Para-Hydrogen Induced Polarization – Production of highly concentrated metabolite precursors and long polarization storage over 10s of minutes

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Introduction: Nuclear magnetic resonance (NMR) comes with the drawback of inherently low sensitivity. In order to improve detection sensitivity and enhance signals of certain compounds, hyperpolarization techniques have been developed.[1-6] Among these methods, para-hydrogen induced polarization (PHIP) is a rapid approach that generates hyperpolarized molecules within seconds.[3] At the conference, I am going to present the most recent advances that have enabled us to generate highly concentrated (50 mM) solutions of metabolites and their precursors (P_{13C} > 50%) with particular applicability for in vivo experiments in the future.[6-9] Furthermore, we show our recent progress in polarizing a library of ^{15}N-enriched compounds in which the hyperpolarized signal can be stored for 10s of minutes enabling the design of long traceable contrast agents.[10,11]

Results and Discussion:
All of our hyperpolarization experiments were performed with our recently introduced pulsed polarization transfer sequence termed ESOTHERIC (Efficient Spin Order Transfer via Relayed Inept Chains).[6,7] This sequence allows for near unity transfer of para-hydrogen spin order to ^{13}C spins. It was optimized to compensate for radiation damping effects which occurred in utilized 7T and 1T spectrometers once concentrations above 1 mM were attempted to be polarized.[9] Applying the new sequence allowed us to achieve more than 50% ^{13}C polarization in 50 mM concentrated solutions of acetate precursors (figure 1). As the developed sequence only requires weak coupling conditions, we have managed to incorporate it into a low field spectrometer at 1T and demonstrate similar polarization results on the acetate precursor. We have subsequently synthesized a variety of metabolite precursors including pyruvate and amino acids and demonstrate their polarization as well as cleavage of the precursor into the respective metabolite.[6-8]

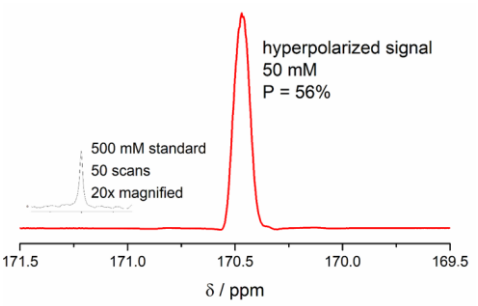

Fig. 1: Hyperpolarized ^{13}C-signal of a highly concentrated acetate precursor.

In addition to the designed metabolite precursors, possibilities to store hyperpolarization for tens of minutes have been investigated in newly designed quaternary ^{15}N-enriched molecules.[11] A library of compounds will be presented and their applicability discussed for future applications. Hyperpolarization of the ^{15}N-nuclei has partly been achieved by utilizing newly designed nanocatalysts and the transfer sequence described above.[10]

Conclusions:
Overall, we have introduced an approach to quickly generated hyperpolarized metabolites and compounds with long polarization storage times. The applicability of this approach in low field systems increases portability and cost efficiency of the shown method.

References:
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