

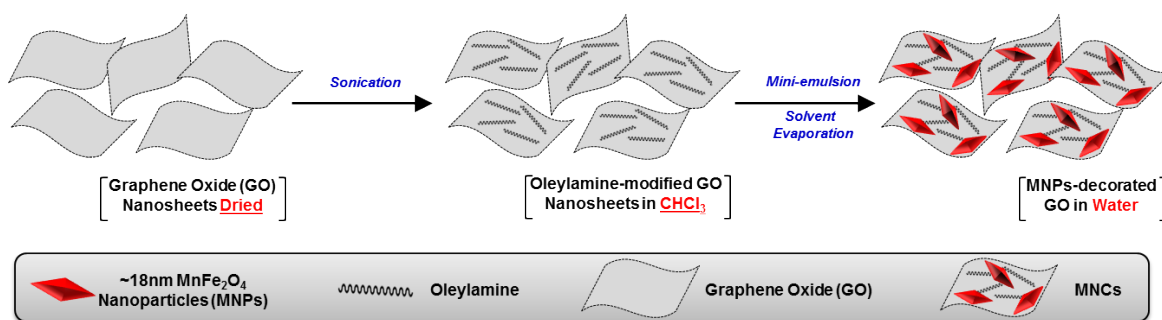
Supporting Information for

**Concentration-dependent Magnetic Hyperthermic Response of Manganese Ferrite-loaded Ultrasmall Graphene Oxide Nanocomposites**

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**S1. MNCs formation**



**Fig. S1** Formation of MNCs from MNPs. (Step 1) Dried graphene oxide were mixed with oleylamine and sonicated to allow graphene oxide to disperse in chloroform. (Step 2) MNPs in chloroform were mixed with graphene oxide disperse in chloroform (with oleylamine attached) and the mixture undergone mini-emulsion/solvent evaporation process. The resultant would be MNPs-decorated GO dispersed in water.

The overall formation of water soluble MNCs is illustrated in **Fig.S1** above.

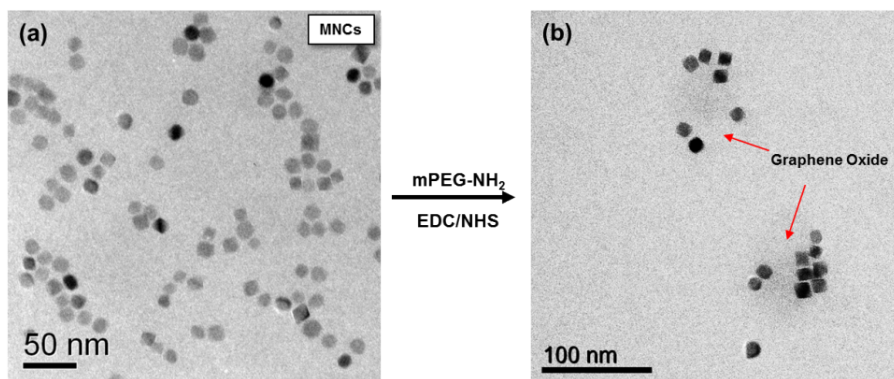
**S2. Scherrer Size**

From the x-ray diffraction (XRD) pattern of MNPs and MNCs given in **Figure 1c** of the manuscript, the mean size of the manganese ferrite crystallites can be calculated from the Scherrer formula:

$$t = \frac{0.9\lambda}{B\cos(\theta)} \quad \dots(1)$$

where  $t$  is the average crystallite size (nm),  $\lambda$  is the wavelength of the x-ray source ( $\lambda_{\text{Cu-K}\alpha} = 0.15418$  nm),  $B$  is the full-width half-maximum (FWHM) of the diffraction peak,  $\theta$  is the diffraction angle. From the Scherrer formula, the average size of the manganese ferrite crystallites can be calculated using the FWHM of the most intense (311) peak. For MNPs and MNCs, the average crystallite size was calculated to be 18.14 and 18.55 nm respectively.

