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Introduction

- In vitro dissolved-phase relaxation measurements are paramount for assessing the feasibility of dissolved-phase HP¹²⁹Xe MRI.
- While significantly different ¹²⁹Xe T_1 values have been reported for xenon dissolved in the same solvent at high field strengths^{1-3,5,7}, no values have been reported at low magnetic field strengths.
- The scope of this work was to quantify 129 Xe T₁ values in several biological solvents at low and high magnetic field strengths to: a) establish the feasibility of dissolved-phase xenon spectroscopy at low magnetic field strengths; b) determine the cause of the significant variation in T_1 values reported in the literature at high field strengths.
- For some of the measurements, hollow fiber membrane exchange modules were used to dissolve xenon in water, which led to the discovery of their fielddependent depolarization effect which has never been reported before.³⁻⁶

Methods

- For T₁ measurements, a HP compatible ventilator was used to bubble HP gas directly into the solvent.⁸ A variable delay was placed between the end of gas delivery and signal acquisition to allow for xenon relaxation in solution. Low field measurements were performed on a home-built NMR spectrometer operating at 2.1 mT.⁹
- For membrane depolarization measurements, gas was flowed through the gasside of the exchange module at a constant rate using the same ventilator, while a peristaltic pump was used to fill the liquid side of the exchange module with pure water. The exhaust gas was then collected in an empty 1.5 mL vial placed in the magnet isocenter to probe its magnetization. The exchange module was placed at various magnetic field strengths, without moving any other components of the setup.

