# Degeneracy in Cryptophane-Xenon Complex Formation in Aqueous Solution

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## Supporting Information

### Sample preparation

Monoacetic acid cryptophane-A (CrAma) was purchased and without further treatment put into distilled water. After sonication for several hours the compound particles were dissolved, the final pH value was 5.3. A volume of 1.5 ml was used in the NMR experiments. By the ratio of the intensities of the xenon NMR signals of freely dissolved xenon and CrAma-bound xenon (see below) the CrAma concentration was estimated to ~ 6.5 μM using a xenon solubility in pure water of 4.32 mM bar$^{-1}$ at 298 K.

### Hp $^{129}$Xe NMR experiments

NMR experiments were performed on a 9.4 T spectrometer (Bruker, Ettlingen, Germany) equipped with a double resonant probe for excitation and detection of $^{1}$H and $^{129}$Xe at 400 MHz and 111 MHz, respectively. The sample was maintained at 298 K during the experiments and saturated with hyperpolarized $^{129}$Xe at various partial pressures. In Figure S1, a $^{129}$Xe-spetrum is shown. Magnetization was excited by a non-selective $\pi/2$-pulse of 30 μs duration, and subsequently detected. Prior to Fourier-Transformation a line broadening of 5 Hz was applied. The xenon partial pressure was 0.02 bar, the polarization of $^{129}$Xe was ~24 %. The signal of freely dissolved $^{129}$Xe was used for referencing the chemical shift scale and set to 193 ppm, the signal of CrAma-bound $^{129}$Xe appears then at 62 ppm.

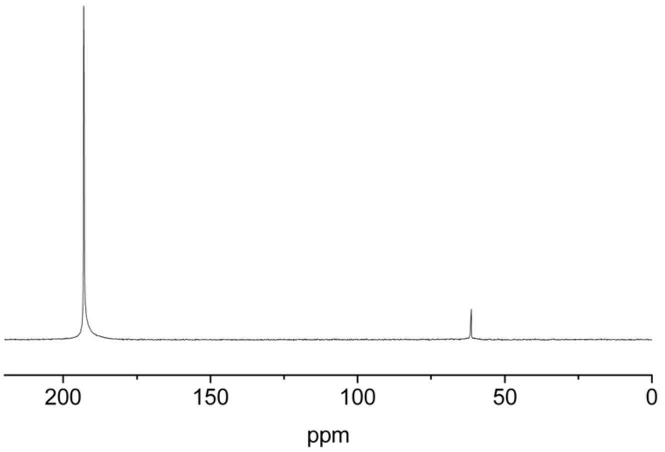

Figure S1: NMR spectrum of $^{129}$Xe in a xenon-saturated solution ($\mathbf{p}_{Xe}$ = 0.02 bar) of CrAma in water.

In the exchange experiments (see Fig. 2(a) main text) a rectangular pulse of length 1.3 ms and excitation bandwidth 384 Hz was applied to the xenon-saturated sample for selective inversion of the magnetization of freely dissolved xenon (at 193 ppm). After a variable delay $\tau_{\mathrm{ex}}$ in the range of 0 ms to 256 ms a Gaussian RF pulse of 1 ms length and an amplitude in terms of the xenon precession frequency of 550 Hz was used for selective excitation of the magnetization of CrAma-bound xenon (at 62 ppm); subsequently, the $^{129}$Xe FID was acquired.

Data Evaluation

A total of 48 exchange experiments were conducted grouped in six series with fixed xenon partial pressures of 0.02, 0.1, 0.2, 0.4, 0.8, and 1.2 bar. For each series eight fixed exchange delays $\tau_{\mathrm{ex}}$ in the range of 0 ms to 256 ms were measured. In each experiment an FID of 16384 complex data points was acquired. After apodization by multiplication with an exponential filter function of width 20 Hz, each FID was Fourier-transformed. The spectra had just one signal (from CrAma-bound xenon) which was phase corrected to absorption-mode, and the baselines were corrected. The signal in each spectrum was integrated over an area of 2 ppm centered at the signal´s maximum amplitude. The software ACD/NMR Processor Academic Edition was used for spectrum integration. The signal intensities obtained in this manner were modeled by functions $Ae^{-R\tau}+B$ in their dependence on the exchange period for each setting of the xenon partial pressure by a non-linear least squares fit (see Fig. 2(b)). In this way (see Fig. 2(c)), the depletion rates were obtained for each setting of xenon partial pressure with error margins given by the standard error in the fit parameter due to deviations of the fitted curve from the data (square root of a main diagonal value of the Covariance Matrix). Kinetic rate constants were extracted by a linear least squares fit where each data point (depletion rate) was weighted by its error margin. The error margins of the rate constants were again obtained as the standard error in the fitting parameter. The software QtiPlot was used for data fitting.

