

## Electronic Supplementary Information (ESI)

### Gold-Iron oxide dimers for magnetic hyperthermia: The key role of chloride ions in the synthesis to boost the heating efficiency

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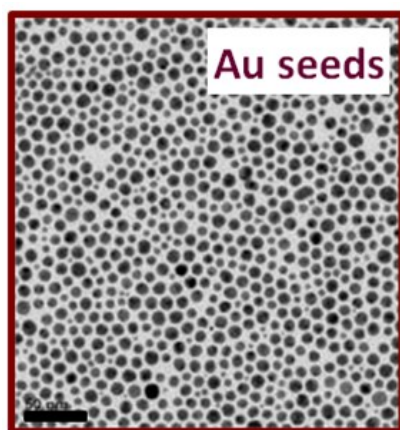
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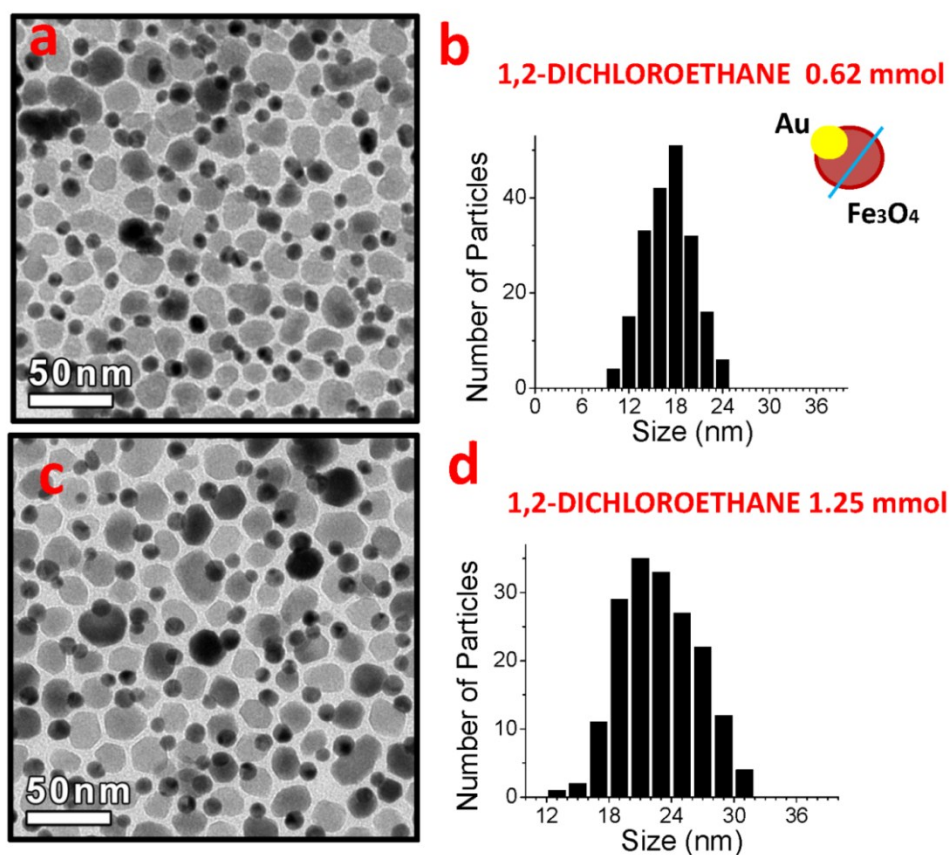
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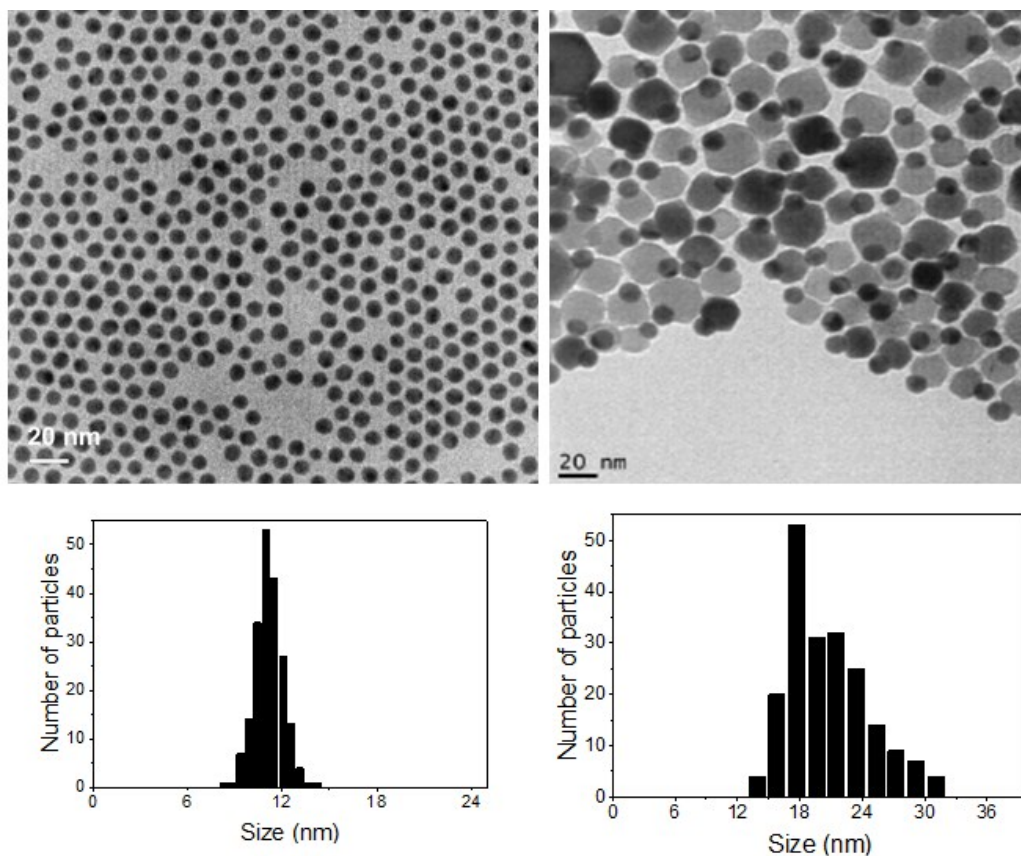
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**Fig. S1.** TEM images of 9 nm Au NPs used as seeds in the two-pot approach.

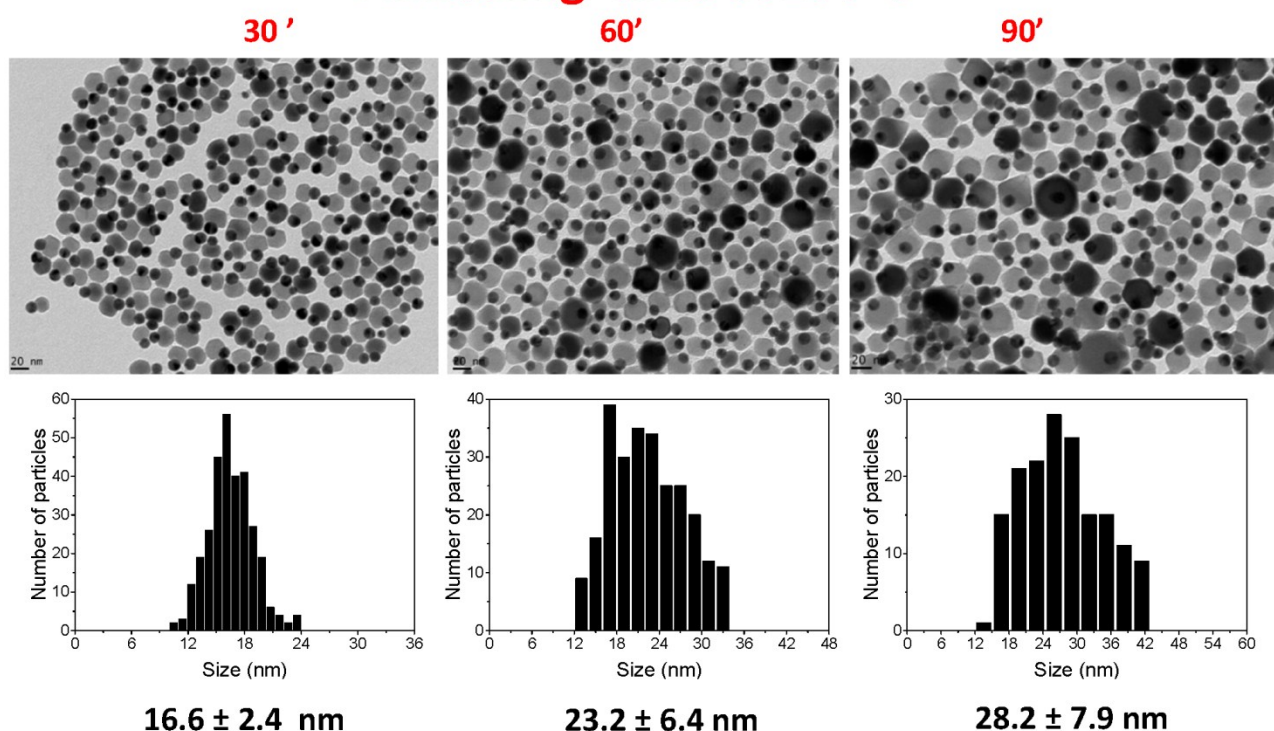


**Fig. S2.** TEM images and corresponding size histograms of gold-iron oxide dimers obtained by using a *two-pot* 200 °C approach and adding 0.62 mmol (a, b), and 1.25 mmol (b, d) respectively of 1,2-Dichloroethane as chloride source. Note that the reaction was stopped after annealing the solution at 200 °C for 90 minutes.



