

Preparation of Radical-Free Hyperpolarized Water using Photo-induced non-persistent Radicals on a “SpinLab-like” dissolution-DNP Polarize

A. Capozzi¹, A. Coi¹, M. Karlsson¹, M. H. Lerche¹, J. H. Ardenkjær-Larsen¹

¹Department of Electrical Engineering, Technical University of Denmark, 2800 Kgs. Lyngby, Denmark

The polarization of nuclear spins in radical-doped frozen amorphous solid samples can be enhanced by dynamic nuclear polarization (DNP) at low temperature and moderate magnetic field (usually between 3.35 T and 7 T). The polarization is maintained in a rapid dissolution procedure to obtain liquid-state hyperpolarized (HP) molecules in solution.¹ Although dissolution-DNP can potentially be employed to increase the polarization of any non-zero nuclear spin species, the method has mainly been used to study biological molecules labeled with ¹³C in a position with a long T₁. The electron spins introduced in the sample, which embody the source for the polarization transfer to the nuclei in the solid state, become unwanted at the moment of dissolution and transfer of the HP liquid since they represent the main source of spin relaxation, and thus polarization loss. A typical example is the short T₁ of water protons (¹H) when a paramagnetic agent is present in the solution.

Nevertheless it has recently been demonstrated that HP water, generated via dissolution-DNP, can be successfully employed to obtain angiographic and perfusion images with high spatial resolution.² These pioneering studies provided a novel contrast agent, free of paramagnetic metal ions such as Gd, and based on water only. However they also clearly established the limitations of the state-of-the-art: even though a polarization of about 80% was obtained at 6.7 T and 1.1 K in the solid state using TEMPOL as polarizing agent, after dissolution, once transferred to the measuring apparatus, only 5% of water proton polarization was left in the liquid state. The main reason of this dramatic polarization's reduction has to be attributed to the time employed in scavenging the nitroxyl radical (the procedure takes about 10 s during which the proton T₁ is still 3 – 4 s)³.

In the present study we show a novel solution to circumvent this issue by employing non-persistent radicals generated by UV-irradiation at low-temperature of pyruvic acid (PA) aqueous solutions. These radicals, in sufficiently high concentration to perform DNP at liquid helium temperature, suffer from thermal stress above 190 K.³ Thus, they are annihilated within the dissolution procedure, when the DNP sample temperature increases, leaving a HP solution naturally free of paramagnetic entities.⁴

The two investigated DNP samples were a mixture of PA:H₂O and [2-¹³C]PA:H₂O 1:1 (v/v). For each sample 60 frozen pellets were made pouring 4.0±0.5 μL droplets of solution into a transparent quartz dewar (Wilmad-LabGlass WG-850-B-Q) filled with liquid nitrogen. The samples were irradiated for 300 s with a high power (20 W/cm²) broadband UV source (Dymax BlueWave 75). X-band ESR measurements (Magnetech MiniScope 5000) showed a radical concentration of 45±5 mM.

Each sample was then transferred to a homebuilt 6.7 T dissolution-DNP polarizer equipped with the GE SPINlab fluid path technology for inserting the sample.⁵ The original sample vial was replaced by a custom-made PTFE reusable threaded vial to facilitate the loading of the temperature sensitive frozen pellets after UV-irradiation.

For both samples, DNP was performed at 6.7 T and 1.1±0.1 K shining microwaves with a nominal output power of 55 mW and at a frequency corresponding to the positive maximum of the sample's ¹H DNP microwave sweep (see Fig. 1). A maximum proton polarization of 35±5% was measured in the solid state for PA:H₂O 1:1 (v/v) after about 45 min of microwave irradiation. In the case of [2-¹³C]PA:H₂O, thanks to the broader UV-generated radical ESR spectrum due to the strong coupling with the ¹³C nucleus at the unpaired electron molecular site (see Fig. 2), a maximum proton polarization of 70±5% was estimated after about 30 min of microwave irradiation. For both samples the dissolution was performed heating 15 mL of D₂O up to 150°C; in the receiver vial 5 mL of HP final solution were collected (2.5 M water final concentration). 500 μL of the latter was then injected into a 5 mm NMR tube and transferred to a Varian 400 MHz high resolution NMR spectrometer. The ¹H signal was acquired sending 1° rf pulses every 2 s. A water proton T₁ of 30.5±0.5 s was measured confirming the absence of radical in the HP solutions.

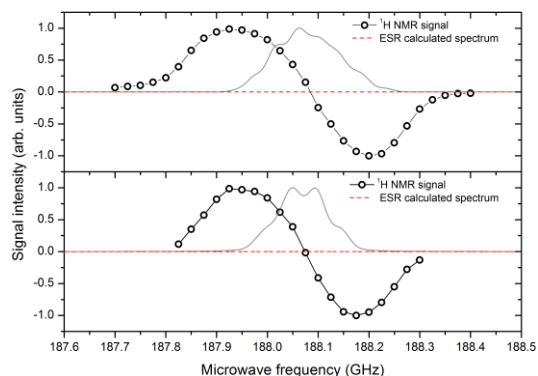


Figure 1 DNP microwave sweep and calculated ESR spectrum at 6.7 T and 1 K for UV-irradiated [2-¹³C]PA:H₂O (top) and PA:H₂O (bottom) 1:1 (v/v).

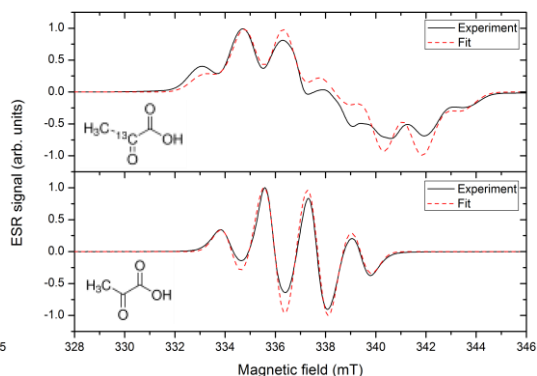


Figure 2 X-band ESR spectrum at 77 K for [2-¹³C]PA:H₂O (top) and PA:H₂O (bottom) 1:1 (v/v) after 300 s of UV-irradiation.

¹ J. H. Ardenkjær-Larsen et al. PNAS **100**, 10158 (2003).

² J. H. Ardenkjær-Larsen et al. MRM **71**, 50 - 56 (2014); K. W. Lipsø et al. JMR, **274**, 65-72 (2016).

³ M. I. Guzman et al. JPCA, **110**, 3619-26 (2006).

⁴ T. R. Eichhorn et al. PNAS **110**, 45 (2013); A. Capozzi et al. JPCC, **119**, 39 (2015).

⁵ R. M. Malinowski et al. JMR, **272**, 141-146 (2016).