

Supplementary material

Robust Water-Based Synthesis of Monodisperse Ultrasmall SPIONs with Tunable T₁-T₂ Relaxometric Behaviour as MRI Contrast Agents

Daniela Meroni,^{1,2} Davide Cicolari,^{3,4} Giorgia Colciago,⁵ Tommaso Taroni,¹ Laura Rossi,⁶ Marco Maria Jacopo Felisi,³ Paola Enrica Colombo,³ Francesco Orsini,^{2,4} Riccardo Vago,^{5,7} Daniela Maggioni,^{1,2,*} Paolo Arosio^{2,4}

¹ *Department of Chemistry, Università degli Studi di Milano, Italy*

² *Consorzio INSTM, Florence, Italy*

³ *Department of Medical Physics, ASST Grande Ospedale Metropolitano Niguarda - Milano, Italy*

⁴ *Department of Physics, Università degli Studi di Milano, Italy*

⁵ *Urological Research Institute, Division of Experimental Oncology, IRCCS San Raffaele Scientific Institute, Via Olgettina, 60, 20132 Milano, Italy*

⁶ *Chemical Engineering Department, TUDelft, The Netherlands*

⁷ *Università Vita-Salute San Raffaele, Via Olgettina, 58, 20132 Milano, Italy*

** Corresponding author: daniela.maggioni@unimi.it*

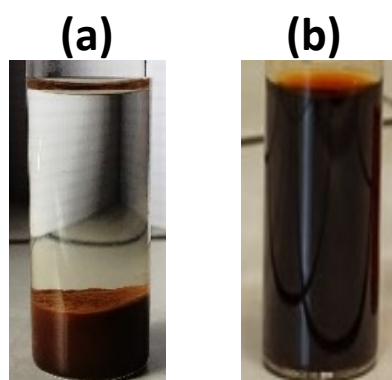


Figure S1. Digital pictures of magnetic nanoparticles synthesized by using as base (a) ammonia, (b) TMAOH.

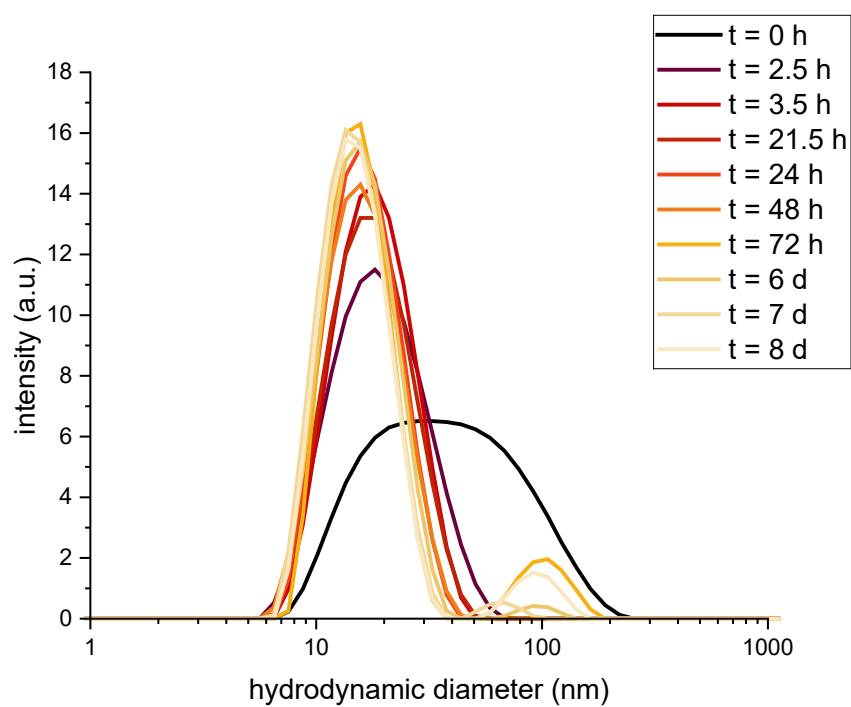


Figure S2. DLS measurements over time of **MNP-6.6** prepared using 50 μL of citric acid to quench the growth step.

