Method and System for Dynamic Nuclear Polarization of Frozen Gases

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Introduction: Advances in hyperpolarized-gas MRI techniques based on optical pumping [1] have enabled new methods of characterizing the structure and function of pulmonary disorders, e.g. COPD [2]. Meanwhile, remarkable progress in Dynamic Nuclear Polarization (DNP) of frozen metabolites such as [1-^{13}C]pyruvate has lead to the development of hyperpolarized metabolic imaging [3]. In this work, we describe a new general approach for producing highly polarized frozen gases using DNP at liquid-helium cryogenic temperatures. This offers a number of advantages compared to optical pumping, such as potentially achieving higher production volumes, since the polarization is performed in the solid phase, at the thousand times higher sample density [4]. The experiments described here showcase our advances in polarizing ^{129}Xe, ^{13}CO$_2$, and ^{15}N$_2$O gases in frozen mixtures with the unpaired electron source (trityl radical) and the glassing agent (1-propanol), and address the unexpected effects of the microstructure of these often inhomogeneous solid matrices on the efficiency of the DNP process.

Methods and Materials: Samples were prepared using a custom-built cryogenic gas-handling manifold. A variety of isotopically-enriched sample gases including ^{129}Xe, ^{13}CO$_2$, and ^{15}N$_2$O, were used to demonstrate the feasibility of our DNP technique. Samples were prepared of a liquid 3:1 mixture (by volume) of (a) 3 mg trityl (Finland acid) radical dissolved in 97 mg 1-propanol and (b) liquefied gas, one of: (i) ^{13}CO$_2$ (Cambridge Isotopes, >99% ^{13}C enriched, <1% ^{18}O), (ii) ^{15}N$_2$O (Cambridge Isotopes, >98% ^{15}N enriched, >98% pure) or (iii) ^{129}Xe (natural, BOC Gases, 99.997% purity, <1 ppm O$_2$, or enriched, Linde, 86% ^{129}Xe enriched, 99% pure) at the (i) 218 K or (ii,iii) 195 K temperature of (i) liquid/solid propylene carbonate or (ii,iii) ethanol/solid carbon dioxide bath at (i) 5.2 atm, (ii) 1.75 atm or (iii) 4.2 atm of the pure gas pressure. After 1 min of vigorous stirring using a hermitically sealed mechanical stirrer driven by a small electric motor enclosed within the gas volume, the bath was rapidly changed to liquid N$_2$ (77 K) and the sample tube was optionally transferred to an annealing bath for about an hour, returned to the liquid N$_2$ bath, and then transferred to our pre-cooled custom-built probe. The probe supported an aluminum microwave chamber (5 cm size, fed by 3/16" ID stainless steel waveguide), containing a two-turn copper NMR coil wrapped around a PEEK sample holder fitted around a vertical 5-mm pyrex tube (Wilmad 504- or 524-PP, 0.77 mm wall) or outside of an open PEEK sample cup. Samples were polarized and monitored at ~1.5 K temperature and 5 T field using our custom-built DNP/NMR system. Thermal polarization and T_1 relaxation times were measured at 1.4 K to investigate potential delivery and transport methods. Annealing of the ^{129}Xe samples was performed by controlling the internal temperature of the probe at ~120 K for over ~4 hours. Annealing of ^{15}N$_2$O samples was performed using ethanol/ethanol ice or toluene/toluene ice bath in a glass dewar during sample preparation.

Results and Discussion: Polarization achieved for ^{129}Xe, ^{15}N$_2$O and ^{13}CO$_2$ frozen mixtures were 21%, 11% and < 1% respectively. Figure 1 shows the NMR spectra of each sample after several hours of DNP at 1.5K at 5T. To the best of our knowledge, the NMR spectrum of ^{13}CO$_2$ is the first reported case of direct polarization of frozen ^{13}CO$_2$. The spectrum of doubly labeled ^{15}N$_2$O was analyzed theoretically to confirm that it represents a superposition of four shifted Pake powder-pattern spectra; a characteristic signature of

Figure 1. NMR spectra of the frozen-gas mixtures during DNP at 5 T and 1.5 K.

