

T1 Nuclear Magnetic Resonance Dispersion of Hyperpolarized [1-13C] Pyruvate

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Introduction:

Hyperpolarized pyruvate is an important NMR probe to study metabolic pathways, such as the citric acid cycle, in real time [1] and as a result, has found many important applications in medical research [2-3]. An important characteristic for hyperpolarized contrast agents is that they possess a spin lattice relaxation time (T1) on the order of tens of seconds for the ¹³C-enriched nucleus. This point is critical in that it permits sufficient time for transfer of the hyperpolarized agent to the MR system, injection into an animal model, metabolism and rapid spectroscopic imaging. These T1 times are largely determined by chemical conformation of the molecule but are influenced by temperature and pH of the solution as well as the strength of the ambient magnetic field and presence of paramagnetic impurities. Relaxation times can be readily measured at 3T using a suitable pulse sequence with the clinical scanner but no such data exists at low field strengths where T1 is much shorter. This information is required to determine the significant loss of polarization as the agent is transported from the polarizer, where it is dispensed at the earth's magnetic field, to the fringe field of the scanner, where it is imaged.

Methods:

[1-¹³C]-enriched pyruvic acid (CIL, Cambridge, MA, U.S.A.) containing 15mM OX63 trityl radical (Oxford Instruments, Abingdon UK) was hyperpolarized using a HyperSense DNP polarizer (Oxford Instruments, Abingdon, UK). After dissolution and buffering, the final solution was 80mM pyruvate. Immediately following collection of the hyperpolarized solution, a 2-mL aliquot was withdrawn, placed in an NMR tube and quickly transferred to a fast field-cycling NMR relaxometer (Spinmaster FFC2000 1T C/DC, Stelar s.r.l., Mede, Italy). The remaining solution was transferred to a 0.55T bench top spectrometer (MQC, Oxford Instruments, Abingdon, UK) where T1 measurements were obtained (5 degree flip angle, 5s repetition time, 100 acquisitions). The sample in the Spinmaster was held at constant relaxation field (B_{RLX}) and temperature (37°C) while the magnetization was quickly sampled at constant intervals (TR), using a small flip angle (α), and an acquisition field (B_{ACQ}) of 0.747 T. Different hyperpolarized samples were used to cover relaxation fields in the range of 0.41mT to 0.55T with TR between 3 and 5 seconds and flip angles between 3° and 5°. T1 times were determined from the Spinmaster relaxation curves at different (B_{RLX}, TR, α) using non-linear least-square estimation with the following model that includes correction for flip angle:

$$S = A(\cos(\alpha))^{t/TR} e^{-t/T_1} + y_0 \quad (1)$$

Results:

Figure 1 shows the T1 nuclear magnetic resonance dispersion of [1-¹³C] pyruvate from 0.41mT to 0.55T. As can be seen, T1 increases very slowly for magnetic fields above 1 mT but, below this point, T1 rapidly decreases towards zero with decreasing magnetic field.

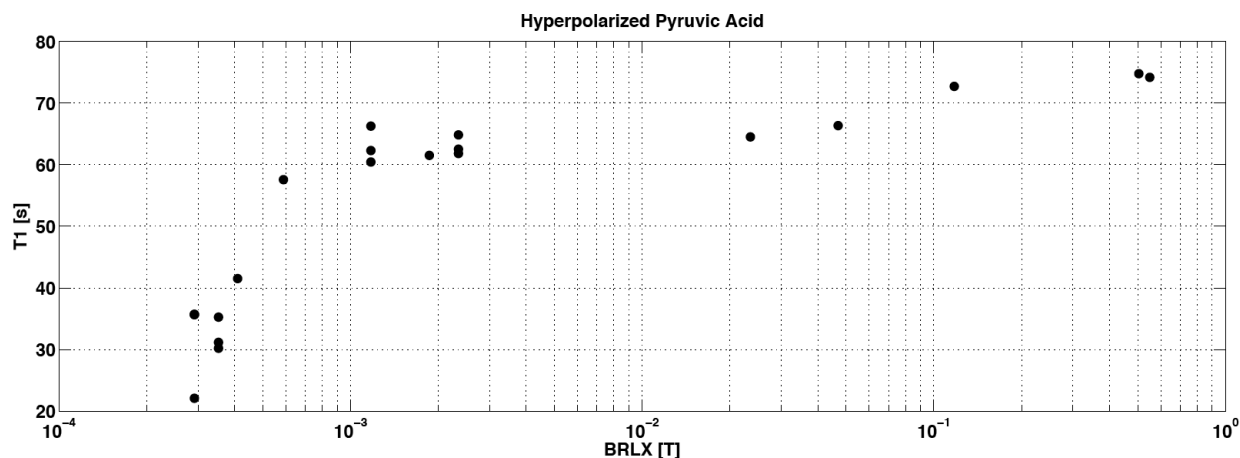


Figure 1. T1 Measurements of Hyperpolarized Pyruvate

Discussion:

The presented measurements suggest that the T1 of hyperpolarized pyruvate is significantly reduced at earth's magnetic field. In addition, the results indicate the importance of keeping the hyperpolarized sample in an environment where the magnetic field is above 1mT and suggest that a holding magnet may be helpful to preserve the hyperpolarised state through long spin-lattice relaxation times.

Conclusions:

Our experiments show that the T1 of hyperpolarized pyruvate is significantly reduced for magnetic fields below 1mT. We believe that the results presented in this work may help to improve the planning of experiments or even improve the design of delivery systems involving hyperpolarized samples such that the time and/or space that hyperpolarized samples spend at low magnetic fields will be minimized.

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