Table S1 – Optimization of the citric acid amount added at the end of the growth step: volume of 3.2 M citric acid aqueous solution added; pH after 20 minutes from the citric acid addition; hydrodynamic diameter by DLS ($\bar{D}_h$) immediately after synthesis and after 7 days.

$V_{\text{citric acid}} \text{ (}\mu\text{L)}$	pH at t = 0	$\bar{D}_h$ at t = 0 (nm)	$\bar{D}_h$ at t = 7 days (nm)
63	3.6	8	n.a.
50	4.5	13	13
38	5	20	22
25	6.5	overlapping peaks at ca. 30 and 120 nm	overlapping peaks at ca. 30 and 100 nm

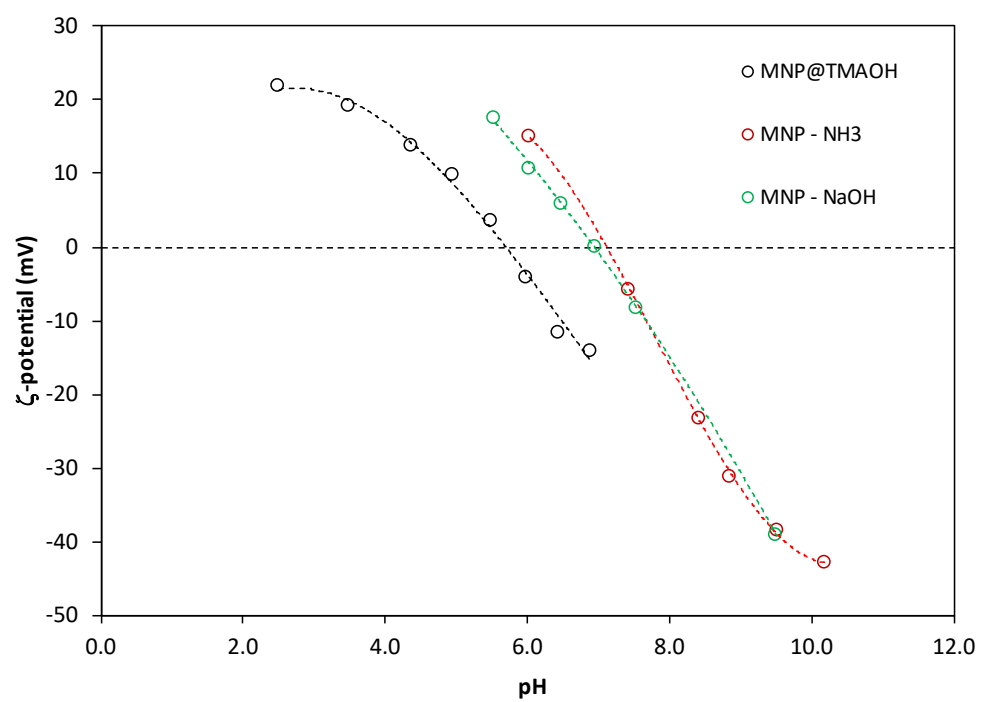


Figure S3. ζ -potential curves as a function of pH for MNPs synthesized with TMAOH, NH_3 or NaOH.

