COMMUNICATIONS

A Rapid and Precise Probe for Measurement of Liquid Xenon Polarization

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The relaxation time of liquid ^{129}Xe is very long (>15 min) and the signal at thermal equilibrium is weak. Therefore, determination of the absolute polarization enhancement of hyperpolarized ^{129}Xe by direct measurement is tedious. We demonstrate a fast and precise alternative, based on the dipolar field created by liquid hyperpolarized ^{129}Xe contained in a cylindrical sample tube. The dipolar field is homogeneous in the bulk of the tube and adds to the external field, causing a shift in the Larmor frequencies of all nuclear spins. We show that the frequency shift of the proton in CHCl$_3$ (chloroform), which dissolves homogeneously in xenon over a fairly broad temperature range, is an excellent probe for ^{129}Xe polarization. Frequency measurements are precise and the experiment is much faster than by direct measurement. Furthermore the ^{129}Xe polarization is minimally disturbed since no rf pulses are applied directly to ^{129}Xe and since chloroform is a fairly weak source of ^{129}Xe relaxation. The experiments are reproducible and require only standard NMR instrumentation.   © 2002 Elsevier Science (USA)

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Hyperpolarized liquid ^{129}Xe is a recently discovered tool to enhance NMR sensitivity in biological systems and organic molecules of interest (*1*). The method is based on polarization transfer via cross-relaxation between hyperpolarized ^{129}Xe and nuclei in nearby molecules, a process called the spin polarization-induced nuclear Overhauser effect (SPINOE). The enhanced nuclear polarization is used to obtain structural and chemical information on molecular systems and also to investigate molecular interactions at the xenon binding sites (*1–5*). In addition, liquid hyperpolarized ^{129}Xe and the SPINOE technique are important in NMR quantum computing (NMRQC) since low polarization at room temperature is one of the main limitations of NMRQC (*6*). A parameter of considerable interest in all of these applications is ^{129}Xe hyperpolarization. Currently, we are only aware of a direct measurement technique: the polarization enhancement is the ratio of the NMR signal of the hyperpolarized ^{129}Xe nuclei to the signal at thermal equilibrium. The initial hyperpolarization is then determined by combining the experimentally measured polarization enhancement with the polarization at thermal equilibrium, which can be calculated theoreti-

cally (high-temperature approximation: $P_{Xe} = \hbar \gamma_{Xe} B_o / 2kT$). Because of the long T_1 of liquid ^{129}Xe (>15 min) and the low gyromagnetic ratio of ^{129}Xe, it is very time-consuming to determine the signal at thermal equilibrium precisely. The results are often only order-of-magnitude estimates.

In this paper, we propose a rapid and precise indirect technique to measure ^{129}Xe polarization, based on frequency-shift measurements of ^{1}H nuclei in molecules dissolved in ^{129}Xe. The frequency shift is induced by the dipolar field created by the hyperpolarized ^{129}Xe molecules. The strength of the dipolar field is proportional to the density and polarization of ^{129}Xe and is also dependent on the shape and size of the sample as well as the orientation of the magnetic dipoles within the sample volume. Mathematically, the total magnetic field H_{Xe} inside the sample can be written as the sum of the nuclear magnetization B_{Xe} of the polarized ^{129}Xe nuclei and the shape-dependent demagnetizing field $H_{d,Xe}$ ($H_{Xe} = B_{Xe} - H_{d,Xe}$). A homogeneous distribution of ^{129}Xe polarized molecules over a cylindrical sample volume is assumed. Calculations of the shape-dependent demagnetizing fields in solid magnets are applicable to a sample of magnetic dipoles in the liquid state (*7*). For cylindrically shaped volumes with magnetic dipole orientation along the axis of the cylinder, the strength of the magnetic field is given by (*7*)

$$H_{Xe} = B_{Xe} - H_{d,Xe} \qquad [1]$$

$$= N_{Xe} P_{Xe} \rho_{Xe} \mu_{Xe}$$

$$\times \left[1 - \frac{4\pi}{a^2 - 1} \left(\frac{a}{\sqrt{a^2 - 1}} \ln(a + \sqrt{a^2 - 1}) - 1 \right) \right] \quad [2]$$

with N_{Xe} the natural-abundance of ^{129}Xe (26%), P_{Xe} the polarization of ^{129}Xe, ρ_{Xe} the density of liquid xenon, μ_{Xe} the nuclear magnetic moment of ^{129}Xe and $a = l_{cylinder} / r_{cylinder}$. In our system, the cylindrical tube has an inner radius $r_{cylinder} = 1.08$ mm (thick wall NMR tube) and the height of the sample volume is $l_{cylinder} \approx 10$ mm. Therefore $l_{cylinder} \gg r_{cylinder}$ and Eq. [2]

