

## Resolution of $^{129}\text{Xe}$ Chemical Shifts at Ultralow Magnetic Field

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In high-field nuclear magnetic resonance (NMR) spectroscopy, the sensitivity of the xenon chemical shift to its environment<sup>1</sup> has been exploited to study porosity and surface interactions in materials<sup>2</sup>, as well as to probe xenon interactions with molecules<sup>3</sup> and proteins<sup>4</sup> in solution. In recent years, polarization enhancement through optical pumping<sup>5</sup> techniques has further advanced the utility of xenon NMR<sup>6</sup> and magnetic resonance imaging (MRI) from high<sup>7</sup> (several Tesla) to ultralow magnetic fields.<sup>8,9</sup> Despite the emergence of research in low-field MRI using laser-polarized xenon, the chemical shift of  $^{129}\text{Xe}$ , widely studied and used at high fields, still remains unexploited at mT fields. The possibility

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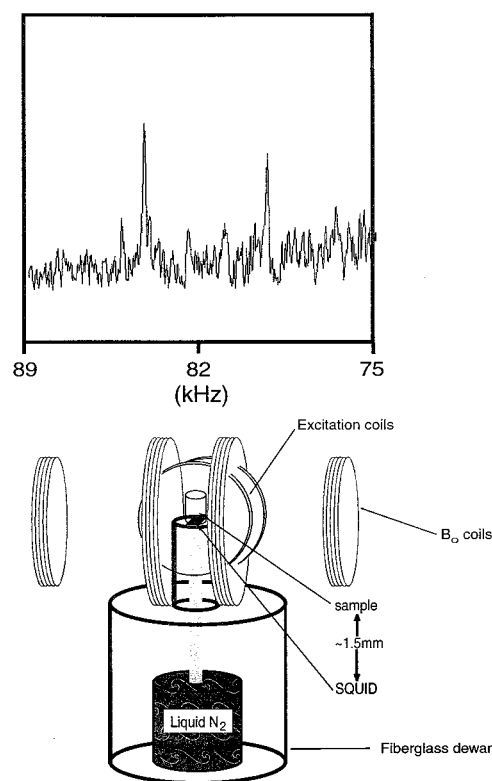
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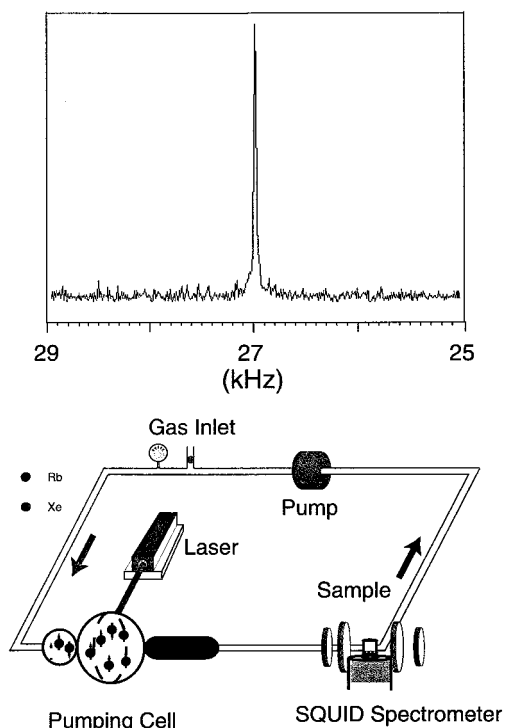


**Figure 1.** Schematic diagram of SQUID spectrometer and NMR spectrum of a 1 mL sample of 2.67 M aqueous solution of trifluoroacetic acid in a magnetic field of 1.98 mT. The spectrum, an average accumulation of 40000 scans at room temperature, shows  $^1\text{H}$  and  $^{19}\text{F}$  signals at 84.3 and 79.3 kHz, respectively.

of obtaining analytical information or performing chemical shift selective imaging without the need for high magnetic fields is an exciting prospect in many circumstances in chemistry and biomedicine.

In this communication we demonstrate examples of analytical information obtainable from ultralow field NMR, highlighting in particular the observation of chemical shifts at such fields. The resolution of chemical shifts in the mT range for common NMR nuclides, such as  $^1\text{H}$  and  $^{13}\text{C}$ , is normally impractical, beyond the issue of sensitivity, because of limitations of spectral resolution due to transverse relaxation. However, certain analytical information, such as the identity and concentration of different nuclei in the same sample, can still be obtained. Figure 1 shows a schematic of the SQUID ultralow field NMR spectrometer<sup>10</sup> and a spectrum from a 1 mL deuterated-trifluoroacetic acid/ $\text{D}_2\text{O}$  solution in water in a static magnetic field of 1.98 mT. The sample consists of 2.67 M deuterated-trifluoroacetic acid to which water is added to provide spin concentrations of about 8 M for  $^{19}\text{F}$  and 12 M for  $^1\text{H}$ . The resonance signals of  $^1\text{H}$  and  $^{19}\text{F}$ , at 84.3 and 79.3 kHz respectively, were excited by irradiation with a single pulse

(10) The detector used in these measurements is a dc SQUID magnetometer fabricated from thin films of the high transition temperature superconductor  $\text{YBa}_2\text{Cu}_3\text{O}_{7-x}$  in a “flip-chip” arrangement (Ludwig, F.; Koelle, D.; Dantsker, E.; Nemeth, D. T.; Miklich, A. H.; Clarke, J.; Thomson, R. E. *Appl. Phys. Lett.* **1995**, *66*, 373.). A SQUID measures magnetic flux directly, and its frequency-independent response enables the sensitive detection of NMR signals at ultralow fields. The magnetometer is operated in a vacuum and cooled to 77 K by a sapphire rod that is thermally anchored to a liquid nitrogen Dewar (see Figure 1). Two pairs of coils provide a magnetic field of up to 4 mT. Their homogeneity, calibrated using a proton sample, is 100 ppm at 2 mT for a cylindrical sample geometry (0.4 cm in radius and 0.42 cm in height). A third pair of coils arranged perpendicularly to the axis of the static field provides the excitation pulses.



