Supporting Information

For

“Utilizing a Water-Soluble Cryptophane with Fast Xenon Exchange Rates for Picomolar Sensitivity NMR Measurements”

Yubin Bai, P. Aru Hill and Ivan J. Dmochowski*

Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104

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HP Xe delivery setup

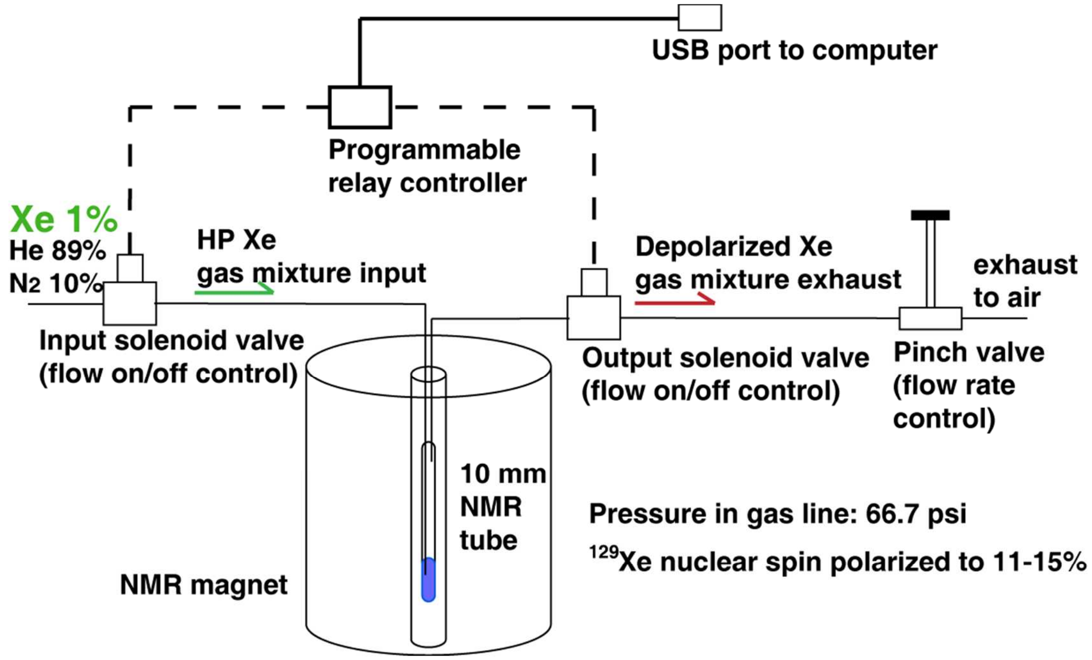

Figure S1. HP Xe gas mixture continuous-flow delivery setup.

Typically the flow rate ranges between 0.6 and 0.8 standard liters per minute (SLM). The sample solution is saturated by HP ^{129}Xe after continuously running the gas line for 20 sec, which is confirmed by monitoring ^{129}Xe signal intensity using small flip-angle pulses.