can further be approximated to give

$$H_{Xe} = N_{Xe} P_{Xe} \, \rho_{Xe} \, \mu_{Xe} \left[1 - \frac{4\pi}{a^2} (\ln(2a) - 1) \right] \qquad [3]$$

$$= N_{Xe} P_{Xe} \, \rho_{Xe} \, \mu_{Xe} * 0.75 \quad \text{(for } a = 10) \qquad [4]$$

$$\approx P_{Xe} \times 0.22 \text{ Gauss} \quad \text{(for T} = -40°C, \text{ low CHCl}_3 \text{ density).}$$
$$[5]$$

A similar expression can be derived for H_H, the dipolar field created by the ^1H nuclei. Note however the proportionality of the dipolar field to the nuclear polarization. In our experiments, the polarization of hyperpolarized ^{129}Xe is at least two orders of magnitude larger than the polarization of ^1H and the density of ^{129}Xe is higher than the density of CHCl$_3$. Taking the difference in nuclear magnetic moment between ^{129}Xe and ^1H into account, it can be derived from Eq. [4] that the ^1H dipolar field is at most 1.5% of the ^{129}Xe dipolar field and can be safely neglected.

Figure 1 shows the frequency shifts of ^1H versus ^{129}Xe polarization expected from Eq. [5] and over the temperature range of interest (ρ_{Xe} changes with temperature and pressure; however, the pressure is the Xe vapor pressure—see sample description below—and is completely determined by temperature, therefore ρ_{Xe} is determined by temperature only). The marked point on the curve, corresponding to a typical setup for our experiments, predicts a frequency shift of 10 Hz for 1% ^{129}Xe polarization.

We have experimentally confirmed the above theoretical prediction by optically pumping ^{129}Xe gas, liquefying the hyperpolarized gas and dissolving CHCl$_3$ in the liquid Xe. We have measured the ^{129}Xe polarization of such samples with the direct measurement technique and compared it with the polarization obtained via the procedure described above. There is a very good agreement as shown later in this paper.
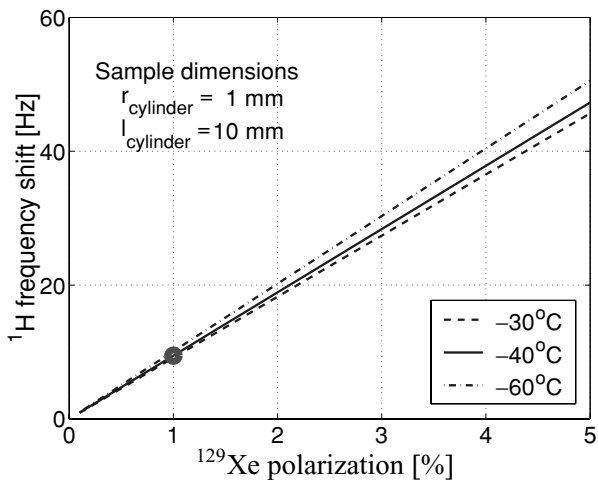

FIG. 1. Theoretically expected frequency shift of ^1H in CHCl$_3$, dissolved in liquid Xe, versus ^{129}Xe polarization. Different curves represent different temperatures (different ρ_{Xe}). The point marked on the graph shows a typical value for our setup.

This method has several advantages over the direct measurement technique. First of all, it is significantly faster due to the huge difference between the relaxation time of ^{129}Xe and ^1H ($T_{1,Xe} > 15$ min and $T_{1,H} < 20$ s). The fastest experiment to determine the ^{129}Xe hyperpolarization of an optically pumped sample *directly* consists of first measuring the hyperpolarized ^{129}Xe signal. Then the ^{129}Xe hyperpolarization is destroyed, e.g., by sending saturation pulses. Finally, the equilibrium ^{129}Xe signal is measured after waiting for a time 3 $T_{1,Xe}$ to allow the ^{129}Xe polarization to build up to 95% of its equilibrium value. The total time of the experiment is therefore larger than 45 min (3 $T_{1,Xe}$). For many experimental setups however, the low gyromagnetic ratio of ^{129}Xe necessitates averaging of the equilibrium ^{129}Xe NMR signal and therefore the experiment often takes more than 2 hs. (average over 3 or more ^{129}Xe NMR signals). The *indirect* technique, in contrast, starts with measuring the initial ^1H resonance frequency. Similarly to the direct technique, the ^{129}Xe hyperpolarization is then destroyed. Finally the equilibrium ^1H resonance frequency is measured. Since the equilibrium ^{129}Xe polarization is smaller than 5×10^{-4}%, the ^1H frequency shift created by the corresponding ^{129}Xe dipolar field becomes too small to resolve, as can be seen from Fig. 1. Therefore the equilibrium ^1H resonance frequency can be determined immediately after saturation of the ^{129}Xe polarization, which means that the indirect method is significantly more rapid than the direct method.

