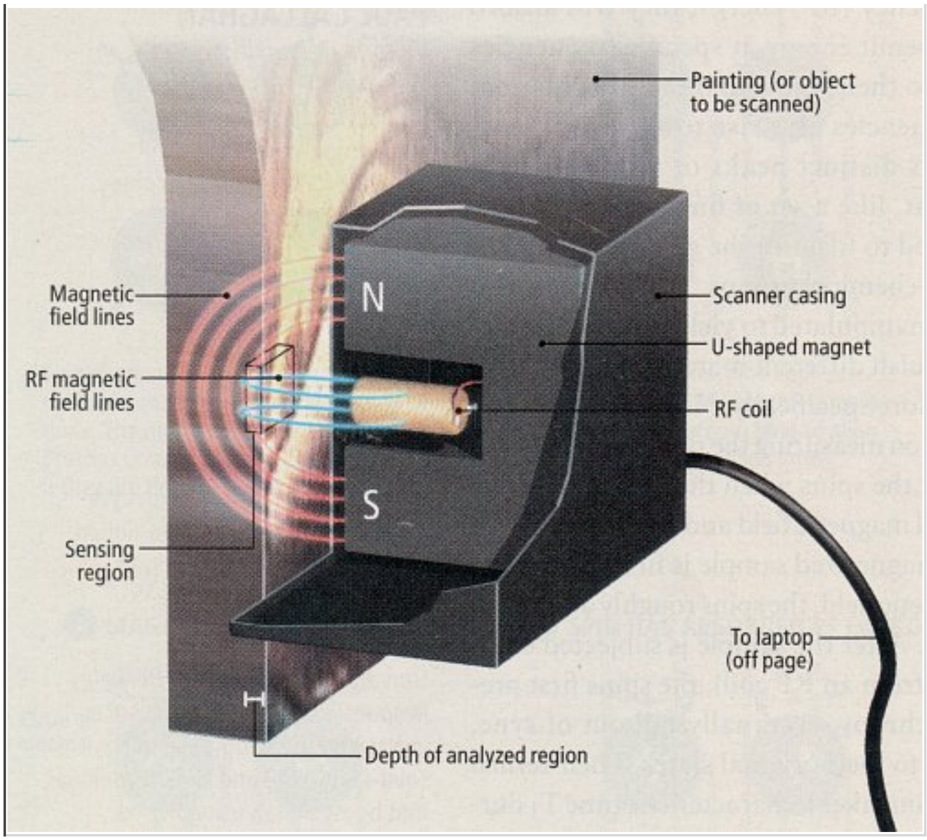


Standard MRI Machine



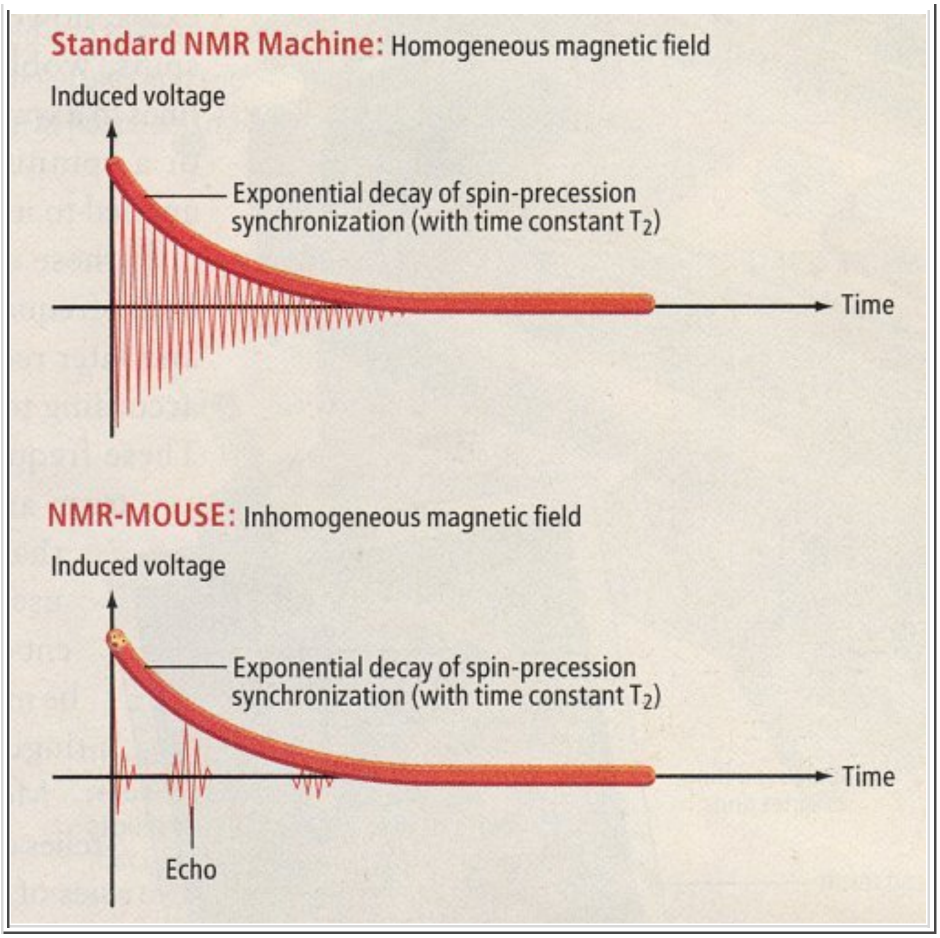
The First Miniaturized NMR Machine

The author's portable materials analyzer, the NMR-MOUSE (shown in cutaway view), consists of a U-shaped magnet that has an RF coil in its gap. The device senses the composition of matter where the magnetic field lines of the magnet and of the RF coil cross each other. Operators place the device at different distances from the surface to analyze slices at different depths.



How Standard and Mobile NMR Differ

A standard NMR machine produces a homogeneous magnetic field and thus can generate a T_2 signal with a single RF pulse. But the NMR-MOUSE cannot do the same because it uses an inhomogeneous magnetic field. It can, however, generate a T_2 signal response by exciting samples with multiple RF pulses that create signals known as echoes. The amplitudes of the echoes can then be assembled into a useful T_2 signal.



Other Uses for the NMR-MOUSE

Beyond analyzing paintings, the NMR-MOUSE has also found applications in industry and science. Manufacturers of automotive tires, for instance, use the device to image and determine the chemical compositions of the many individual layers of different rubber compounds that make up a tire (in some cases, a competitor's product). A conventional NMR tomography machine would not work on a standard steel-belted tire, for example, because the strong magnetic field it creates would attract the belt, whose ferrous nature would also disrupt the results. Other users employ the technology to evaluate the environmental damage done to aging polymer materials such as polyethylene.

Scientists have also applied the NMR-MOUSE to the study of Ötzi the Iceman, the ancient, partially thawed-out mummy discovered in 1991 by climbers in the Alps. In 2006 the sensor probe successfully mapped a cross section of the Iceman's well-preserved skin, subcutaneous tissue and skull bone at the Museum of Archaeology in Bolzano, Italy. -- B.B.