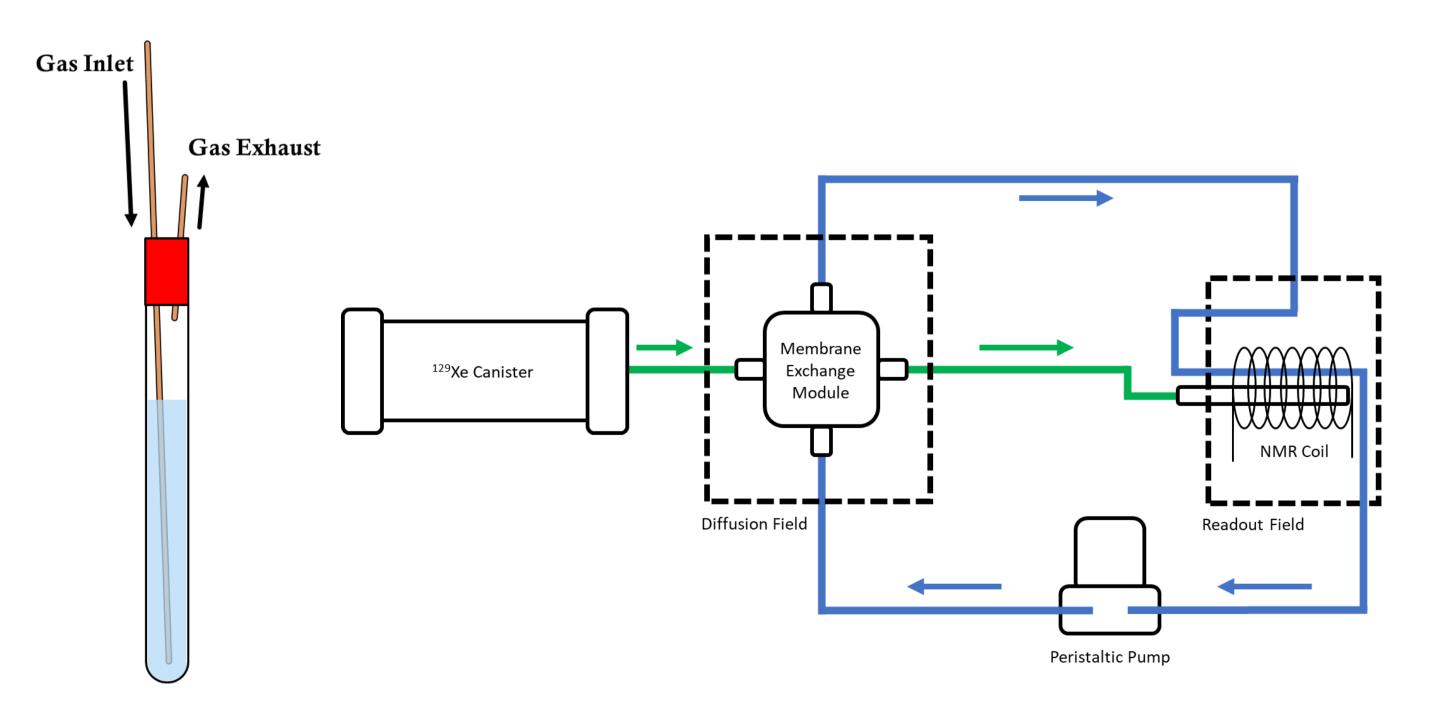


Figure 1: (Left) Illustration of sample used for T1 measurements. Gas flows from the ventilator into the NMR tube through PEEK tubing. An exhaust tube is used to prevent pressure build up in the NMR tube. (Right) Experimental setup used for membrane depolarization studies. Gas is flown through the exchange module into an empty vial placed inside the readout magnet.

