Low-field magnetic resonance imaging with a high-T_c dc superconducting quantum interference device

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A spectrometer incorporating a high transition temperature dc superconducting quantum interference device (SQUID) is used to obtain nuclear magnetic resonance signals from protons in mineral oil at room temperature in fields up to 3 mT. The spatial separation between the SQUID magnetometer at 77 K and the sample at room temperature is less than 1 mm. At 2 mT, the signal is easily resolved in a single scan. Two-dimensional images of samples consisting of pieces of lucite or glass immersed in mineral oil are obtained at 2 mT. © *1999 American Institute of Physics.*
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In nuclear magnetic resonance (NMR) experiments, the precession frequency ω of the nuclear spins is proportional to the local magnetic field $B(\mathbf{r})$. By controlling the local strength of the magnetic field with a combination of the static homogeneous field B_0 and externally applied field gradients, one can determine the spatial distribution of the nuclear spins from the measured spectrum.[1] This technique is widely used, notably in medical magnetic resonance imaging (MRI). In conventional NMR experiments, in which a resonant circuit (Faraday detector) is used to detect the precessing magnetization, the induced voltage, V, is proportional to ωM, where M is the net magnetization of the spins. Since the magnetization is also proportional to the frequency, V scales as ω^2. Thus, the signal-to-noise (S/N) ratio increases rapidly as the magnetic field is increased. On the other hand, the large magnetic fields required by conventional MRI result in a large and expensive system that may not be appropriate for the study of small samples. Furthermore, an endemic problem in high-field MRI arises from the spatial variation in magnetic susceptibility, for example, at liquid-gas or solid-gas interfaces.[2] These variations lead to local magnetic field gradients that can cause distortion and limit the resolution. Since the spurious gradients are proportional to the applied field, these problems are largely eliminated at low fields. On the other hand, in low-field NMR (say, below 10 mT), the frequency is low (below 500 kHz) and the signal correspondingly weak.

One way of enhancing the signal strength at low frequencies is to use hyperpolarized ^{129}Xe or ^{3}He nuclei in which the magnetization is enhanced by several orders of magnitude over the thermal equilibrium value by the optical pumping of alkali metal vapor.[2–5] Tseng *et al.*[2] imaged voids

filled with hyperpolarized ^{3}He, and demonstrated that magnetic resonance images obtained in a magnetic field as low as 2.1 mT can have a higher quality than the corresponding images obtained at high field, 4.7 T. For imaging of protons in biological samples, however, the magnetization and precession frequency in a field of 2 mT are too small for practical MRI experiments with conventional detectors. In fact, these authors estimate that, with their low-field MRI system, it would take roughly two months to obtain images of thermally polarized proton samples at 2.1 mT of a quality comparable to their images of hyperpolarized ^{129}Xe. This acquisition time is much too long for practical applications.

An alternative approach is to use a dc superconducting quantum interference device (SQUID) as the NMR detector. Since the SQUID is a flux-to-voltage transducer, it detects the sample magnetization directly, rather than its time derivative. The signal therefore scales with ω, rather than with ω^2, resulting in a higher S/N ratio in low fields than with a conventional Faraday detector.[6] In fact, low transition temperature (low-T_c) SQUIDs have been successfully used for MRI of room temperature samples at 10 mT[7] and of helium temperature samples at 1 mT.[4] Kumar *et al.*[8] have used a high-T_c SQUID to detect NMR spectra in a field as low as 23 mT. In this letter, we describe the implementation of a high-T_c SQUID spectrometer for the detection of spatially resolved NMR signals from protons in thermal equilibrium at room temperature, and we present images obtained at 2 mT.

A simplified sketch of the dewar and coils is shown in Fig. 1. The static magnetic field B_0 in the z direction is produced by a Helmholtz pair. The transmitter coils consist of a second Helmholtz pair perpendicular to the first, and are used to apply pulses of oscillating magnetic field with amplitude B_1 in the y direction. A gradient field dB_z/dz is applied by a pair of Maxwell coils situated outside the static field coils. The dc SQUID multiloop magnetometer[9] is operated in vacuum and separated from the sample, which is less than 1 mm away, by a sapphire window.[10] The SQUID is
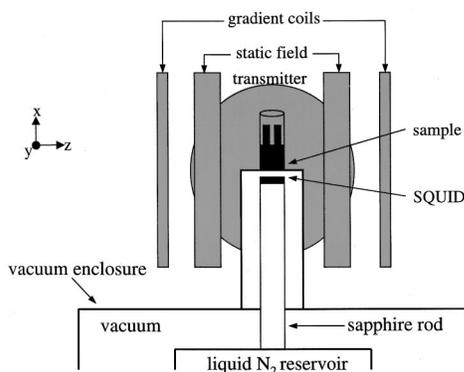
FIG. 1. Configuration of NMR apparatus. The overall height is 0.35 m.

