

Supplementary Information

Multifunctional Polymeric Scaffolds for Enhancement of PARACEST Contrast Sensitivity and Performance: The Effects of Random Copolymer Variations

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Supplementary Information S1

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Supplementary Information S2

1. Proton constant data for M2

Table S1. Proton Constants of M2 and DOTA-(gly)₄ at 1.0 M KCl and 25 °C.

Species	M2	DOTA-(gly) ₄ ^a
LogK ₁ ^H	8.93 ± 0.03	9.19 ± 0.02
LogK ₂ ^H	6.38 ± 0.03	6.25 ± 0.03
LogK ₃ ^H	4.08 ± 0.04	4.08 ± 0.04
LogK ₄ ^H	3.44 ± 0.04	3.45 ± 0.04
LogK ₅ ^H	2.95 ± 0.03	3.20 ± 0.03
LogK ₆ ^H	—	1.40 ± 0.05

Table S2. Stability Constants (logK) of DOTA-(gly)₄ Complexes with Some Metal Ions at 1.0 M KCl and 25 °C.

Ligand	Species	Ca ²⁺	Mg ²⁺	Cu ²⁺	Zn ²⁺	Eu ³⁺ ^b
DOTA-(gly) ₄ ^a	MLH ₄	3.00 ± 0.03	—	—		1.90 ± 0.01
	MLH ₃	3.96 ± 0.02	—	3.46 ± 0.07		2.40 ± 0.01
	MLH ₂	3.98 ± 0.04	—	3.35 ± 0.07		2.96 ± 0.01
	MLH ₁	4.23 ± 0.02	—	4.38 ± 0.07		3.45 ± 0.01
	ML	9.82 ± 0.04	4.34 ± 0.03	13.39 ± 0.03		14.84 ± 0.08
	MLH ₋₁	—	—	9.37 ± 0.02		9.61 ± 0.06

^aValues taken from: Baranyai, Z.; Brucher, E.; Ivanyi, T.; Kiraly, R.; Lazar, I.; Zekany, L. *Helv. Chim. Acta* **2005**, 88, 604-617. ^bValues measured by the “out-of-cell” technique.

Supplementary Information S3

2. CEST spectra and CEST fitting results

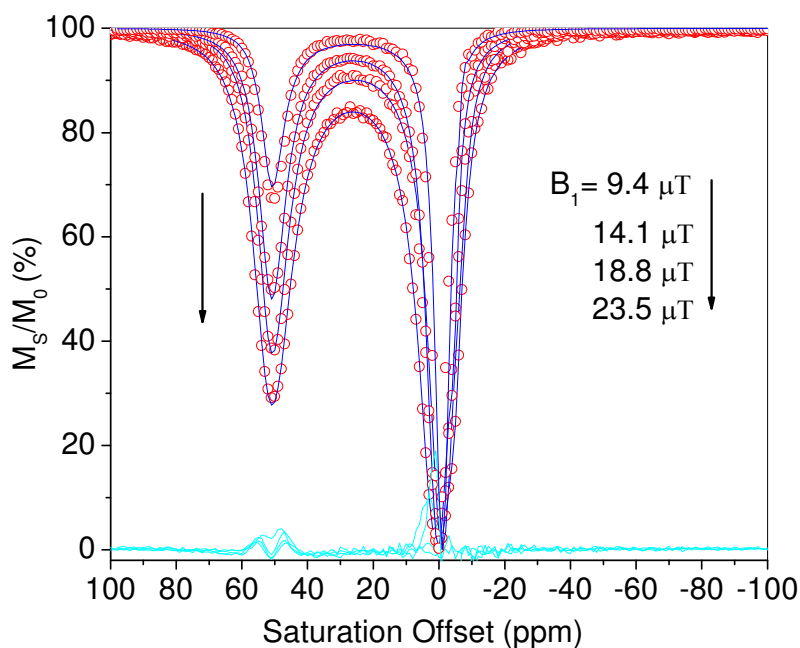


Figure S1a. Changes in the CEST spectra of Eu-DMAA 1.1 with the increase of presaturation pulse intensity B_1 recorded at pH 7.6 and 9.4 T. $[\text{Eu}^{3+}] = 30 \text{ mM}$ and sat. time = 2 s. Symbols: experimental data. Lines: fitted data to the Bloch equations.

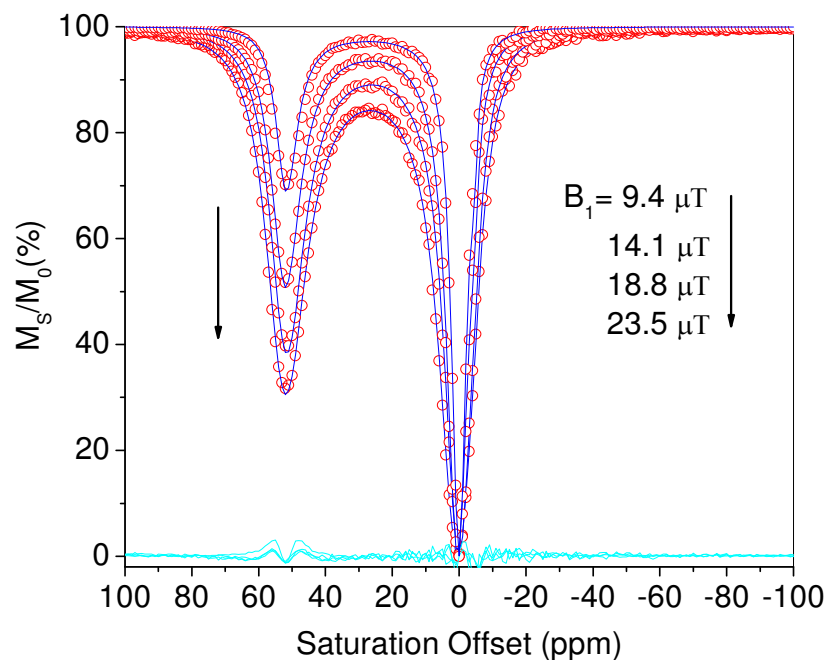


Figure S1b. Changes in the CEST spectra of Eu-DMAA 2.0 with the increase of presaturation pulse intensity B_1 recorded at pH 6.6 and 9.4 T. $[\text{Eu}^{3+}] = 30 \text{ mM}$ and sat. time = 2 s. Symbols: experimental data. Lines: fitted data to the Bloch equations.