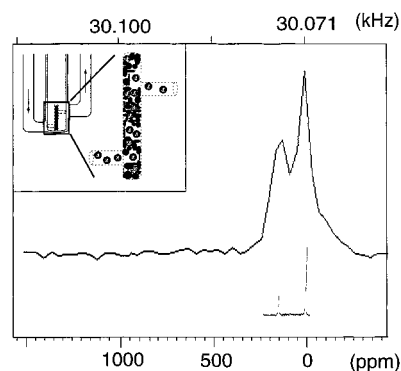
**Figure 2.** Schematic diagram of apparatus used to circulate laser polarized  $^{129}\text{Xe}$  and spectrum of SQUID-detected NMR signal of laser-polarized xenon gas (1 atm natural abundance) at room temperature. The magnetic field is 2.28 mT corresponding to a resonance frequency of 27 kHz.

applied at 82 kHz. At such low fields the thermal nuclear spin polarization is minuscule ( $\sim 10^{-9}$ ), presenting a significant challenge for signal acquisition using conventional NMR detectors. With the enhanced sensitivity of SQUID detection only 40000 averages were required. Such multinuclei NMR can be a useful tool for nuclide selective imaging and a diagnostic probe for molecular structure and chemistry. The added ability to resolve chemical shifts at ultralow fields, for which optically pumped xenon is uniquely suited, would further extend the analytical power of this technique.

Figure 2 shows a schematic of the circulating flow optical pumping apparatus used to provide a continuous source of laser polarized xenon<sup>11</sup> and a spectrum of laser-polarized xenon in a magnetic field of 2.28 mT. With the  $1 \times 10^7$  enhancement in polarization from optical pumping,<sup>11</sup> a signal-to-noise ratio (SNR) of 20 is obtained after only 100 scans, despite the fact that the spin density in gaseous, natural abundance  $^{129}\text{Xe}$  is about 3000 times lower than for protons in liquid water. Figure 3 shows a spectrum obtained from optically pumped xenon flowing through powdered polypropylene at 2.54 mT (upper trace). Also shown is a spectrum of Xe in polypropylene obtained in a highly homogeneous 4.3 T high-field magnet (lower trace).<sup>12</sup> The sample cell, shown in the inset, has a volume of 0.03 mL. The peak at 0 ppm arises from the free xenon gas, while the peak at about 200 ppm corresponds to xenon adsorbed on the polypropylene,

(11) We built a circulating flow optical pumping apparatus to provide a constant source of laser-polarized xenon gas. The system is based on earlier designs [(a) Driehuys, B.; Cates, G. D.; Miron, E.; Sauer, K.; Walter, D. K.; Happer, W. *Appl. Phys. Lett.* **1996**, *69*, 1668. (b) Brunner, E.; Seydoux, R.; Haake, M.; Pines, A.; Reimer, J. A. *J. Magn. Reson.* **1998**, *130*, 145.], but has been adapted for re-circulating flow and for operation with the SQUID detector. Typical polarization is 1–2%, an enhancement of about  $10^7$  over thermal polarization at 2 mT. The gas mixture consists of 1 atm natural abundance xenon, 1 atm nitrogen, and 5 atm helium.

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**Figure 3.** SQUID-detected NMR spectrum showing chemical shifts of laser-polarized xenon flowing over polypropylene at room temperature in a magnetic field of 2.54 mT. The peak at 30.071 kHz (0 ppm) arises from the free xenon gas while the peak at 30.077 kHz ( $\sim 200$  ppm) is due to xenon adsorbed on polypropylene. The low-field chemical shifts are consistent with the sharp peaks obtained by high-resolution high-field NMR at 4.3 T shown as the lower trace. The upper frequency scale (kHz) corresponds to the low-field spectrum.

consistent with high-field results.<sup>12</sup> The line widths, substantially higher than susceptibility-limited broadening,<sup>13</sup> are dominated by the inhomogeneity of the magnetic field, as evidenced by the appearance of spin-echoes following refocusing  $180^\circ$  pulses. Additional significant contributions include broadening caused by gas flow and exchange between the free and adsorbed xenon, as indicated by the increase in line widths when the gas flow-rates are increased.<sup>14</sup> It is anticipated that high spectral resolution will be possible with enhancements to the apparatus currently under way, including the design of more homogeneous magnets including shim coils, and modifications to the optical pumping apparatus to enable stop-flow and variable-temperature experiments. To the best of our knowledge, these experiments demonstrate the first resolution of  $^{129}\text{Xe}$  chemical shifts obtained at such low magnetic fields.

In summary, we have used a SQUID detector incorporated into an optical pumping NMR spectrometer to resolve the chemical shift of  $^{129}\text{Xe}$  in different physicochemical environments in a static magnetic field of 2.54 mT. These results open the way for the use of xenon chemical shifts for diagnostic chemical and biomedical NMR analysis, and chemical-shift resolved MRI and microscopy in molecules, materials, and organisms at ultralow magnetic fields. In particular, the combination of laser polarization and SQUID detection will enable the extension of xenon NMR, a powerful high-field probe of molecular conformation and environments,<sup>15</sup> to the regime of low-field.

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**Supporting Information Available:** Further information about the low-field SQUID spectrometer and the optical pumping apparatus (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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