### S3. HRTEM of MNCs

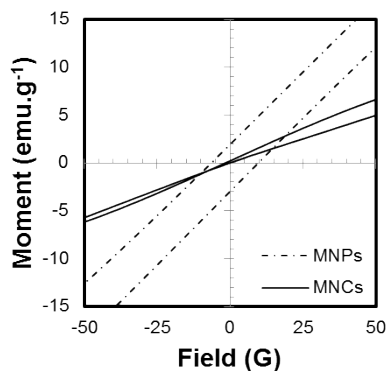


**Fig. S2** High magnification TEM image of (a) MNCs dispersed in water and (b) MNCs-tagged with PEG (MW 5000) dispersed in water.

The low contrast of ultra-small GO sheet does not allow the presence of GO to be observed under TEM. However, a further experiment to enhance the contrast was done by tagging MNCs with higher molecular weight polymer mPEG-NH<sub>2</sub> (MW5000) using carbodiimide chemistry, EDC/NHS reagent. The high magnification TEM image of MNCs-tagged with PEG showed a slight contrast enhancement which indicated the presence of the sheet-like structure. It was clear that the nanoparticles were well anchored on GO sheets. From the image, the lateral size matched very well with the AFM analysis. (**Fig. 4**).

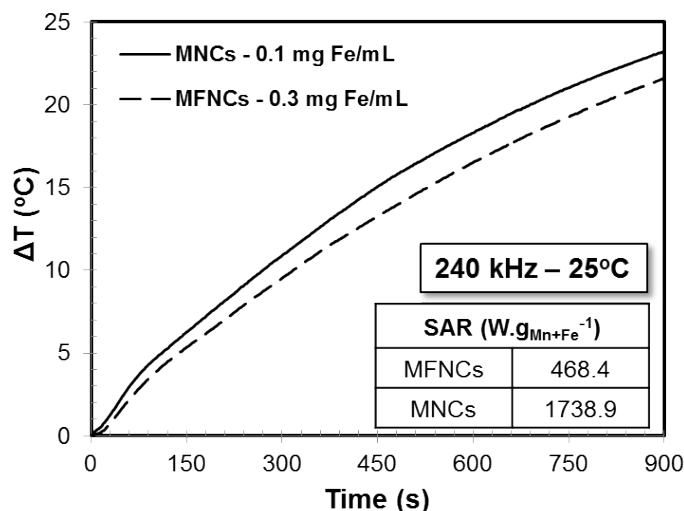
### S4. MNPs and MNCs Hysteresis Loop

The close-up view of the hysteresis loop profile of MNPs and MNCs near the zero field, in **Fig. S3**, suggested that both MNPs and MNCs only exhibited negligible remnant magnetization and coercive field which were typically the characteristic behavior of superparamagnetic materials.



**Fig. S3** A close-up view of the hysteresis loops of MNPs and MNCs at room temperature (300K) near zero field.

## S5. Hyperthermic Response of Amphiphilic Polymer-coated MNPs



**Fig. S4.** Time-dependent temperature curve of MNPs decorated on oleylamine-modified GO (0.1 mg Fe.mL<sup>-1</sup>) and MNPs water solubilized by using amphiphilic copolymer based on PMAO (denoted as MFNCs; 0.3 mg Fe.mL<sup>-1</sup>) at 60 kA.m<sup>-1</sup> with 240kHz frequency (inset: SAR values).