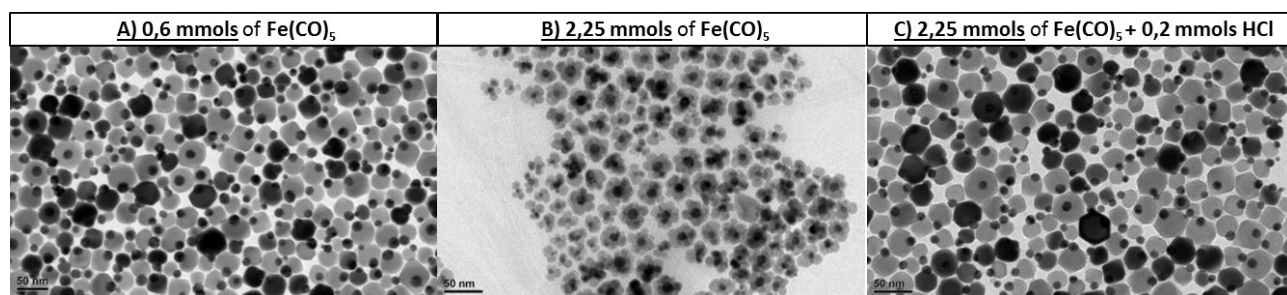
**Fig. S3.** TEM images and corresponding size histograms for *One-pot 200* synthesized gold-iron oxide dimers obtained by adding the Au precursor solution at the very beginning of the reaction. Au NPs were already formed after the vacuum step at 100 °C for 45 minutes (left). After 90 minutes at 200°C, dimers having an iron oxide domain of  $20.8 \pm 4.0$  nm and Au NPs of  $11.2 \pm 0.9$  nm were obtained (right).

## Annealing time at 200°C

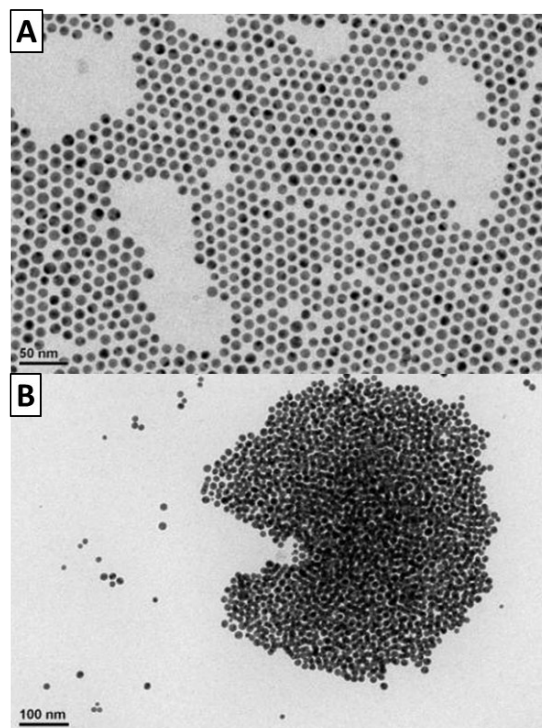


**Fig. S4.** TEM images and corresponding size histograms for *One-pot 200* synthesized gold-iron oxide dimers performed under the same conditions but halting the reaction at 200°C after 30, 60 or 90 minutes. Scale bar corresponds to 20 nm. The Au NPs have an average size of  $11.4 \pm 1.2$  nm

***One-pot Chloride mediated synthesis of gold-iron oxide:*** 20 mL of 1-Octadecene, 3 mL of oleylamine and 1 mL of oleic acid were mixed in a 100 mL three neck round bottom flask and degassed at 120 °C for 30 minutes. Then, at this temperature, a fresh solution containing 0.12 mmols (40 mg) of  $\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$  and 0.5 mL oleylamine in 5 mL 1-Octadecene was injected to the initial solution under a nitrogen blanket. Soon after injection, the solution was heated up to 150 °C and kept for 30 minutes. The solution was then cooled down to 65 °C and a defined volume of a 2M solution of HCl in diethyl ether was added (for instance 120  $\mu\text{L}$  to have an addition of 0,2 mmol of HCl for dimers of Figure S5C). The reaction mixture was then heated to 150 °C and a solution containing 1 mL of 1-Octadecene and 300  $\mu\text{L}$  of  $\text{Fe}(\text{CO})_5$  (2.25 mmols) was injected. Soon after the injection the solution temperature was increased to 200 °C at a heating rate of 7 °C/min and kept for 90 minutes. Dimers were collected following the washing protocol above reported.



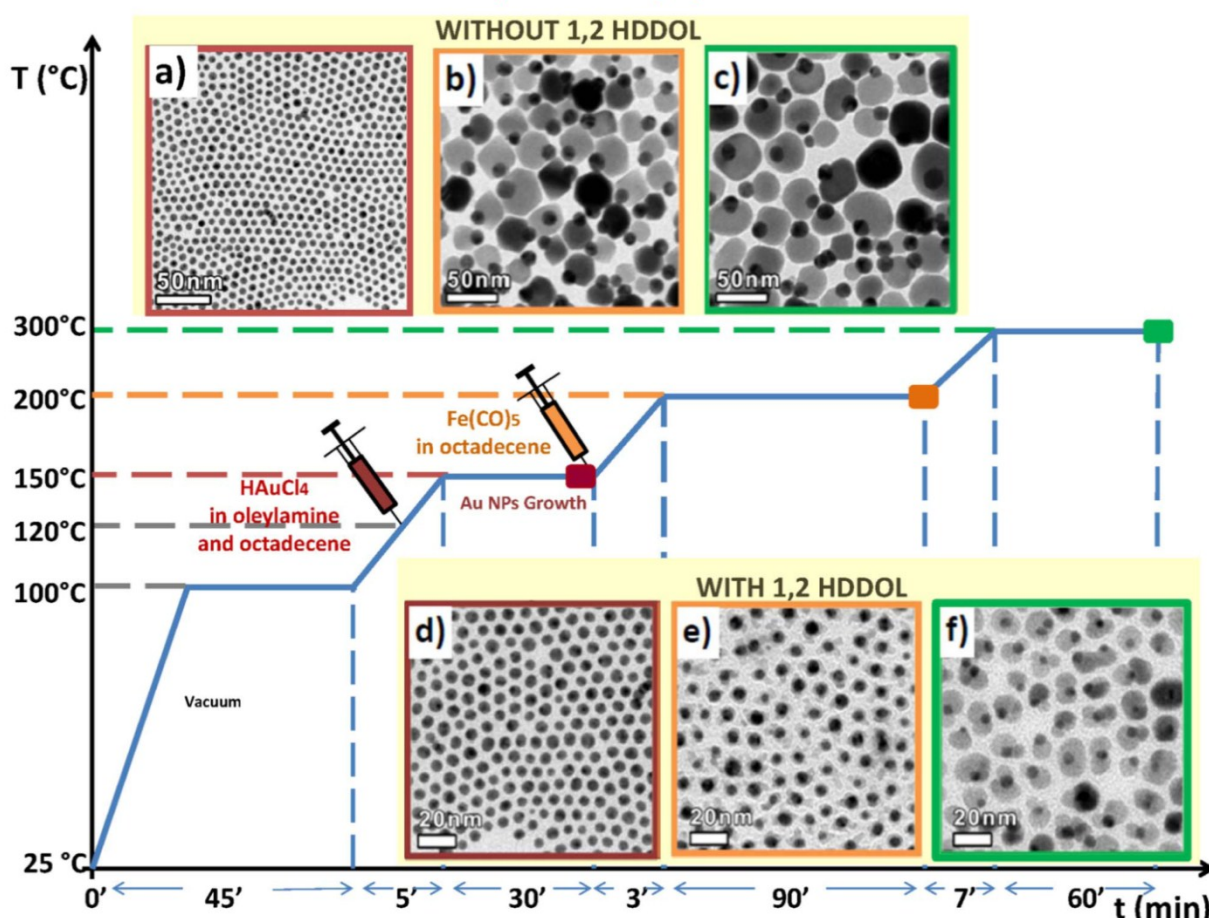
**Fig. S5.** TEM images for gold- iron oxide dimers produced by *one-pot 200* protocol obtained by increasing the amount of  $\text{Fe}(\text{CO})_5$  while keeping all the parameters constant. Increasing the relative ratio of Fe:Cl from 1:25 (A) to 5 (B) favors the formation of flower-like dimers. When using more  $\text{Fe}(\text{CO})_5$  (2.25 mmols) (C) to recover the dimer shape the ratio Fe:Cl needs to be decreased by addition of extra chloride ions. Adding 0.2 mmols of HCl in diethyl ether (2M) to the 0.48 mol of chloride ions deriving from the gold precursor (reaching an overall Fe:Cl ratio of 3.3) restores the dimers-like dumbbell dimers (C). All samples were produced following a *one-pot 200* procedure injecting 0.6 mmol (A) or 2.25 mmol (B and C) of  $\text{Fe}(\text{CO})_5$  to a solution containing 1-Octadecene (20mL), oleic acid (1mL), oleylamine (3mL) and 0.12 mmol (40 mg) of  $\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$ . The synthesis was stopped after the solution was aged at 200 °C for 90 minutes.