Supplementary Information S4

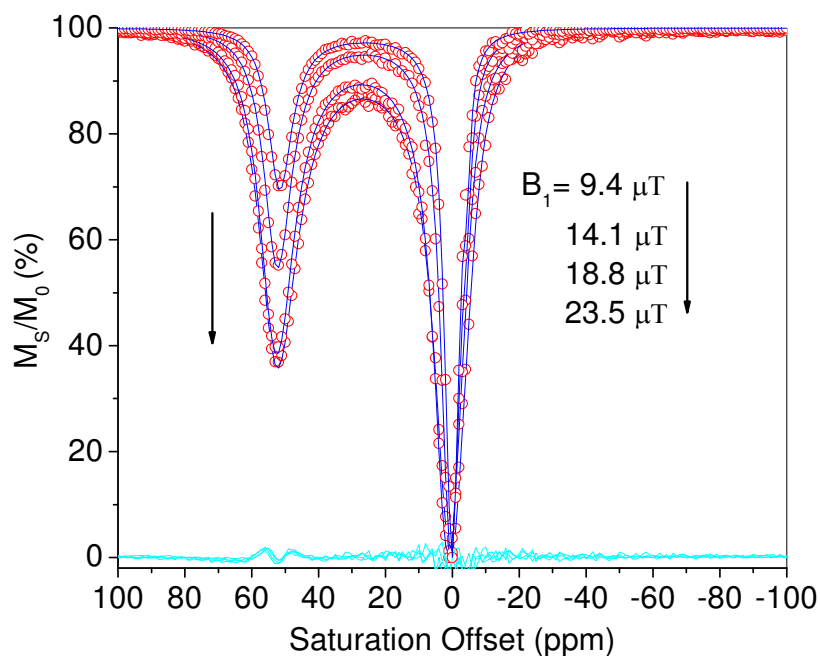


Figure S1c. Changes in the CEST spectra of Eu-DMAA 2.1 with the increase of presaturation pulse intensity B_1 recorded at pH 6.6 and 9.4 T. $[\text{Eu}^{3+}] = 30 \text{ mM}$ and sat. time = 2 s. Symbols: experimental data. Lines: fitted data to the Bloch equations.

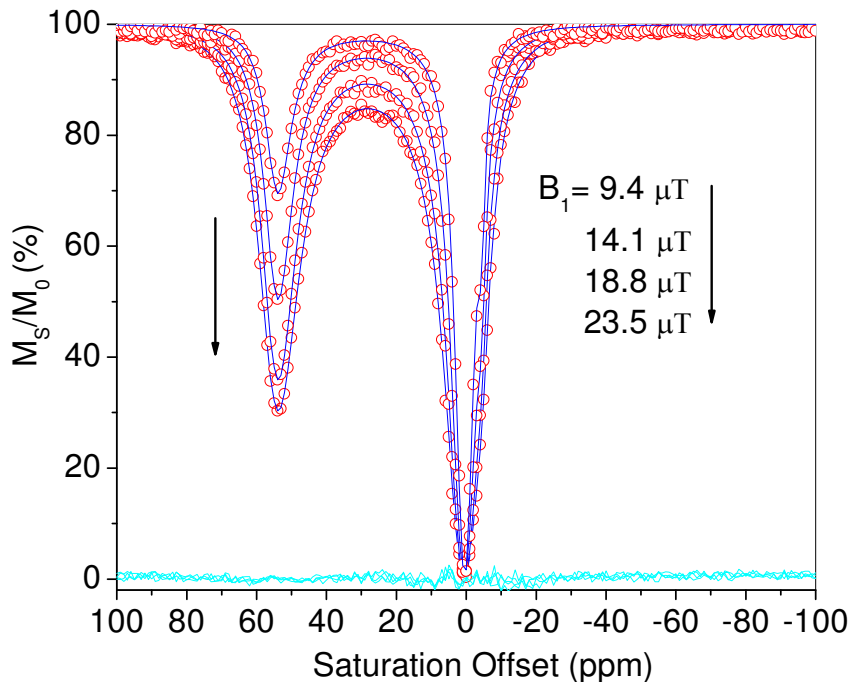


Figure S1d. Changes in the CEST spectra of Eu-DMAA 3.0 with the increase of presaturation pulse intensity B_1 recorded at pH 7.5 and 9.4 T. $[\text{Eu}^{3+}] = 30 \text{ mM}$ and sat. time = 2 s. Symbols: experimental data. Lines: fitted data to the Bloch equations.

