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Measuring non-invasively and in a local way the *in vivo* extra-cellular pH is of importance for the diagnosis of insidious pathologies such as various cancers. For one decade, the use of hyperpolarized agents has been proposed; each method possesses its own advantage and inconvenience, and their applicability in the *in vivo* domain is not always straightforward. For instance, some years ago, we proposed the use of cage-molecules bearing ionizable groups, in which laser-polarized xenon exhibits a pH-dependent chemical shift.[1] However extracting pH from measurement of the absolute chemical shift of caged xenon or even of the chemical shift difference between free and caged xenon is susceptible to be biased by external parameters such as temperature and magnetic susceptibility fluctuation.

Here we present an approach which is simple and fast to implement and which should be exempt of most of the problems encountered *in vivo*. The idea is to perform a differential measurement by using a pair of pH-sensitive $^{129}$Xe NMR-based sensors. The method is rendered very pH-sensitive *via* the choice of two xenon host molecules in which the frequency of the noble gas signal varies in opposite manner with the $H^+$ concentration. For this proof-of-concept, the two cryptophanes described in Figure 1 have been used. The measurement is shown to be independent of temperature and ionic strength.

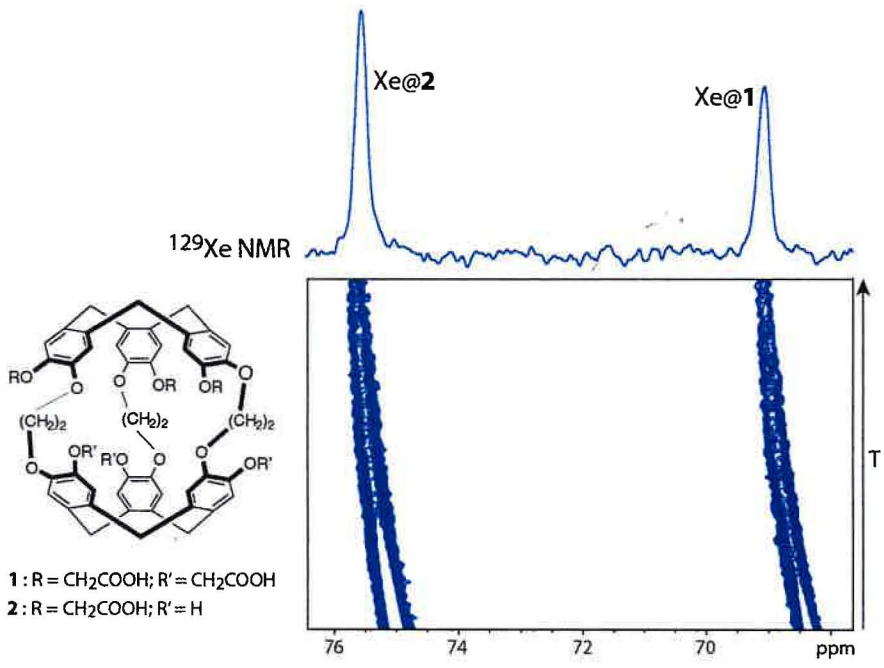


**Figure 1.** High field region of the $^{129}$Xe NMR spectrum of an aqueous solution containing the two cryptophanes **1** and **2** at 1 µM each. Evolution as a function of temperature.

(1) Berthault, P.; Desvaux, H.; Wendlinger, T.; Gyejacquot, M.; Stopin, A.; Brotin, T.; Dutasta, J.-P.; Boulard, Y. *Chem. – A Eur. J.* **2010**, *16*, 12941.

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