

Supporting information

T1/T2 Dual functional iron oxide MRI contrast agent with super stability and low hypersensitivity benefited by ultrahigh carboxyl group density

Chongchong Miao,^a Fenglin Hu,^a Yuanpeng Rui,^b Yourong Duan,^c Hongchen Gu^{*a}

*Corresponding autho - Hongchen Gu hcgu@sjtu.edu.cn

^a Nano Biomedical Research Center, School of Biomedical Engineering & MED-X Research Institute,
Shanghai Jiao Tong University, 1954 Huashan Road, Shanghai, 200030, P.R. China

^b Department of Radiology, Putuo Hospital, Shanghai University of Traditional Chinese Medicine,
Shanghai 200062, China

^c State Key Laboratory of Oncogenes and Related Genes, Shanghai Cancer Institute, Renji
Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200032, China

Table S1 Crystalline interplanar spacing of CS015 and contrast with JCPDS card No. 39-1346 and 19-0629. $L = 591$, $d = L/5R$

	sample	No.39-1346	No.19-0629	hkl
d value	2.949 ± 0.019	2.953	2.967	220
	2.531 ± 0.024	2.5177	2.532	311
	2.116 ± 0.009	2.0886	2.0993	400
	1.631 ± 0.006	1.6073	1.6158	511
	1.492 ± 0.008	1.4758	1.4845	440

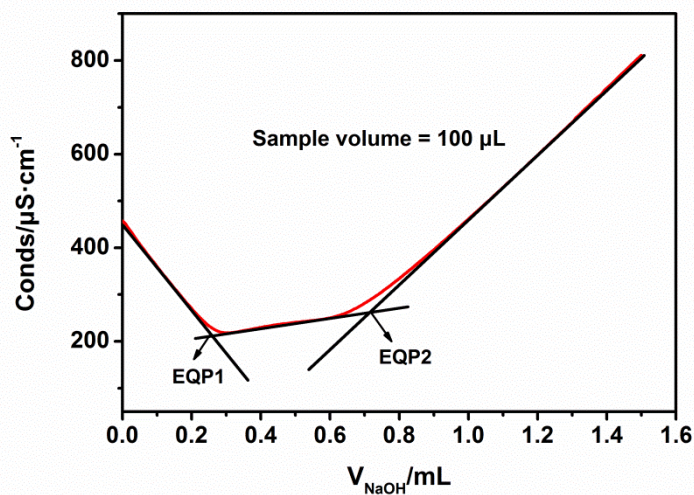


Fig. S1 Conductivity titration of free carboxyl using 0.1 M NaOH with 100 μL CS015 sample.

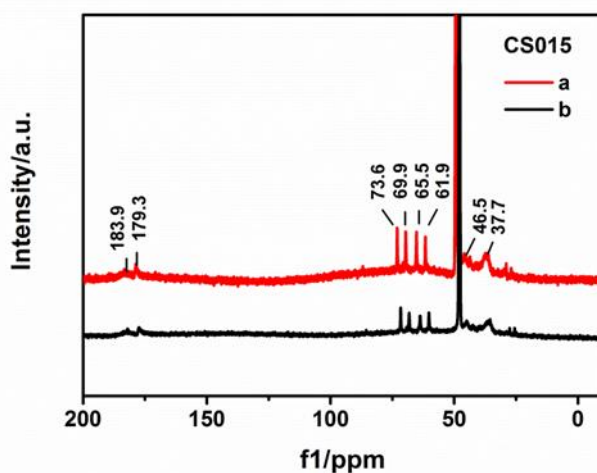


Fig. S2 ^{13}C NMR spectra of neutralized filter (a) and dialyzed neutralization filter (b) after decomposition CS015.

