Thermally-Activated Clustering of Xe Atoms Increases ^{129}Xe T_1 in Solid-State DNP Mixtures

Huseyin Kara[1,2], Nicholas N. Kuzma[2], Philip Manasseh[3], Mehrdad Pourfathi[2], Stephen J. Kadlecek[2], and Rahim R. Rizi[2]

[1]Astronomy and Physics, University of Pennsylvania, Philadelphia, PA, United States, [2]Radiology, University of Pennsylvania, Philadelphia, PA, United States, [3]Department of Chemistry, Earlham College, Richmond, IN, United States

Introduction: Hyperpolarized ^{3}He MRI has found many ground-breaking applications for *in-vivo* human lung imaging. However, due to the limited world supply of ^{3}He, development of hyperpolarized ^{129}Xe as an alternative is receiving renewed interest. Many properties of ^{129}Xe, such as its much higher solubility in blood and lipids, lower diffusion coefficient, and a possibility of polarization storage in the frozen state can offer an advantage over ^{3}He as an imaging agent, despite the weaker magnetic moment and modest natural abundance of the ^{129}Xe isotope. Optical pumping of ^{129}Xe is a well-established method for producing hyperpolarized xenon gas, but offers challenges in scaling up the production volume due to low density of xenon gas in the optical pumping cell. On the other hand, recent reports [1,2] show a potential for Dynamic Nuclear Polarization (DNP) to produce large volumes of hyperpolarized ^{129}Xe in the solid state. Storage and transportation of such cryogenically-produced ^{129}Xe is crucial in clinical applications and requires long spin-lattice relaxation times. On the other hand, DNP rates and achievable polarization levels are dependent on T_1 values as well. In this study we investigated how T_1 relaxation times are affected by spontaneous formation of pure-xenon clusters in xenon/1-propanol/trityl matrix typically used for DNP. By using vigorous mechanical stirring of the liquid mixture at 195-K temperature and 4.2-atm pressure followed by a rapid cool-down to 77 K, we could achieve a nearly homogenous Xe/1-propanol/trityl solid mixture. Exposing this mixture to ~125 K temperature for several hours led to partial clustering of pure xenon in the solid matrix, as did a delay in cooling down the liquid after stirring it. Cluster formation led to effective segregation of ^{129}Xe spins from the unpaired electrons of the radical molecules and was observed to significantly increase spin-lattice relaxation times, as well as DNP time constants, both inside the clusters and in the solid matrix.

Methods: We used a home-built hybrid DNP/NMR system based on an Oxford TMR7/88/15 Teslatron^{MR} superconducting magnet with an integrated ^{4}He-cooled variable-temperature insert monitored by an Oxford ITC-503 controller. We irradiated the sample with microwaves at 140 GHz, generated by a computer-controlled primary microwave source at 7.78 GHz and 18.3 dBm followed by a ×18 frequency multiplier integrated with a narrow-band 140 GHz/70 mW microwave amplifier. Our custom-made probe supported an overmoded cylindrical aluminum microwave chamber (~5 cm in height and diameter), which was directly coupled to an overmoded circular stainless-steel waveguide and contained a two-turn copper NMR saddle coil wrapped around a PEEK sample holder that accommodated a vertical 5-mm glass sample tube. We prepared the samples using a hermetically-sealed retractable electric stirrer from a 3:1 mixture (by volume) of (a) 3 mg Finland acid radical dissolved in 97 mg 1-propanol and (b) liquid ^{129}Xe (BOC Gases, 99.997% purity, <1 ppm O$_2$) at the 195 K temperature of ethanol/dry ice bath and 4.2 atm ^{129}Xe gas pressure. After 1 min of vigorous stirring we changed the bath to liquid nitrogen (LN$_2$, at 77 K), then transferred the sample tube to our pre-cooled probe within several minutes. ^{129}Xe NMR spectra were acquired with our home-built broadband NMR spectrometer. After applying baseline adjustment, FFT, and zero-phase correction, single-peak spectra were numerically integrated. Multi-peak spectra were fitted to double-Gaussian line shapes, and the individual peak integrals were computed from the fit parameters. In cases where the narrow peak's sligh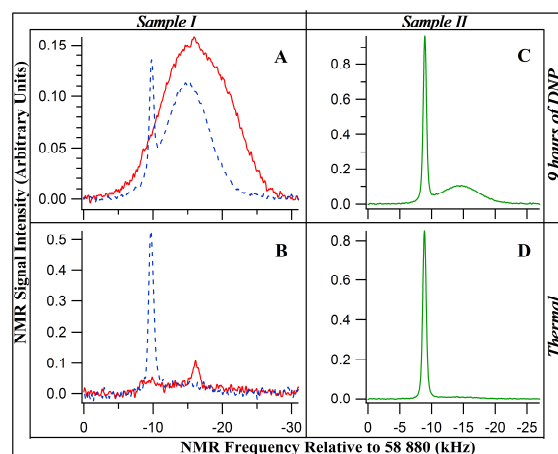tly non-Gaussian tail overlapped the broad peak significantly, a linear combination of a Gaussian and a Lorentzian of the same full width at half maximum was used instead of a pure Gaussian to represent the narrow peak in multi-peak fits. To obtain T_1 values, the time evolution of each peak integral $I(t)$ was fitted to a single exponential: $I(t) = A_0 + A_1 \exp(-t/T_1)$, where t is time, and A_0, A_1, and T_1 are the free parameters of the fit.