**Fig.S4** depicted time-dependent temperature curve of (i) MNCs sample (0.1 mg Fe.mL<sup>-1</sup>) and (ii) MNPs water solubilize inside amphiphilic copolymer based on poly (maleic anhydride-*alt*-1-octadecene) or PMAO (denoted as MFNCs; 0.3 mg Fe.mL<sup>-1</sup>). The water solubilization of MNPs using this polymer has been previously published by our group. [1] The measurements were under AMF with amplitude: 60 kA.m<sup>-1</sup> and frequency 240 kHz. From the comparison, it can be seen that even at concentration of 0.3 mg Fe.mL<sup>-1</sup>, the heating efficiency was far below 0.1 mg Fe.mL<sup>-1</sup> MNCs. The required time for 0.3 mg Fe.mL<sup>-1</sup> to reach 42°C was around 625 seconds, much longer than the required time for 0.1 mg Fe.mL<sup>-1</sup> MNCs to reach 42°C (535 seconds). Such results clearly demonstrated that the use of GO actually allow faster MNPs relaxation as compared to the polymer coating. When polymer coating was used, the presence of “encapsulation” coating acted as heat barrier (low heat conductivity) that slow down the heat release to the solvent/environment.

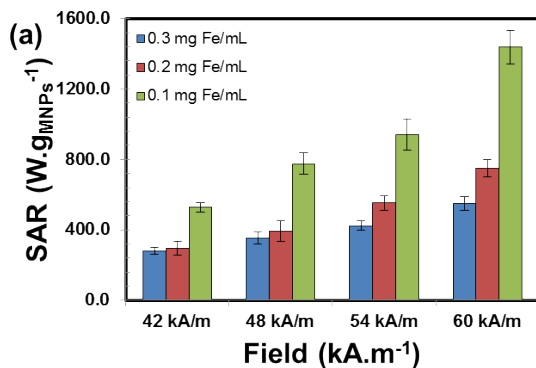
## S6. Hyperthermia – Physiological Limitation

**Table S1.** Tabulated ( $Hf$ ) values used in experiment.

Field $H$ ( $\text{kAm}^{-1}$ )	Frequency (kHz)	$Hf$ ( $\text{A.m}^{-1}\text{s}^{-1}$ )
42	240	$1.01 \times 10^{10}$
48	240	$1.15 \times 10^{10}$
54	240	$1.30 \times 10^{10}$
60	240	$1.44 \times 10^{10}$

The presence of alternating magnetic field indeed would induce a nonselective heating of both cancerous as well as healthy tissue due to the autonomously generated eddy current. The limitation of  $Hf < C$  reported by R. Hergt and S. Dutz, was based on 10 cm diameter coil (where  $H$  is the amplitude of alternating magnetic field,  $f$  is the frequency,  $C$  is the constant,  $C = 5 \times 10^9 \text{ Am}^{-1}\text{s}^{-1}$ ). [2] In our experiment, coil with 3.4 cm diameter was used as opposed to 10 cm diameter used in the Hertz and Dutz. As reported by Dipak *et al.*, since the energy absorbed due to eddy currents is known to be proportional to the exposure area of the tissues ( $E_{\text{Eddy}} \sim D^2$ , where  $D$  is the diameter of coil), the  $Hf$  limit can be extended to around nine-times ( $\sim 8.65$  times) as compared to the limit reported by, *i.e.*  $\sim 4\text{--}4.5 \times 10^{10} \text{ Am}^{-1}\text{s}^{-1}$ . [3] Therefore, based on our experimental set-up, field amplitude of 42 – 60  $\text{kA.m}^{-1}$  and 240 kHz frequency resulted in  $Hf$  that can be considered well below the limit ( $\sim 1\text{--}1.5 \times 10^{10} \text{ Am}^{-1}\text{s}^{-1}$ , see **Table S1**).