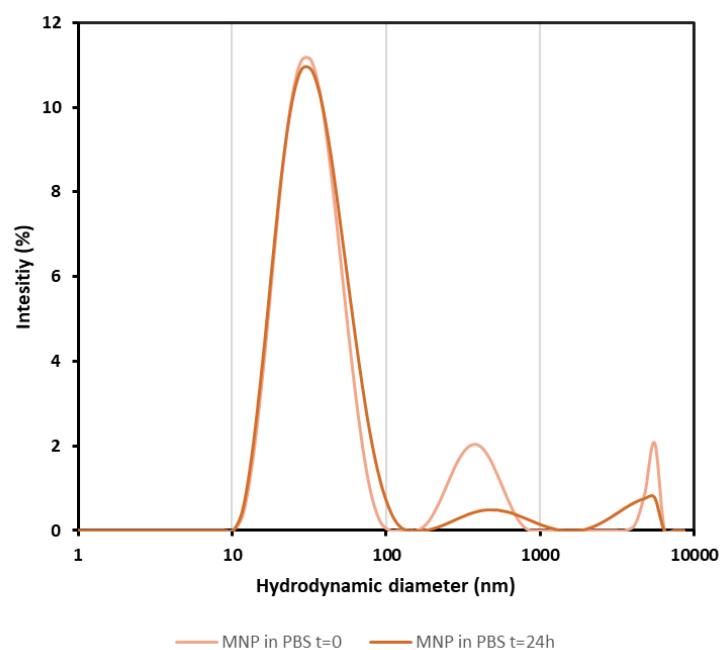


Figure S4. DLS size distribution by intensity of MNP@citrate in 0.01 M PBS at $t=0$ and after 24 h at room temperature.

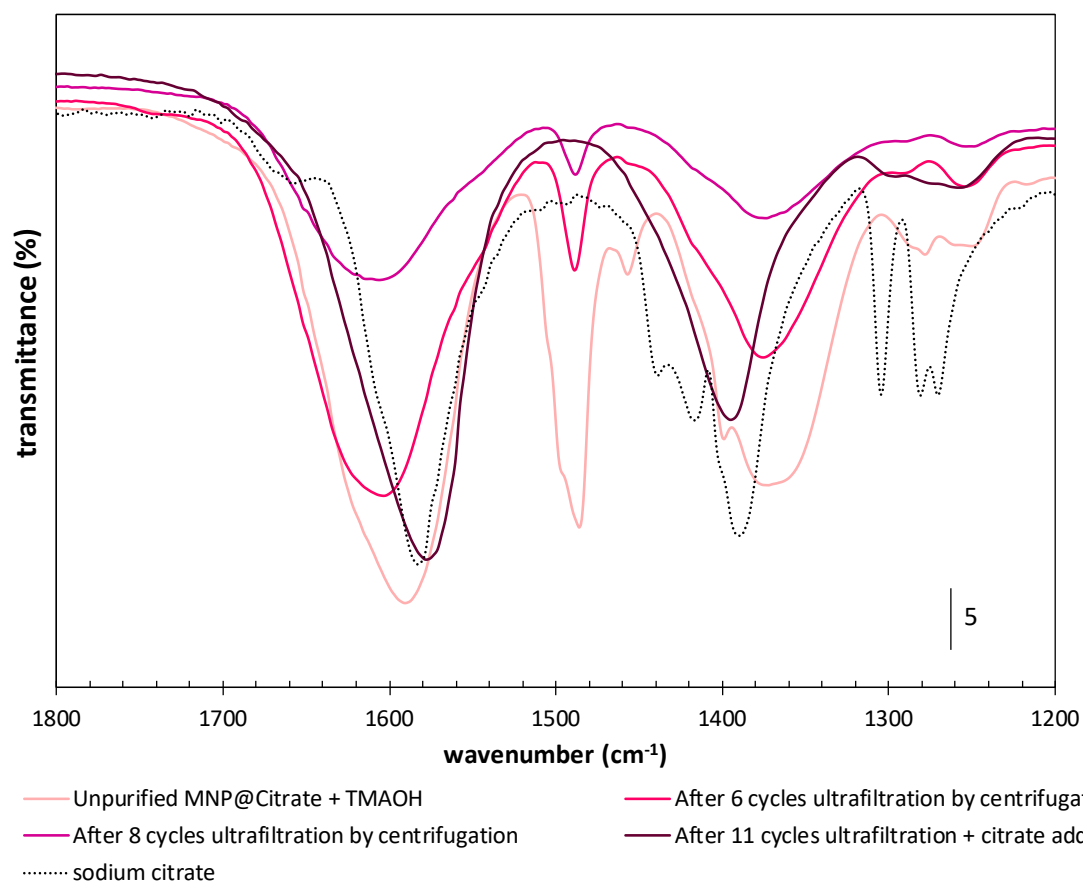


Figure S5. ATR-FTIR spectra before and after purification by ultrafiltration by centrifugation: effect of the number of centrifugation cycles and of the addition of sodium citrate as stabilizer.