FIG. 2. Proton NMR signal obtained from 1 ml of mineral oil at room temperature (a) in a single pulse at 2 mT and (b) after 10 000 averages at 59 μT.

cooled by a 0.1 m long sapphire rod thermally anchored to the liquid nitrogen reservoir. The SQUID is operated in a flux-locked loop[11] with a bandwidth of 0–1.1 MHz: the voltage across the SQUID is amplified, integrated and fed back as a magnetic flux via a single-turn copper loop. The voltage across the feedback resistor is amplified, filtered, and stored in a computer. Above a few kilohertz, the measured system flux noise is $25 \mu\Phi_0/\text{Hz}^{1/2}$, where $\Phi_0 = h/2e$ is the flux quantum, corresponding to a field noise of 30 fT/Hz$^{1/2}$.

As a sample for our proton NMR experiments, we used mineral oil, which has a high proton density as well as a relatively short spin-lattice relaxation time $T_1 \sim 100$ ms, making it possible to pulse frequently and thereby to improve the S/N ratio by signal averaging. Our experiments were performed in a static magnetic field $B_0 = 2.037$ mT, at which the central proton resonant frequency is 86.72 kHz. An 86.7 kHz pulse of duration 120 μs is applied to the transmitter coil to produce the excitation pulse. With the amplitude adjusted to give a field of 58.6 μT at the sample, this pulse tips the magnetization by 54° from the z direction towards the x-y plane, allowing an optimal repetition rate of 25 Hz for our experiment. The flux-locked loop is disabled during the excitation pulse, and enabled 200 μs after it is completed. During the free induction decay (FID) the magnetization of the sample precesses in the x-y plane and is detected by the SQUID.

The sensitivity of the spectrometer is sufficient to detect the proton NMR signal produced by 1 ml of mineral oil in a field of 2 mT without signal averaging as shown in Fig. 2(a).[12,13] As a further demonstration of the sensitivity, Fig. 2(b) shows the Fourier transform of the spin echo from the protons in 1 ml of mineral oil at room temperature in 59 μT, a field comparable to that of the Earth. The proton signal at 2.57 kHz is clearly visible; the data were averaged over 10 000 pulses. Proton NMR in the Earth's field was reported long ago;[14] however, these measurements required 500 ml of mineral oil and prepolarization in a field of 10 mT. More recently, Mohoric̆ *et al.*[15] demonstrated MRI of phantoms in which the nuclear spins were prepolarized in a high magnetic field which was subsequently turned off nonadiabatically for low-field imaging.

For our proton imaging experiments, we used phantoms consisting of hollow glass cylinders filled with mineral oil and pieces of glass or lucite. The inner dimensions of the phantoms were chosen to correspond roughly to those of the magnetometer. The fact that the SQUID magnetometer does
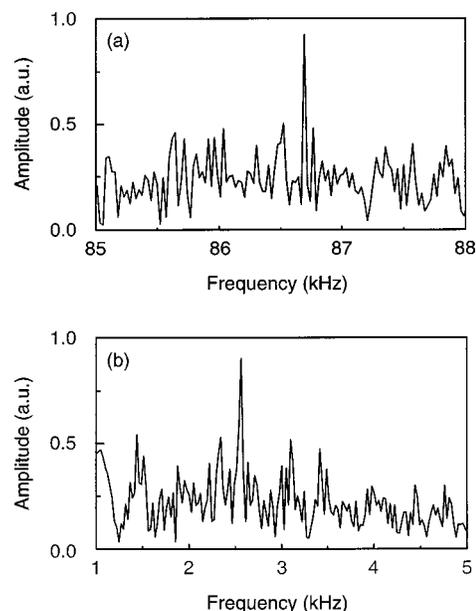
not enclose the sample allows us, in principle, to investigate samples that are large compared to its diameter. However, the sensitivity of the device is highest in a region that corresponds roughly to its diameter, in this case 7 mm. By choosing cylinders of roughly this size, we find that we do not need to correct for distortions that result from spatial changes in the sensitivity of the magnetometer. For the imaging procedure we employed the pulse sequence described above and a projection-reconstruction method.[16] The data were collected with the sample in a static gradient of 2 mT/m. For each orientation of the sample, 30 000 FIDs were averaged. A Fourier transform of these data delivers a one-dimensional projection. After a total data acquisition time of 8 h, 24 projections were obtained by sequential 15° rotations of the sample around the x axis. Finally, the image of the sample was reconstructed by filtered backprojection with a generalized Hamming filter.[16] Two examples are shown in Figs. 3(a) and 3(b). The pixel size corresponds to 0.575 mm, or 49 Hz in frequency space. We chose this size so that the pixel diagonal, approximately 0.8 mm, was equal to the spatial resolution Δz determined by the full width half maximum linewidth, $\Delta f \approx 70$ Hz, of the proton NMR line without an applied gradient. This linewidth is determined largely by the inhomogeneity of the static magnetic field. For a gradient $G = 2$ mT/m, the spatial resolution is given by $\Delta z = 2\pi\Delta f/\gamma G \approx 0.8$ mm, where $\gamma = 26.7 \times 10^7$ Hz/T is the gyromagnetic ratio for protons.