**Fig. S6.** TEM images of a *two-pot 300* synthesis approach replacing  $\text{Fe}(\text{CO})_5$  by  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ . A) TEM images of an aliquot taken after aging the solution for 90 minutes at 200 °C and B) the final product after the solution was kept at 300 °C for 60 minutes.



# One-pot approach

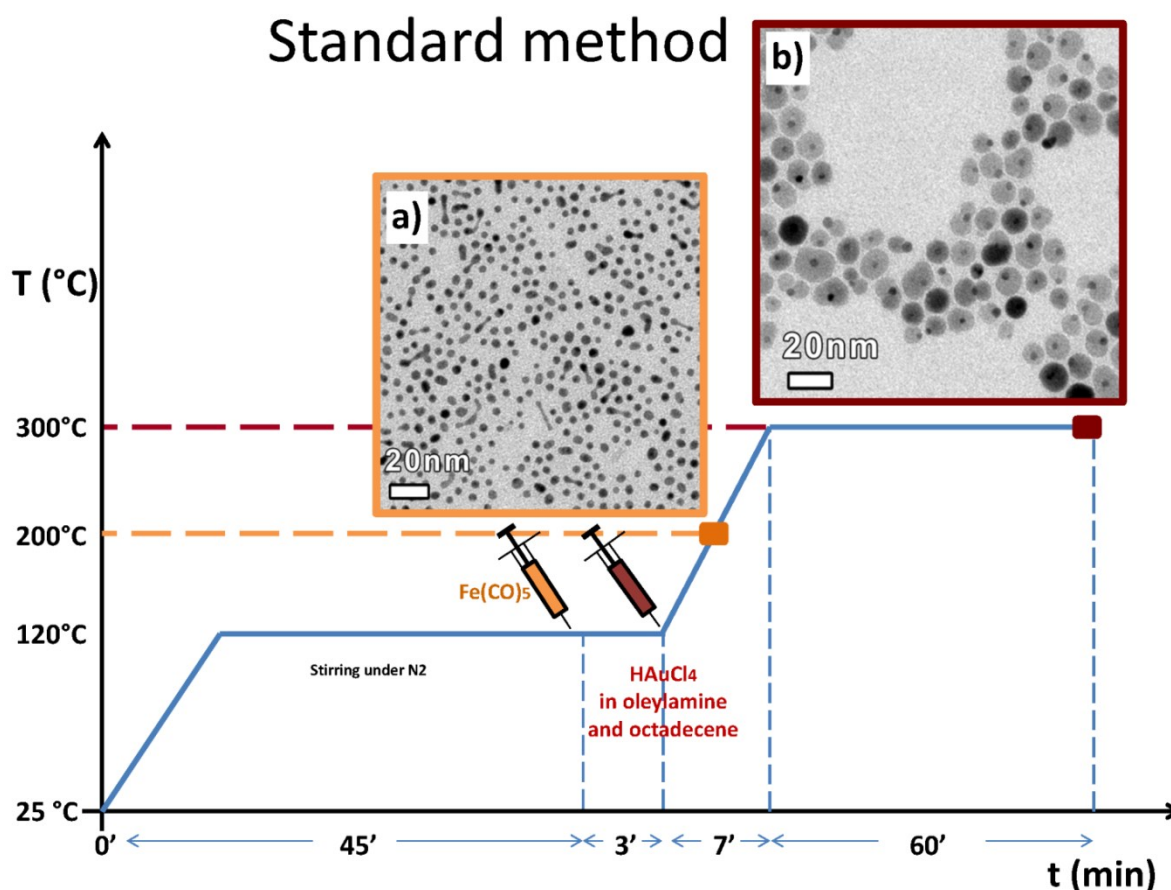


**Fig. S7.** One-pot 200 synthesis of gold-iron oxide dimers performed without (a,b,c) and with (d,e,f) 1,2-HDDOL (1,2-hexadecandiol). Temperature diagram and relevant steps (injection of precursor and annealing times) are also depicted. Upper TEM panels refer to aliquots taken at different time of the reaction of the dimer synthesis done in absence of 1,2-HDDOL (a, b, c), lower TEM panels refers to the aliquots taken for the dimers synthesis performed in presence of 1,2-HDDOL (e, f, g). TEM images, framed with different color codes, correspond to different aliquots of the synthesis identified in the diagram by the corresponding color code spots. Similar results were found by using other alkyl diols (*i.e.* 1,2-Dodecanediol, data not shown) or using the two-pot method (data not shown).

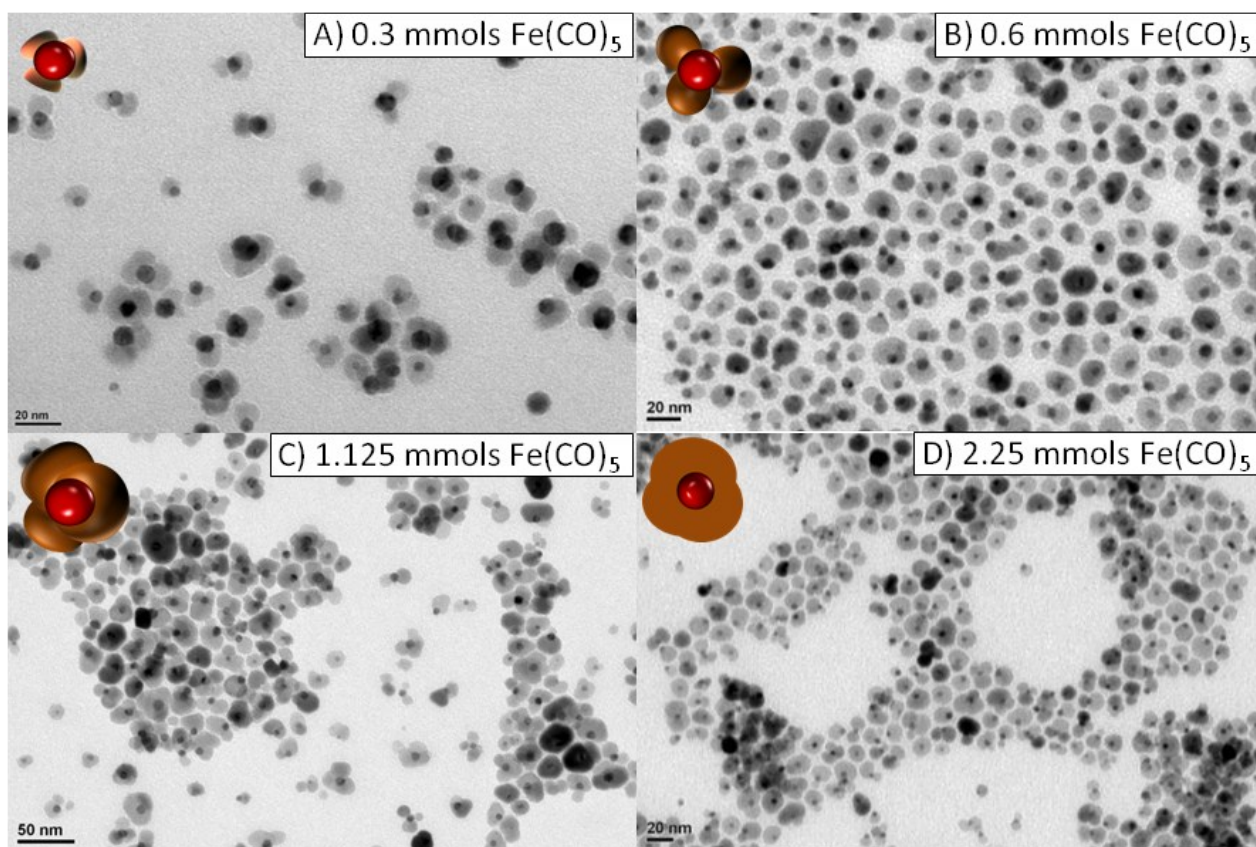
**Standard synthesis of gold-iron oxide dimers by Sun method using 1-2-HDDOL:** To compare the performance of our dimers with other dimers already available, we reproduced a literature report synthesis.<sup>8</sup>

Briefly, 20 mL of 1-Octadecene, 10 mmols (2.58 g) of 1,2-Hexadecanediol, 2 mL of oleylamine and 1.9 mL of oleic acid were mixed in a 100 mL three-neck round bottom flask and stirred under a gentle flow of nitrogen at 120 °C for 20 min. Then under a nitrogen blanket, 0.30 ml  $\text{Fe}(\text{CO})_5$  (2 mmol) was injected into the solution. After 3 min, the gold precursor solution consisting of 40 mg  $\text{HAuCl}_4 \cdot (\text{H}_2\text{O})_3$  (0.12 mmol), 0.5 ml oleylamine