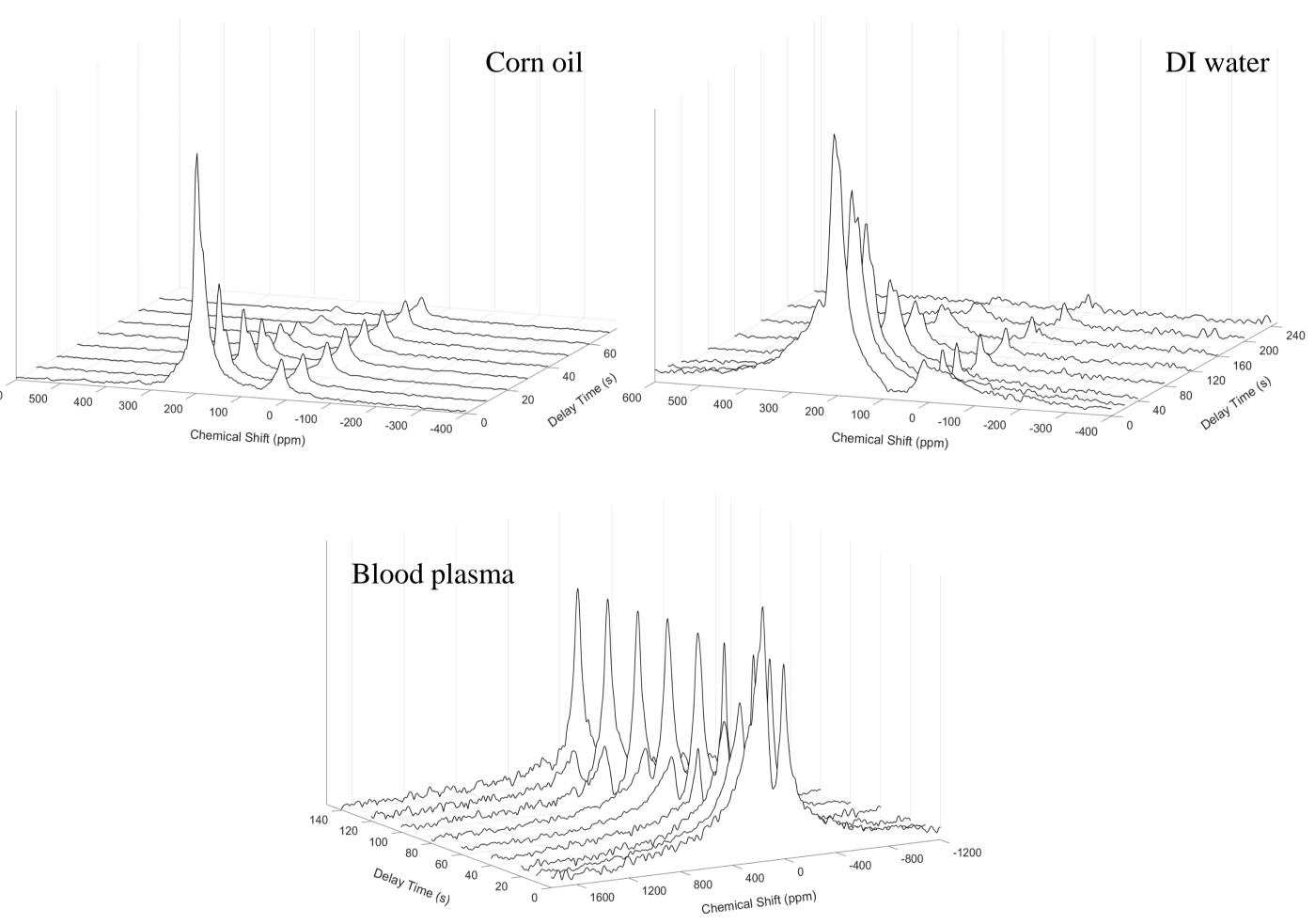
Funding

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Dissolved-phase ¹²⁹**Xe longitudinal relaxation at low and high magnetic field strengths** Nicholas Bryden^{1,2}, Michele Kelley^{1,2}, Christian T McHugh^{1,2}, Rosa T Branca^{1,2}

Results and Discussion

- The spectral resolution of the instrument allowed to correct for the relaxation of the gas phase signal and to independently quantify the longitudinal relaxation of the dissolved-phase signal.
- Longitudinal relaxation measurements at 2.1 mT returned T_1 values for ¹²⁹Xe dissolved in DI water, corn oil, and blood plasma of 49, 11, and 19 s, respectively.
- To our knowledge, these are the first T_1 values reported for ¹²⁹Xe dissolved in these solvents at low field strengths.