Supplementary Information S5

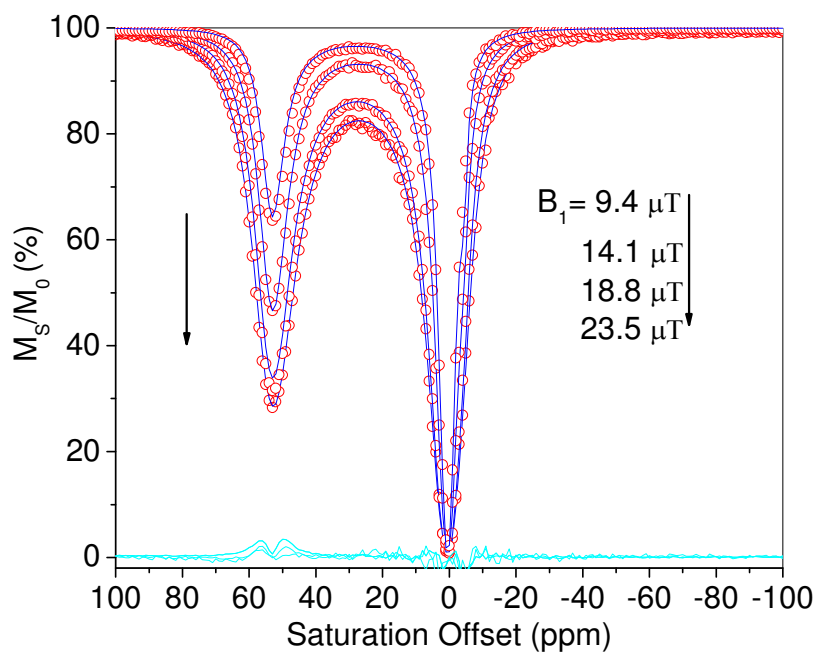


Figure S1e. Changes in the CEST spectra of Eu-DMAA 3.1 with the increase of presaturation pulse intensity B_1 recorded at pH 7.0 and 9.4 T. $[\text{Eu}^{3+}] = 30 \text{ mM}$ and sat. time = 2 s. Symbols: experimental data. Lines: fitted data to the Bloch equations.

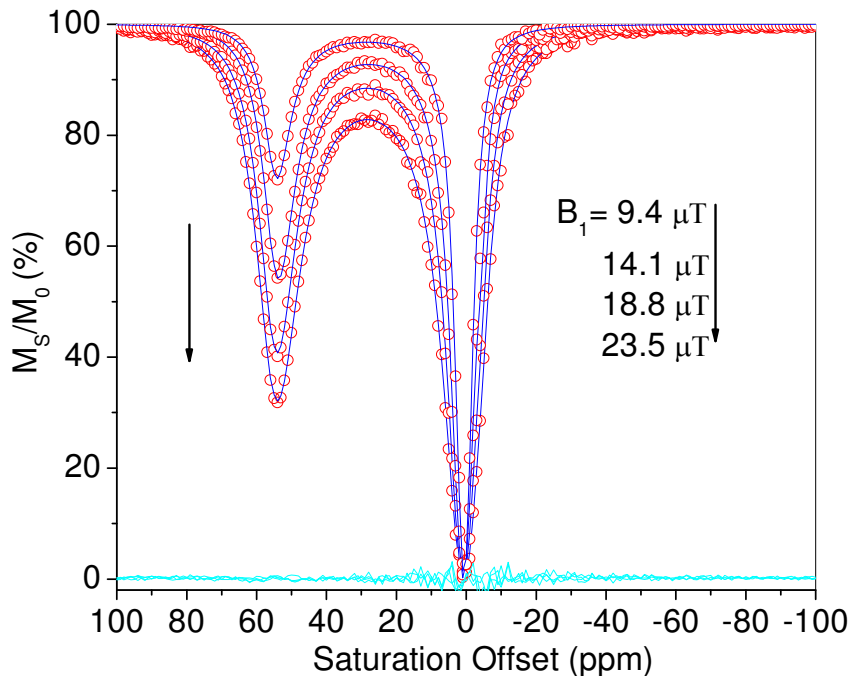


Figure S1f. Changes in the CEST spectra of Eu-DMAA 4.1 with the increase of presaturation pulse intensity B_1 recorded at pH 6.7 and 9.4 T. $[\text{Eu}^{3+}] = 30 \text{ mM}$ and sat. time = 2 s. Symbols: experimental data. Lines: fitted data to the Bloch equations.

Supplementary Information S6

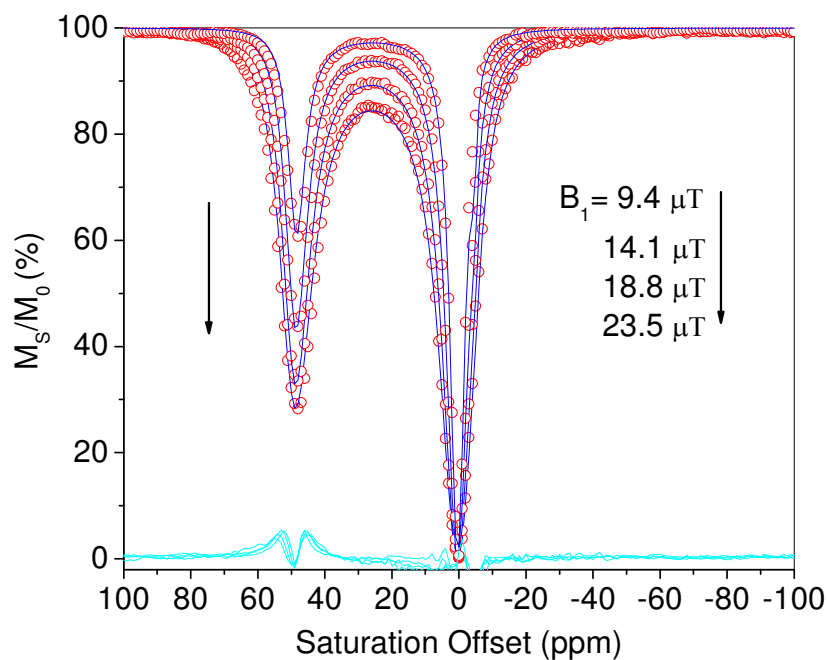


Figure S1g. Changes in the CEST spectra of Eu-DAMPS 1.1 with the increase of presaturation pulse intensity B_1 recorded at pH 6.7 and 9.4 T. $[\text{Eu}^{3+}] = 30$ mM and sat. time = 2 s. Symbols: experimental data. Lines: fitted data to the Bloch equations.