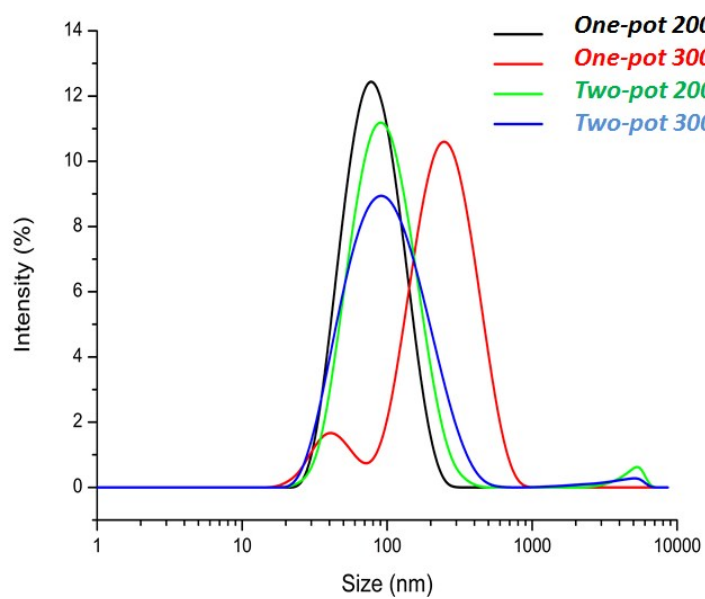
(1.5 mmol) and 5 ml ODE was injected into the solution. The solution turned to dark red instantly after the injection, indicating the formation of gold nanoparticles. The mixture was heated to reflux ( $\sim 300^\circ\text{C}$ ) for 45 min, cooled down to room temperature, and exposed to air for an extra hour to ensure the formation of  $\text{Fe}_3\text{O}_4$  (Fig. S8). In a series of experiments following the same standard protocol also only the iron precursor amount was varied from 0.3 to 2.25 mmol, providing dimers as shown in Fig. S9. Similar results were obtained when replacing 1,2-Hexadecanediol with 1,2-Dodecanediol (data not shown).



**Fig. S8.** Temperature diagram along with the most relevant steps (injection of precursors) for the standard procedure reported by Sun and coworkers. Note that in this procedure 1,2-HDDOL is used. TEM micrographs represent aliquots collected at  $200^\circ\text{C}$  where Au NPs were already nucleated (orange frame) and the iron oxide-gold dimer obtained at  $300^\circ\text{C}$  at the end of the synthesis.

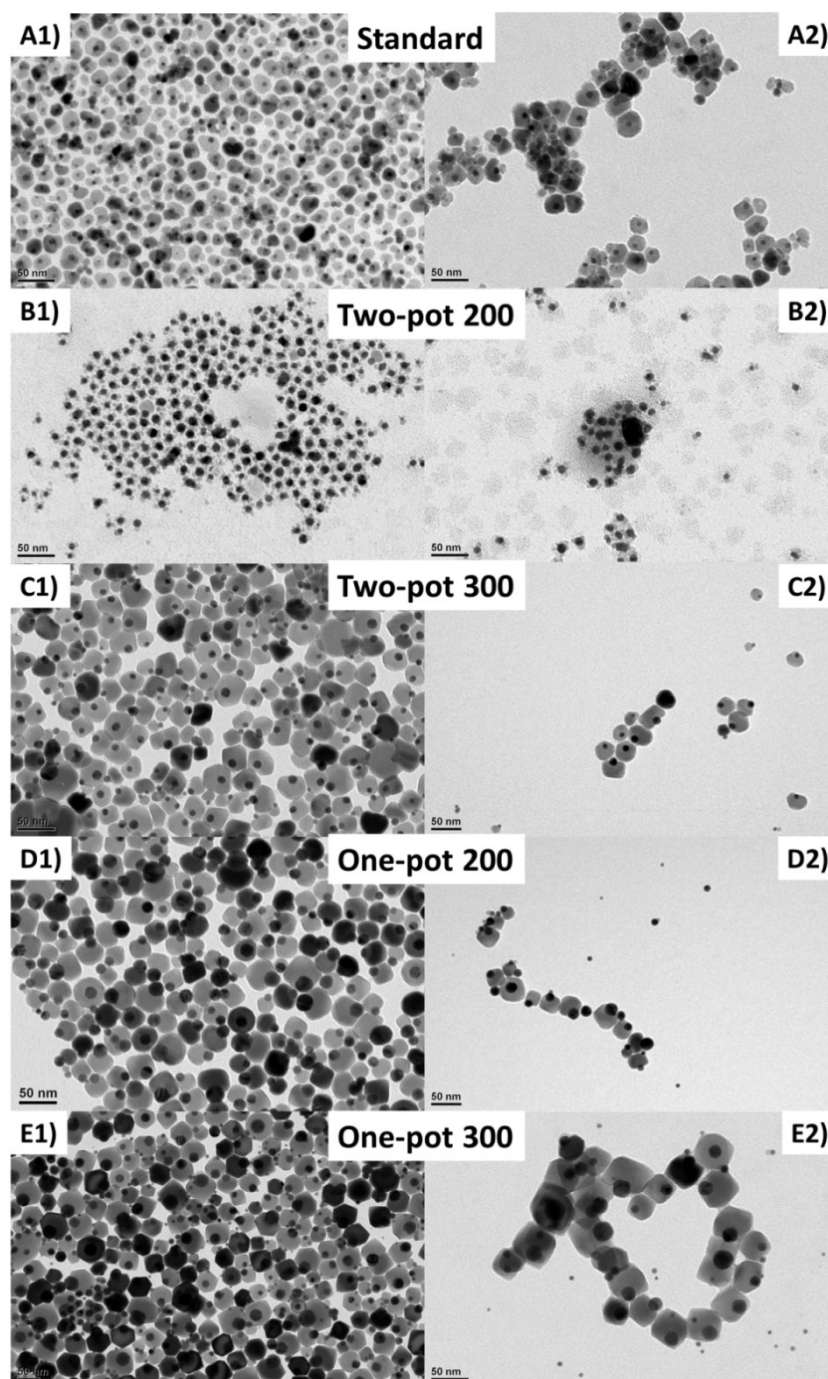


**Fig. S9.** TEM images of gold-iron oxide dimers synthesized following a standard protocol available in which the iron precursor ( $\text{Fe}(\text{CO})_5$ ) was varied from 0.3 mmols (a), to 0.6 mmols (b), 1.125 mmols (c) or 2.25 mmols (d), respectively and it was injected at 150 °C into a solution of oleylamine, oleic acid,  $\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$ , 1,2-HDDOL and 1-Octadecene. (see scheme in Figure S8 that summarizes the different steps of this procedure).