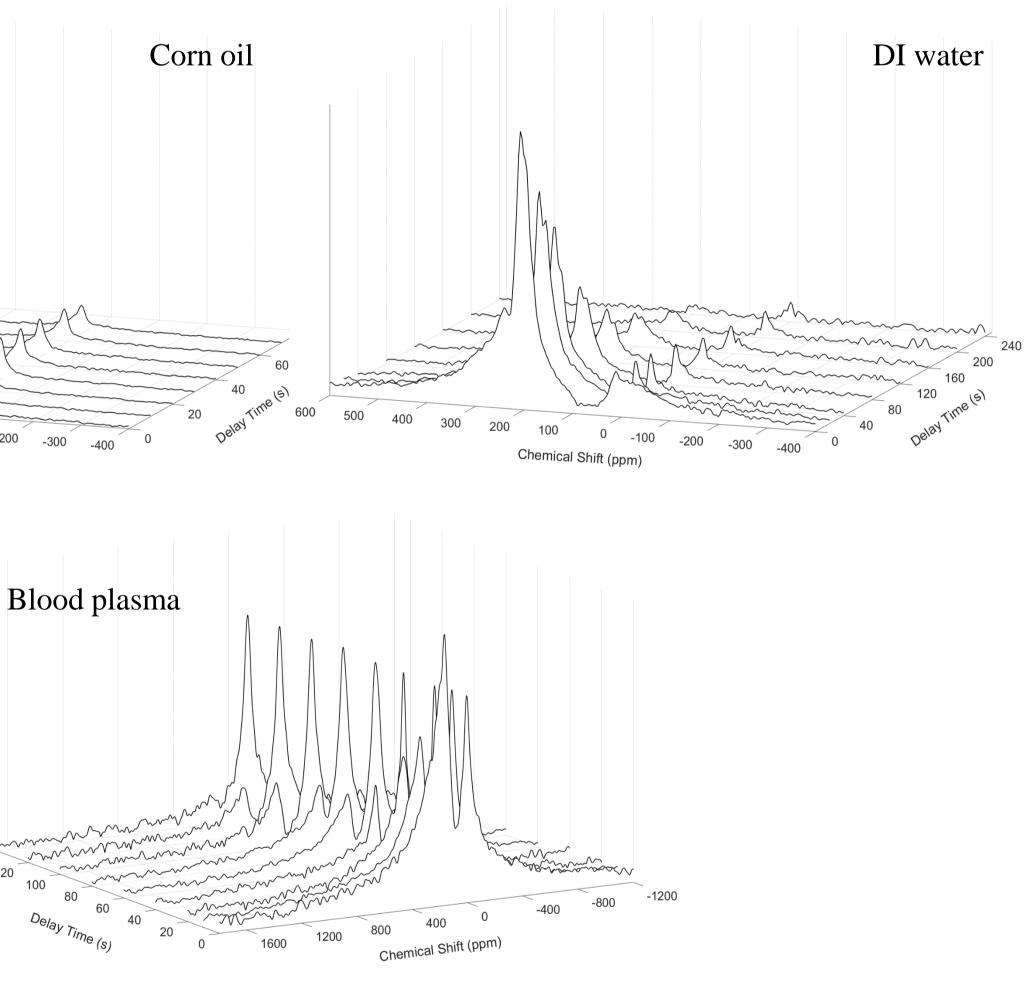


Figure 2: Low field relaxation measurements of hyperpolarized ¹²⁹Xe dissolved in corn oil (top left), water (top right), and blood plasma (bottom). All spectra were collected using a single transient. The higher SNR of the oil-dissolved spectra is explained by the much higher solubility of xenon in oil.

- Using the same method, measurements performed at high magnetic field strengths (11.7 T), returned T_1 values of ¹²⁹Xe dissolved in DI water, corn oil, blood plasma, saline, and 20% intralipid of 97, 16, 20, 72, and 18 s, respectively.
- Significant variation in previous measurements made at high field may be explained by the sensitivity of the previously used small flip angle method to error in flip angle calibration, which can be summarized by the following expression:

$$\frac{T_1 - T_1'}{T_1 T_1'} = \frac{1}{\tau} \ln(\frac{\cos\theta'}{\cos\theta})$$

- depolarization even at a field strength of 1.5 T.
- placed at 12 mT or 2.3 mT.
- equation:^{10,11}

$$M(B_0) = M_0 e^{\frac{1}{10T_0} \left(\frac{1}{1 + (\gamma_{Xe}^2 - \gamma_H^2)B_0^2 \tau_c^2} + \frac{3}{1 + \gamma_{Xe}^2 B_0^2 \tau_c^2} + \frac{6}{1 + (\gamma_{Xe}^2 + \gamma_H^2)B_0^2 \tau_c^2}\right)}$$

the membranes.

