Hyperpolarization of hetero nuclei via adiabatic field cycling of parahydrogenated molecules

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Introduction

Over the last few years NMR hyperpolarization methods (1, 2) have gained new interest in the field of (pre-) clinical MR (3,4). This renewed interest is mostly caused by the large improvements in sensitivity that hyperpolarization schemes provide. Dynamic nuclear polarization (DNP) has since become commercially available (HyperSense, Oxford Instruments / OXO63, GE Healthcare). Another promising method, the so-called para-hydrogen induced polarization (PHIP) makes use of the macroscopic spin order contained in para-hydrogen gas (pH_2) to produce hyperpolarization. Field cycling following a para-hydrogenation reaction allows for polarization transfer from the pH_2 protons to other protons and hetero nuclei (e.g. ^{13}C, ^{31}P) of the hydrogenated substrates. Here we analyze interactions involved in field cycling polarization transfer following para-hydrogenation. In contrast to previous studies (5) we try to expand our simulation to include all nuclei and couplings present in the para-hydrogenated molecule.

Background

A problem in ^1H MR spectroscopy is the large overlap in the relatively narrow ^1H spectrum causing several metabolite signals to coincide. This problem is usually overcome by observing the corresponding signals of hetero nuclei like ^{31}P and ^{13}C of the metabolites, which offer much higher resolving power because of their relatively wider spectra. A drawback of hetero nuclear MR spectroscopy is the intrinsic low sensitivity of this technique. In regular non-hyperpolarized MR about one order of sensitivity can be gained by using optimized pulse sequences (6,7) and or measuring at higher field strengths. By performing a para-hydrogenation reaction at low magnetic field while ramping the field adiabatically up, nuclear spin polarization of other protons and hetero nuclei in the hydrogenated molecule can be brought close to unity, thereby enhancing especially hetero nuclear MR by several orders of magnitude. Another advantage of using hyperpolarized hetero nuclear MR might be the relatively longer relaxation times of most hetero nuclei compared to proton, which allows observation of slower metabolic processes as compared to 'conventional' hyperpolarized ^1H MR spectroscopy.

Theory

The principle of field cycling following para-hydrogenation can best be analysed by looking at the density operator of the para-hydrogenated molecule expressed in the eigen basis of the field Hamiltonian of detection. The para-hydrogenation reaction is assumed taking place at low magnetic field (<μT). As the applied field adiabatically increases, the evolution of the spin density operator is given by the solution of the Liouville-von Neumann equation (Eq. 1) where $\hat{\sigma}(0)$ is the density operator at the end of the para-hydrogenation reaction and $\hat{H}$ is the high resolution Hamiltonian of the para-hydrogenated molecule. The Hamiltonian of the hydrogenated molecule takes the form (Eq. 2).

$$\hat{\sigma}(t) = \exp(-i\hat{H}t)\hat{\sigma}(0)\exp(i\hat{H}t)$$

Equation 1: Spin density operator for adiabatic field increase.

$$\hat{H} = -\sum_i \gamma_i B_o \hat{I}_z + \pi \sum_{ki \neq l} J_{kl} \hat{I}_k \cdot \hat{I}_l$$

Equation 2: High resolution Hamiltonian of the para-hydrogenated molecule.

Simulations

The evolution of the density operator under field cycling was simulated as described above using Matlab ® (Natick, MA, USA). Deviations from an ideal case example (two protons originating from pH_2 + hetero nucleus) as described in (5) as well as other biologically potentially interesting substrates were analyzed including additional nuclear spins and different topologies of scalar couplings. The effects of duration and shape of the field ramp were investigated as well as deviations from the adiabaticity conditions. Inclusion of additional (moderately) coupled spins into the simulation next to only the protons originating from the pH_2 and the hetero nucleus proved to dramatically alter overall polarization transfer effectiveness and or the optimal shape for field cycling trajectories. Fig. 1 shows the maximal ^{19}F polarization of para-hydrogenated 3-Fluorostyrene.

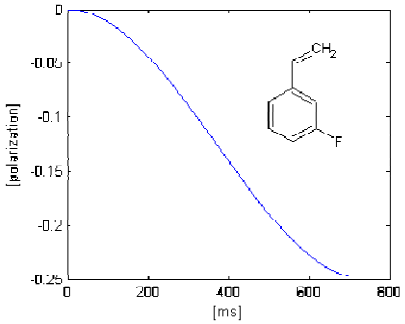

Figure 1: Optimal ^{19}F polarization trajectory of 3-Fluorostyrene.

Discussion and conclusion

The numerical simulation of the field cycling experiment after para-hydrogenation is of great help in the selection of the optimal biologically interesting para-hydrogenatable substrates as well as for determining optimal field cycling conditions for the specific nucleus to be observed. The number of spins and the topology of the J-interaction was found to dramatically affect the effectiveness of the field cycling method.

References

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