Second, the indirect technique is more precise as it is based on frequency measurements of ^1H nuclei instead of on signal-integrated intensities of ^{129}Xe nuclei, which have a low gyromagnetic ratio. Furthermore, the direct tehnique is exposed to two possible sources of error which are not present in the indirect technique. Tip angle and receiver gain are normally not identical when the initial versus equilibrium ^{129}Xe signal is recorded. Therefore the direct method requires accurate knowledge of these parameters to derive the initial ^{129}Xe polarization and as a result, the method is more susceptible to error.

Third, due to the indirect nature of the measurement, the ^{129}Xe hyperpolarization itself is not destroyed (not even partially) during the ^1H frequency measurements. Furthermore, the presence of only 10 mol% CHCl$_3$ does not noticeably change $T_{1,Xe}$ and hence the ^{129}Xe polarization that is achieved with or without the presence of CHCl$_3$ is assumed to be the same. Negative ^{129}Xe enhancements can now be measured accurately as well without radiation damping effects, from which the direct measurement technique suffers (8). Finally, the proposed method should work for any molecules that dissolve in xenon or that serve as a solvent for xenon (e.g., liquid benzene (1)), provided that the ^{129}Xe density and the ^{129}Xe hyperpolarization are high enough to create resolvable resonance frequency shifts. For example, a 0.1 M solution of ^{129}Xe (enriched) with a polarization of 10% will introduce a shift in the ^1H Larmor frequency of 1.9 Hz.

We propose that the newly developed polarization measurement technique be used when research with optically pumped liquid ^{129}Xe is performed. It will speed up the process of

optimizing the parameters of the optical pumping apparatus during the building stage and can be used thereafter as a verification tool. The technique also allows to characterize the loss of polarization when liquefying ^{129}Xe, when used in conjunction with polarization measurements in the gas phase. Furthermore, in SPINOE experiments, both the polarization of ^{129}Xe and the nucleus of interest have to be determined. This can now be done with one simple $\pi/2$ readout pulse on the nucleus of interest: the signal integrated intensity of the observed resonance peak gives information on the polarization of the nucleus itself, while the frequency shift determines the ^{129}Xe polarization.

The optical pumping setup consists of three ultrapure gas tanks (N$_2$, He, and natural-abundance Xe) which are connected to a Pyrex glass cell ($\phi = 1.5''$, length $= 6''$) containing solid Rb. The gases flow through a zirconium filter (NuPure Mdl 600 XL) before entering the pumping cell, to decrease the amount of O$_2$ to the ppb level. A typical gas mixture consists of 12% natural-abundance Xe, 2% N$_2$, and 86% He at a total pressure of 3.5 atm. The high percentage of Xe is a compromise between having sufficient ^{1}H signal from dissolved CHCl$_3$ (see Xe : CHCl$_3$ molar ratio below) and preserving ^{129}Xe polarization in the gas phase (self-relaxation increases with increasing Xe partial pressure (9)). Once the gases are inside the cell, a saturated Rb vapor is produced by heating the cell to 110°C and a magnetic field of 25 Gauss is applied using a pair of Helmholtz coils. High-power (up to 100 W) circularly polarized laser light (Optopower A100FCRB diode array laser), tuned to the D1 transition of Rb (795 nm), polarizes the Rb electrons.

After 20 min of Rb–Xe spin exchange, the gas mixture is passed through a cold trap which condenses the highly polar-ized ^{129}Xe. The ^{129}Xe polarization is maintained by permanent magnets which produce a magnetic field of 1–3 kG over the cold trap volume. Once all Xe is condensed, the cold trap is rapidly heated and Xe is transferred and frozen (77 K) in an attached high-pressure NMR tube (New Era NE-CAV5-H-120) containing 20 μl of degassed ^{13}CHCl$_3$. The sample tube is then disconnected from the optical pumping setup and lowered into a 2.1 T magnet. The temperature of the sample in the magnet can be controlled from -100°C to 16°C, which covers most of the liquid Xe range (-112°C to 16°C). For a typical experiment, we operate at -40°C, maximizing $T_{1,H}$ while keeping as much Xe in the liquid phase as possible. Xe and ^{13}CHCl$_3$ liquefy and mix homogeneously (Xe : ^{13}CHCl$_3$ molar ratio $= 5:1$ to $8:1$). NMR signals are monitored using a home-built spectrometer.