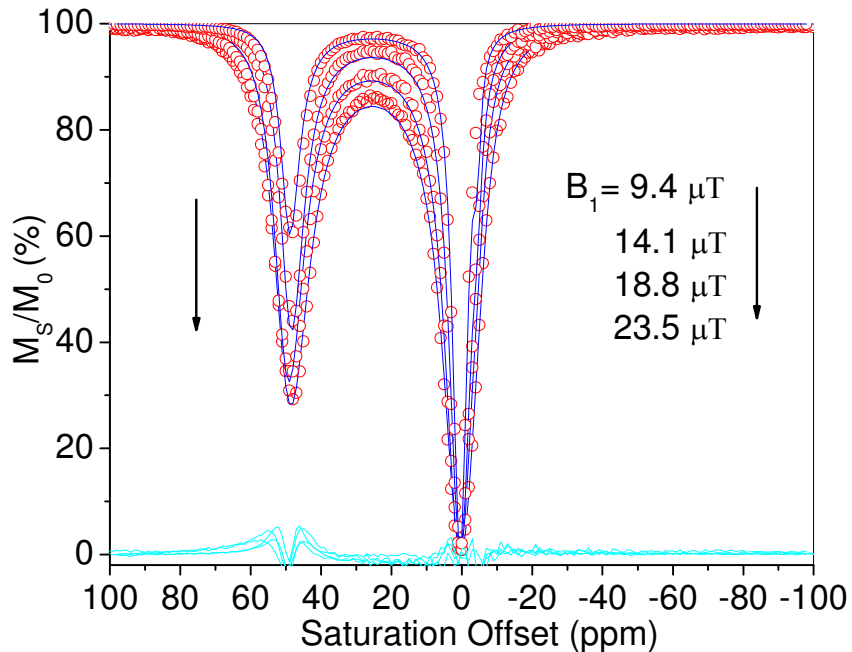


Figure S1h. Changes in the CEST spectra of Eu-DAMPS 2.0 with the increase of presaturation pulse intensity B_1 recorded at pH 6.9 and 9.4 T. $[\text{Eu}^{3+}] = 30$ mM and sat. time = 2 s. Symbols: experimental data. Lines: fitted data to the Bloch equations.

Supplementary Information S7

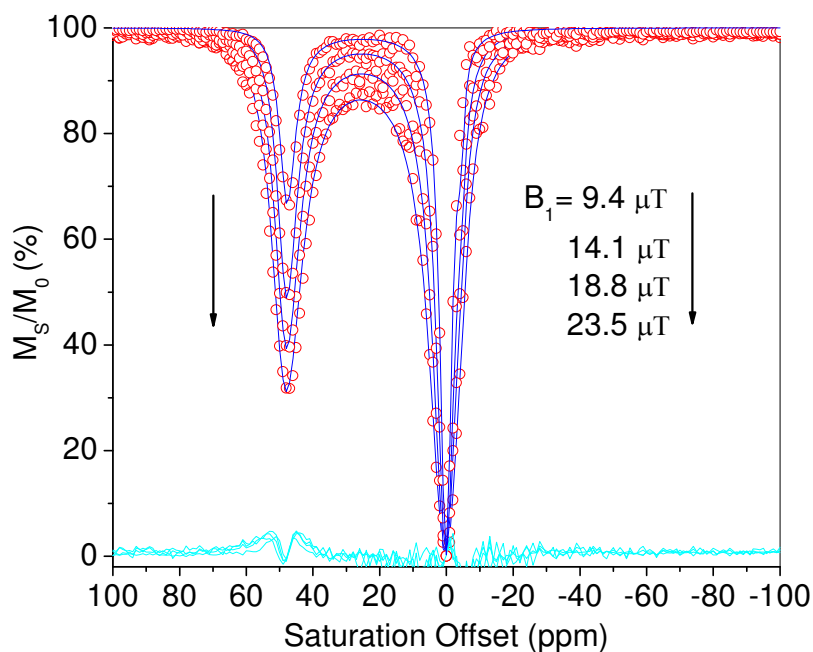


Figure S1i. Changes in the CEST spectra of Eu-DAMPS 2.1 with the increase of presaturation pulse intensity B_1 recorded at pH 7.5 and 9.4 T. $[\text{Eu}^{3+}] = 30 \text{ mM}$ and sat. time = 2 s. Symbols: experimental data. Lines: fitted data to the Bloch equations.

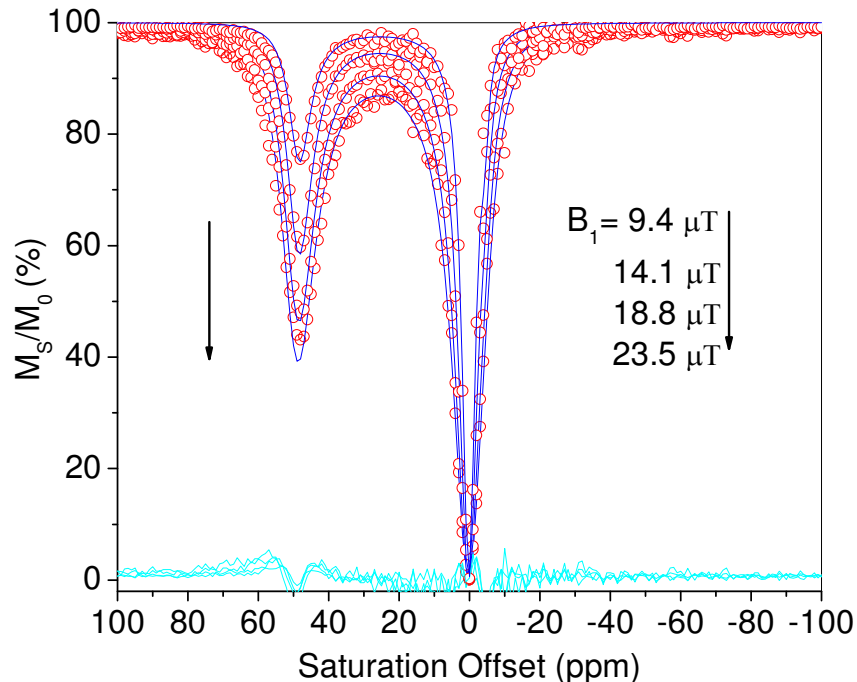


Figure S1j. Changes in the CEST spectra of Eu-DAMPS 3.1 with the increase of presaturation pulse intensity B_1 recorded at pH 8.0 and 9.4 T. $[\text{Eu}^{3+}] = 30 \text{ mM}$ and sat. time = 2 s. Symbols: experimental data. Lines: fitted data to the Bloch equations.