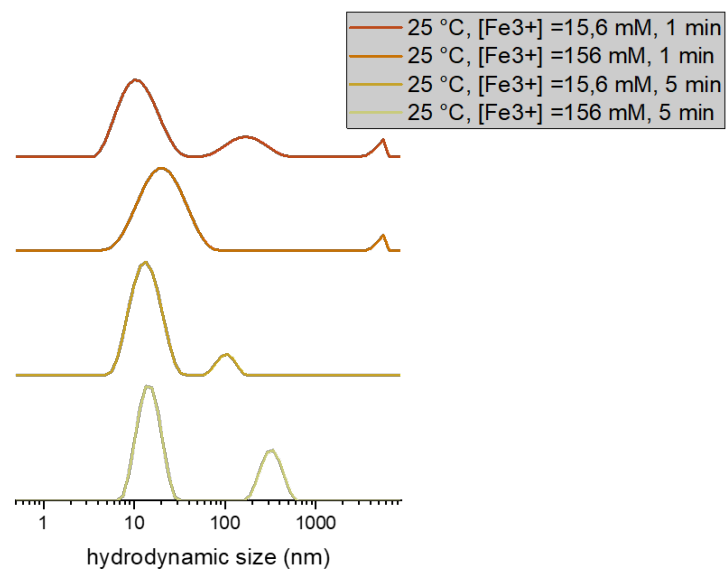


Figure S6. DLS size distribution by intensity of samples synthesized at different concentrations (156 and 15.6 mM), and different growth times (1 and 5 min), all other parameters being equal ([TMAOH]/[Fe³⁺] = 4.8, 25 °C).

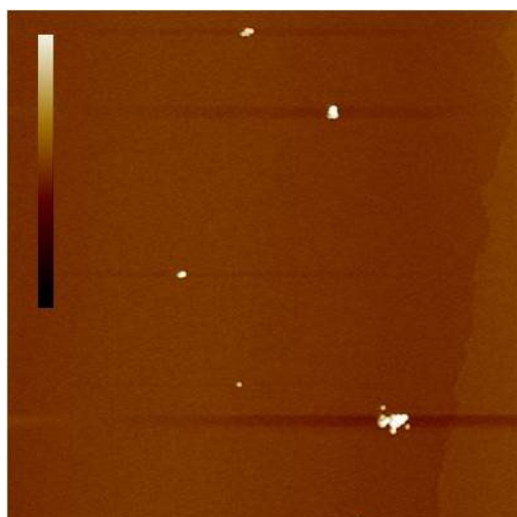


Figure S7. AFM topography image of the MNP-4.0 sample on a mica support. Scan area: $1 \times 1 \mu\text{m}^2$. Vertical false-colour scale bar: 15 nm.