In a first experiment, we compare the results of the direct and indirect procedure for measurement of liquid ^{129}Xe polarization. The ^{129}Xe signal is measured at the start of the experiment and at the end, when thermal equilibrium is reached. From the signal enhancement, the initial hyperpolarization is derived (see result in table in Fig. 2b). As discussed before, the precision of this direct measurement technique is poor. During the experiment, the frequency shift over time of ^{1}H is also monitored (see Fig. 2a). The time constant of the exponential ^{1}H frequency shift curve is 16 min, which is equal to the measured $T_{1,Xe}$. This is in accordance with our theory: the frequency shift decreases because the ^{129}Xe polarization decreases, therefore the time constants must be the same. The polarizations derived from the respective procedures are compared in the table in Fig. 2b. The agreement is very good.
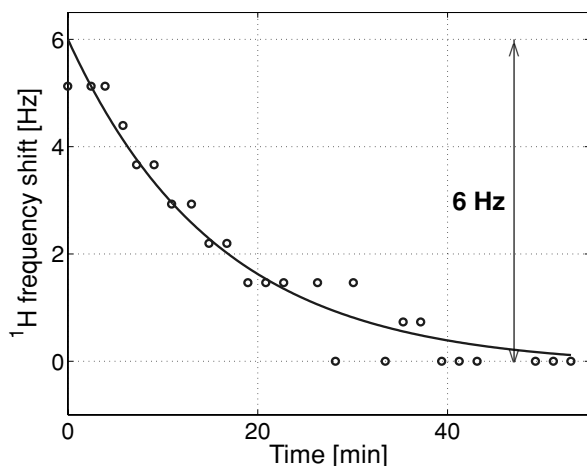
	^{129}Xe polarization	
Direct measurement	Indirect measurement	
0.8 ± 0.5 %	6 Hz $\Downarrow$ 0.6 ± 0.1 %	

(a)   (b)

FIG. 2. (a) Frequency shift of the ^{1}H resonance peak over time after mixing CHCl$_3$ with hyperpolarized liquid ^{129}Xe. The total ^{1}H frequency shift is equal to 6 ± 1 Hz. The precision of the frequency measurement is limited by the resolution of the spectrometer (0.7 Hz) and frequency fluctuations increase over time as the ^{1}H polarization decreases (SPINOE effect) and as signals become harder to resolve (this can be avoided by applying larger tip angle pulses; the pulses we used have very small tip angle ($<10°$) for reasons not related to the subject of this paper). The last three datapoints are then obtained after saturation of the ^{129}Xe nuclei and while applying pulses with larger tip angle. (b) ^{129}Xe polarization derived from the direct and indirect measurement procedures. The results are in very good agreement.

A second experiment is performed with $^{13}CHCl_3$ (labeled chloroform). Both the ^1H and ^{13}C frequency shifts are monitored (see Fig. 3). We expect to see a factor of 4 difference in the overall frequency shift of the respective nuclei, due to the difference in gyromagnetic ratios ($\gamma_H \approx 4\gamma_C$). The experimentally determined ratio is $\frac{20.6 \pm 1\ [Hz]}{4.5 \pm 1\ [Hz]} = 4.6 \pm 1$, in good agreement with theoretical expectations.

A final set of experiments is performed in which the orientation of the ^{129}Xe polarization is reversed. The upper curve in Fig. 4 shows the ^1H frequency shift when ^{129}Xe is polarized parallel with the magnetic field. The lower curve displays the results of a second experiment in which ^{129}Xe is polarized antiparallel with respect to the magnetic field. As expected, the sign of the ^{129}Xe polarization is reflected in the sign of the frequency shift.

We have also noted that when a π-pulse is applied to ^{129}Xe, the ^1H frequency shifts to a new value, reflecting a reversed ^{129}Xe dipolar field.

