# Optimal glass forming solvent and photo-induced radicals yield 129Xe hyperpolarization via sublimation-DNP to biomedical imaging standards

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## Introduction

The unique properties of Hyperpolarized (HP) $^{129}$Xe provide a highly sensitive probe to local environment. HP $^{129}$Xe has been extensively used to study materials, surfaces, protein structure [1]. It also leads to several biomedical MRI applications, in particular the study of human lung function [2] and perfusion imaging [3]. More recently use of HP $^{129}$Xe biosensors opens new perspectives in the field of molecular imaging [4]. $^{129}$Xe is classically hyperpolarized using the well-established spin exchange optical pumping (SEOP) method. Production of 1L/hour of natural abundance xenon hyperpolarized at 5% to 20% is often reported. In optimized conditions, hyperpolarization of small amounts of enriched $^{129}$Xe up to 90% has been measured [5]. Besides SEOP, sublimation-DNP was proposed as an alternative technique to produce HP $^{129}$Xe with the promising advantages of a larger throughput and use of a generic dissolution-DNP hardware able to polarize different nuclear species [6]. The large-scale implementation of this technique was precluded by the limited polarization level achievable (namely 5-7% in routine with natural abundance Xe) [7]. It has been recently shown that non-persistent radicals can be produced by means of UV irradiation of frozen solid-state samples containing Pyruvic Acid (PA) [8].
In the present study we show the influence of the physico-chemical properties of the DNP glass-forming solvent on the maximum achievable $^{129}$Xe polarization in two cases: using nitroxyl radicals (TEMPO) and UV-induced radicals as polarizing agents.

## Methods

A nitroxyl radical (TEMPO) is dissolved in a glass-forming solvent (e.g. 2-methyl-propane-1-ol). Liquid natural abundance xenon is then incorporated before freezing the sample. The solid-state sample is placed in a home-made dissolution-DNP polarizer operating at 5T and 1.15K [9]. When $^{129}$Xe reaches its maximum polarization, a sublimation procedure allows to recover almost all the gas incorporated at the beginning. The HP xenon is then transferred to a distant 9.4 T rodent MRI scanner. In the case of UV-induced radicals, PA is mixed with the glass-forming solvent (in ratio 1:10) instead of TEMPO. After freezing, the solid-state sample is irradiated by UV light for 1h before placing it in the dissolution-DNP polarizer. The MR acquisition in the scanner was performed by means of a dual tuned $^{1}$H/$^{129}$Xe Alderman-Grant RF coil. The samples were then imaged using a 3D bSSFP sequence (TR/TE 5ms/2.5ms; flip angle=22°; 1.2 mm in-plane resolution) (Figure 1)

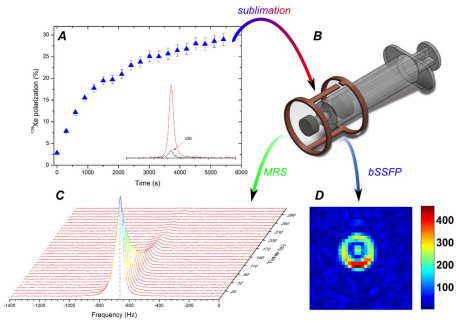


**Figure 1A** DNP polarization time evolution. **B** 9.4 T rodent MRI scanner experimental set-up. **C** HP $^{129}$Xe relaxation inside a plastic syringe. **D** HP $^{129}$Xe image using a 3D bSSFP sequence.

## Results and discussion

Figure 2 shows a typical solid-state NMR spectrum of 8.2 M natural abundance xenon dissolved in 2-methyl propan-1-ol, with a broad peak corresponding to $^{129}$Xe well mixed in the glass-forming solvent (solely due to the solvent see blue curve) and a sharp peak corresponding to pure $^{129}$Xe crystals. A systematic study of maximum achievable polarization and xenon concentration (Figure 3A) shows a solubility threshold that depends on the polarity of the solvent (Figure 3B). As for clinical applications of lung imaging or centralized production of HP tracers, producing a large amount of HP gas is of particular interest, 2-methyl pentan-1-ol would be the solvent of choice, but at the expense of a lower polarization level when using TEMPO. UV-induced radicals present a sharper EPR line; so that they lead more efficient DNP process yielding a 6-fold polarization level in the case of 2-methyl pentan-1-ol. Depending on sample optimization we were able to obtain highly polarized (>50%) tens of mL $^{129}$Xe gas or hundreds of mL of $^{129}$Xe polarized at around 20%. Moreover the gas volume could be easily increased (10 times) scaling up the DNP hardware as already shown [10].

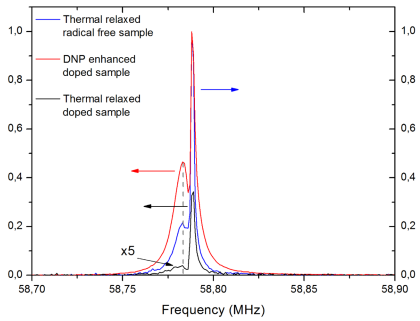


**Figure 2** Solid-state $^{129}$Xe NMR spectrum of a sample containing 8.2 M xenon dissolved in 2-methyl propan-1-ol.

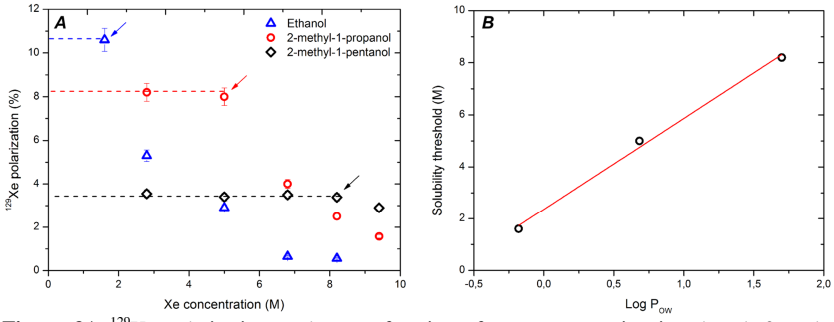


**Figure 3A** $^{129}$Xe polarization study as a function of gas concentration in ethanol, 2-methyl propan-1-ol and 2-methyl-pentan-1-ol. **B** Solubility threshold as a function of solvent polarity (Log $P_{OW}$).

## Conclusions

We demonstrate that the maximum achievable volume and $^{129}$Xe polarization strongly depends on the physico-chemical properties of the glass-forming agent in which xenon is embedded, and that sublimation-DNP compares favorably with SEOP when sample preparation is optimized. This versatility yields sublimation-DNP to the advanced biomedical imaging standards.

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## References

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