

# Producing Hyperpolarized Gases via Dynamic Nuclear Polarization and Sublimation

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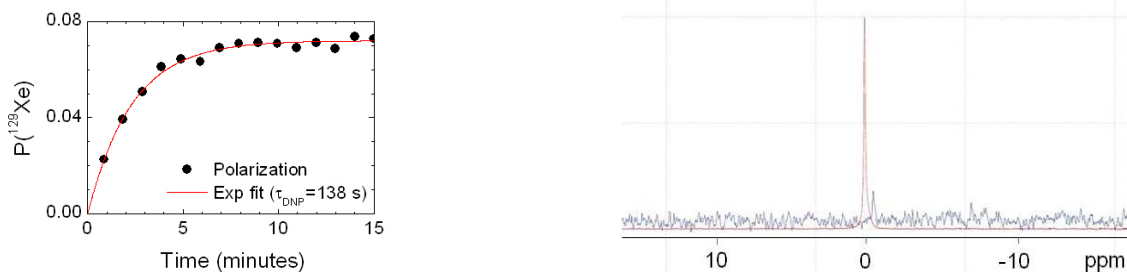
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## Introduction

Hyperpolarized <sup>129</sup>Xe has been extensively used for lung imaging and its potential as blood tracer for in vivo vascular and perfusion imaging applications was demonstrated. <sup>129</sup>Xe and other isotopes of NMR-active noble gases can be polarized via optical pumping [1, 2]. This method allows for the production of highly polarized gases, up to 70% for <sup>129</sup>Xe under optimum conditions, but large throughputs (1-5 L/h of xenon gas at atmospheric pressure) are only possible under less favorable conditions where the polarization level is limited (to about 20% in the case of <sup>129</sup>Xe) [3]. Large volumes are needed for clinical applications since 0.5-2 L of hyperpolarized xenon gas (the natural abundance of <sup>129</sup>Xe being 26.4%) have to be delivered to a patient for pulmonary examination. Below, we describe a general method to produce room-temperature hyperpolarized gases via Dynamic Nuclear Polarization (DNP) combined with a sublimation procedure. The new method is used to hyperpolarize <sup>129</sup>Xe in xenon gas at natural isotope abundance.

## Methods

We first liquefied xenon gas in a glass tube pressurized at 500 kPa by lowering the temperature to 170 K. Because liquid xenon is non-polar, an additional solvent had to be used to dissolve the standard nitroxide radicals commonly used for DNP. We mixed equal volumes of liquid xenon and isobutanol containing between 60 and 100 mM of TEMPO (2,2,6,6-Tetramethylpiperidine-1-oxyl). After a settling time of about 5 minutes, the two liquids were homogeneously mixed, and the resulting homogenous mixture was rapidly frozen by plunging the glass tube in liquid nitrogen. The pressure was subsequently released to atmospheric pressure. A volume of about 0.2 ml of the solid mixture was inserted in the sample holder of custom-designed DNP polarizers [4,5]. DNP was performed at 1.15±0.05 K in either a 3.35 T or a 5 T polarizer. Solid-state <sup>129</sup>Xe NMR measurements led to the determination of the nuclear polarization  $P = 3 \pm 0.3\%$  at 3.35 T and  $P = 7 \pm 0.5\%$  at 5 T (see Fig.1), where  $P$  is the ratio between the population difference of the two nuclear spin energy levels and the total number of nuclear spins. The sublimation step was performed using 1 mL of water heated to 310 K and pressurized with helium gas at 250 kPa. The procedure yielded 35 ml of hyperpolarized xenon gas in less than 15 min.



**Figure 1.** *Left:* <sup>129</sup>Xe polarization curve at 1.2 K in  $B_0 = 5$  T; *Right:* FT of a hyperpolarized <sup>129</sup>Xe FID acquired at 7.05 T following a single 90 degree pulse (red) superimposed with the FT of the thermal equilibrium FID averaged over 1000 experiments with 90 degree pulses (blue).

## Results and Discussion

The <sup>129</sup>Xe nuclear spin polarization of the resulting room-temperature hyperpolarized gas was measured in a high-resolution 7.05 T NMR spectrometer using a 5 mm probe. The pressure in the NMR tube was stabilized at 10 kPa above atmospheric pressure using an overpressure valve and the temperature in the probe head was maintained at 25° C using a thermostated air flow. Figure 1 (right) shows the hyperpolarized NMR signal (red) and the thermal equilibrium NMR signal (blue) averaged over 1000 experiments on a reference xenon gas sample pressurized to 1 MPa. The enhancement is 4200, which amounts to a nuclear spin polarization of 2.7 %. By comparing this value with solid-state measurements, we deduced that about 10 % of the polarization was lost during the whole sublimation and sample transfer procedure. The sublimation step was only performed on samples polarized at 3.35 T, but from the 5 T solid-state polarization measurements, the polarization after sublimation is expected to be about  $6.3 \pm 0.5\%$ .

## Conclusions

The optimization of the composition of the solid sample is expected to lead to further improvements of the <sup>129</sup>Xe polarization. It was demonstrated that the maximum <sup>13</sup>C polarization in <sup>1-13</sup>C-labeled acetate and glycine is twice as large if the solvents protons are replaced by deuterons [6]. It might therefore be of advantage to use deuterated isobutanol. TEMPO is likely not to be the most efficient paramagnetic substance for polarizing xenon. Photo-induced radicals created directly in liquid xenon from precursors could be more efficient [7]. There would then be no need for an additional solvent and this would increase throughput by a factor 2. Most importantly, using <sup>129</sup>Xe-enriched xenon gas would shorten the polarization time constants as a consequence of enhanced spin diffusion. Since cross relaxation to the fast relaxing <sup>131</sup>Xe spins is the most efficient spin-lattice relaxation mechanism at low temperature [8], reducing the concentration of <sup>131</sup>Xe spins would additionally most likely lead to increased final <sup>129</sup>Xe polarizations.

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