

Nuclear Spin-Noise Spectra of Hyperpolarized Systems**

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By resorting to spin systems with a polarization P driven far out of thermal equilibrium, thanks to optical pumping^[1] or dynamic nuclear polarization,^[2] NMR signals can be improved by a factor $K = P/P_{\text{th}}$ ranging between 10^3 and 5×10^5 , where P_{th} is the thermal equilibrium polarization. Thus, the limit of detection in a single acquisition by Faraday induction after an excitation pulse is reduced from $N \approx 10^{17}$ to 10^{13} spins.^[3] Other detection schemes, such as nuclear spin noise,^[4] usually disregarded owing to sensitivity limitations,^[5] can also benefit from this improvement. This method, which consists of the detection of the noise absorption at the Larmor frequency has been applied to characterize the NMR probe quality,^[6] optimize NMR signals,^[7] and has recently been used in magnetic resonance imaging (MRI).^[8] Since nuclear spin noise is observed through fluctuations of the transverse magnetization, and is proportional to $\sqrt{N}$, it is expected to be of low sensitivity. However, the nuclear spin noise is amplified by nonlinear coupling between an intense bulk nuclear magnetization and the coil (radiation damping, RD),^[9] an effect enhanced at high polarization, and we show experimentally that nuclear spin noise is readily observable in the case of dilute hyperpolarized samples. With a continuous monitoring capability, nuclear spin noise allows the determination of longitudinal (T_1) and also transverse ($T_2^* = 1/r_2$) self-relaxation times without destroying the hyperpolarization. This determination of relaxation times would otherwise be biased as rf pulses in classical detection schemes would destroy the hyperpolarization. Finally, since RD is primarily dependent on the coil specifications and spin concentration, we show herein that the conditions of spin-noise detection are fully renewed, thereby giving access to new applications in spectral and dynamics characterization, low spin number detection, and MRI.

Assuming a Lorentzian resonance line for the nuclear susceptibility, McCoy and Ernst derived a formulation for the nuclear spin noise,^[5] which depends on the spin polarization level and on λ_r , the RD characteristic rate at P_{th} .^[10] When applied to a hyperpolarized solute ($\lambda_r \ll r_2$) with perfect

tuning conditions,^[7] the theoretical equation for the noise spectral density becomes:

$$W^U(\omega) = W_c \left[1 + \frac{r_2^2 - (r_2 + K\lambda_r)^2}{(r_2 + K\lambda_r)^2 + (\omega - \omega_0)^2} \right] + W_a \quad (1)$$

where W_c and W_a are, respectively, the noise spectral densities of the coil and of the preamplifier around the Larmor frequency. The nuclear spin-noise spectra of laser-polarized xenon dissolved in deuterated cyclohexane, observed through a dip at the resonance frequency ω_0 , is shown in Figure 1. The polarization is higher in the case of Figure 1 a with $K \approx 20000$

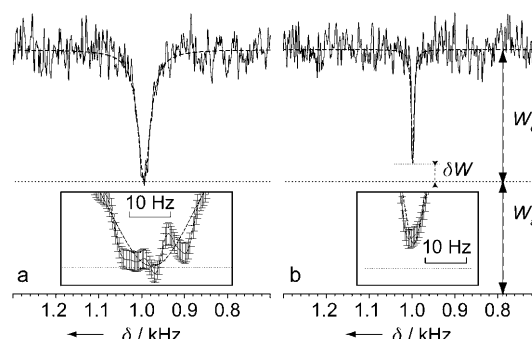


Figure 1. Hyperpolarized ^{129}Xe spin-noise spectra ($\text{SNR} > 10$) obtained by averaging power spectra of 3 Hz absolute resolution for a) $9 < t < 95$ s and b) $973 < t < 1059$ s after the introduction of xenon in the NMR tube ($t = 0$). W_c and W_a are the noise spectral densities of the coil and of the preamplifier around the Larmor frequency, respectively. Inserts: Expansions around the resonance. The best-fit theoretical curves to Equation (1) (----) and the preamplifier noise level (.....) are superimposed.

than in Figure 1 b with $K \approx 3000$. The higher polarization induces a larger RD contribution which is expressed by a broader line and the absorption of the whole noise of the coil by nuclear spins. From the difference δW (Figure 1 b) between the preamplifier noise level W_a and the dip depth equal to $W_a + W_c r_2^2 / (r_2 + K\lambda_r)^2$, the quantity r_2 can be determined. The shape of the spin-noise spectrum close to ω_0 differs from a pure Lorentzian shape (Figure 1 a). It appears broader and contains other line shapes. This behavior is similar to effects that are observed due to spectral clustering^[11] that result from the nonlinear effects^[12] observed at high magnetization, and induces new phenomena, such as chaotic behavior^[13] or multiple maser emission.^[14]

Figure 2 shows the continuous monitoring of the spin noise and thus provides information on the spin dynamics. The time dependence of the term $(r_2 + K\lambda_r)$, which is proportional to the line width was determined using Equation (1). The experimental spin-noise spectra allow direct determination of $K_0\lambda_r$, T_2^* , and T_1 using $K = K_0 e^{-t/T_1}$. In fact,

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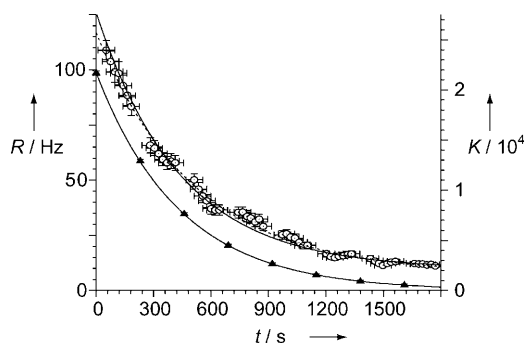


Figure 2. Temporal evolution of R ($[r_2 + K\lambda_r]$, $\circ$) as determined by fitting the nuclear spin-noise spectra (signal averaging for 83 s), and of the enhancement factor K ($\blacktriangle$) measured after small flip angle pulse excitation (extracted value of $T_1 = (438 \pm 6)$ s). Similar exponential decays appear for the spin-noise line-width analysis from which $K_0\lambda_n$, T_2^* , and T_1 can be determined. -----: $T_1 = 438$ s, —: best-fit $T_1 = (505 \pm 19)$ s.

the temporal variation of the integral of the spin absorption spectrum enables an alternative determination of these parameters (Supporting Information, Figure S1).