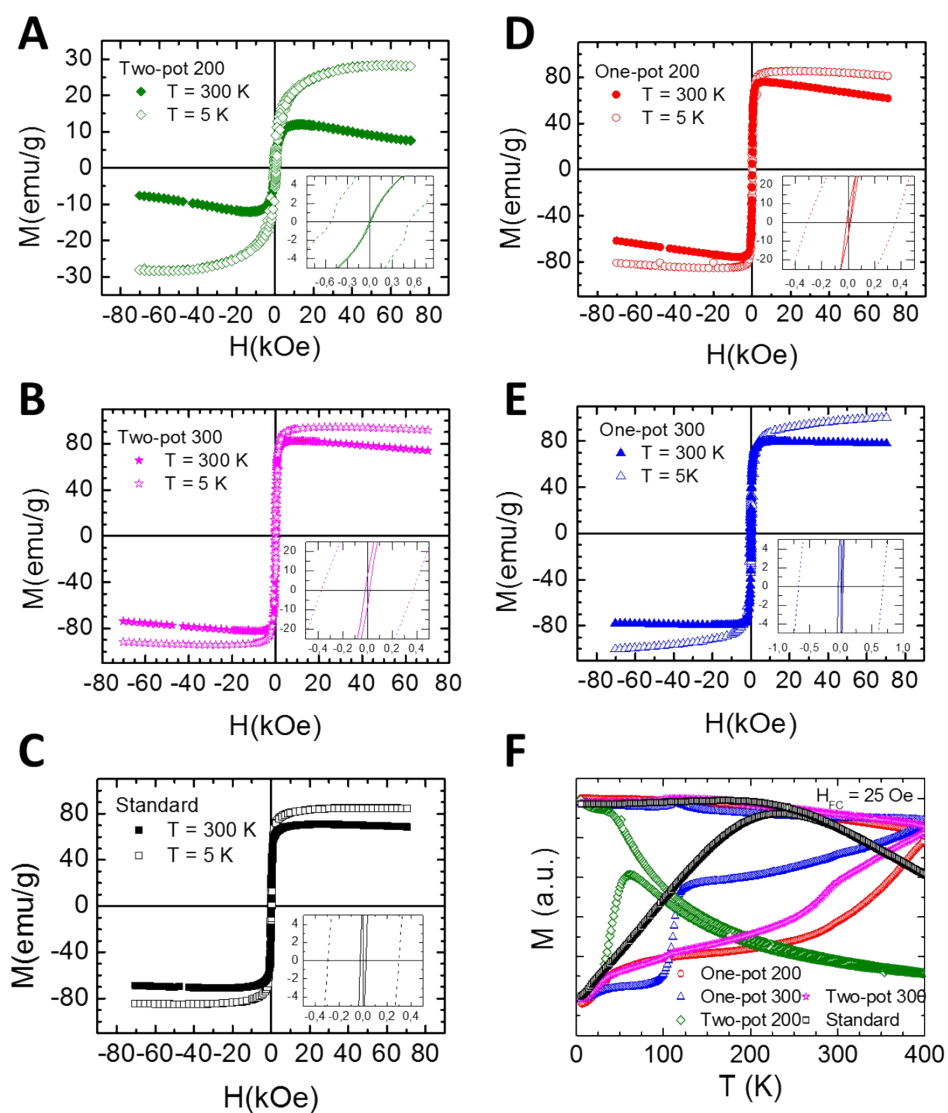




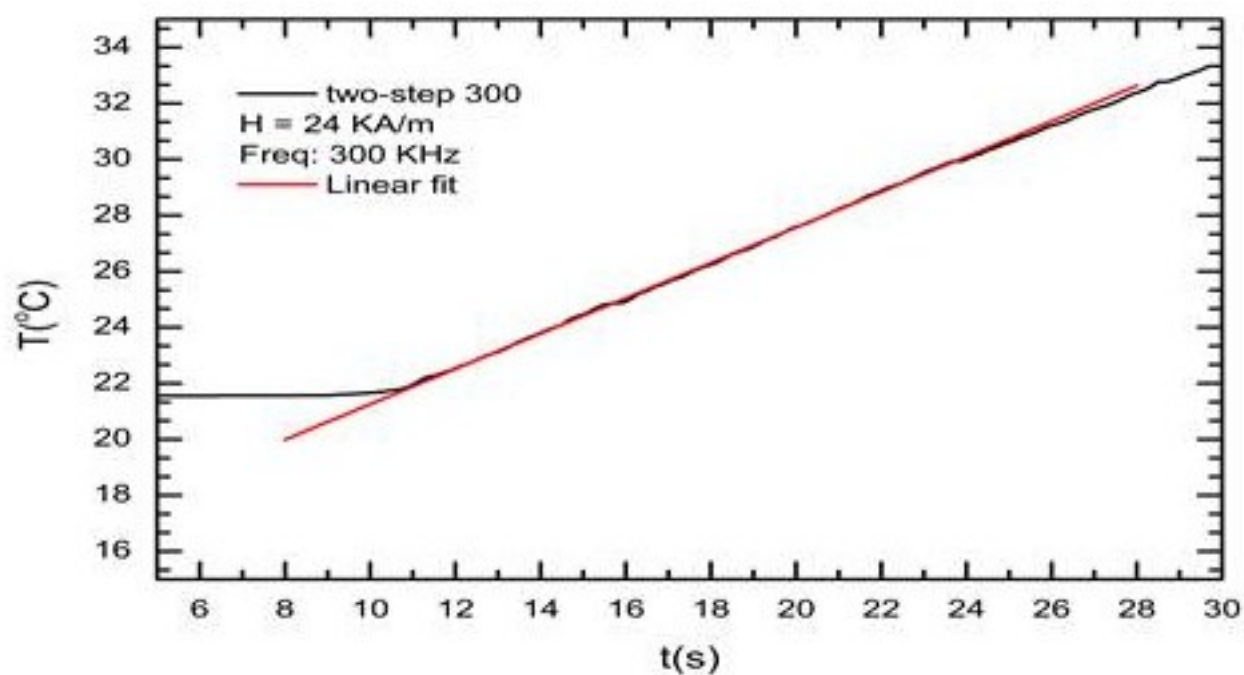
**Fig. S10.** Dynamic light scattering measurements of gold-iron oxide dimers synthesized by using different approaches: One-pot at 200 °C (black line); one-pot at 300 °C (red line); two-pot 200 °C (green line); two-pot at 300 °C (blue line). As shown, all the samples have a good colloidal stability except for the one-pot 300 °C which shows a partial aggregation.



**Fig. S11:** TEM images for water soluble gold-iron oxide dimers synthesized by using different approaches: Standard (A1-A2); *two-pot 200* (B1-B2); *two-pot 300* (C1-C2); *one-pot 200* (D1-D2) and *one-pot 300* (E1-E2); Samples show good colloidal stability with exception of sample *one-pot 300* which shows a partial aggregation.

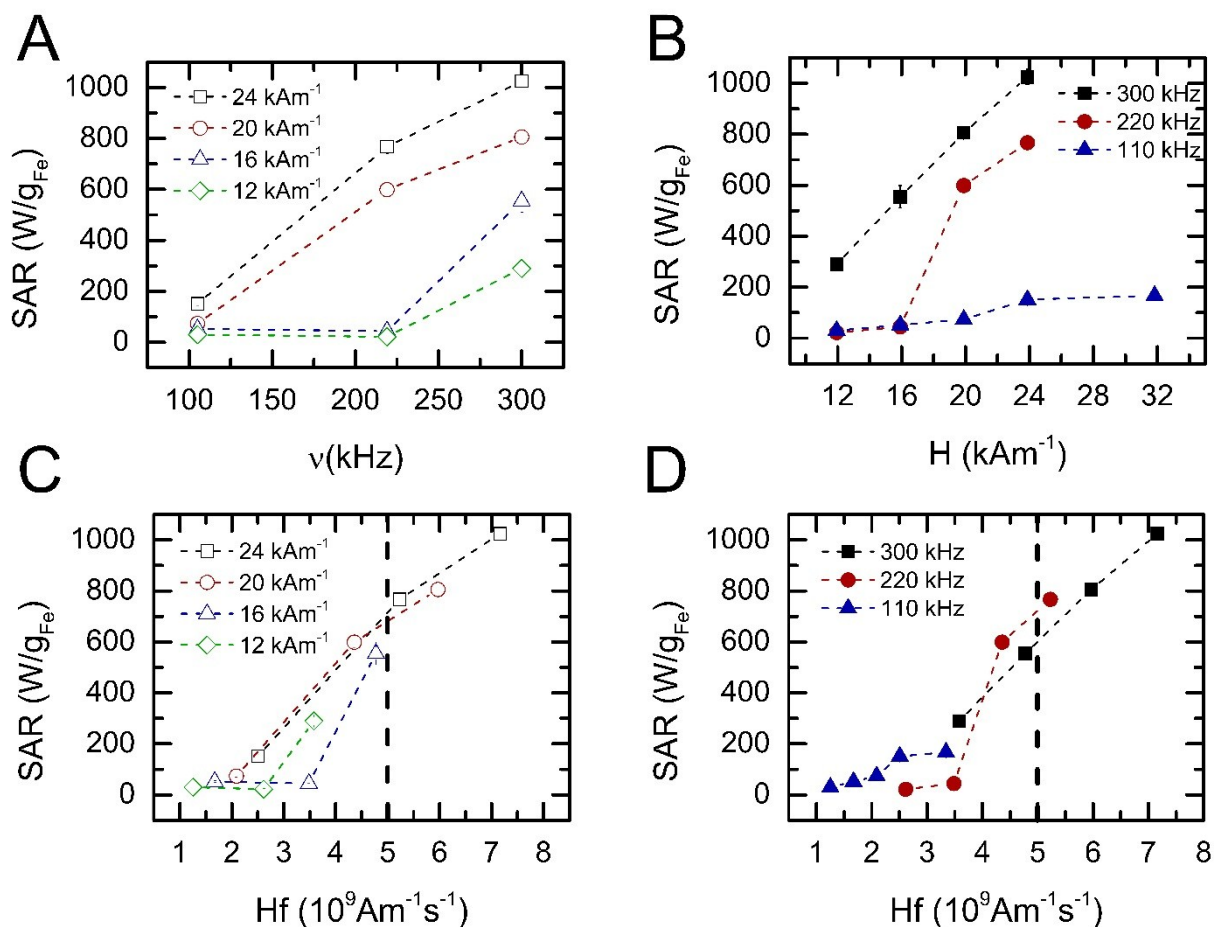


**Fig. S12.** Hysteresis loops at 5 K (black open squares) and 300 K (red squares) for gold-iron oxide dimers synthesized by using five different approaches: (A) two-pot 200, (B) two-pot 300, (C) standard, (D) one-pot 200 and (E) one-pot 300 °C. Insets show low field detail of the magnetization hysteresis loops showing the coercive fields at 5 K (black line) and 300 K (red line). F) Zero field cooled-field cooled curves for gold-iron oxide dimers synthesized by using five different synthesis approaches (One-pot 200 (open red circles  $\circ$ ), one-pot 300 (open blue triangles  $\Delta$ ), two-pot 200 (open green rhombi  $\diamond$ ), two-pot 300 (open pink stars  $\star$ ) and Standard (open black squares  $\square$ )).



