# Optimization of polarization transfer sequence timing for parahydrogen induced polarization

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## Introduction

Parahydrogen Induced Polarization (PHIP) achieves a hyperpolarized proton state by hydrogenation of a double or triple bond with parahydrogen [1]. A commonly used molecule for PHIP is $^{13}C_1$-Hydroxyethylacrylate which is hydrogenated to Hydroxyethylproprionate (HEP) by a water-soluble catalyst. The hyperpolarization can be transferred to heteronuclei, such as $^{13}C$, using a modified version of the refocused INEPT sequence (PH-INEPT+, [2]) to enable $^{13}C$-MRI and MRS and to enlarge the lifetime of the hyperpolarized state. The aim of the current study was to optimize the PH-INEPT+ sequence for $^{13}C$-MRI/MRS studies of $^{13}C_1$-HEP to enable optimal and selective polarization transfer.

## Materials and Methods

Spin dynamics simulations were accomplished using the program SIMPSON which is based on a numerical evaluation of the Liouville-von Neumann equation [3]. They were performed for the transfer of thermal polarization using the refocused INEPT and for the hyperpolarized state using the PH-INEPT+



Fig. 1. Polarization transfer sequences. (a) Refocused INEPT and (b) PH-INEPT+.

sequence (Fig.1). The first five protons of the HEP molecule were taken into account in the simulations. The initial density operator of the thermal polarization is the sum of all $I_z$-spin-operators and $I_{1z}I_{2z}$ for the PHIP state [1] with 1 and 2 being the hyperpolarized protons. Experimental validation was performed using a 7T spectrometer (Avance 300, Bruker). For this purpose a modified version of the membrane method for parahydrogen application developed by Roth et al. [4] was used, allowing a constant hyperpolarization level in the spectrometer for ~10 minutes. Experiments employed $\tau_2$=14ms and the $\tau_1$ optima found in the simulations between 0 and 60ms.
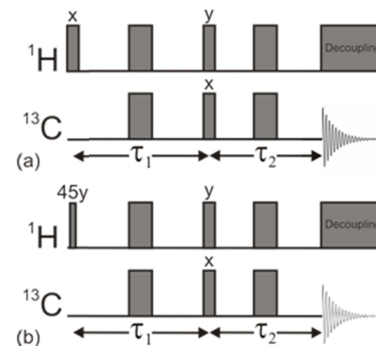
## Results & Discussion

A comparison of $\tau$ delays for the thermal polarization and PHIP (Fig.2) shows that there is an important difference between the two cases. Even though the position of the local optima is the same, the global $\tau_1$ optimum in the PHIP case is not reached at the first $\tau_1$ optimum, however, at the fourth local $\tau_1$ optimum at 27.5ms. The difference in the maximal amplitude of the optima is due to the different norms of the initial density operators. The experiments reproduce the simulation results adequately (Fig.3).
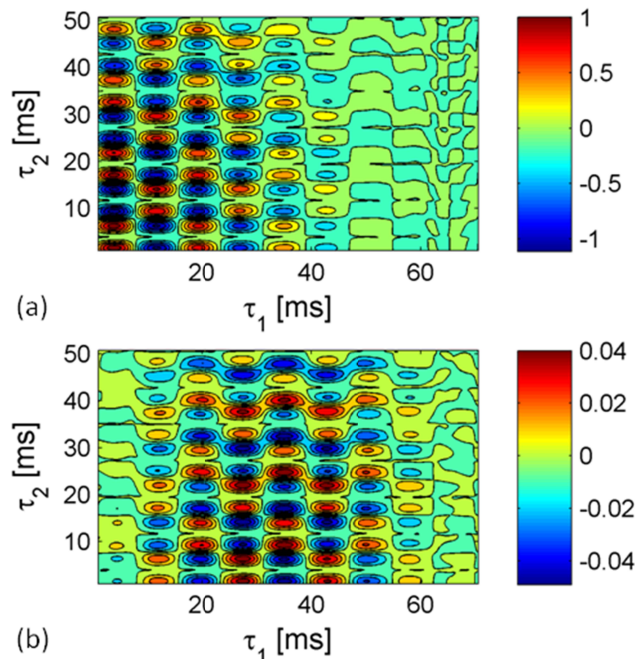


Fig. 2. Simulations of polarization transfer to Carbon-13 with different $\tau$ delays for (a) the thermally polarized protons and (b) the PHIP protons.



Fig. 3. Experimental validation of simulation result for a fixed $\tau_2$ delay of 14ms. Error bars shows experimental measurements, the line depicts the simulation results. The experimental data was scaled to fit with the optimum at 27.5ms.

## Conclusion

In conclusion, we have shown the different behavior of thermally polarized and a PHIP polarized molecule when applying polarization transfer sequences for observation of heteronuclei (e.g. $^{13}C_1$-HEP). To achieve an optimal polarization transfer it is not only necessary to modify the pulse sequence elements, but also to choose an adapted timing of the pulse combinations.

## Acknowledgement

## References

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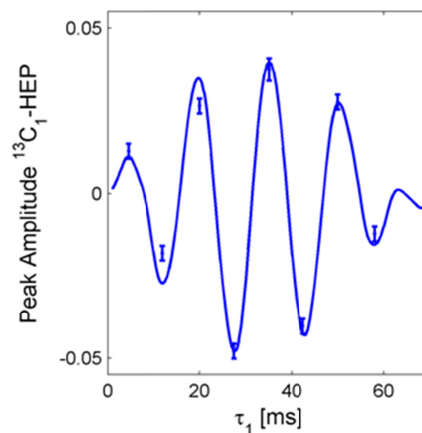[4] Roth et al. Angew. Chemie 49, 8358-62 (2010)