ITC controls at 310 K

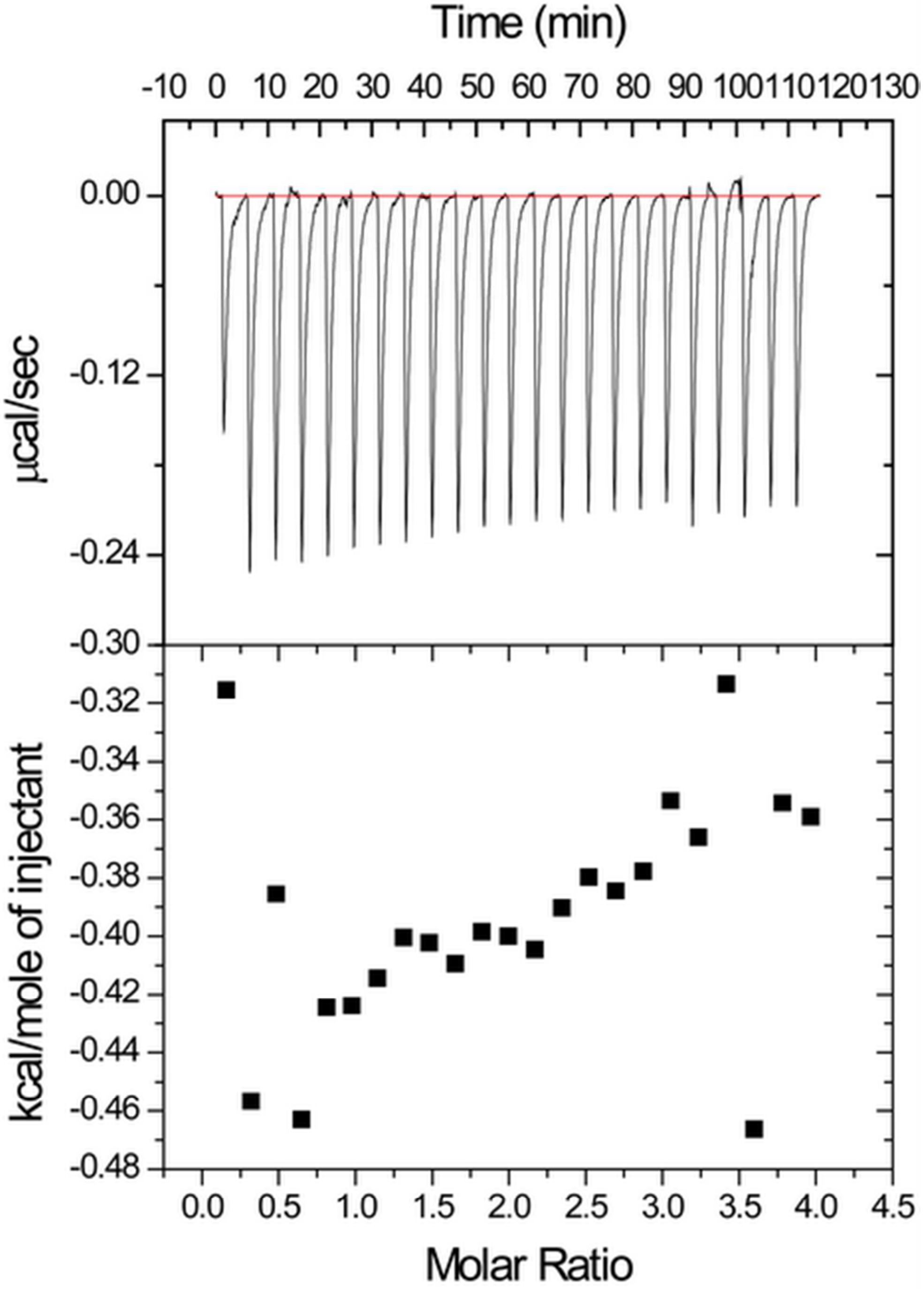

Figure S2. ITC buffer controls at 310 K. Water titrated into 20 mM phosphate buffer, pH 7.5.