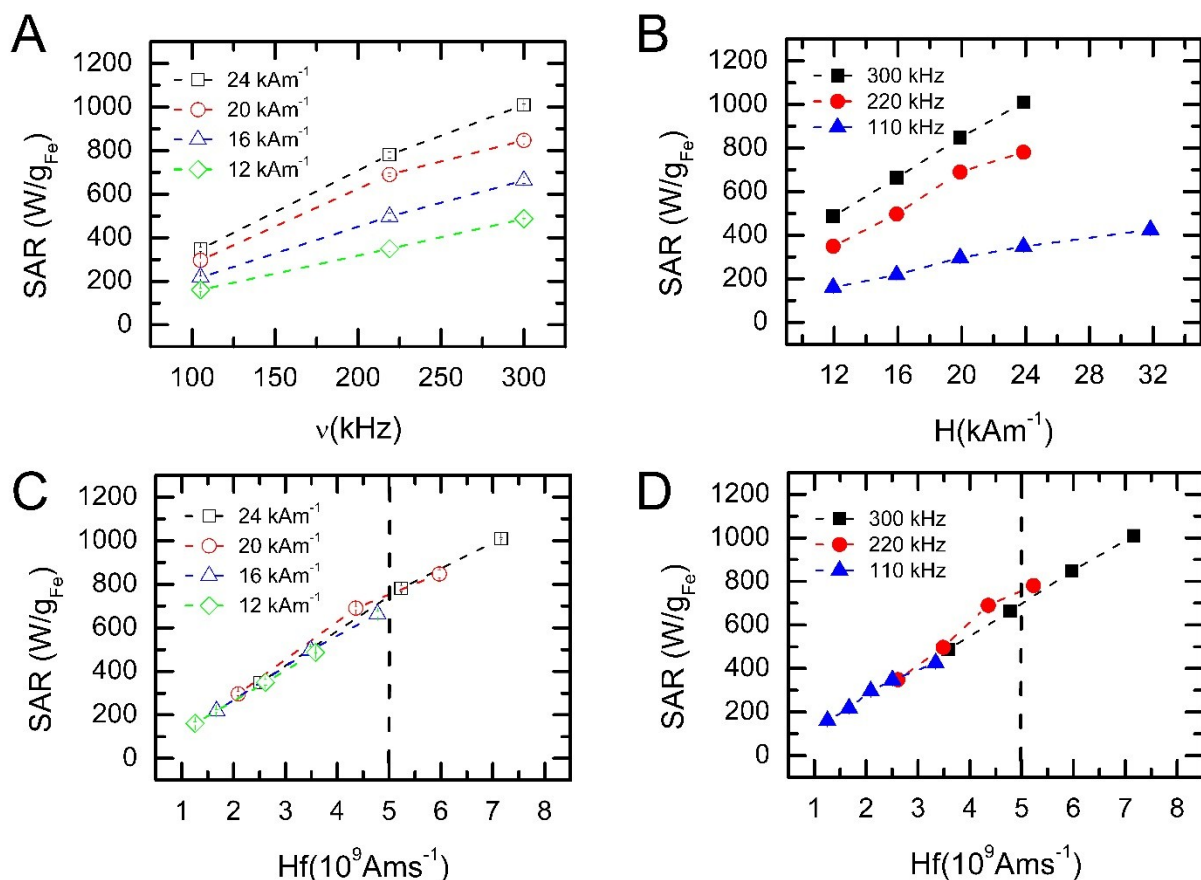
**Fig. S13:** Typical temperature versus time curve recorded under the alternating magnetic field (in this case at 24Kam-1 and 300 KHz. and the corresponding fitting to calculate the SAR value (red line) for gold-iron oxide dimers synthesized by using a two-pot 300 approach.

## Two-pot 300



**Fig. S14.** SAR values for gold-iron oxide dimers prepared by using gold NPs as seeds and reaching 300°C (two-pot 300). SAR values are reported as a function of: **A**) Frequency at different applied magnetic field amplitudes 24 kA m<sup>-1</sup> (open black squares  $\square$ ), 20 kA m<sup>-1</sup> (red open circles  $\circ$ ), 16 kA m<sup>-1</sup> (blue open triangles  $\triangle$ ) and 12 kA m<sup>-1</sup> (green open rhombi  $\diamond$ ). **B**) Applied Magnetic field at different frequencies 300 kHz (black squares  $\blacksquare$ ), 220 kHz (red circles  $\bullet$ ) and 110 kHz (blue triangles  $\blacktriangle$ ). **C**) The  $H \cdot f$  factor at different applied magnetic field amplitudes 24 kA m<sup>-1</sup> (open black squares  $\square$ ), 20 kA m<sup>-1</sup> (red open circles  $\circ$ ), 16 kA m<sup>-1</sup> (blue open triangles  $\triangle$ ) and 12 kA m<sup>-1</sup> (green open rhombi  $\diamond$ ) and **D**)  $H \cdot f$  factor at different frequencies 300 kHz (black squares  $\blacksquare$ ), 220 kHz (red circles  $\bullet$ ) and 110 kHz (blue triangles  $\blacktriangle$ ). Dimers were synthesized by injecting at 150 °C 0,06 mmols of iron pentacarbonyl in a solution of oleylamine, oleic acid, 1-Octadecene and containing Au NPs. The mixture was heated up to 200 °C and kept at this temperature for 90 minutes. The solution was then further heated up to 300 °C and kept at this temperature for 60 minutes. Each experimental data point was calculated as the mean value of at least 4 measurements and error bars indicate the standard deviation.

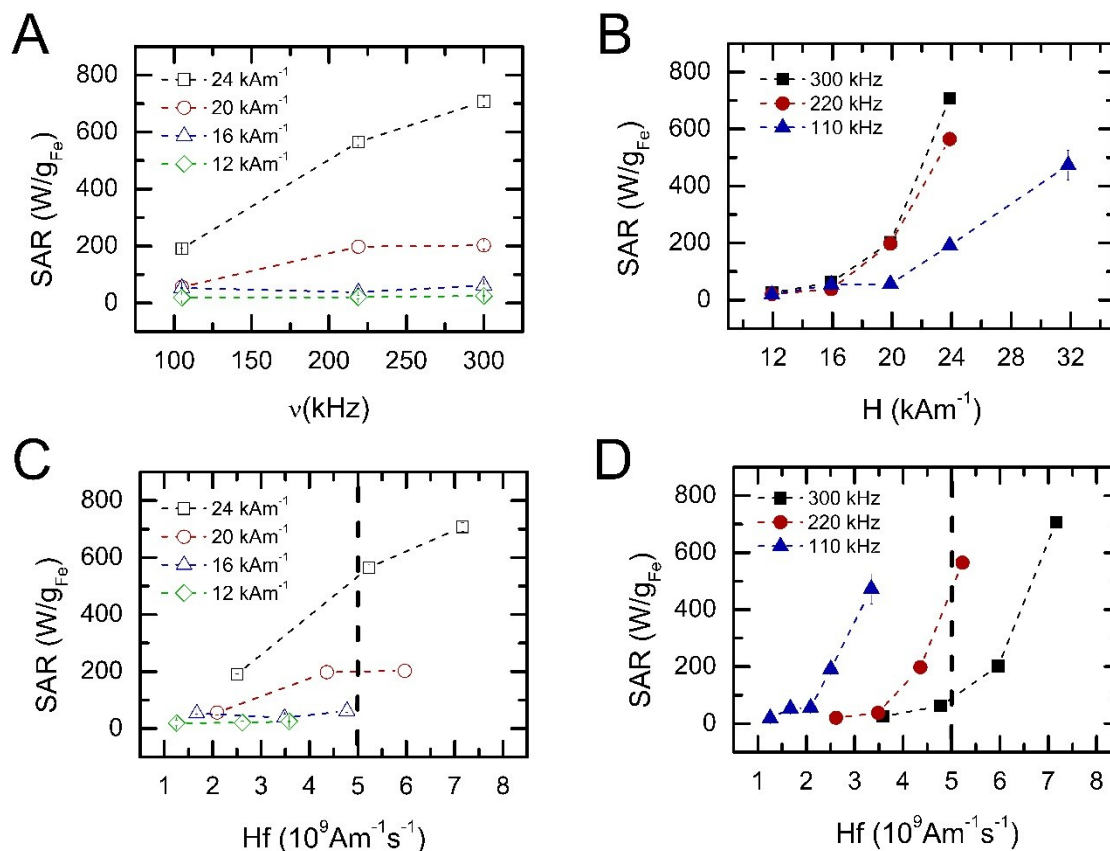
# One-pot 200



**Fig. S15.** SAR values for gold-iron oxide dimers prepared by one-pot method at 200°C as a function of: A) Frequency at different applied magnetic field amplitudes 24 kA m<sup>-1</sup> (open black squares  $\square$ ), 20 kA m<sup>-1</sup> (red open circles  $\circ$ ), 16 kA m<sup>-1</sup> (blue open triangles  $\triangle$ ) and 12 kA m<sup>-1</sup> (green open rhombi  $\diamond$ ). B) Applied Magnetic field at different frequencies 300 kHz (black squares  $\blacksquare$ ), 220 kHz (red circles  $\bullet$ ) and 110 kHz (blue triangles  $\blacktriangle$ ). C) The H·f factor at different applied magnetic field amplitudes 24 kA m<sup>-1</sup> (open black squares  $\square$ ), 20 kA m<sup>-1</sup> (red open circles  $\circ$ ), 16 kA m<sup>-1</sup> (blue open triangles  $\triangle$ ) and 12 kA m<sup>-1</sup> (green open rhombi  $\diamond$ ). And D) as a function of the H·f factor at different frequencies 300 kHz (black squares  $\blacksquare$ ), 220 kHz (red circles  $\bullet$ ) and 110 kHz (blue triangles  $\blacktriangle$ ). Dimers were synthesized by using 0,06 mmols of iron pentacarbonyl injected at 150 °C in a solution of oleylamine, oleic acid, HAuCl<sub>4</sub>·3H<sub>2</sub>O and 1-Octadecene before heating up the mixture up to 200 °C for 90 minutes. Each experimental data point was calculated as the mean value of at least 4 measurements and error bars indicate the standard deviation.