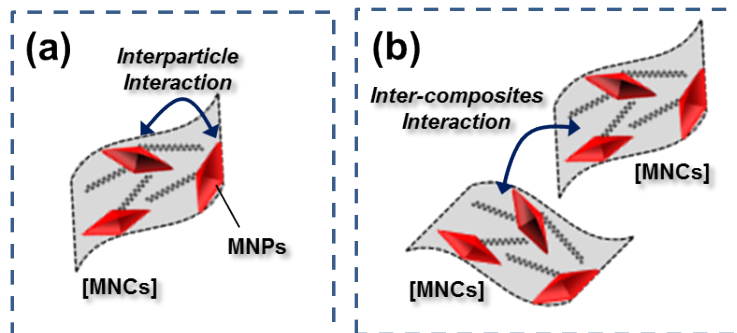
## S7. MNCs - Hyperthermia Results



(b) SAR ( $\text{W.gMNP}^{-1}$ )	Field ( $\text{kA.m}^{-1}$ )			
	42	48	54	60
0.3 mg Fe.mL <sup>-1</sup>	$280.8 \pm 17.8$	$353.4 \pm 34.4$	$424.1 \pm 25.7$	$550.9 \pm 40.0$
0.2 mg Fe.mL <sup>-1</sup>	$294.8 \pm 38.2$	$393.6 \pm 38.2$	$553.4 \pm 42.9$	$750.9 \pm 49.2$
0.1 mg Fe.mL <sup>-1</sup>	$528.7 \pm 28.0$	$775.6 \pm 28.0$	$941.1 \pm 87.3$	$1437.8 \pm 96.6$

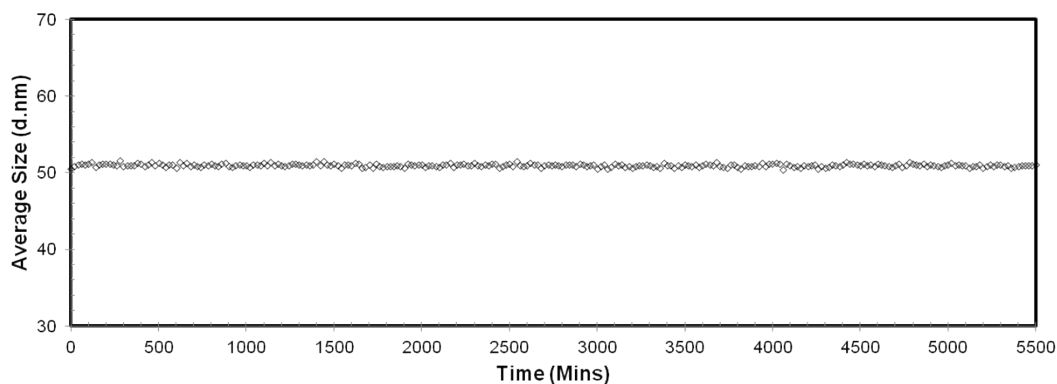
**Fig. S5.** (a) Histogram plot of the MNCs SAR values and (b) tabulated SAR values of MNCs, measured at 240 kHz frequency at various concentration and applied alternating magnetic field (AMF). The SAR values were expressed in the ferrite/oxide mass.

The SAR values of the MNCs samples in water measured at 240kHz frequency at various concentration and at various applied alternating magnetic field (AMF) were plotted in a histogram (see **Fig. S5a**). The respective SAR values were given in the table shown in **Fig. S5b**.



**Fig. S6.** Schematic illustration of (a) interparticle interaction and (b) inter-composites interactions.

## S7. MNCs – Colloidal Stability



**Fig. S7.** Time-dependent hydrodynamic size of MNCs in water at 37°C.

The magnetic nanocomposites MNCs were highly stable in water at 37°C. No significant aggregation was observed from the dynamic light scattering (DLS) experiment up to more than 90 hours, as suggested in **Fig. S7**.

## Reference

- [1]. E. Peng, E. S. G. Choo, C. S. H. Tan, X. Tang, Y. Sheng and J. Xue, *Nanoscale*, 2013.
- [2]. R. Hergt and S. Dutz, *J. Magn. Magn. Mater.*, 2007, **311**, 187-192.
- [3]. D. Maity, P. Chandrasekharan, C.-T. Yang, K.-H. Chuang, B. Shuter, J.-M. Xue, J. Ding and S.-S. Feng, *Nanomedicine*, 2010, **5**, 1571-1584.