Supplementary Information S8

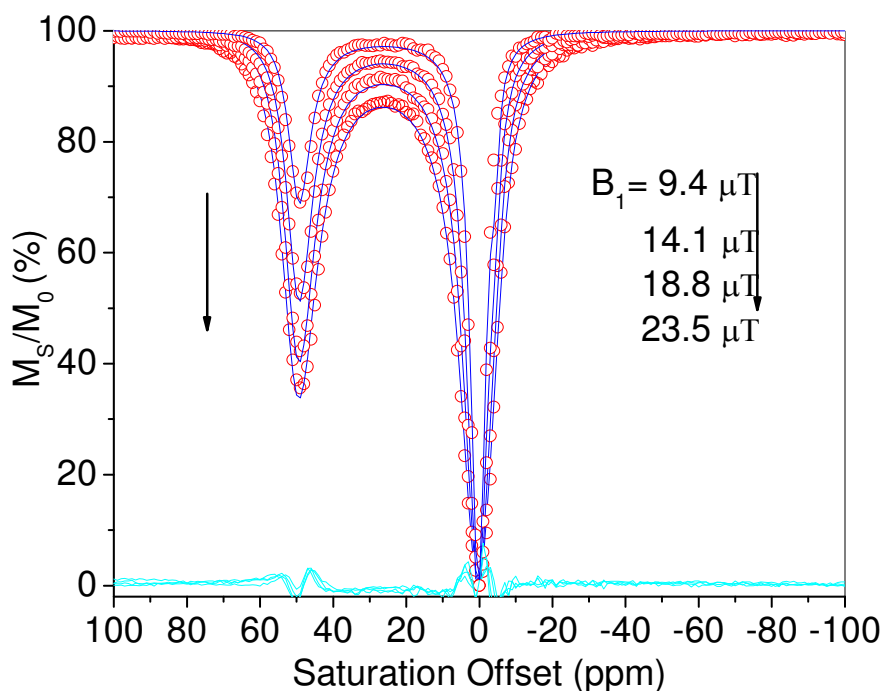


Figure S1k. Changes in the CEST spectra of Eu-DAMPS 4.1 with the increase of presaturation pulse intensity B_1 recorded at pH 7.7 and 9.4 T. $[\text{Eu}^{3+}] = 30$ mM and sat. time = 2 s. Symbols: experimental data. Lines: fitted data to the Bloch equations.

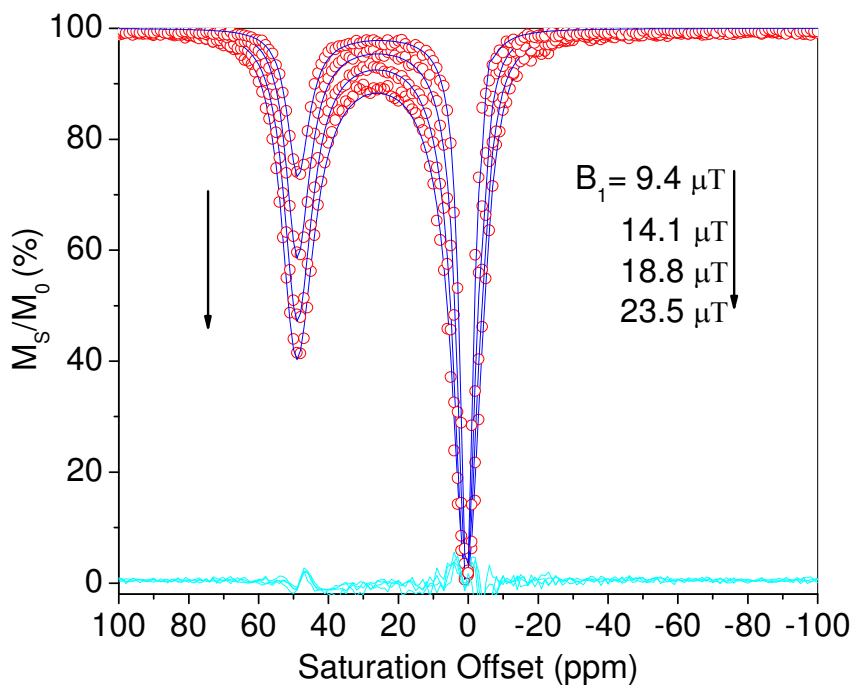


Figure S1l. Changes in the CEST spectra of Eu-DNIPAM 3.0 with the increase of presaturation pulse intensity B_1 recorded at pH 7.3 and 9.4 T. $[\text{Eu}^{3+}] = 30$ mM and sat. time = 2 s. Symbols: experimental data. Lines: fitted data to the Bloch equations.

