HIGH POLARIZATION OF NUCLEAR SPINS MEDIATED BY NANOPARTICLES AT MILLIKELVIN TEMPERATURES

David G Gadian[1], David T Peat[2], Kelvin Goh[2], Anthony J Horsewill[2], and John R Owers-Bradley[2]
[1]*UCL Institute of Child Health, London, United Kingdom,* [2]*School of Physics & Astronomy, University of Nottingham, Nottingham, United Kingdom*

Introduction There is intense interest in the development of techniques that can generate high levels of nuclear spin polarization. Here we report on a novel strategy that could prove to be widely applicable. The central notion is that as the temperature is reduced and the magnetic field is increased, the equilibrium nuclear polarization will increase, according to the Boltzmann distribution. For example, at 7 millikelvin (mK) and a field of 16T (conditions achievable with commercially-available technology), the equilibrium polarization of ^{13}C nuclei would be approximately 50%, i.e. ~100,000-fold greater than typical room temperature values. The main problem with this so-called brute-force approach is that it may take an excessively long time (possibly many years) for the nuclear polarization to approach thermal equilibrium at very low temperatures. Here we describe investigations that address this problem.

Purpose Our goal was to use the brute-force approach to achieve high polarizations of nuclei such as ^{13}C and ^{15}N with a view to using pre-polarized ^{13}C- or ^{15}N-labelled agents to probe tissue metabolism *in vivo*. We explored the possibility that selected nanoparticles (including metallic nanoparticles) might act as low temperature relaxation agents.

Methods Samples were prepared by mixing nanoparticles with 50/50 water/glycerol solutions containing 2 molar 1-^{13}C-labelled sodium acetate and 1 molar sodium phosphate. The volume ratio was one part nanoparticle to 4 or 8 parts of solution, and the resulting mixtures had a wet sandy consistency. Copper (size 25nm), silver (size 20-30nm), aluminium (size 18nm), and graphene (size 11-15nm) nanoparticles were obtained from SkySpring Nanomaterials Inc; platinum (size <50nm) and copper (II) oxide (size <50nm) nanoparticles were obtained from Sigma Aldrich. Experiments were carried out using a spectrometer that operates at any chosen field up to 15T, and forms part of a dilution refrigerator-cooled system that yields sample temperatures as low as 10mK.

Results ^{1}H T1 measurements at 2.45T revealed that copper, copper (II) oxide and platinum nanoparticles are highly effective relaxation enhancers at millikelvin temperatures, with copper showing the greatest enhancement. However, aluminium and silver nanoparticles were ineffective, while graphene nanoparticles showed intermediate effects. ^{13}C data were obtained at 9.74T using a volume ratio of 1 part copper nanoparticles to 8 parts solution (see Fig. 1). The estimated ^{13}C $T_{1/2}$ value (time to reach 50% of equilibrium polarization) at 19mK was about 40 hours, and was only 3 times as long as the value at 770mK. For comparison, the ^{13}C $T_{1/2}$ value measured in the presence of aluminium nanoparticles was at least one year, which gives some indication of the degree of enhancement conferred by the copper nanoparticles. Further experiments were carried out at 14T and 15mK using a 1:4 volume ratio of copper nanoparticles to solution. Under these conditions the ^{13}C polarization reached 6% after 24 hours, and the $T_{1/2}$ for growth towards the equilibrium polarization of 23% was estimated to be about 60 hours.

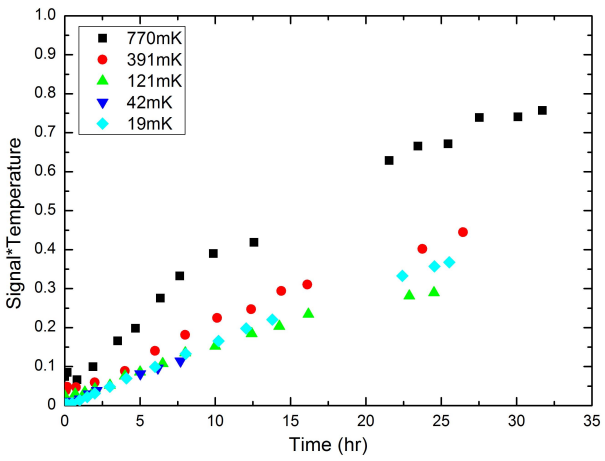

Figure 1. ^{13}C signal x temperature as a function of time. The end-point (normalized to 1.0) should be the same for all timecourses.

Discussion Our exploration of metallic nanoparticles as low temperature relaxation agents was based on well-known observations that the nuclei of metals such as silver, copper, platinum and aluminium continue to display measurable T1 relaxation even at ultra-low temperatures in the millikelvin range. However, at this stage it is not clear why copper and platinum (as well as the non-metal copper oxide) are effective, while silver and in particular aluminium are not.

Conclusions While further experiments are required in order to establish mechanisms, it is evident that this methodology will enable us to generate and store large-scale quantities of highly polarized materials. A wide variety of applications are envisaged, including investigations of tissue metabolism following dissolution and subsequent administration of pre-polarized ^{13}C or ^{15}N-labelled agents. For human studies, an additional feature is that the nanoparticles should be easily removable on dissolution. With further developments, including the use of polarization transfer techniques and simultaneous polarization of many samples, outputs of ten or more samples per day should be feasible.

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