Strategies to prolong the T_1 times in hyperpolarized ^{13}C and ^{15}N biomolecules

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Introduction

Hyperpolarization techniques have gained great attention recently with the promise of NMR signal enhancement of over 50000 fold. This holds the potential for real time *in-vivo* studies of metabolic reactions which were not obtainable before. Functional, metabolic imaging may also become available.

All techniques share the same liability, which is the decay of hyperpolarization from the moment of generation. This decay defines the period in which the hyperpolarized agent has to be administered, metabolized, and detected. In this work we investigate deuteration as means to increase the lifetime (T_1) of hyperpolarization agents, exemplified on the molecules succinate (SUC) [1], 2-hydroxyethyl 1-^{13}C-propionate (HEP) [2], 1-^{13}C tetrafluro-proprionate (TFPA) [3] and ^{15}N choline (Ch) for PASADENA methodology of hyperpolarization [4, 5, 6]. Biomedical applications for all of these molecules are envisaged.

Experimental

^{13}C hyperpolarization > 15% was achieved for SUC-$d_{2,3}$, HEP-$d_{2,3,3}$, TFPA-$d_{2,3,3}$ with procedures and automated setup described before [1, 2, 3, 6). The decay of the longitudinal magnetization of these compounds was probed with small-excitation-angle pulses (SEA, ~8°) in intervals of 20s. The T_1 decay constants were extracted, taking into account the loss of magnetization due to the excitation pulse. In case no precursor molecule for hyperpolarization was available (non-deuterated SUC, Ch) the T_1 was determined on a high-resolution spectrometer (7T, 14T, Varian).

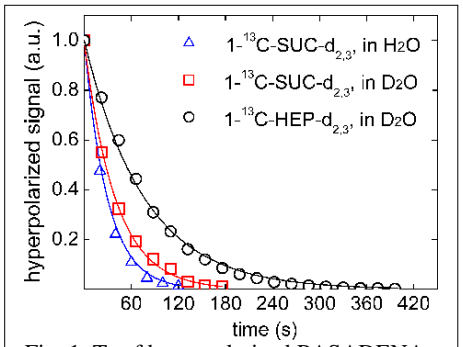

Fig. 1. T_1 of hyperpolarized PASADENA agents 1-^{13}C-SUC-$d_{2,3}$ and 1-^{13}C-HEP was increased by deuteration.

Results

The T_1 decay times for the molecules under investigation are given in Table 1. Molecular deuteration proved to have a strong impact on the T_1 of the molecules under investigation, which was extended further when D_2O was employed.

Conclusions

Hyperpolarization techniques promise to overcome the single greatest impediment of NMR, the inherently low sensitivity. However, the lifetime of this effect is not longer than several seconds. While longitudinal decay is intrinsic to all spins, it can be decreased significantly by molecular deuteration, and further improved when combined with deuterated solvent. Recent work in our laboratory has shown no significant difference in the metabolism of deuterated 1-^{13}C-succinate-$d_{2,3}$ as compared to the non-deuterated molecule in cellular human cancer [1]. The results suggest that molecular deuteration is a very promising approach to increase the lifetime of hyperpolarization, leading to a wider range of imaging agents for bio-medical applications *in-vivo*.

Molecule	T1 (s) (a)	T1 (s) (b)	T1 (s) (c)
1-^{13}C SUC	6*	27	40
1-^{13}C HEP	40	50	77
1-^{13}C TFPA	38	50	70
1-^{15}N CHO	48		72**

(a): Protonated molecule, in H2O
(b): Deuterated molecule, in H2O
(c): Deuterated molecule, in D2O
* Reference (1). ** Non-deuterated Ch in D_2O.

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