EARTH'S FIELD MRI USING CONTINUOUS SABRE HYPERPOLARIZATION

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Introduction

The goal of hyperpolarization is to access the vast majority of nuclear spins (99.9997 % of ^{1}H per Tesla) which do not contribute to the signal of conventional MRI. Methods employing parahydrogen (pH_2) are unique in providing fast, cost-efficient hyperpolarization in the liquid state. Until recently, the spin order of pH_2 was added to a molecule by a one-way hydrogenation reaction[1], followed by a pulse sequence to transfer the para-order to another nucleus[2,3]. In 2009, multi-nuclei signal amplification by reversible exchange (SABRE) was demonstrated using an Ir-catalyst in a low magnetic field[4] (Fig. 1).

Two major limitations of hyperpolarization in general are its lifetime and single-use-character: Usually, all hyperpolarized (i.e. non-equilibrium) magnetization returns to thermal equilibrium after a single 90° excitation. Thus, there is no recovery of hyperpolarization; it can only be used once. Dedicated pulse sequences are thus required to image hyperpolarization efficiently. In combination with a relatively short lifetime, the diagnostic application of hyperpolarized agents remains challenging.

Here, we describe a method of continuously hyperpolarizing, exciting and detecting a given number of molecules multiple times for > 10 min after a single application of pH_2. The potential of this quasi-permanent hyperpolarized state is demonstrated by fast MRI in the earth field (EFMRI).

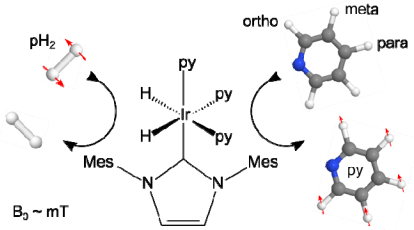

Fig. 1: Schematic repr. of SABRE: the spin order of pH_2 (red arrows) is transferred to pyridine (py) polarization by a reversible exchange.

Fig. 2: Photograph of reaction chamber connected to PTFE tubing (inner diam. 31 mm, vol. 12 ml).

Methods: ^{1}H MR spectra and images of a reaction chamber (Fig. 2) filled with water or hyperpolarized pyridine were acquired using a earth's field MRI system (Terranova-MRI, Magritek, New Zealand). Before signal was excited and acquired at earth field (B_0), an additional static magnetic field (B_P) was generated to enhance the bulk polarization of H_2O (20 mT for 4 s) or to enable SABRE (6.5 mT for 4 s). For SABRE, 20 mg of pyridine (py, CAS 110-86-1, Carl Roth, Germany) and 5 mg of catalyst $[Ir(H)_2(IMes)(py)_3]Cl$] (University of York, UK) were dissolved in 3 ml of perdeuterated methanol (CAS 811-98-3, Carl Roth). pH_2 enriched to ≈ 96 %[5] was injected through PTFE tubing at variable pressure.

Results

No MR signal was observed from py before pH_2 was supplied. After initial activation of the catalyst and injection of pH_2, strong hyperpolarized signal was observed for 128 consecutive, full 90° acquisitions (Fig. 3). Within 3 scans after the injection, the signal decreased rapidly to ≈30 % of the maximum intensity. In the following 15 min, the decay was much slower (e.g. by ≈35 % at 9 bar). This remarkable effect may be attributed to the fact that the SABRE reaction is ongoing, pH_2 is impervious to r.f. pulses and available in excess in the reaction chamber.

A spin echo image of hyperpolarized py was acquired in 4 min. (Fig. 4, right), and provided higher SNR as an image of 6 ml water acquired in 2h 16 min (32-fold signal averaging, Fig. 4, left). Note, the molecular concentration of py was much lower (≈20 mM) as the concentration of water (56 M).

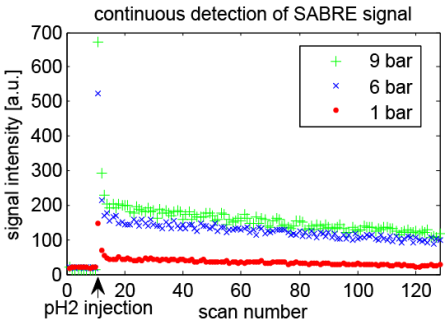

Fig. 3: ^{1}H signal intensities of 128 serial MR spectra of hyperpolarized pyridine (TR=8s). For acquisition 1-10, residual pH_2 resided in the reactor at 1 bar; in between N=10 and 11, fresh pH_2 was injected for 1s at the indicated pressure (^{1}H frequency 2407 Hz, no shaking of chamber).

Discussion and Conclusion

In its literal sense, the experiments described here do not provide for continuous polarization. The fields for detection and polarization are different: No repolarization takes place during signal read out. Even though, the signal gain compared to much higher concentrated water, prepolarized at 20 mT, is tremendous. As all EFMR systems typically comprise a step for prepolarizing the sample, this method may be easily integrated in existing setups.

In conclusion, the two challenges of hyperpolarization, its lifetime and single-use-character, are circumvented by the method presented. Introducing the concept of signal averaging to hyperpolarization, fast, low-field MRI (≈mT) becomes feasible. While challenges (such as a biocompatible chemistry) remain, the possibility of polarizing a specific molecule multiple times, potentially *in vivo*, offers a wide range of new perspectives for the emerging field of nuclear hyperpolarization.

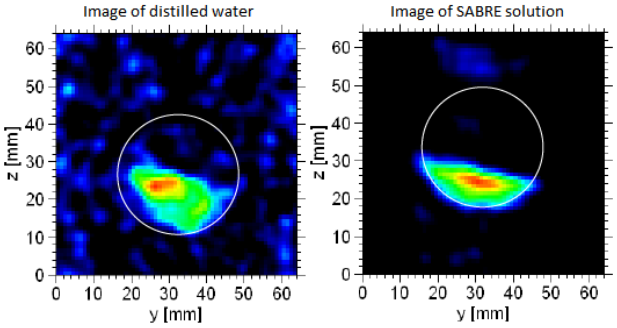

Fig. 4: 2D projection spin-echo MRI of distilled water (left, 6 ml, N=32, 2h 16' 32'') and hyperpolarized pyridine (right, 3 ml, N=1, 4min 16s). White circles indicate the reaction chamber (FOV 64 mm^2, matrix size 32^2, 1x zero fill., interp. resolution 1 mm^2, TE 150 ms, TR 8 s).

References [1] Bowers and Weitekamp J. Am. Chem. Soc., (1987), 109 (18), 5541–5542 [2] Goldman (2005) 6,575–581 [3] Haake et al., J. Am. Chem. Soc., (1996),118(36),8688–8691.[4] Adam et al. (2009) Science, 323,1708–1711 [5] Hövener et al. (2012) NMR Biomed. DOI: 10.1002/nbm.2873.