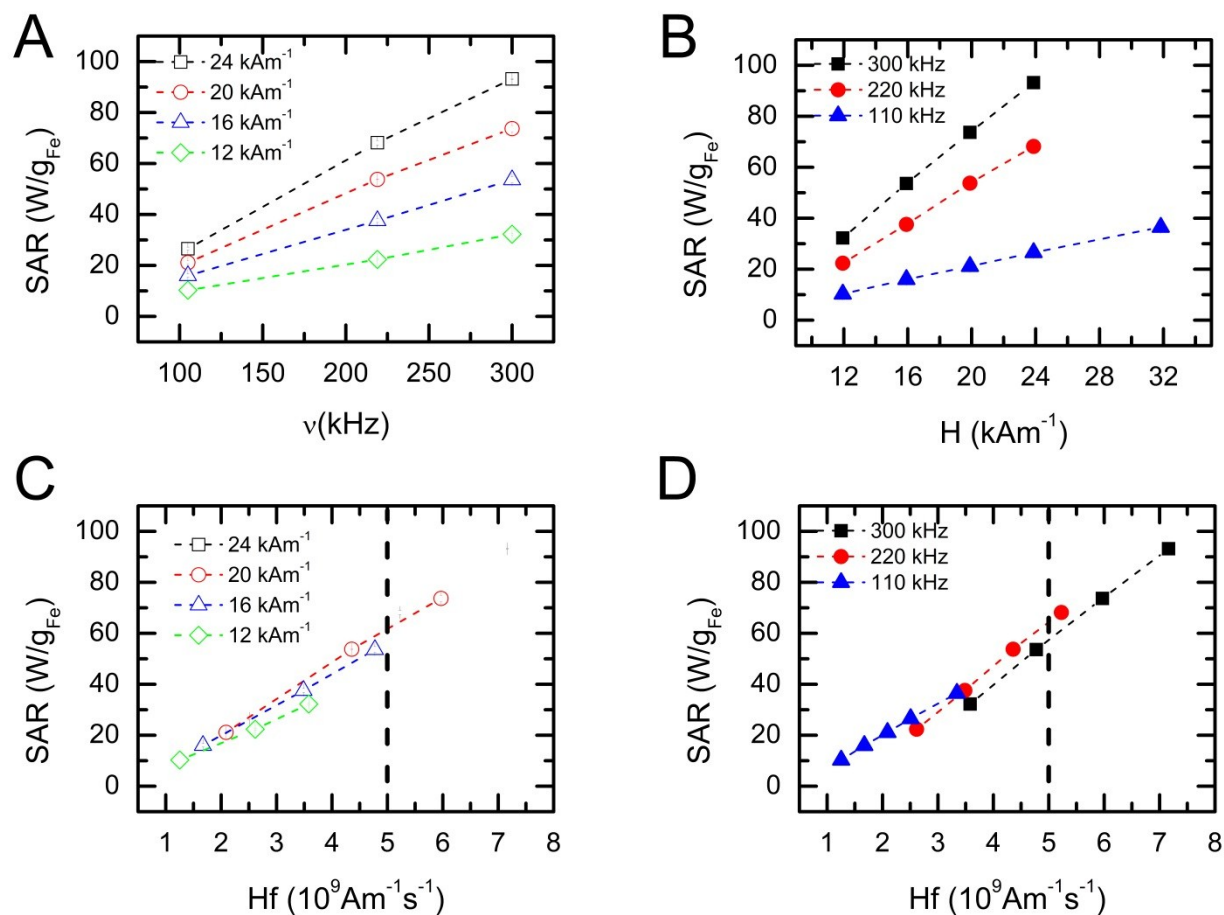


# One-pot 300



**Fig. S16.** SAR values for gold-iron oxide dimers prepared by the one-pot 300 approach. SAR are reported as a function of: **A**) Frequency at different applied magnetic field amplitudes 24 kAm<sup>-1</sup> (open black squares  $\square$ ), 20 kAm<sup>-1</sup> (red open circles  $\circ$ ), 16 kAm<sup>-1</sup> (blue open triangles  $\triangle$ ) and 12 kAm<sup>-1</sup> (green open rhombi  $\diamond$ ). **B**) Applied Magnetic field at different frequencies 300 kHz (black squares  $\blacksquare$ ), 220 kHz (red circles  $\bullet$ ) and 110 kHz (blue triangles  $\blacktriangle$ ). **C**) The H-f factor at different applied magnetic field amplitudes 24 kAm<sup>-1</sup> (open black squares  $\square$ ), 20 kAm<sup>-1</sup> (red open circles  $\circ$ ), 16 kAm<sup>-1</sup> (blue open triangles  $\triangle$ ) and 12 kAm<sup>-1</sup> (green open rhombi  $\diamond$ ). And **D**) H-f factor at different frequencies 300 kHz (black squares  $\blacksquare$ ), 220 kHz (red circles  $\bullet$ ) and 110 kHz (blue triangles  $\blacktriangle$ ). Dimers were synthesized by using a modified protocol in which 0,06 mmols of iron pentacarbonyl were injected at 150 °C in a solution of oleylamine, oleic acid, HAuCl<sub>4</sub>·3H<sub>2</sub>O and 1-Octadecene. The resulting mixture was heated up to 200 °C and kept for 90 minutes. Finally the solution was heated up to 300 °C and kept at this temperature for 60 minutes. Each experimental data point was calculated as the mean value of at least 4 measurements and error bars indicate the standard deviation.

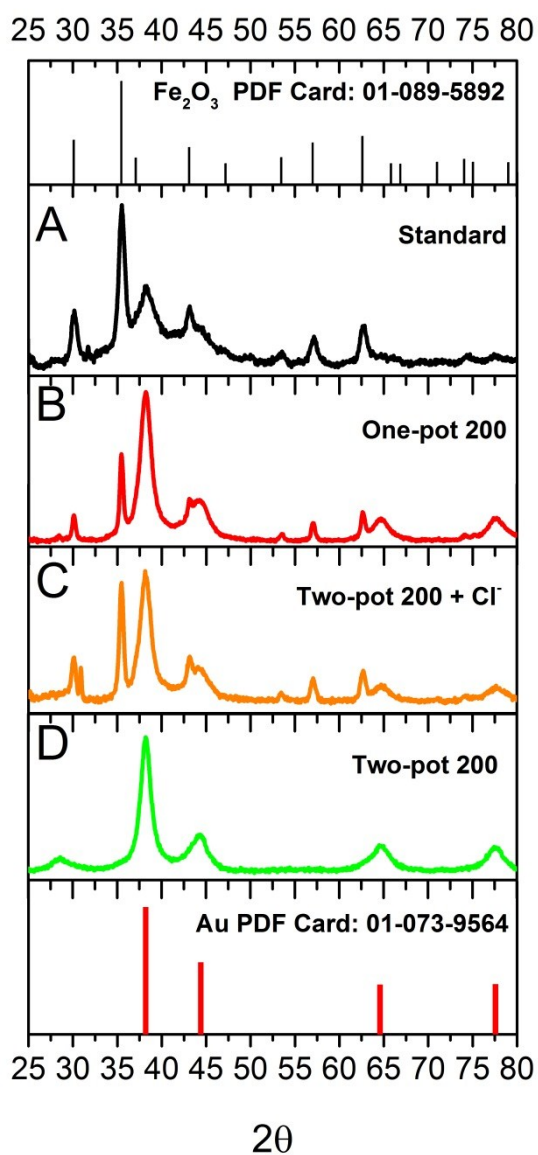
# Standard



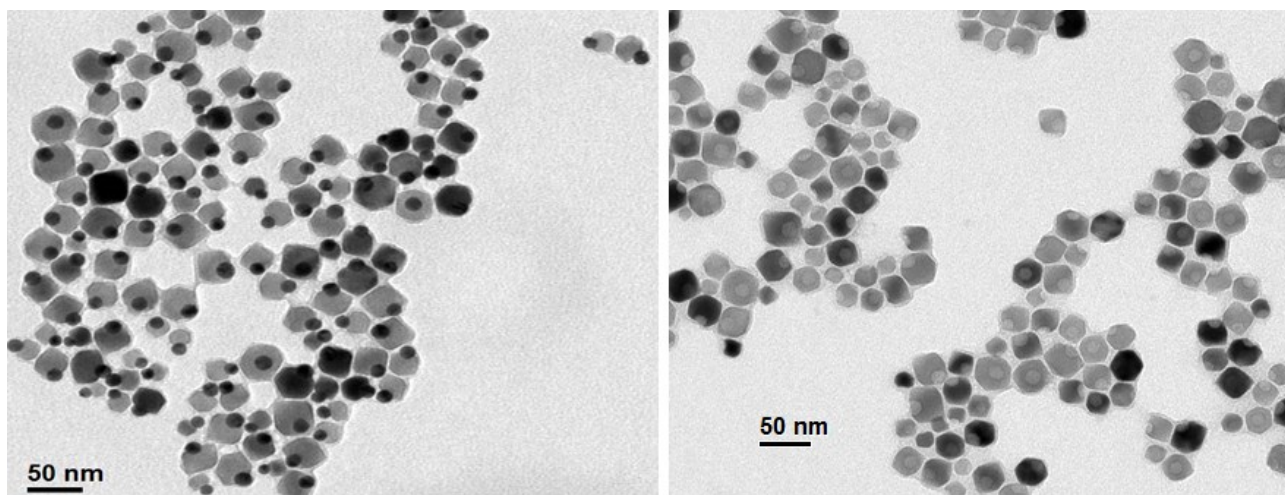
**Fig. S17.** SAR values for gold-iron oxide dimers prepared by literature method as a function of: **A)** Frequency at different applied magnetic field amplitudes 24 kA m<sup>-1</sup> (open black squares  $\square$ ), 20 kA m<sup>-1</sup>, (red open circles  $\circ$ ), 16 kA m<sup>-1</sup> (blue open triangles  $\triangle$ ) and 12 kA m<sup>-1</sup> (green open rhombi  $\diamond$ ). **B)** Applied Magnetic field at different frequencies 300 kHz (black squares  $\blacksquare$ ), 220 kHz (red circles  $\bullet$ ) and 110 kHz (blue triangles  $\blacktriangle$ ). **C)** The H·f factor at different applied magnetic field amplitudes 24 kA m<sup>-1</sup> (open black squares  $\square$ ), 20 kA m<sup>-1</sup>, (red open circles  $\circ$ ), 16 kA m<sup>-1</sup> (blue open triangles  $\triangle$ ) and 12 kA m<sup>-1</sup> (green open rhombi  $\diamond$ ). And **D)** as a function of the H·f factor at different frequencies 300 kHz (black squares  $\blacksquare$ ), 220 kHz (red circles  $\bullet$ ) and 110 kHz (blue triangles  $\blacktriangle$ ). Dimers were synthesized by using a standard reported procedure in which 0,06 mmols of iron pentacarbonyl were injected at 150 °C in a solution of oleylamine, oleic acid, HAuCl<sub>4</sub>·3H<sub>2</sub>O, 1,2- HDDOL and 1-Octadecene before heating up the mixture up to 300 °C for 30 minutes. Each experimental data point was calculated as the mean value of at least 4 measurements and error bars indicate the standard deviation.

