

Generation of hyperpolarised materials for magnetic resonance using high-field cryogenics

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Introduction

Several approaches have been adopted for hyperpolarising nuclei. Here, we report initial studies investigating the extent to which high-field cryogenics (ie the so-called brute-force approach), in conjunction with relaxation switches and low-field thermal mixing, can be used to generate large increases in nuclear polarisation on a realistic timescale. The central notion is that at high field and low temperature, the equilibrium nuclear polarisation will increase according to the Boltzmann distribution. The main problem is that it may take an excessively long time for the polarisation to approach thermal equilibrium at very low temperatures. Relaxation agents and polarisation transfer techniques provide potential approaches to overcoming the problem. We tested the proposition that lanthanides such as dysprosium and holmium (which have very short electron spin relaxation times at room temperature) might act as relaxation switches, generating effective relaxation at low temperatures but not at room temperature (1). We also evaluated low-field thermal mixing (2) as a means of transferring polarisation from relatively rapidly relaxing ¹H nuclei to more slowly-relaxing ¹³C nuclei.

Methods

Experiments were performed on samples of 1-¹³C sodium acetate, using three spectrometers operating at temperatures of 4.2K or below. ¹H and ¹³C T1 relaxation measurements were carried out using lanthanide-DTPA chelates as relaxation switches; such chelates offer the advantage of low toxicity.

Results

Of the lanthanides tested, holmium proved to be the strongest relaxation agent, followed by dysprosium (see Table). At 3.35T and 1.6K, ¹³C T1 values could be reduced from over 10 hours to 8 minutes and ¹H T1 values from over 1 hour to 16 s.

Lanthanide DTPA chelate	Concentration of lanthanide ion	¹³ C T1	¹ H T1
Cerium	25mM	85min	3.2min
Dysprosium	18mM	30min	33s
Europium(III)	34mM	≥400min	87min
Holmium	24mM	8min	16s
Praseodymium	24mM	≥400min	38min
Samarium	21mM	≥600min	39min

¹H and ¹³C T1 values at 3.35T and at a temperature of 1.6K for water/glycerol (1:1) solutions of 2 molar 1-¹³C sodium acetate in the presence of a range of different lanthanides complexed to DTPA

We explored the effectiveness of low-field thermal mixing in experiments carried out at 4.2K on 1-¹³C sodium acetate powder, exploiting a field cycling NMR spectrometer designed to deliver magnetic field switches of 10T s⁻¹. The incorporation of a brief (<0.5s duration) low-field (<0.005T) thermal mixing step immediately prior to data acquisition resulted in an increase in the rate of polarisation of the ¹³C nuclei with a time constant more in keeping with the ¹H T1 than with the ¹³C T1, indicating the effectiveness of low-field thermal mixing. We also carried out a series of proof-of-concept experiments using a further spectrometer coupled to a dilution refrigerator. In one experiment, we initially exposed a solution of 2 molar 1-¹³C sodium acetate/2mM holmium DTPA to a field of 12T and temperature of 1.0K for 26 hours, allowing the ¹H nuclei to approach thermal equilibrium. The temperature was then reduced to 32mK, and we were able to show that low-field thermal mixing was highly effective at this temperature, yielding a ¹³C polarisation that was approximately 70% of that corresponding to equilibrium at the starting conditions of 12T and 1.0K, ie approximately 1,000 greater than the equilibrium polarisations that are typical of clinical spectroscopy.

For clinical studies, after the polarisation process it is necessary to warm the sample to room temperature without causing undue loss of polarisation. We tested the extent of polarisation loss in a frozen water/glycerol (1:1) solution of 2 molar 1-¹³C sodium acetate/2mM holmium-DTPA, using a 3.35T spectrometer coupled to a rapid warming/dissolution/transfer/measurement system. In initial experiments with as yet non-optimised technology, approximately 50% of the ¹³C polarisation was preserved following rapid warming, dissolution (in deuterium oxide), and transfer from the cold (1.6K) 3.35T system to a nearby 9.4T spectrometer. Furthermore, the relaxivity of holmium-DTPA at 20°C and 11.7T was only 0.004s⁻¹mM⁻¹ for a 100mM 1-¹³C sodium acetate solution. We conclude that the holmium-DTPA will exert only very small relaxation effects during the warming-up and subsequent measurement times.

Discussion

We believe that this enhanced brute-force approach will enable us to generate large scale quantities of highly polarised materials on a realistic timescale. Among the technical advantages of this approach, the polarisation process does not involve any resonance phenomena or radiofrequency irradiation. In addition, the process is completely broadband; thus a wide range of nuclear species could be polarised simultaneously. For these reasons, we envisage that our methodology and technology could play a very useful role in the preparation and analysis of highly polarised materials in the basic and clinical sciences.

References

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- (2) Abragam A and Proctor WG (1958). Spin temperature. Phys. Rev. 109:1441-1458