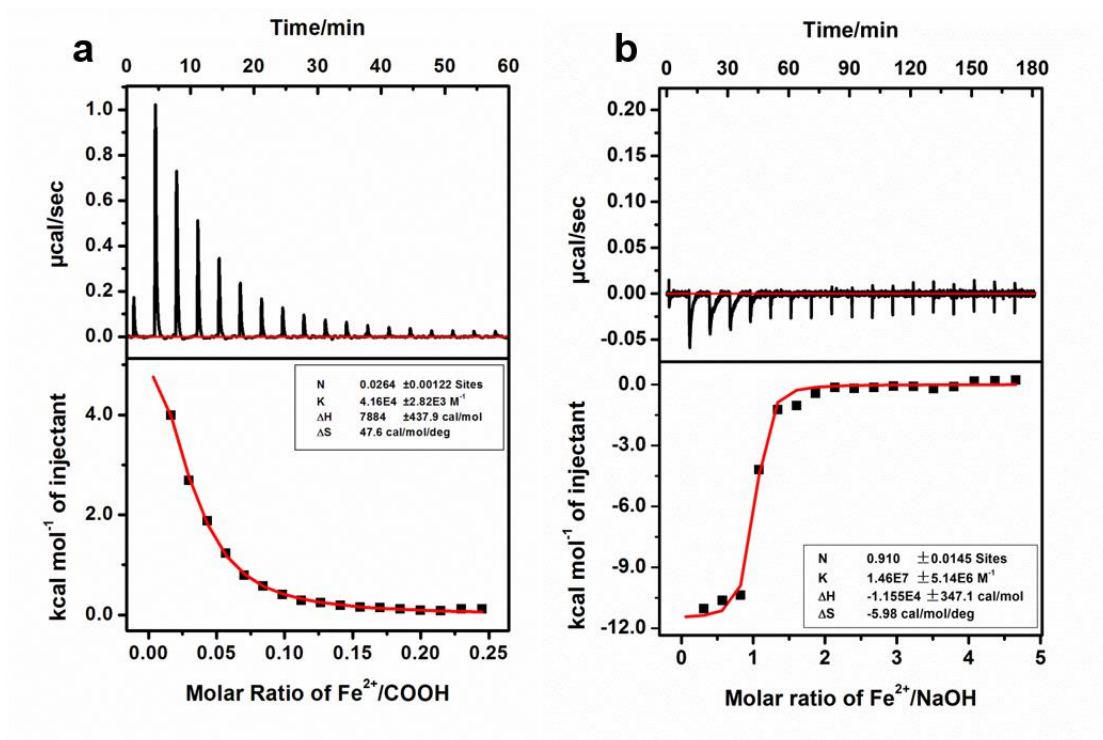
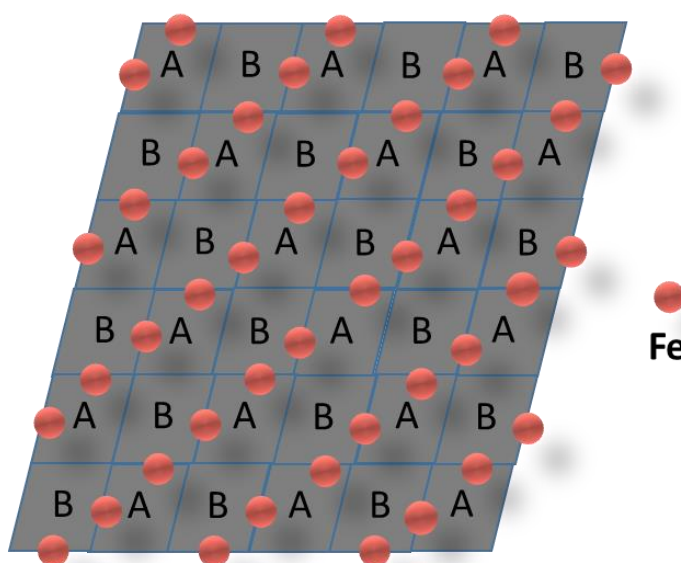


Fig. S3 Raw ITC thermo-gram (up) and corresponding Wiseman diagram (down) of (a) interaction between CS015 (1.5 mM COOH) under pH 5.5 and 2 mM FeCl_2 , (b) 2 mM FeCl_2 and NaOH (pH 8.9, same pH with 1.5 mM COOH).

