Retaining Polarization by exploiting reduced T1 relaxation of hyperpolarized spins at low field in solution

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Introduction:

Techniques to retain highly polarized spins in solution via dynamic nuclear polarization (DNP) have enabled ^{13}C NMR and MR imaging studies with very high signal-to-noise in short acquisition times (*1,2*). An important consideration for performing hyperpolarized (HP) ^{13}C MR studies is matching the T_1 relaxation time of the HP ^{13}C labeled probe with the time scale of the metabolic process being investigated. For example, HP [1-^{13}C]pyruvate has been very successful in measuring fast metabolic fluxes such as the flux of pyruvate to lactate catalyzed by LDH. However, extending [1-^{13}C]pyruvate's T_1 relaxation time may allow improved visualization of HP TCA intermediates. In this study, the field dependence of solution state T_1 relaxation times of hyperpolarized [1-^{13}C]pyruvate, between low field (< 0.1T) and 11.7T (125MHz) and 14.1T (150MHz), is exploited to retain higher amounts of residual polarization.

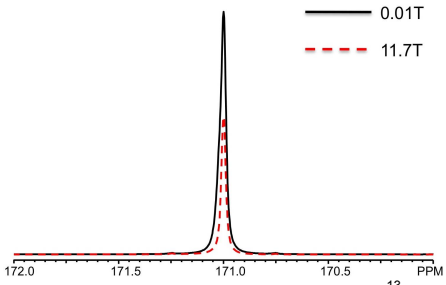

Figure 1. Representative hyperpolarized ^{13}C spectra 90 secs after evolution in 0.01T (black) and 11.7T (red) magnetic field.

Experimental Methods:

Samples of [1-^{13}C]pyruvate (Isotec) either neat or doped with a DOTA based Gd^{3+} complex and containing 15mM OX063 trityl radical (Oxford Instrument) and nearly identical in weight were polarized. After full solid-state build-up (SSbu) the samples were dissolved using a Hypersense^{TM} DNP polarizer (Oxford Instrument) as described elsewhere (*3*). The dissolved samples were rapidly transferred to a high field NMR spectrometer, and either in the first case parked for 90 secs. in the stray field region on top of the NMR magnet (~ 0.01T for 11.7T and 0.05T for 14.1T) and in a second case positioned in the magnet center and waited 90 sec. before the start of acquisition. Both polarization and T_1 measurements were performed in 11.7T and 14.1T spectrometers (Varian Inc.). T_1 decay NMR data was acquired at 3 secs intervals applying a small tip angle (< 8°) excitation pulse. Polarization measurements were calculated based on the thermal signal of the same dissolution sample after the completion of the T_1 decay acquisition while waiting a sufficient recycle delay (5 x T_1). T_1 relaxation times were estimated by performing a mono-exponential fit to the signal decay curve taking into account magnetization lost as a function of excitation. All Polarization and T_1 measurement data were collected at 37□.

Results and Discussion:

By evolving the hyperpolarized spins in low field, a dramatic increase in relaxation rate is indirectly observed as a 50% increase in residual polarization relative to the solution positioned inside the center of the high field as shown in *Figure 1*. Pre-polarized solutions were left 90 secs on top of both 11.7 and 14.1 T magnets in fields of 0.01T and 0.05T, and the residual polarization was subsequently measured in the bore of the magnet. The residual polarization observed for [1-^{13}C] pyruvate was 31% and 26% at 0.01T and 0.05T, versus 18% and 13% at 11.7 and 14.1T, respectively (Figure 2). The estimated T_1 relaxation times were 49.3 ± 1.6 secs, and 42.1 ± 0.3 secs at 11.7T, and 14.1T respectively for the pyruvate solutions. The field dependency of T_1 relaxation times is caused by increased chemical shift anisotropy (CSA) with field (eq. 1) and it is known that ^{13}C T_1s for carbonyl carbons decrease

$$\frac{1}{T_1^{CSA}} = \frac{2}{15}\gamma_C^2 B_0^2 (\Delta\sigma)^2 \left(1 + \eta^2/3\right)\tau_c \qquad (1)$$

with increasing field strength (□ B_o^2) (4).

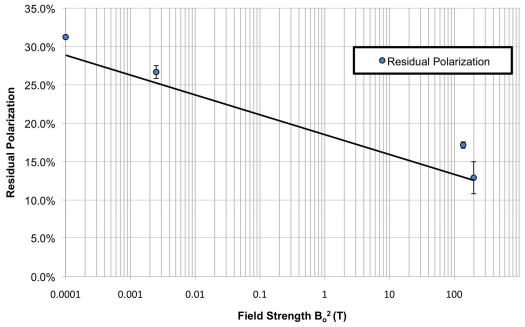

Figure 2. Plot of residual polarization as a function of squared field strength.

This study demonstrates the feasibility of dramatically reducing the loss of polarization of a HP ^{13}C carbonyl labeled probe after dissolution by taking advantage of its longer T_1 relaxation time at low field (< 0.1T). Future studies include the investigation of different time points and field strengths to optimize the low field strength necessary to preserve the hyperpolarized spins. For *in vivo studies*, it is possible that hyperpolarized spins could be allowed to evolve inside of animals at low field and subsequently transport them into the magnet at a later time to observe slower enzyme kinetics.

References

1. JH. Ardenkjaer-Larsen et al. *Proc Natl Acad Sci* USA 2003; 100:p10158
2. K. Golman et al. *PNAS* 2006; 103(30):11270-11275
3. S. J.Kohler *et al*., *Magn. Reson. Med.* (2007), **58**, 65
4. C. Pattaroni and J. Lauterwein *Mag. Res. Chem.* 1987; 25:745-751

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