Depletion rate by Bloch-McConnell equations

The exchange experiments described in this publication were performed on aqueous solutions of hyperpolarized $^{129}$Xe in the homogeneous, static field of a strong superconducting solenoid (9.4T). The highly polarized xenon was prepared by a polarizer in the weak fringe field and adiabatically transferred to the sample in the solenoid´s center. The $^{129}$Xe magnetization was therefore aligned along the static field in the beginning of the experiment. After selective inversion exchange of longitudinal magnetization occurred while transversal magnetization was only generated for read out in the end of an experiment. It is thus sufficient to restrict the analysis to the exchange of longitudinal magnetization. The dynamics of xenon longitudinal magnetization in the free pool, $M_{Xe}(t)$, and in the cryptophane-bound pool, $M_{CXe}(t)$, can be described by the Bloch-McConnell equations[1]

$$\dot{M}_{Xe}(t) = M_{Xe}^{0} R_{1Xe} - (k_{on} + R_{1Xe}) M_{Xe}(t) + k_{off} M_{CXe}(t) \qquad [S1]$$

$$\dot{M}_{CXe}(t) = M_{CXe}^{0} R_{1CXe} + k_{on} M_{Xe}(t) - (k_{off} + R_{1CXe}) M_{CXe}(t) \qquad [S2]$$

with $M_{Xe}^{0}$ and $M_{CXe}^{0}$ for the thermal equilibrium magnetizations, $R_{1Xe}$ and $R_{1CXe}$ for the longitudinal relaxation rates, and $k_{on}$ and $k_{off}$ for the inverse live times of xenon in the free and cryptophane-bound pools, respectively

For the analysis of the exchange experiments equations [S1] and [S2] can be simplified by using prior information. As was shown in the main text, the relaxation rates $R_{1CXe}$ and $R_{1Xe}$ , which are in the less than one tenth or one hundredths Hertz range, respectively, can be completely neglected in comparison to the depletion rate $R_d = k_{off}$ which has a lower bound of $c \approx 19$ Hz . The relaxation rates can thus be equally well neglected in comparison to $k_{off}$ in [S1] and [S2]. In addition, the constant terms $M_{Xe}^{0} R_{1Xe}$ and $M_{CXe}^{0} R_{1CXe}$ are negligible because of the very low thermal polarization in comparison to the hyperpolarized magnetizations $M_{Xe}(t)$ and $M_{CXe}(t)$ prevailing in the experiments. In consequence, the system [S1] and [S2] becomes

$$\dot{M}_{Xe}(t) = -(k_{on} + R_{1Xe})M_{Xe}(t) + k_{off}M_{CXe}(t) \qquad \text{[S1']}$$

$$\dot{M}_{CXe}(t) = k_{on}M_{Xe}(t) - k_{off}\,M_{CXe}(t)\ . \qquad \text{[S2']}$$

The general solution is of the form of a bi-exponential function $A\,e^{\lambda_- t} + \mathrm{B}e^{\lambda_+ t}$ for each magnetization pool.[2] The rates $\lambda_{\mp}$ are the roots of the characteristic polynomial of the coefficients-matrix of eqs. [S1'] and [S2'],

$$\lambda_{\mp} = -\frac{k_{on} + k_{off} + R_{1Xe}}{2} \mp \sqrt{\left(\frac{k_{on} + k_{off} + R_{1Xe}}{2}\right)^2 + k_{off}R_{1Xe}}\ . \qquad \text{[S3]}$$

On neglecting the relaxation rate $R_{1Xe}$ in comparison to $k_{off}$ once again, and, equivalently, $k_{off}R_{1Xe}$ against $(k_{on} + k_{off} + R_{1Xe}/2)^2$, the one rate vanishes $\lambda_+ = 0$, while the single rate $\lambda_- = -(k_{on} + k_{off})$ remains. Thus, the magnetization in both pools behaves according to a function $A\,e^{\lambda_- t} + \mathrm{B}$.

From xenon spectra taken at dynamic equilibrium (see Fig. S1) the ratio of the intensities of the xenon NMR signals of CrAma-bound xenon (at 62 ppm), $M_{\mathrm{CXe}}$ to freely dissolved xenon (at 193 ppm), $M_{\mathrm{Xe}}$, , was $M_{\mathrm{CXe}} / M_{\mathrm{Xe}}$ = 0.068, 0.015, 0.007, 0.004, 0.002, and 0.001 at the various xenon partial pressures used in the exchange experiments of $p_{\mathrm{Xe}}$ = 0.02, 0.1, 0.2, 0.4, 0.8, and 1.2 bar, respectively. Because $M_{\mathrm{Xe}}k_{\mathrm{on}}=M_{\mathrm{CXe}}k_{\mathrm{off}}$ holds in this situation, $k_{\mathrm{on}}$ may be safely neglected in comparison to $k_{\mathrm{off}}$, yielding the relation $R_{\mathrm{d=}}$ $k_{\mathrm{off}}$ used in the main text.

## References

1. McConnell, H. M. *J. Chem. Phys.* **1958**, *28*, 43 –431.
2. Braun, M. *Differentialgleichungen und ihre Anwendungen*; 3. Auflage, Springer-Verlag: Berlin, 1994.