Figures 3(c) and 3(d) show the same two images after digital smoothing with Gouraud shading. This color interpolation routine subdivides each image pixel and linearly interpolates the values of the resulting subpixels. It then assigns a color based on the predefined color mapping.

We note that the averaging time to obtain the images in Fig. 3 is still quite long, about 8 h. It should be possible to lower the noise of the magnetometer by about a factor of 2 by using additional positive feedback[11] to eliminate the noise contribution of the preamplifier. Even lower noise, below 10
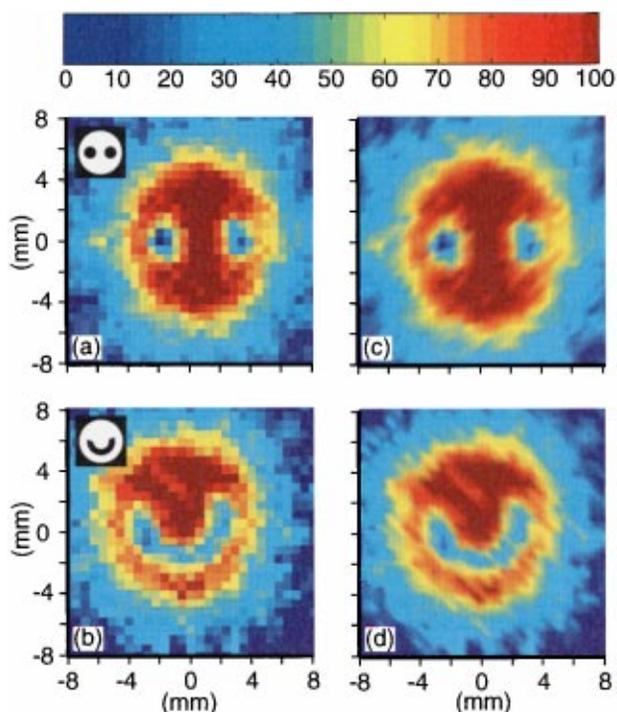
FIG. 3. (Color) (a), (b) Two-dimensional images of a hollow cylinder containing mineral oil and (a) two glass rods, (b) a ''U''-shaped plexiglass piece (shown in the upper left corners). The mineral oil volume was about 0.6 ml in (a) and 0.4 ml in (b). Both images were obtained from 24 projections with 30 000 proton NMR signals averaged per projection in a magnetic field of 2 mT. (c), (d) Digitally smoothed versions of these images obtained with a linear interpolation color shading scheme known as Gouraud shading. The color bars show the color map used in the shading.
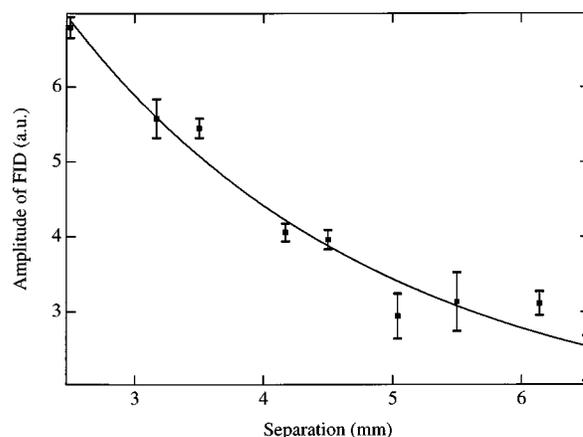

FIG. 4. Amplitude of FID decay from mineral oil sample at 3 mT vs spatial separation between the top of the sapphire window and the bottom of the sample cell. The curve is an empirical fit to the data.

$fT/Hz^{1/2}$,[17,18] has been demonstrated with high-T_c, flip-chip magnetometers. An improvement in S/N ratio by a factor of 3 would enable us to acquire images of the same quality in under one hour. Alternatively, we could make use of the improved S/N ratio to reduce the pixel size.

We emphasize that the configuration in Fig. 1 is designed to image small samples, and that the sensitivity falls off rapidly as the separation between the SQUID and the sample increases beyond a certain value. To illustrate this point, we measured the NMR signal from mineral oil at 3 mT as a function of sample separation from the magnetometer. The lateral dimensions of the cell were comparable to those of the magnetometer, its bottom was 125 μm thick, and the height of the mineral oil was about 40 mm. The amplitude of the Fourier transform of the FID versus separation is shown in Fig. 4. The curve is an empirical fit to the data. We see that the amplitude falls to roughly 1/e of its initial value in 3 mm, which represents an effective ''sensing depth'' of the spectrometer.

In conclusion, we have shown that it is possible to obtain magnetic resonance images of protons in fields of about 2 mT with a pixel size of about $0.6 \times 0.6 \, mm^2$ in a reasonable averaging time. This technique could be extended to small objects, for example, of biological or geological interest, simply by placing them on the window. For many situations, the long averaging times may well be acceptable. However, it would be of considerable interest to enhance the signal by means of dynamic nuclear polarization[19] or by using hyperpolarized ^{129}Xe.[2]

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