All these experiments support the above theory that the frequency shift of the ^1H nuclei in dissolved $CHCl_3$ is directly proportional to the dipolar field created by the hyperpolarized ^{129}Xe nuclei. The proportionality factor is dependent on the shape and size of the sample volume and the density and the orientation within the sample volume of the ^{129}Xe nuclei. All those sample parameters can be determined easily and hence the ^{129}Xe polarization is known if the ^1H frequency shift of a dissolved species is known.
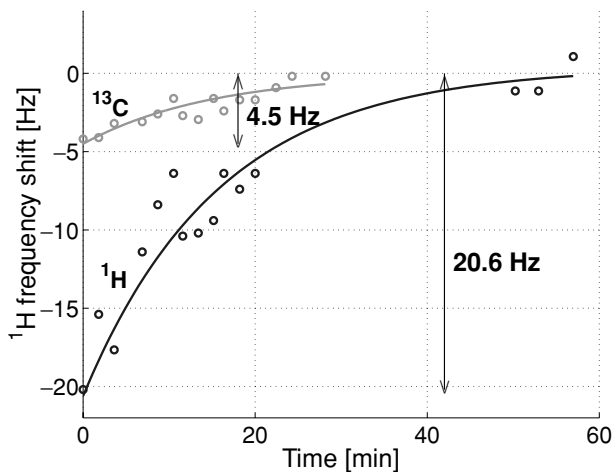

FIG. 4. Frequency shift of the ^1H resonance peak over time for ^{129}Xe polarized parallel (upper curve) and antiparallel (lower curve) to the magnetic field.

FIG. 3. Frequency shift of the ^{13}C and ^1H resonance peaks over time after $^{13}CHCl_3$ is mixed with hyperpolarized ^{129}Xe. There is approximately a factor of 4 difference in frequency shift due to the difference in gyromagnetic ratio ($\gamma_H \approx 4\gamma_C$). The data are obtained by simultaneously applying small tip angle pulses ($<10°$) to ^{13}C and ^1H. The small tip angle and the fact that a few pulses have been applied to ^{129}Xe during the coarse of the experiment (even when small tip angles were used) explain the frequency fluctuations in the presented data. There is a lack of datapoints in the ^1H curve between $t = 20$ and 40 min resulting from negative enhancement of the ^1H nuclei: the polarization has to pass through absolute 0 polarization before the positive equilibrium polarization is restored. Since NMR signals are proportional to absolute polarization, there is a time interval during which no signals can be detected.
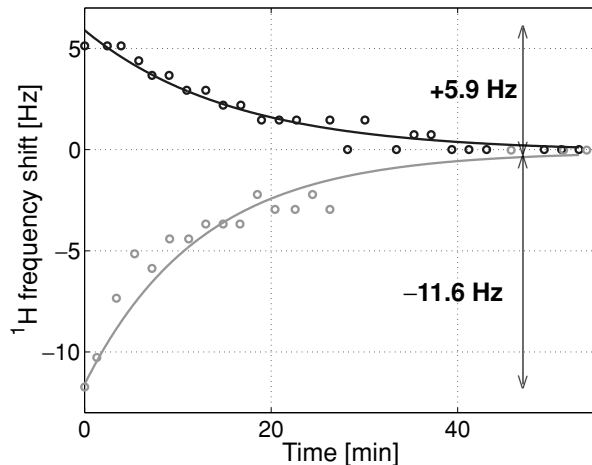
For completeness of the experimental discussion, we remark that ^{129}Xe resonance frequency shifts are observed during the experiments which can not be explained with the above theory. The obseved shifts are much larger than predicted (30 to 50 Hz shifts are observed when only a few Hz are expected) and the shifts always correspond to a decrease in Larmor frequency. We suspect that the shifts are a temperature effect rather than a dipolar field effect. As discussed above, the sample is frozen when inserted in the magnet and then heated to $-40°C$ using a temperature control system. Even though the temperature sensor, which is in contact with the bottom of the sample tube, reads the target temperature at the start of the experiment (4 min after insertion of the sample in the magnet), the sample itself might not have warmed up yet to $-40°C$. Since the dependence of the ^{129}Xe Larmor frequency on temperature is very strong ($\Delta f = 15$ to 20 Hz/$°C$) for natural abundance xenon at $-40°C$ and in a 2.1 T magnetic field (10, 11), it seems reasonable to attribute the observed ^{129}Xe frequency shifts to an increase in sample temperature (1 to 3$°C$).

In conclusion, we have demonstrated a new technique for determining liquid ^{129}Xe polarization. The technique is very fast and more precise than the current measurement procedure. Moreover, indirect probing minimally disturbs the ^{129}Xe polarization enhancement. Applications can be found in testing during the building stage of an optical pumping apparatus as well as for acquisition of information on the experiment itself, e.g., SPINOE experiments.

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