Fundamentals of Hyperpolarization

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Highlights

- Dynamic Nuclear Polarization (DNP) transfers polarization from free radical electrons to nuclei
- Multiple mechanisms for polarization transfer are in play at different field strengths
- Dissolution DNP is generally best carried out at intermediate field strengths
- Sample preparation can drastically change the efficiency of the DNP process

Target Audience: M.D. and Ph.D. researchers with a specialty or developing need to improve their knowledge in cellular and molecular imaging concepts and applications.

Objectives

1. Describe the phenomenon of Dynamic Nuclear Polarization in the solid state
2. Understand the impact of sample preparation on the absolute polarization
3. Evaluate properties of molecules that would suggest them as new imaging agents

Background

Metabolic imaging using MR has traditionally been handicapped by poor sensitivity and by limited chemical shift resolution in *in vivo* ^{1}H spectra. Carbon-13 spectra are spread across a much larger range of chemical shifts, but ^{13}C spectroscopy has much lower sensitivity than its ^{1}H analogue. Carbon-13 detection limits can be lowered significantly by pre-polarizing a molecular imaging contrasts agent by DNP prior to its injection into the study subject. The phenomena of DNP was first predicted by Overhauser (1) and was quickly demonstrated experimentally by Slichter (2). In 2003, it was demonstrated that the DNP method could be used to produce a highly sensitive metabolic contrast agent (3).

Methods

DNP requires the presence of a free radical electron to be located proximal to the nuclei that are the targets for enhancement. For low gyromagnetic ratio nuclei like ^{13}C and ^{15}N, narrow electron spin resonance (ESR) line radicals like trityl, tris{8-carboxyl-2,2,6,6-tetra[2-(1-hydroxyethyl)]-benzo(1,2-d:4,5-d)bis(1,3)dithiole-4-yl}methyl sodium salt, or BDPA, 1,3-bisdiphenylene-2-phenylallyl (4), produce significantly higher polarizations than wide line radicals like TEMPO (5), DPPH (6), or galvinoxyl (7). The DNP process exploits the dipolar interactions between the electron Zeeman system (EZS), the electron dipolar system (EDS), and the nuclear Zeeman system (NZS) to produce non-Boltzmann population distributions for the nuclei. At currently available field strengths for commercial pre-polarizers, thermal mixing is the primary mechanism for DNP enhancement. This has strong consequences for the choice of matrix that the target sample is solubilized in (8). Kinetics of the polarization process is also subject to manipulation suing isotopic labeling of the solvents (9). Previous studies at lower field strengths utilized 3He based refrigerators to produce very high polarizations (10).

Results

DNP in the solid state is field and temperature dependent. As the field strength increases, the power dependence of the microwave irradiation also becomes pronounced. Pyruvic acid is a ubiquitous target for DNP studies. One reason is that the free acid makes a nearly ideal target for DNP due to the high concentration of the neat acid and the lack of interfering nuclei.

Discussion

While thermal mixing produces large polarizations of ^{13}C using current DNP systems, significant improvements in the absolute polarization are still possible. Optimization of the sample matrix for DNP can lead to 2x gains in sensitivity without unduly complicating sample preparation. New methods that could accelerate the production of polarized samples would have substantial benefit for throughput and cost of doing molecular imaging with DNP enhanced ^{13}C imaging.

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