Supplementary Information S9

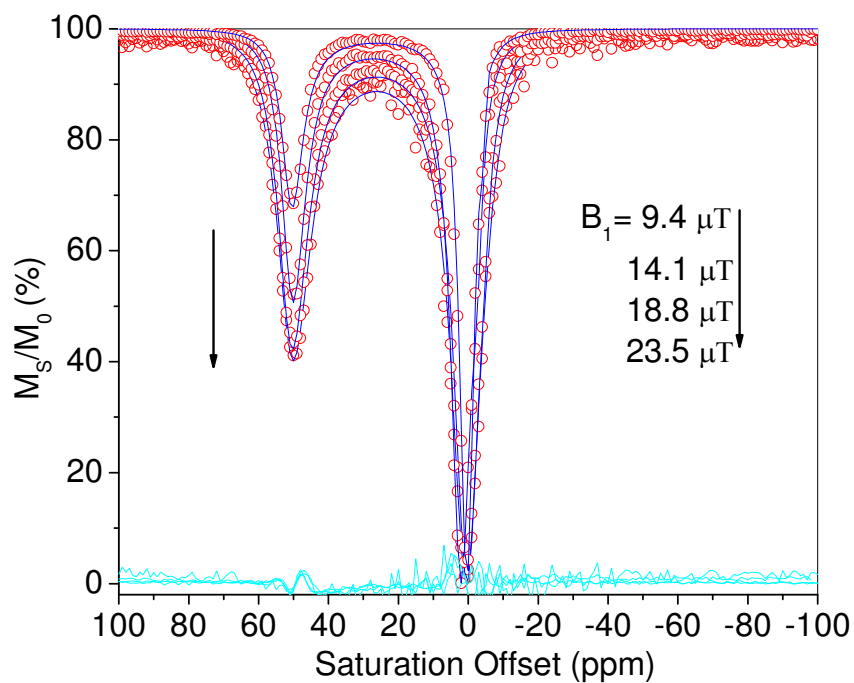


Figure S1m. Changes in the CEST spectra of Eu-DNIPAM 4.0 with the increase of presaturation pulse intensity B_1 recorded at pH 6.8 and 9.4 T. $[\text{Eu}^{3+}] = 30 \text{ mM}$ and sat. time = 2 s. Symbols: experimental data. Lines: fitted data to the Bloch equations.

Supplementary Information S10

3. The agent concentrations dependence of CEST intensity ($1 - M_S/M_0$) for Eu-DAMPS and Eu-DNIPAM

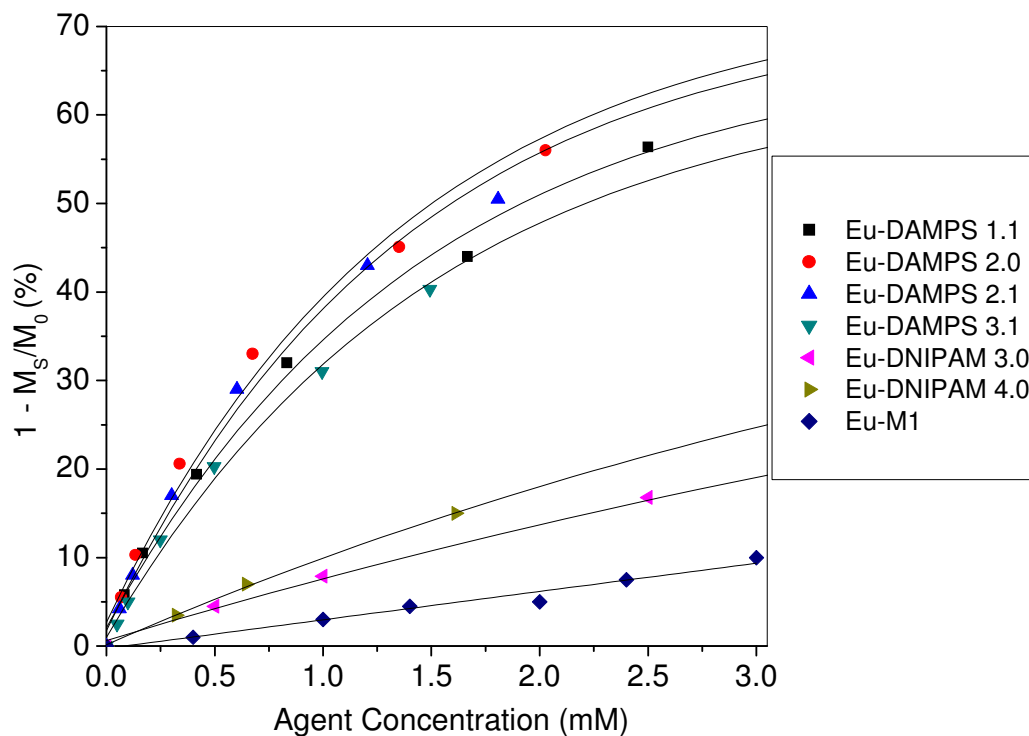


Figure S2. The agent concentrations dependence of CEST intensity ($1 - M_S/M_0$) for Eu-DAMPS and Eu-DNIPAM recorded at 9.4 T, 298 K and neutral pH. $B_1 = 14.1 \mu\text{T}$ and sat. time = 2 s. Scatter: experimental data; line: fitting data to an exponential decay.

Supplementary Information S11

4. pH dependence of transmittance spectra for Eu-DMAA 4.1

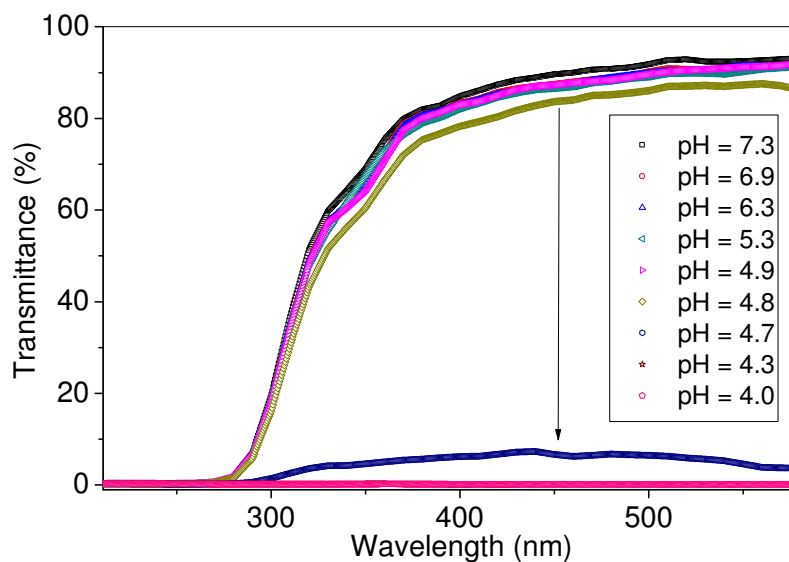


Figure S3. pH dependence of transmittance spectra for Eu-DMAA 4.1 (2 wt %) in aqueous solution.