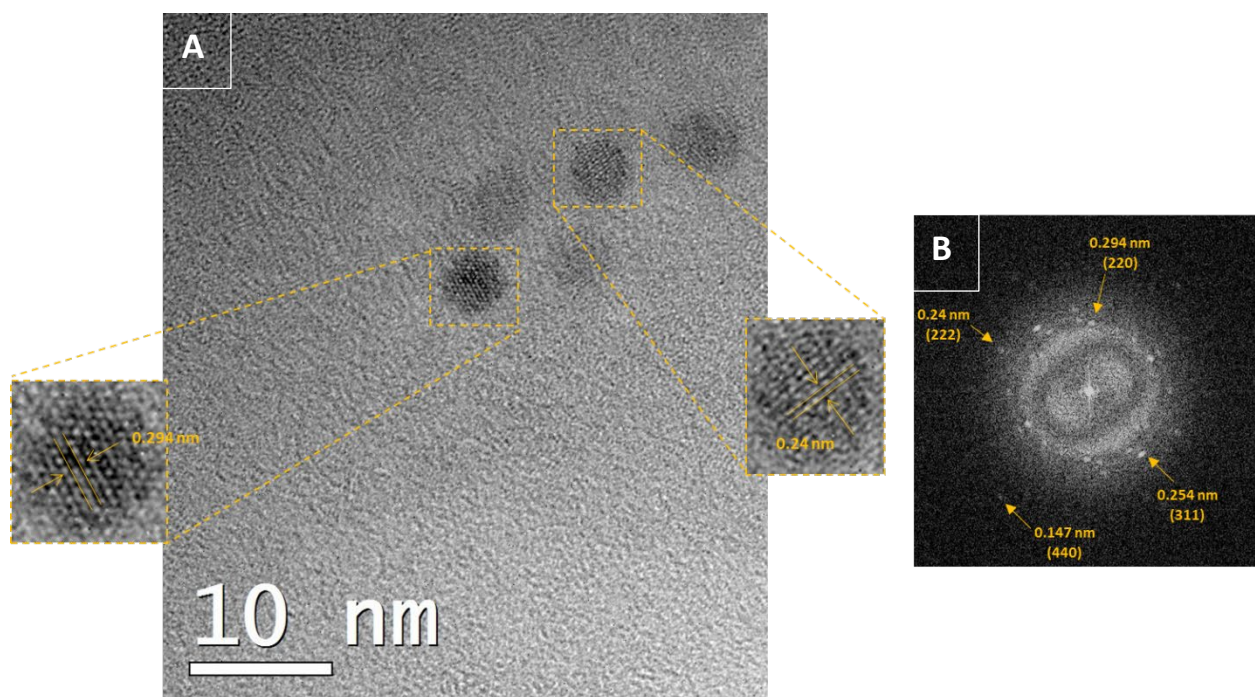


Figure S8. HRTEM analysis of **MNP-5.3**: HRTEM image (A) and corresponding fast Fourier transform (FFT) image (B). Inset magnified images of two nanoparticles highlighting two different interplanar distances.

