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 13C NMR and MR imaging studies with very high signal-to-noise in short acquisition times (1, 2). An important consideration for performing hyperpolarized (HP) 13C MR studies is matching the T1 relaxation time of the HP 13C labeled probe with the time scale of the metabolic process being investigated. For example, HP [1-13C]pyruvate has been very successful in measuring fast metabolic fluxes such as the flux of pyruvate to lactate catalyzed by LDH. However, extending [1-13C]pyruvate’s T1 relaxation time may allow improved visualization of HP TCA intermediates. In this study, the field dependence of solution state T1 relaxation times of hyperpolarized [1-13C]pyruvate, between low field (~0.1T) and 11.7T (125MHz) and 14.1T (150MHz), is exploited to retain higher amounts of residual polarization.

Experimental Methods:
Samples of [1-13C]pyruvate (Isotec) either neat or doped with a DOTA based Gd3+ 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™ 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 T1 measurements were performed in 11.7T and 14.1T spectrometers (Varian Inc.). T1 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 T1 decay acquisition while waiting a sufficient recycle delay (5 x T1). T1 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 T1 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 [1-13C] 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 T1 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 T1 relaxation times is caused by increased chemical shift anisotropy (CSA) with field (eq. 1) and it is known that 13C T1s for carbonyl carbons decrease

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

(1)

with increasing field strength (\( B_0 \)).

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

This study demonstrates the feasibility of dramatically reducing the loss of polarization of a HP 13C carbonyl labeled probe after dissolution by taking advantage of its longer T1 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
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