Ötzi the Iceman and car tires are only two of the many study subjects for the NMR-MOUSE.

Pioneers of Portable NMR

The budding technical field or "mobile NMR" has been advanced by many distinguished researchers worldwide. Here are a few of the leaders:

Paul Callaghan
Victoria University, Wellington, New Zealand
Produced innovations in NMR, microscopy, developed NMR methods for the molecular study of soft and porous materials, and invented novel portable NMR spectrometry devices

Eiichi Fukushima
New Mexico Resonance Albuquerque, N.M.
Created NMR methods to analyse technical processes and developed new mobile NMR technologies

Alexander Pines *University of California, Berkeley*
Responsible for multiple advances to NMR methodology, including solid-state NMR and NMR techniques that boost signals using hyperpolarization effects.

MOBILE NMR PROBE (right) developed by Paul Callaghan (holding drill at left), Mark Hunter and other researchers was dropped into a drill hole to assess the physical properties of Antarctic sea ice.

Further Reading

- **The NMR-MOUSE, a Mobile Universal Surface Explorer.**
  G. Eidmann, R. Savelsberg, Peter Blümler and Bernhard Blümich in *Journal of Magnetic Resonance, Series A,* Vol. 122, No. 1, pages 104-109; September 1996.
- **Well Logging.**
  R. L. Kleinberg in *Encyclopedia of Nuclear Magnetic Resonance,* Vol. 8. Edited by David M. Grant and R. K. Harris. Wiley, 1996.
- **NMR Logging Principles and Applications.**
  George R. Coates, Lizhi Xiao and Manfred G. Prammer. Halliburton Energy Services, 1999.
- **Essential NMR.**
  Bernhard Blümich. Springer, 2005.
- **Mobile Single-Sided NMR.**
  Bernhard Blümich, Federico Casanova and Juan Perlo in *Progress in Nuclear Magnetic Resonance Spectroscopy* Vol. 52, No. 4, pages 197-269; April 14, 2008.

- **Virtual Institute for Portable NMR**
- **Simply Physics: The Home of MRI Physics Put Simply**