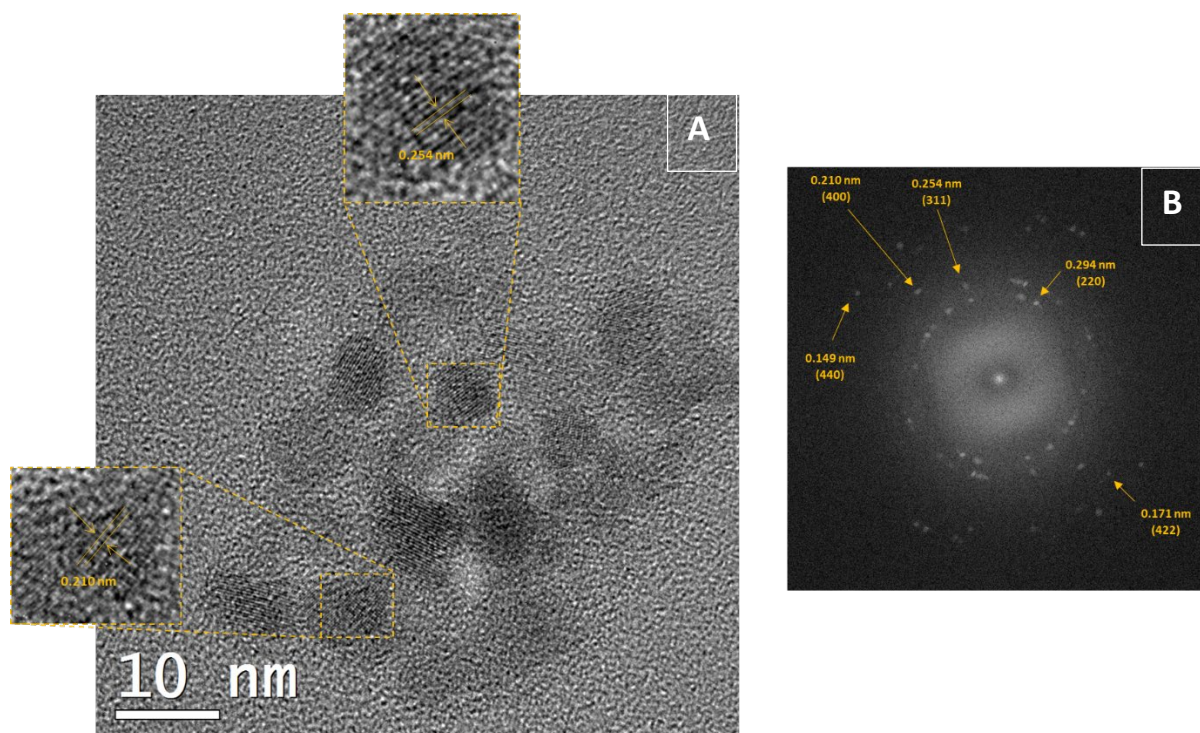


Figure S9. HRTEM analysis of **MNP-4.0**: HRTEM image (A) and corresponding fast Fourier transform (FFT) image (B). Inset magnified images of two nanoparticles highlighting two different interplanar distances.

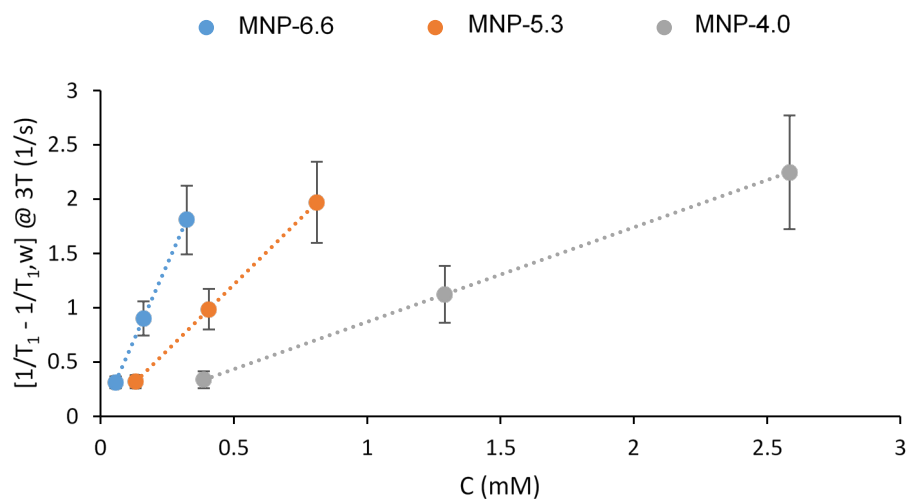


Figure S10. Longitudinal relaxation time (T_1) dependence as a function of MNP concentration (C) for the **MNP-6.6**, **MNP-5.3**, and **MNP-4.0** samples.

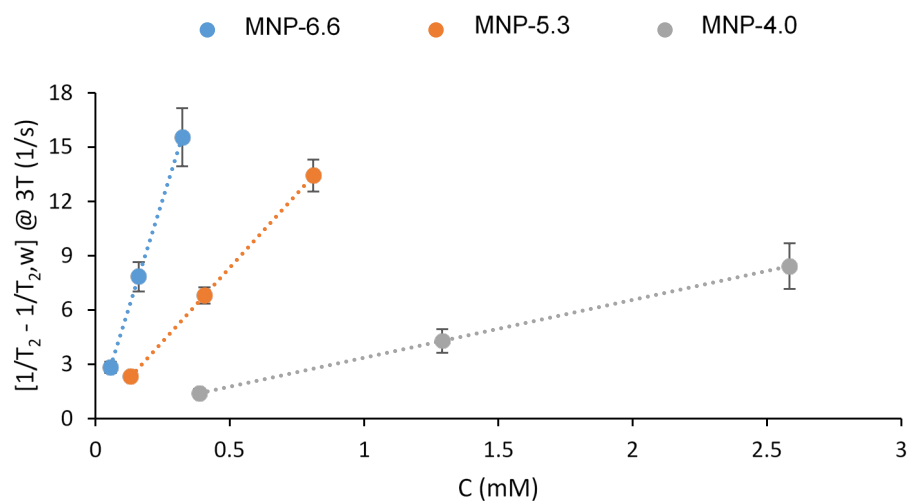


Figure S11. Transverse relaxation time (T_2) dependence as a function of MNP concentration (C) for the **MNP-6.6**, **MNP-5.3**, and **MNP-4.0** samples.