Figure 2: A: Temperatures measured during annealing of ^{15}N$_2$O samples in ethanol/ethanol-ice bath at ~154 K (dashed line), 160-175 K (thin solid line) and in toluene/toluene ice bath at ~180 K (thick solid line).
B: Corresponding ^{15}N NMR spectra after 3.7 hours of DNP at 1.5 K.
C: Corresponding time evolution of the ^{15}N NMR spectrum integrals during DNP at 1.5 K.

two different chemical shift anisotropy (CSA) tensors further split by the direct dipole-dipole interaction between the neighboring ^{15}N spins. The same analysis was performed for ^{13}CO$_2$, demonstrating a much simpler single Pake pattern due to CSA. Consistent with the previous observations, the measured T_1 relaxation times at 1.4 K for these gases were very long: 102 ± 24 minutes, 7.8 ± 0.1 and 20 ±10 hours for ^{129}Xe, ^{15}N$_2$O and ^{13}CO$_2$ samples respectively. Controlled annealing of the ^{129}Xe and ^{15}N$_2$O significantly increased the relaxation times: 34.6 ± 0.7 and 33 ± 0.3 hours respectively. Similarly to the case of ^{129}Xe [4], we inferred that annealing frozen ^{15}N$_2$O mixtures close to 180 K leads to spontaneous formation of pure ^{15}N$_2$O clusters in the ^{15}N$_2$O/1-propanol/trityl matrix. However, contrary to the case of ^{129}Xe, the micron-size clustering in these mixtures dramatically *increases* the maximum polarization achieved during DNP, as shown in Figure 2. We explain this unexpected result by extremely long T_1 relaxation times in pure ^{15}N$_2$O, combined with unhindered spin-diffusion from the trityl-containing matrix into the clusters, whereas a spin-diffusion bottleneck in the ^{129}Xe system effectively decouples ^{129}Xe spins in the clusters from the highly polarized ^{129}Xe in the matrix. This explanation is also supported by the gradual sharpening of the Pake patterns over time during DNP, suggesting the growth of the pure ^{15}N$_2$O relative to that of matrix ^{15}N$_2$O.

Conclusion: We have demonstrated a novel method of preparation and conditioning the frozen mixtures of ^{129}Xe, ^{15}N$_2$O and ^{13}CO$_2$ gases and trityl (Finland acid) radical dissolved in 1-propanol glassing agent that is suitable for hyperpolarization using DNP technology. We have also studied the effects of sample inhomogeneity on relaxation and DNP efficiency of ^{129}Xe and ^{15}N$_2$O and determined that annealing-induced clustering dramatically increases the species' relaxation times, potentially facilitating the transport of the hyperpolarized samples. However, this temperature-induced pure-gas clustering affects the efficiency of DNP in radically opposite ways in the ^{129}Xe and ^{15}N$_2$O systems studied so far. Currently, we are investigating and improving our techniques to achieve the DNP of large samples. Ultimately, our goal is to polarize biologically interesting gases and substrates in large quantities for transport to nearby facilities.

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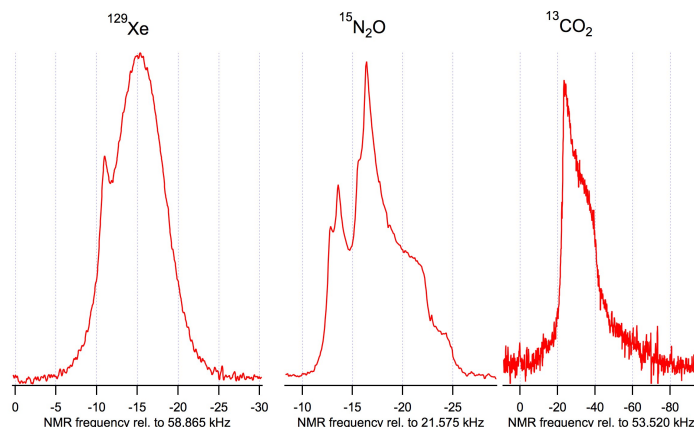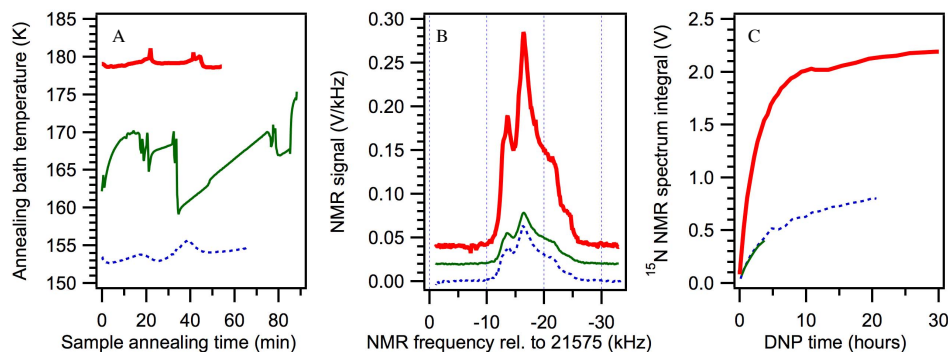[4] N. N. Kuzma *et al.*, *Journal of Chemical Physics,* vol. 137, art. # 104508, 2012.