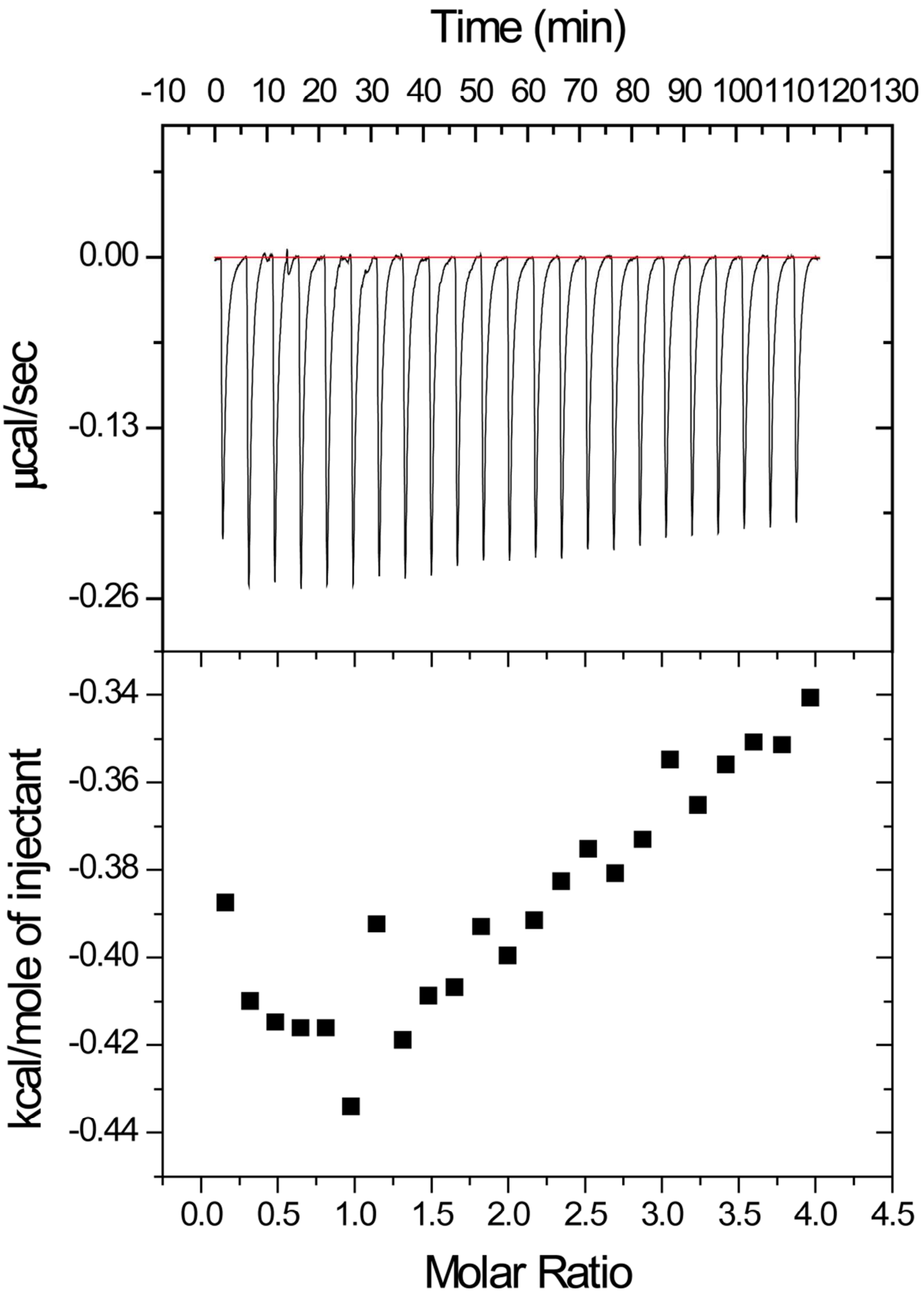

Figure S3. ITC buffer controls at 310 K. Water titrated into a solution of 131 μM TAAC in 20 mM phosphate buffer, pH 7.5.

