

Dynamic nuclear polarization of doubly-labeled $^{15}\text{N}_2\text{O}$

Nicholas N. Kuzma¹, Huseyin Kara^{1,2}, Mehrdad Pourfathi¹, Philip Manasseh³, Rajat K. Ghosh¹, Stephen J. Kadlecsek¹, Giuseppe Pileio⁴, Pär Håkansson⁴, Malcolm H. Levitt⁴, and Rahim R. Rizi¹

¹Radiology, University of Pennsylvania, Philadelphia, PA, United States, ²Astronomy and Physics, University of Pennsylvania, Philadelphia, PA, United States,

³Department of Chemistry, Earlham College, Richmond, IN, United States, ⁴School of Chemistry, Southampton University, Southampton, Hampshire, United Kingdom

Introduction: Hyperpolarized *in-vivo* markers enhance MRI signals by many orders of magnitude, making it possible to image trace amounts of substances of interest and their metabolism. However, most compounds in the hyperpolarized state exhibit relatively short magnetization life-time due to fast T_1 relaxation (typically less than a minute). This severely restricts storage and transportation of the hyperpolarized agent, and limits the physiological time scales accessible with the technique. An emerging development enables polarization storage in quantum-mechanical singlet states of a coupled system of two nuclear spins of the same species with slightly different chemical shifts, such as two nitrogen nuclei in doubly labeled $^{15}\text{N}_2\text{O}$ [1]. A recent relaxation study of $^{15}\text{N}_2\text{O}$, a non-toxic anesthetic gas, reports relatively long

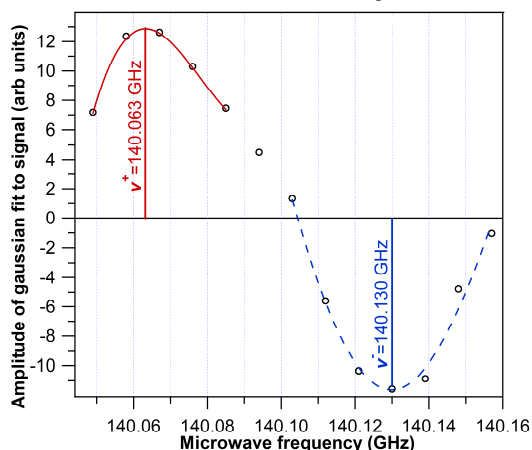


Figure 1. The dependence ^{15}N NMR signals on the microwave frequency after 8 min of DNP. The polarization was destroyed by a train of hard NMR pulses at the beginning of each measurement.

7.5–8 μs dead time delay. The free-induction decay signals were base-line adjusted, Fourier transformed, and subjected to a zero-order phase correction and a 170-Hz Gaussian broadening. Gaussian line shapes were fitted to the experimental powder-spectrum patterns to estimate spectral integrals.

Results and discussion: Figure 1 (open circles) shows a microwave frequency sweep performed over the 140.04–140.16 GHz range, where an ^{15}N NMR spectrum was taken after 8 min of DNP at each microwave frequency. Vertical solid lines show two optimal microwave frequencies chosen for DNP towards the ground state of the nuclear spin system ($\nu^+ = 140.063$ GHz) and the excited (inverted) state ($\nu^- = 140.130$ GHz). The solid and dashed curves are plotted to guide the eye. Figure 2 shows the temporal evolution of ^{15}N NMR spectra at four time-points during DNP at ν^+ . Each experimental spectrum can be interpreted as a superposition of four powder-spectrum patterns. These are produced by a combination of two different chemical-shift-anisotropy

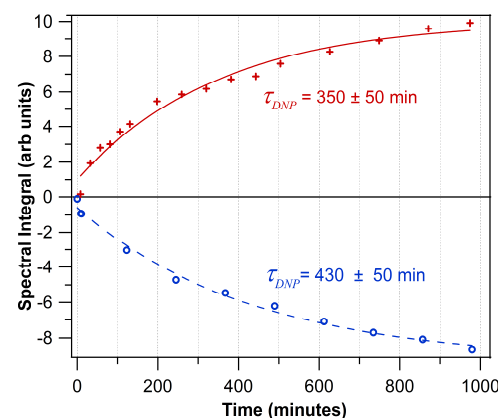


Figure 3. Temporal evolution of ^{15}N NMR spectral integrals during DNP at the ν^+ and ν^- microwave frequencies (+ and o symbols). Solid (—) and dashed (---) lines are single-exponential fits to the data.

time constant. The solid-line fit to the ν^+ data set yields the polarization time constant of $\tau_{\text{DNP}}^+ = 350 \pm 50$ min, within the error bars of the time constant for the “spin-down” DNP at ν^- : $\tau_{\text{DNP}}^- = 430 \pm 50$ min.

