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Multiplexed Magnetic Resonance Imaging With Parahydrogen Induced Spin Polarization

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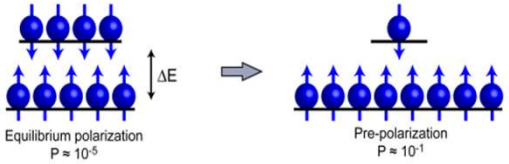
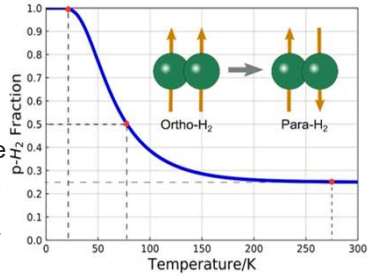
Hyperpolarization for Magnetic Resonance Signal Enhancement



The sensitivity and resolution of magnetic resonance (MR) imaging is limited by a low population difference of nuclear spin states at the thermal equilibrium. Hyperpolarization techniques increase this population difference and hence the achieved signal amplitudes by orders of magnitude. Parahydrogen induced polarization (PHIP) allows hyperpolarization of nuclear spins at low cost. [1] The signal enhancement provided by PHIP makes it promising to probe metabolites below the detection limit of conventional MRI.

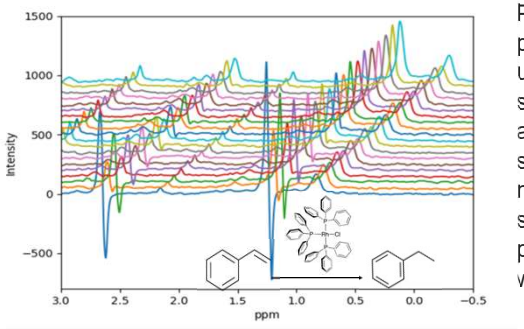
Parahydrogen Induced Polarization

PHIP generates nuclear spin hyperpolarization by incorporation of molecular hydrogen (H_2) in the antiparallel para-spin state into a target compound of interest. In a hydrogenation reaction, the pairwise addition of para-H_2 to two magnetically inequivalent sites of the substrate breaks the symmetry of para-H_2 and allows the desired signal to be enhanced by up to ~10,000 fold.



The singlet para-H_2 is generated by passing the hydrogen gas through a spin-flip catalyst at low temperature. The para-spin state is enriched due to the requirement for an antisymmetric total wave function, and increased population of the J = 0 rotational state of H_2.

Hyperpolarized NMR Spectroscopy

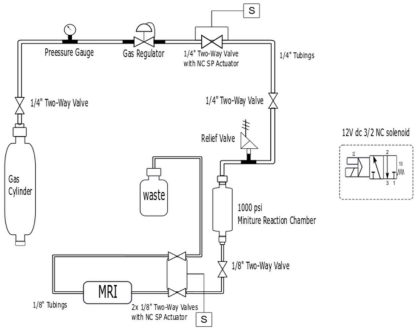


Parahydrogen induced polarization is produced by reacting para-H_2 with styrene, using Wilkinson's catalyst. The antiphase signals at ~1.2 and 2.7 ppm, with positive and negative signs, are strongly enhanced signals of the target compound. Each odd-number scan represents a hyperpolarized spectrum measured after bubbling the para-H_2, while the even-number scans were measured at thermal equilibrium.

[1] Bowers, C. R.; Weitekamp, D. P. *J. Am. Chem. Soc.*, **1987**, *109(18), 5*541-5542.

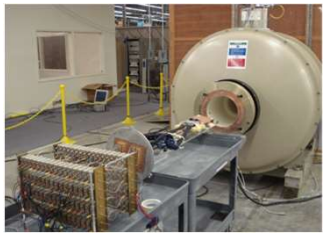
Development of Portable Para-H_2 Polarizer for MRI

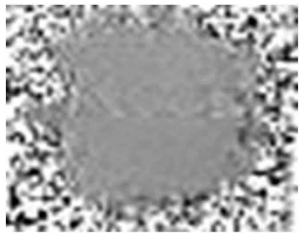
We are developing a portable and low-cost instrument for generating PHIP at the site of an MR scanner. In this instrument, para-H_2 preloaded in the gas cylinder will be rapidly injected into a reaction chamber, where a mixture of dissolved substrate and catalyst will be contained. After a hydrogenation reaction, the product will be injected into an MRI system for data analysis. The image shows a prototype for the development of the fluid delivery system. Automated valves are incorporated into the setup to provide accurate control over the injection timing. The schematic of the instrument includes the gas cylinder to supply para-H_2, the flow path to the reaction chamber, and the flow path into the MRI scanner.



Development of Fast MRI Acquisition

Metabolic imaging using PHIP hyperpolarized substrates requires fast MR data acquisition. This requirement is both due to the limited lifetime of the hyperpolarized spin state, and due to the time-dependent nature of a metabolic process. We are developing fast MRI that enables the acquisition of 64 images during a 60 ms pulse at a rate of >1000 frames per second. The fast MRI system coupled with the PHIP will potentially provide the means to acquire time-resolved images of metabolites at low concentration.





The image shows a front view of the 4.7 T MRI scanner with a 64-channel receiver coil inside of a transmit coil, prior to loading into the magnet. The coil array is interfaced to 64 transmit/receive switches and 64 preamplifiers, shown in the foreground of the picture. This system has been used to obtain MR images at 1000 images per second. An example of an MR image captured at this frame rate is shown to the right.