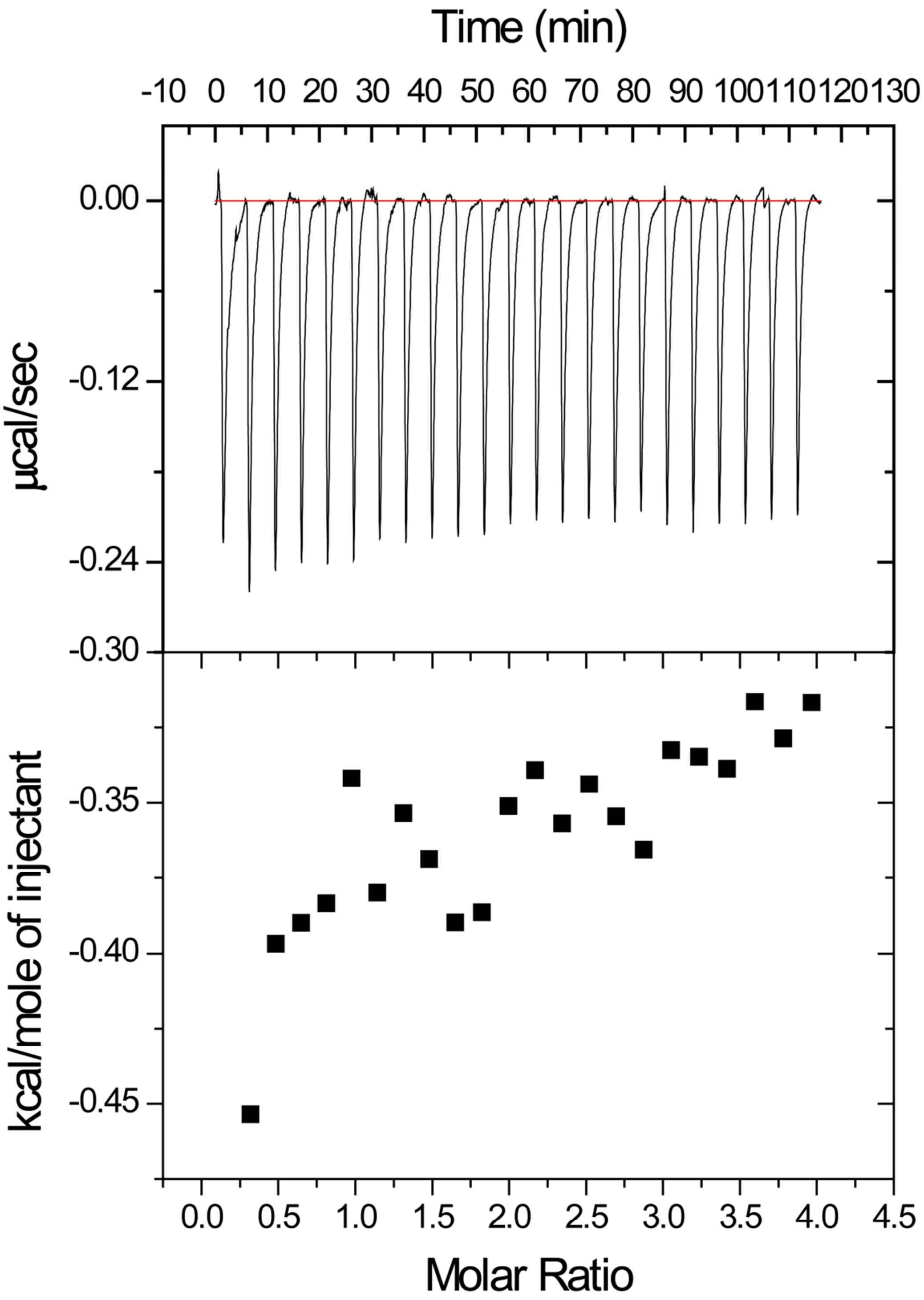

Figure S4. ITC buffer controls at 310 K. Xenon-saturated water (3.31 mM) titrated into 20 mM phosphate buffer, pH 7.5.

Describing HP Xe depolarization rate

1. HP Xe concentration in sample

In the Hyper-CEST experiment, the concentration of Xe is estimated as:

xenon partial pressure in gas line × mole fraction solubility (at 320 K, 1 atm) × molarity of water = $0.045 \times 4.95 \times 10^{-5} \times 55.5$ M = 0.12 mM.

With the given isotope abundance (26%), and hyperpolarization level (10%), the HP Xe concentration becomes:

$0.12 \text{ mM} \times 26\% \times 10\% = 3.1\ \mu\text{M}$.

2. Rate of xenon depolarization

Various physical-chemical processes are involved in Hyper-CEST-mediated depolarization through TAAC. In the following equations, "Xe*" stands for hyperpolarized species (difference of "spin down" and "spin up" species). Therefore the first derivative can be approximated by a combination of Hyper-CEST induced depolarization (k_{crypt}, the first-order rate constant for cryptophane-mediated Xe* depolarization) and T_1 relaxation (k_1).

$$\frac{d[\text{Xe*}]}{dt} = -k_{crypt}[\text{Xe*}] - k_1[\text{Xe*}] \tag{S1}$$

3. Fitting existing Hyper-CEST data

As demonstrated, depletion of the hyperpolarized xenon can be modeled using simple first-order kinetics with rate constant k:

$$-k = -k_{crypt} - k_1$$

Therefore exponential fit for the on-resonance Hyper-CEST curve can provide the total first-order rate constant, as the data in Figure 3 provide the relative HP Xe concentration at different time points of Hyper-CEST polarization transfer.