Figure 1: ^{129}Xe NMR spectra after 9 hours of DNP at v^+ = 140.067 GHz microwave frequency (**A,C**) and after thermally relaxing 1.43 K (**B,D**). **A, B**: Solid (dashed) lines: spectra in sample I before (after) the annealing process of Fig. 2A. **C, D**: Spectra in sample II after extreme annealing.
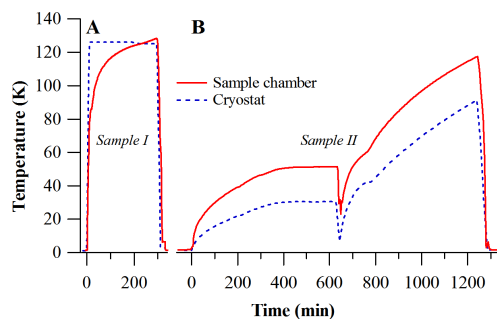

Figure 2: Temperature as a function of time during the annealing process. **A**: Annealing of the homogeneous sample I. **B**: Extreme annealing of imperfectly mixed sample II.

Results and Discussion: During the DNP process, either v^+=140.067 GHz or v^-=140.166 GHz microwave frequencies were used to pump the nuclear Zeeman spin system towards either its ground state or the excited state (i.e. population inversion), respectively. Figure 1A shows the low-temperature DNP spectra before and after annealing of sample I. The single broad peak (solid line) represents a homogenous Xe/1-propanol/radical matrix. Its line width and frequency are consistent with the known values of 1-propanol-induced broadening and chemical shift of ^{129}Xe. After undergoing an annealing process (Fig. 2A), the narrow peak appears in the dashed-line spectrum of Fig. 1A, with line width and frequency consistent with the broadening and the chemical shift of ^{129}Xe in pure xenon. The annealing had also reduced the line width and increased the chemical shift of the broad peak, indicating a reduced number of 1-propanol molecules surrounding an average ^{129}Xe atom in the matrix after annealing.
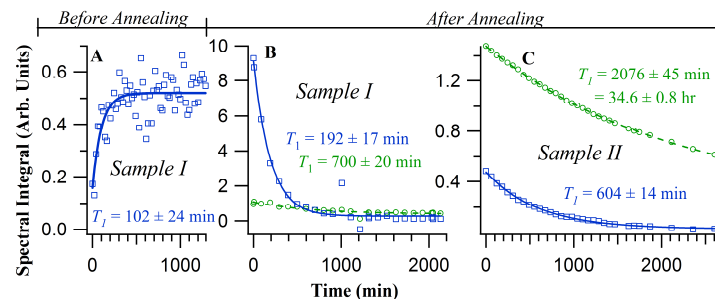
Figure 1B shows the averaged thermal-polarization spectra at 1.43 K before (solid line) and after (dashed line) the annealing, providing further evidence that this process forced the majority of Xe atoms into pure-xenon clusters. An extreme case of annealing (sample II, Fig. 2B) can be seen in ^{129}Xe spectra shown in Figs. 1C and 1D, where the narrow peak appeared to be much more pronounced. Figure 3 shows vastly different T_1 values in the three cases (homogeneous sample I, same sample after annealing, and sample II after extreme annealing). We found the relaxation time to be T_1=102 ± 24 min before annealing in sample I (Fig. 3A). Annealing this sample resulted in T_1=192 ± 17 min for the broad peak (matrix) and a much longer T_1=700 ± 20 min for the narrow peak (pure Xe clusters), as shown in Fig. 3B. A case of extreme annealing resulted in T_1=604 ± 14 min for the broad peak (matrix) and T_1=2076 ± 45 min for the narrow peak (clusters) in sample II (Fig. 3C).

Conclusion: T_1 relaxation times of hyperpolarized ^{129}Xe in DNP experiments strongly depend on the preparation method and the thermal history of the sample. Annealing solid samples at 125 K significantly prolongs T_1 relaxation times, thus making it easier to store hyperpolarized ^{129}Xe for clinical imaging. However, both the polarization rate and the ultimate achievable polarization were found to decrease upon annealing due to spontaneous formation of pure xenon clusters in the Xe/solvent/radical matrix.

Figure 3: ^{129}Xe T_1 relaxation data at 1.43 K, 5 T (squares: broad peak - ^{129}Xe in the matrix; circles: narrow peak - ^{129}Xe in pure Xe clusters) and the exponential fits (solid and dashed lines). Sample I before (**A**) and after (**B**) annealing. Sample II (**C**) after extreme annealing.

References: [1] A. Comment *et al.*, Phys. Rev. Let. **105**, 018104 (2010). [2] J.-H. Ardenkjaer-Larsen *et al.*, US patent 8,003,077, filed 2003, issued 2011.