5. Temperature dependence of transmittance spectra for DNIPAM 4.0 and Eu-DNIPAM 4.0

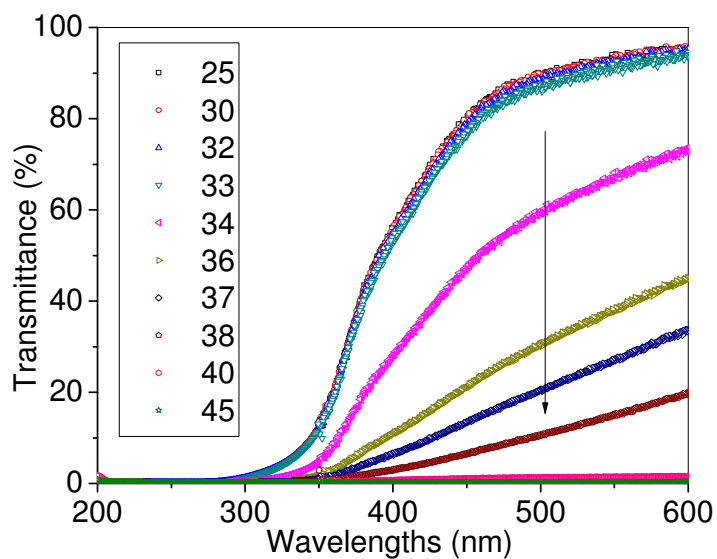


Figure S4a. Temperature (°C) dependence of transmittance spectra for DNIPAM 4.0 (2 wt %) in aqueous neutral solution.

Supplementary Information S12

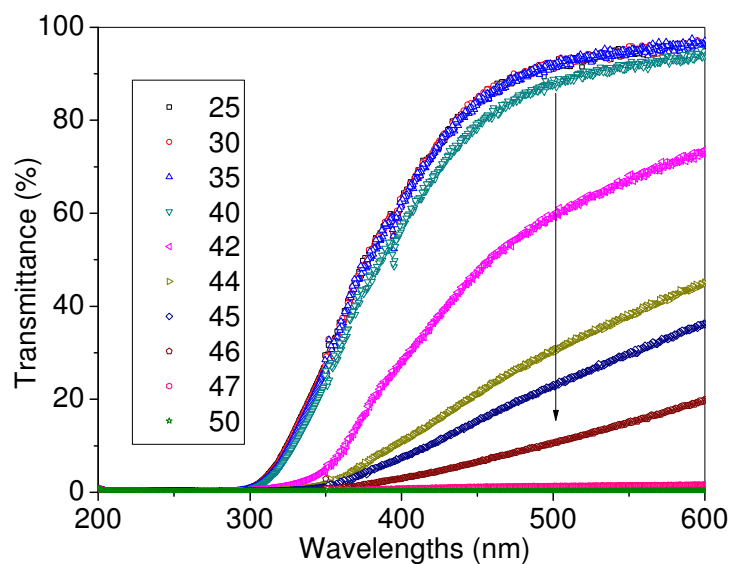


Figure S4b. Temperature (°C) dependence of transmittance spectra for Eu-DNIPAM 4.0 (2 wt %) in aqueous neutral solution.

6. pH dependence of CEST spectra for Eu-DMAA 4.1 and Eu-DAMPS 4.1

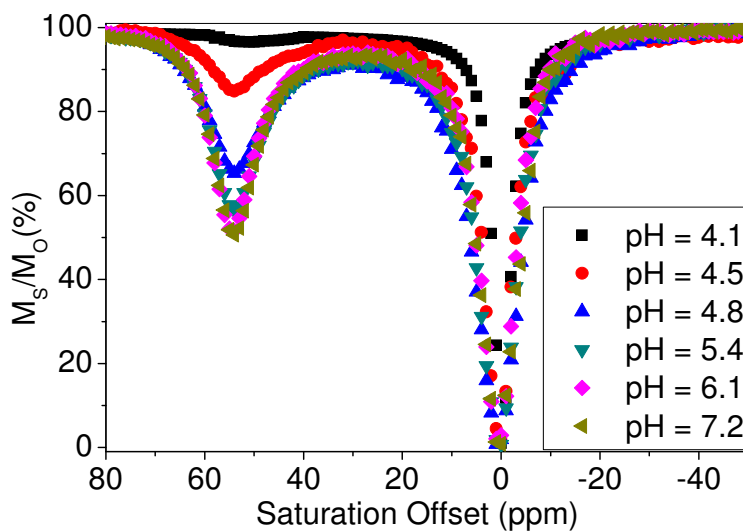


Figure S5a. pH dependence of CEST spectra for Eu-DMAA 4.1 recorded at 9.4 T and 25 °C. $[\text{Eu}^{3+}]_{\text{initial}} = 30 \text{ mM}$, $B_1 = 14.1 \text{ } \mu\text{T}$, sat. time = 2 s.