Obvious exothermic peaks were appeared during the reaction of Fe^{2+} with CS015. After CS015 was adjusted to pH 5.5 (the same pH with Fe^{2+} at 4 mM), exothermic peaks were barely seen in Fig. S3a. Furthermore, as CS015 was replaced by NaOH with same pH in Fig. S3b, the exothermic peaks appeared again demonstrated that the exothermic peaks may have a relationship with the concentration of OH^- . As hydroxylation of Fe^{2+} was thermopositive, it was assumed to be hydroxylation heat of Fe^{2+} with OH^- and formed $[\text{Fe}(\text{OH})(\text{OH}_2)_5]^+$.¹

Table S2 Crystal structure parameters of Fe₃O₄

Compound	Crystallographic system	Space group	Stacking of closed packed anions	Unit cell dimensions nm (a b c β°)	Z
Magnetite	Cubic	Fd3m	ABCABC[111]	0.8369	8

**Fig. S4** The arrangement of Fe atoms on the surface of Fe₃O₄ particles.

Conformation calculation process of CS015

In this section, solid state content, Fe concentration using AAS instrument and weight loss using TGA analyzer were detected. The conformation was studied as below:

1. Percentage of Fe₃O₄: $\omega(\text{Fe}_3\text{O}_4)\% = \frac{C_{\text{Fe}} \times 232}{(56 \times 3 \times C_s)} \times 100\% = 47.88\%$ (C_s was the solid state content (63.09±0.25 mg/mL), C_{Fe} was 16.21±0.05 mg/mL, 232 g·mol⁻¹ was the molar weight of Fe₃O₄).
2. Organic percentage: $\omega(\text{org})\% = 42.71\% \pm 2.87$ from TG result.

3. Relative organic content vs per gram Fe₃O₄: $m(\text{org}) = 42.71\% / 47.88\% = 0.89 \text{ g}$.
4. Molar weight of PAA chains were 1000. The total number of PAA chains per gram Fe₃O₄ were $N(\text{chains}) = 0.89 / 1000 \times 1000 = 0.89 \text{ mM}$.
5. A 5.1 nm Fe₃O₄ core mass: $m = \pi/6 \times 5.1^3 \times 5.21 \times 10^{-21} = 3.61 \times 10^{-19}$, the quantity of 5.1 nm core in every gram Fe₃O₄: $N = 1/m / (6.02 \times 10^{23}) \times 1000 = 4.60 \times 10^{-3} \text{ mM}$. There were $0.89 / 4.60 \times 10^{-3} = 193$ PAA chains on every core. The grafting density was calculated to be $193 / 81.6 = 2.35 \text{ chains/nm}^2$.
6. Crystal structure of Fe₃O₄ was inverse spinel and the parameters of the crystal were summarized in Table S2.² According to the inverse spinel structure, the arrangement of Fe atoms on the surface of Fe₃O₄ particles was plotted in Fig. S4. The area of every orthogon was $(0.8369/2)^2 = 0.176 \text{ nm}^2$ and the amount of orthogons on the surface of a 5.1 nm Fe₃O₄ core was $81.6 / 0.176 = 464$. Therefore, the amount of Fe atoms on a 5.1 nm Fe₃O₄ core surface was 464.
7. The amount of COOH on every PAA chain that chelated with surface Fe was $464 / 193 = 2.40$.

Combining the analyzed data with crystal structure of Fe₃O₄, we deduced that the number of COOH in one PAA chains that chelating with surface Fe atoms was about 3. As repeated unit length of PAA was 0.25 nm³ and the number of COOH one PAA chain was $1000 / 72 = 14$ (72 g·mol⁻¹ was the molar weight of acrylic acid). If COOH that coordinated with Fe atoms was equally distributed in one PAA chain (every 3 COOH), the length of particle would be $5.1 + 3 \times 0.25 \times 2 / 2 = 5.75 \text{ nm} < 18 \text{ nm}$ (Number diameter), which was much smaller than Number diameter detected by DLS. Hence, the distribution of COOH was unequally on the particles surface and we deduced a “brush-like” conformation.

References

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2. R. J. Hill, J. R. Craig, G. V. Gibbs, *Phys. Chem. Minerals*, 1979, **4**, 317-339.
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