To obtain a correct signal-to-noise ratio (SNR), averaging of several hundred spin-noise spectra is required. A resolution of 3 Hz is usually not required for a broad line, as observed in Figure 1 a. Thus, the minimum duration required to detect the nuclear spin noise can be significantly reduced by adjusting the spectral resolution to the spin resonance width. Spin-noise spectra with a SNR greater than five can be obtained by signal averaging over 3.6 s (Supporting Information, Figure S2). By overlapping the time intervals during which signal averaging is performed, with a constant spectral resolution, the number of points in a given amount of time can be increased (Figure 2).

The noise power of the preamplifier W_a is typically one half of the whole detected noise ($W_a + W_c$), thereby reducing the achievable SNR (Figure 1). But technical solutions exist that can decrease the preamplifier noise through cooling or enhancing the coil quality factor,^[15] or potentially by taking advantage of the disappearance of the constraint on the impedance matching between the probe and the amplifier. As an alternative we have decided to resort to a small solenoid immersed in the solution and inductively coupled to the probe coil, a design inspired by the recent magic angle coil spinning development.^[16] Typical spectra obtained after rf excitation and using the spin-noise scheme are shown in Figure 3 a, b, respectively. Without special care, however, such a design leads to a degradation of the overall field homogeneity.

The sensitivity enhancement induced by this microcoil has been characterized by using the same protocol as that described above for the classical probe (Supporting Information, Figure S3). The RD characteristic rate λ_r is 10–25 % larger than that obtained with the classical probe at a similar xenon concentration. The NMR-active volume is, however, 40 times lower. Therefore, the increase in the rate clearly indicates that, in terms of the number of spins and for spin-noise detection, a sensitivity enhancement by a factor of 50 has been achieved by resorting to the inductively coupled

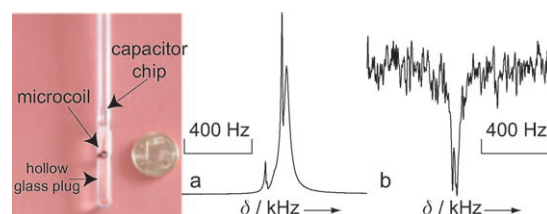


Figure 3. Picture of the microcoil located inside the NMR tube. a) Laser polarized ^{129}Xe spectrum acquired after a small flip angle excitation pulse and b) noise power spectrum of the same sample. The small peak corresponds to Xe in the hollow plug, the narrow signal to the bulk phase, and the wider signal to Xe inside the microcoil as validated, by magnetic resonance imaging experiments.

microcoil. Concomitantly, an improvement by a factor of four has been observed for pulse experiments.^[17] This method represents an appealing feature for the molecular imaging applications based on MRI and hyperpolarized species,^[18] where the number of polarized spins N remains large compared to the number of cell receptors.^[19]

Using this microcoil, a spin-noise spectrum of a solution containing 8 mmol L^{-1} ^{129}Xe can be obtained from five minutes of signal averaging (Supporting Information, Figure S4). This method corresponds to a noise detection of about 4×10^{16} spins, that is below the detection limit at thermal equilibrium after one 90° pulse. By extrapolation to a $50 \mu\text{m}$ diameter solenoid,^[15] this leads to a threshold for spin-noise detection of about 7×10^{11} hyperpolarized spins, a value below the sensitivity limit of the classical pulse scheme. In fact, the pulse approach depends on the whole number of spins, whereas noise detection only requires a significant RD contribution ($r_2 + K\lambda_r \neq r_2$), which requires a sufficient concentration, thus rendering noise detection more efficient for small samples. Finally, this detection scheme applied to hyperpolarized samples is magnetic field independent.^[20]

Herein we showed that unlike thermal equilibrium situations for hyperpolarized spin systems, the nuclear spin-noise approach appears to be an attractive way to continuously characterize the spin system, in particular using the determination of the apparent transverse relaxation time.^[14] We have also shown that in combination with this approach, microcoils afford a sensitivity enhancement by about two orders of magnitude, a value that can still be increased by using multilayers and/or smaller solenoids. These two aspects open new perspectives for exploring highly polarized spin systems applied to biosensors.

Experimental Section

86 % enriched ^{129}Xe from Cortecnet was polarized by spin-exchange optical pumping^[1] using our home-built apparatus.^[21] After isolation, it was transferred to the previously degassed NMR tube. The experiments were conducted at 297 K on a 11.7 T BRUKER spectrometer equipped with a 5 mm ^{129}Xe - ^1H probe from RS2D having a quality factor for xenon of 265. The probe was carefully tuned according to the reception circuit.^[7] The experiment consisted of the alternation of simple acquisitions after a 2° excitation pulse, followed by 218 s of time domain signal acquisitions for determination of the spin-noise spectrum. Power spectrum averaging performed using Scilab was computed for the given spectral resolutions, time domain

periods, and numbers of points added by zero filling. The microcoil used was a 3.6 mm long and 1.7 mm diameter solenoid composed of 19 turns with a 150 μm diameter wire connected to a 4.7 pF capacitor chip from ACT.

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