### X-Ray Diffraction

XRD measurements were performed on a Rigaku SmartLab X-ray diffractometer operating at 40 kV and 150 mA. The diffractometer was equipped with Cu source and a Gobel mirror in order to have a parallel beam and it was used in 2-theta/omega scan geometry for the acquisition of the data. Specimens for XRD measurement were prepared by dropping a concentrated solution of dimers onto a zero background silicon substrate.



**Fig. S18.** XRD patterns for of gold-iron oxide dimers synthesized by using different approaches: A) standard approach , B) One-pot at 200 °C, C) Premade at 200 °C with chloride ions and D) Premade at 200 °C without chloride ions. Patterns were compared to the Au (PDF Card: 01-073-9564) and  $\text{Fe}_2\text{O}_3$  (PDF Card: 01-089-5892) cards.



**Fig. S19.** TEM image of gold-iron oxide dimers with iron oxide domain of 26 nm and gold domain of 13 nm deposited from a water solution (A). TEM image of the same dimers after having etched the gold with Lugol solution (B).

#### ***Elemental Analysis***

An inductively coupled plasma atomic emission spectrometer (ICP-AES, iCAP 6500, Thermo) was used for the elemental analysis of iron and gold and thus allowing to evaluate corresponding concentrations of IONCs. The samples were prepared by digestion of 25  $\mu\text{L}$  of dimer solution in 2.5 mL of *aqua regia* overnight. Subsequently, the sample was diluted with deionized water to a final volume of 25 mL and used for the elemental analysis.

**Table 1.** Synthesis conditions for the samples reported in the main text and in the SI. Note that the amounts of ODE, OLA and OA are reported in the experimental section.

Samples	Procedure	HAuCl <sub>4</sub> (mmols)	Fe(CO) <sub>5</sub> (mmols)	1.2-HDDOL (mmols)	HCl(2M)* (mmols)	1.2 DCl† (mmols)	FeCl <sub>3</sub> ·6H <sub>2</sub> O (mmols)	T (°C)
Fig. 1B	Two-pot		0.6		-			200
Fig. 1C	Two-pot		0.6					300
Fig. 1D	One-pot	0.12	0.6					200
Fig. 1E	One-pot	0.12	0.6					300
Fig. 2A	Two-pot		0.6		0.12			200
Fig. 2C	Two-pot		0.6		0.24			200
Fig. 2E	Two-pot		0.6		0.48			200
Fig. 3C	One-pot	0.12	0.6					200
Fig. S2A	Two-pot		0.6			0.62		200
Fig. S2C	Two-pot		0.6			1.25		200
Fig. S3	One-pot	0.12	0.6					200
Fig. S4A	One-pot	0.12	0.6					200
Fig. S4B	One-pot	0.12	0.6					200
Fig. S4C	One-pot	0.12	0.6					200
Fig. S5A	One-pot	0.12	0.6					200
Fig. S5B	One-pot	0.12	2.25					200
Fig. S5C	One-pot	0.12	2.25		0.2			200
Fig. S6	Two-pot						0.6	300
Fig. S7A	One-pot	0.12	0.6					150
Fig. S7B	One-pot	0.12	0.6					200
Fig. S7C	One-pot	0.12	0.6					300
Fig. S7D	One-pot	0.12	0.6	10				150
Fig. S7E	One-pot	0.12	0.6	10				200
Fig. S7F	One-pot	0.12	0.6	10				300
Fig. S8A	Standard	0.12	2	10				200
Fig. S8B	Standard	0.12	2	10				300
Fig. S9A	Standard	0.12	0.3	10				300
Fig. S9B	Standard	0.12	0.6	10				300
Fig. S9C	Standard	0.12	1.25	10				300
Fig. S9D	Standard	0.12	2.25	10				300
Fig. S11A	Standard	0.12	2	10				300
Fig. S11B	Two-pot		0.6					200
Fig. S11C	Two-pot		0.6					300
Fig. S11D	One-pot	0.12	0.6					200
Fig. S11E	One-pot	0.12	0.6					300
Fig. S19	One-pot	0.12	0.6					200

\*HCl(2M)= HCl in Diethyl Ether 2M

†1.2-DCL=1.2-Dichloroethaner



Mössbauer spectra were recorded in transmission geometry using a <sup>57</sup>Co/Rh γ-ray source mounted on an electromagnetic driving unit submitted to a triangular velocity form. Experiments were carried out at 300K and 77K using a bath cryostat. The samples were prepared by drying ferrofluid solution containing both Au and Fe oxide nanoparticles: the quantity of powder is optimized to about 3 mg of Fe/cm<sup>2</sup>, slightly lower than the usual 5 mg of Fe/cm<sup>2</sup>, in order to establish an efficient compromise between Fe and Au elements.

The fitting procedure was done using the home-made unpublished MOSFIT software involving magnetic sextets and quadrupolar components with lorentzian lines.

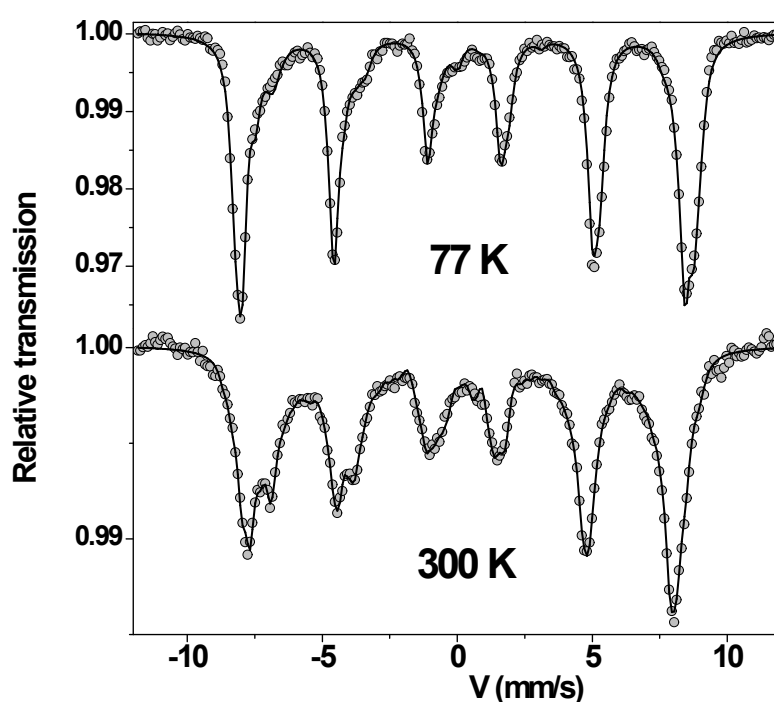


Fig S20: Mössbauer spectra at 300 and 77 K. As shown, the hyperfine structures are very complex because of the presence of both maghemite and magnetite in addition to that of superparamagnetic relaxation phenomena (particularly at 300 K) contributing to broaden the lines. The modelling at 300 K consists in considering 2 overlapped distributions of hyperfine fields, corresponding to octahedral and tetrahedral Fe species while that at 77 K results from a discrete number of magnetic components. The relevant parameter is the mean value of the isomer shift ( $0.44 \pm 0.01$  and  $0.55 \pm 0.01$  mm/s at 300K and 77K, respectively) which gives rise to an estimation of the mean valency state and consequently to the Fe atomic proportions of maghemite ( $46 \pm 2\%$  and  $48 \pm 2\%$ , respectively) and magnetite ( $54 \pm 2\%$  and  $52 \pm 2\%$ , respectively), assuming

ideal stoichiometric phases and the same values of the recoilless Lamb-Mössbauer  $f$  factor. For sake of simplicity we labelled the dimers as  $\text{Au-Fe}_x\text{O}_y$ .