Supplementary Information S13

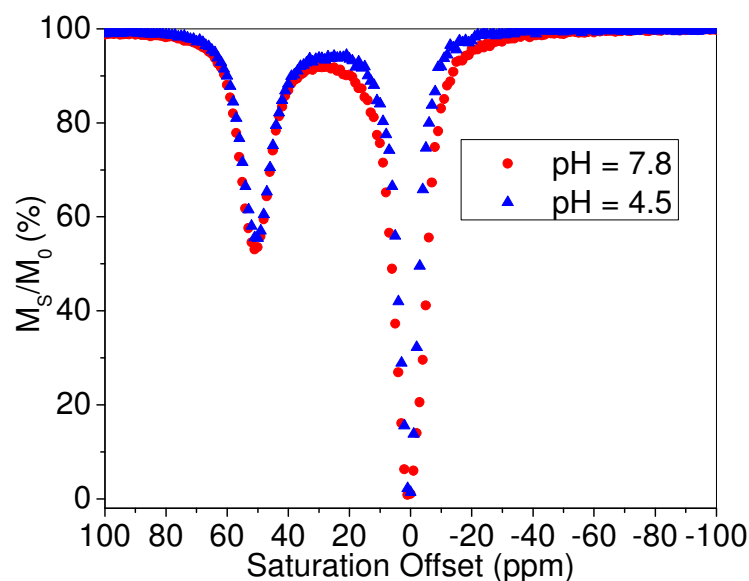


Figure S5b. pH dependence of CEST spectra for Eu-DAMPS 4.1 recorded at 9.4 T and 25 °C. $[\text{Eu}^{3+}] = 30 \text{ mM}$, $B_1 = 14.1 \text{ } \mu\text{T}$, sat. time = 2 s.

7. Temperature dependence of CEST spectra for Eu-DNIPAM 4.0 and Eu-DMAA 4.1 in plasma

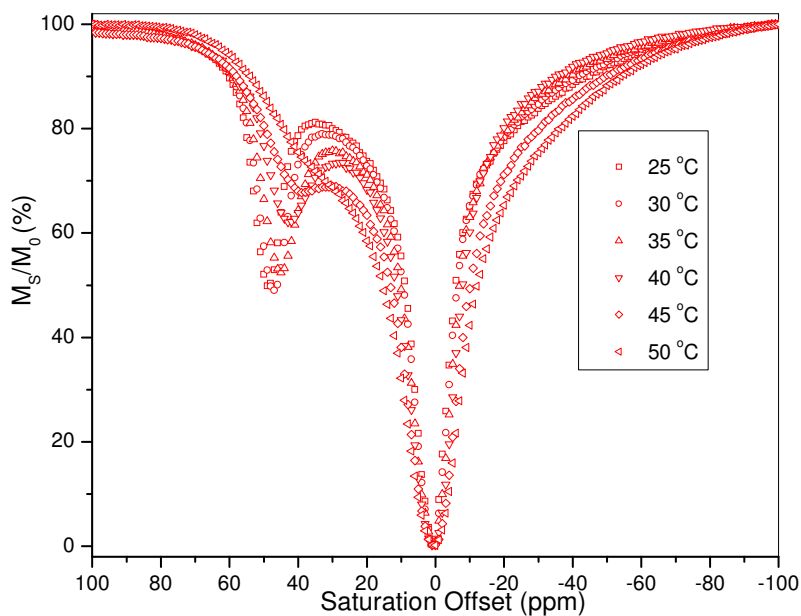


Figure S6a. Temperature dependence of CEST spectra for Eu-DNIPAM 4.0 recorded at 9.4 T under neutral pH in plasma. $[\text{Eu}^{3+}] = 30 \text{ mM}$, $B_1 = 14.1 \text{ } \mu\text{T}$, sat. time = 2 s.

Supplementary Information S14

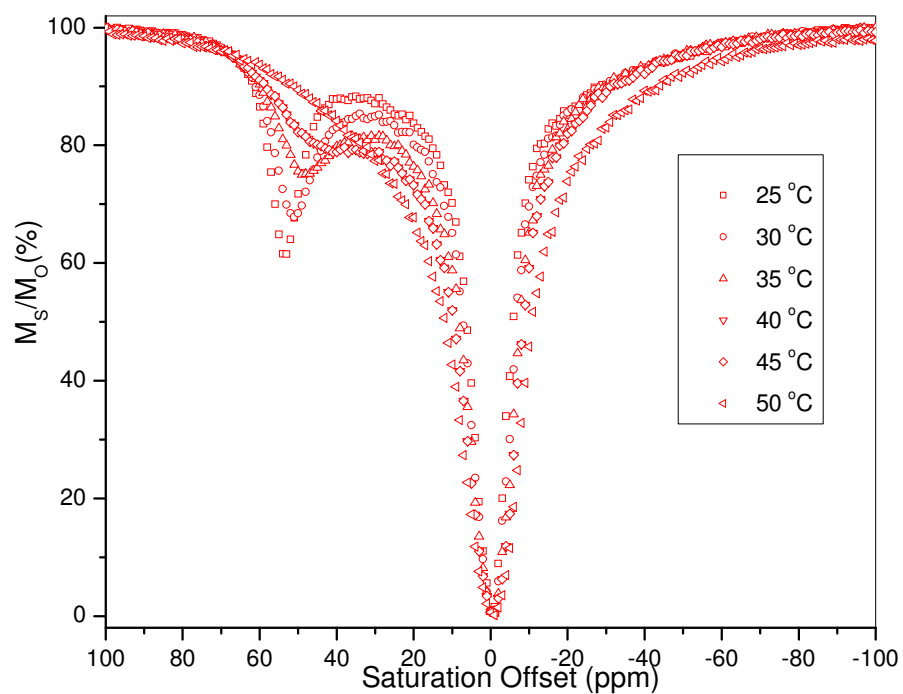


Figure S6b. Temperature dependence of CEST spectra for Eu-DMAA 4.1 recorded at 9.4 T under neutral pH in plasma. $[\text{Eu}^{3+}] = 30 \text{ mM}$, $B_1 = 14.1 \text{ } \mu\text{T}$, sat. time = 2 s.