Conclusion: This is the first report of dynamic nuclear polarization of doubly-labeled $^{15}\text{N}_2\text{O}$. Sample polarization during DNP at 1.5 K and 5 T was monitored *in-situ* by solid-state NMR as a function of microwave frequency in the range 140.04–140.16 GHz. The fastest initial polarization rate occurred at $\nu^+ = 140.063$ GHz and $\nu^- = 140.130$ GHz microwave frequencies, corresponding to positive and negative polarizations of the nuclear spin system. Maximum ^{15}N polarization was $(11 \pm 4)\%$.

References: [1] G. Pileio, M. Carravetta, and M. H. Levitt, *Proc. Natl. Acad. Sci. USA* **107**, 17135 (2010).

[2] R. K. Ghosh, S. J. Kadlecsek, J. H. Ardenkjaer-Larsen, B. M. Pullinger, G. Pileio, M. H. Levitt, N. N. Kuzma, and R. R. Rizi, *Magn. Reson. Med.* **66**, 1177 (2011).

[3] P. Håkansson *et al.*, “Solid-state ^{15}N polarimetry of hyperpolarized $^{15}\text{N}_2\text{O}$ based on modeling of NMR spectral patterns”, *ISMRM* (2012)

tensor for each of the two ^{15}N involved, further split by spin-orientation-dependent dipolar coupling to a spin- $1/2$ intramolecular ^{15}N neighbor. The ^1H magnetic moments of the surrounding 1-propanol molecules contribute to a Gaussian isotropic dipolar broadening which depends on sample preparation and thermal history. Detailed modeling [3] of solid-state ^{15}N spectra such as those shown in Fig. 2 yields the maximum achieved ^{15}N polarization of $(11 \pm 4)\%$. Figure 3 shows the temporal evolution of ^{15}N NMR spectral integrals during DNP for both positive (ν^+ frequency) and negative (ν^- frequency) polarizations. These experimental “spin-up” and “spin-down” curves were fitted to the single-exponential functional forms:

Materials and methods: We used a home-built hybrid DNP/NMR system based on an Oxford TMR7/88/15 Teslatron^{MR} superconducting magnet with an integrated ^4He -cooled variable-temperature insert monitored by an Oxford ITC-503 controller. A computer-controlled primary microwave source (Giga-tronics SNY-0410-510-01) operating at 7.78 GHz and 18.3 dBm was followed by a $\times 18$ frequency multiplier integrated with a narrow-band 140 GHz/70 mW microwave amplifier (ELVA DCOIMA-06/140/70). Our custom-made probe supported an overmoded cylindrical aluminum microwave chamber (~ 5 cm in height and diameter). This 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 which accommodated a vertical 5-mm sample tube. We prepared the samples using a hermetically-sealed retractable electric stirrer from a 3:1 mixture (by volume) of (a) 3 mg trityl (Finland acid) radical dissolved in 97 mg 1-propanol and (b) liquid N_2O (Cambridge Isotope Labs, 98+% purity) at the 195 K temperature of ethanol/dry ice bath and 1.75 atm N_2O gas pressure. After stirring the sample vigorously for 1 minute, the bath was changed to liquid nitrogen (LN_2 , 77 K) and the sample was transferred to the pre-cooled probe within several minutes. $^{15}\text{N}_2\text{O}$ NMR spectra were acquired using a home-built broadband NMR spectrometer at the 21.565-MHz ^{15}N NMR frequency

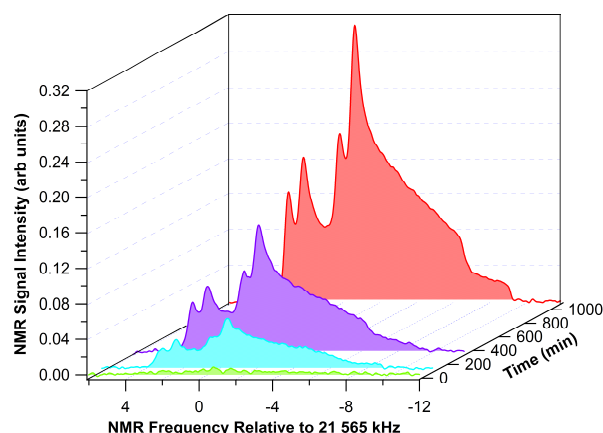


Figure 2. Temporal evolution of ^{15}N NMR spectra during DNP at the ν^+ microwave frequency. The first spectrum at time $t = 0$ was taken when DNP began as the sample was cooled down to 1.4 K temperature.

$A_0 + A_1 \cdot \exp(-t/\tau_{\text{DNP}})$, where A_1 and A_0 parameterize the initial and the ultimate spectral integrals, t is time, and τ_{DNP} is the DNP time constant. The solid-line fit to the ν^+ data set yields the polarization time constant of $\tau_{\text{DNP}}^+ = 350 \pm 50$ min, within the error bars of the time constant for the “spin-down” DNP at ν^- : $\tau_{\text{DNP}}^- = 430 \pm 50$ min.

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