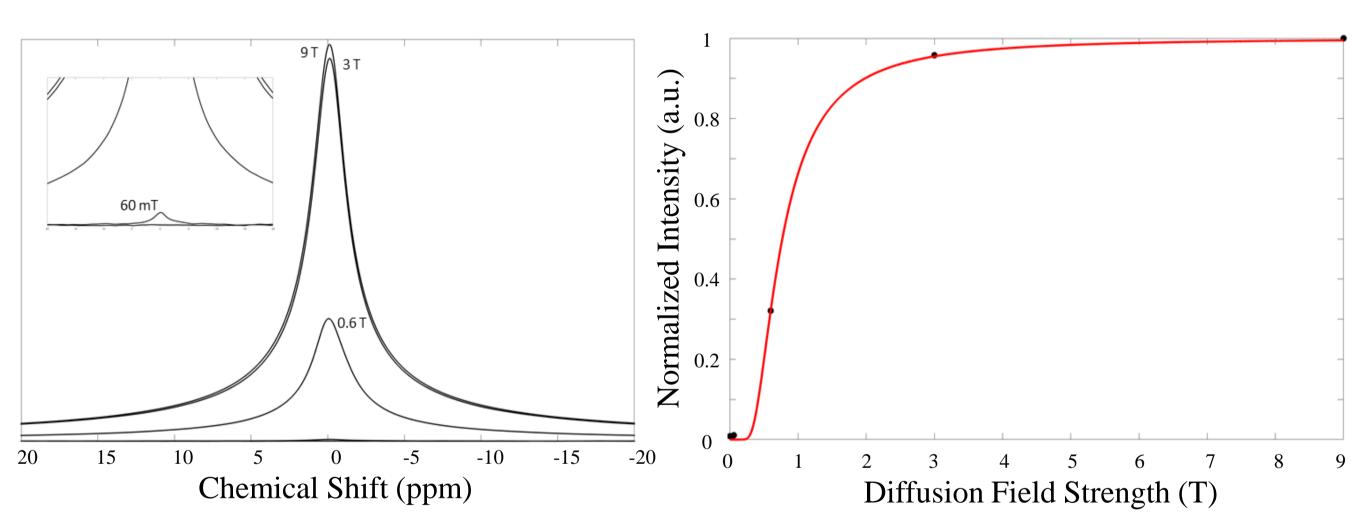


Figure 3: (Left) Example of spectra acquired with the membrane exchange modules placed at various magnetic field strengths. All spectra were acquired by flowing the same amount of HP xenon gas through the membrane fibers. (Right) Normalized intensities extracted from the data plotted against the corresponding diffusion field strengths.



Dissolved-phase ¹²⁹Xe T_1 values obtained at low field are only slightly lower than the values obtained at high field. While these values support the feasibility of dissolved-phase xenon studies in the low field regime, for *in vivo* dissolved-phase studies the T_1 of xenon in blood will be the limiting factor. An exact measurement of this value at low field was attempted unsuccessfully as the use of membrane fibers is evidently not an option at lower field strengths due to excessive depolarization of the gas diffusing in these membranes.

References

- M. Albert, V. Schepkin, T. B., J. Comput. Assist. Tomogr. 19, 975–978 (1995).
- 3. Norquay, G. et al, Magn. Reson. Med. 74, 303–311 (2015).

- Bifone, A. et al., Proc. Natl. Acad. Sci. U. S. A. 93, 12932–12936 (1996).
- Nouls, J., Concepts Magn. Reson. Part B Magn. Reson. Eng. 49B, 78-88 (2011).
- Bryden, N., Antonacci, M., Kelley, M. & Branca, R. T., J. Magn. Reson. 332, 107076 (2021).
- 10. A. Abragam, Principles of Nuclear Magnetism. Oxford University Press, New York (1961).
- 11. Driehuys, B., Cates, G. D. & Happer, W., Phys. Rev. Lett. 74, 4943–4946 (1995).

• The membrane exchange module study revealed significant (> 30%) gas

• No detectable signal was observed when the exchange module was

• Data agrees well with our current theoretical understanding of HP ¹²⁹Xe surface relaxation and its field dependence, summarized by the following

• The strong relaxation that xenon undergoes while diffusing across these exchange membranes not only prevents their use at low field strengths, but also suggests that for high field studies these membrane modules need to be located as close as possible to the magnet isocenter, not only to reduce transfer time, but to prevent significant xenon relaxation through

Conclusions

Wolber, J., Cherubini, A., Dzik-Jurasz, A. S. K., Leach, M. O. & Bifone, A., Proc. Natl. Acad. Sci. U. S. A. 96, 3664–3669 (1999).

^{4.} Baumer, D., Brunner, E., Blümler, P., Zänker, P. P. & Spiess, H. W., Angew. Chemie - Int. Ed. 45, 7282–7284 (2006).

^{5.} Cleveland, Z. I., Möller, H. E., Hedlund, L. W. & Driehuys, B., Journal of Physical Chemistry B vol. 113 12489–12499 (2009). 6. Norquay, G., Leung, G., Stewart, N. J., Wolber, J. & Wild, J. M., Magn. Reson. Med. 77, 1399–1408 (2017).