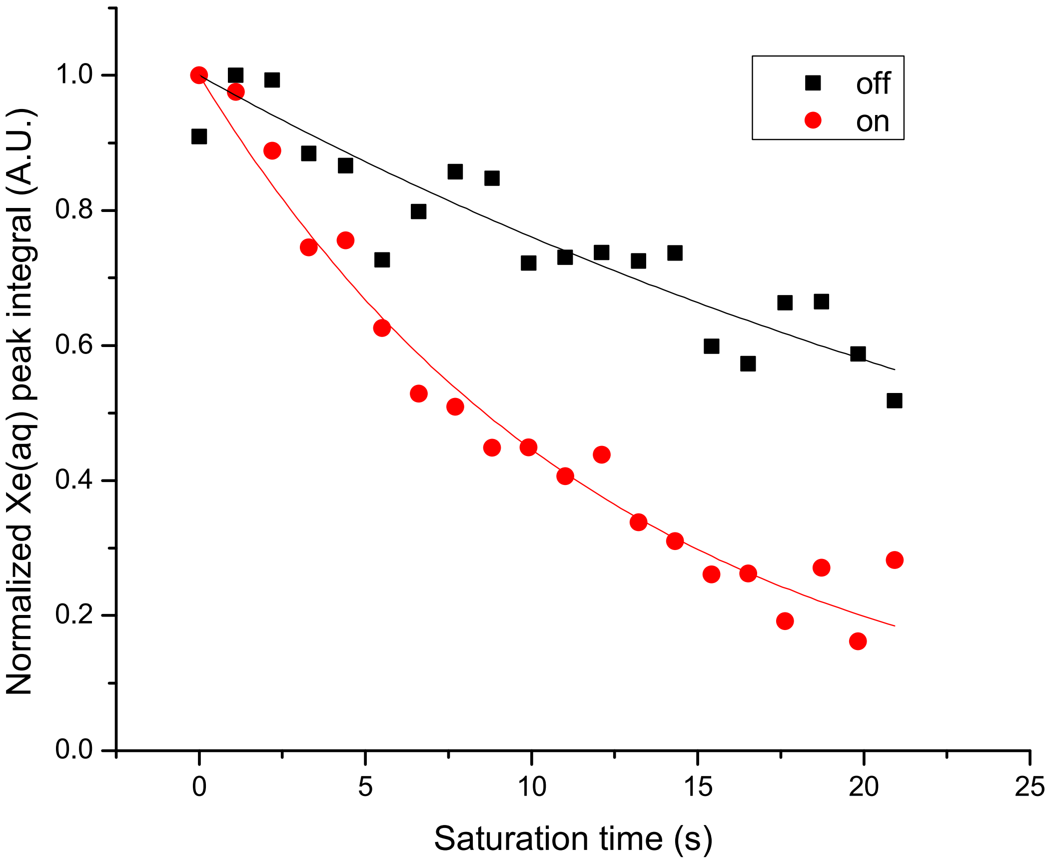

Figure S5. Exponential fit on Hyper-CEST mediated HP Xe overall depolarization in 14 pM TAAC solution (another trial, same parameters as Fig 3 in main text). Depolarization lifetimes were fitted to be 12 ± 1 s (on) and 36 ± 2 s (off).

Giving rate constant:

$$-k = -k_{crypt} - k_1 = -\frac{1}{12} = -0.083 \text{ s}^{-1}$$

The off-resonance T_1 relaxation was fit to be 36 seconds, giving:

$$-k_1 = -\frac{1}{36} = -0.028 \text{ s}^{-1}$$

$$k_{crypt} = 0.055 \text{ s}^{-1}$$

At time zero of saturation, the HP Xe concentration is:

$$[\mathrm{Xe}^*] = 3.1\ \mu\mathrm{M}$$

So using 14 pM TAAC and the described pulse sequence, the starting depolarization rate due to the selective saturation is:

$$k_{crypt}[\mathrm{Xe}^*] = 0.055 \times 3.1 \times 10^{-6} = 0.17\ \mu\mathrm{M} \cdot \mathrm{s}^{-1}$$

On a per cryptophane basis, the rate becomes:

$$\frac{k_{crypt}[\mathrm{Xe}^*]}{[\mathrm{TAAC}]} = \frac{0.055 \times 3.1 \times 10^{-6}}{14 \times 10^{-12}} = 1.2 \times 10^{4}\ \mathrm{s}^{-1}$$

which describes for each cryptophane, twelve thousand Xe-129 atoms get depolarized in a second.

Following similar calculations, the virus capsid biosensor[1] had a 100-fold slower depolarization rate:

$$\frac{k_{crypt}[\mathrm{Xe}^*]}{[\mathrm{TAAC}]} = \frac{0.0046 \times 2.5 \times 10^{-6}}{125 \times 0.7 \times 10^{-12}} = 1.3 \times 10^{2}\ \mathrm{s}^{-1}$$

References

(1) Meldrum, T.; Seim, K. L.; Bajaj, V. S.; Palaniappan, K. K.; Wu, W.; Francis, M. B.; Wemmer, D. E.; Pines, A. *J. Am. Chem. Soc.* **2010**, *132*, 5936.