

**Synthesis of double-responsive magnetic latex particles via seeded emulsion polymerization using macroRAFT block copolymers as stabilizers**

*Thiago Rodrigues Guimarães, Muriel Lansalot, \* Elodie Bourgeat-Lami\**

Univ Lyon, Université Claude Bernard Lyon 1, CPE Lyon, CNRS, UMR 5265, Chemistry, Catalysis, Polymers and Processes (C2P2), 43, Bd. du 11 Novembre 1918, F-69616 Villeurbanne, France.

**SUPPORTING INFORMATION**

**Contents**

1. EXPERIMENTAL DETAILS .....	2
1.1. Materials .....	2
1.2. Methods .....	2
1.3. Characterization .....	8
2. SUPPLEMENTARY DATA .....	10
2.1. Synthesis of PDMAEMA and PDMAEMA- <i>b</i> -PS macroRAFT .....	10
2.2. Clusters formation .....	12
2.3. Magnetic latex particles .....	13
2.4. Magnetic properties of FA@IONP, clusters and hybrid particles .....	14
2.5. Thermo-responsive properties of PDMAEMA-TTC .....	16
3. REFERENCES .....	16

# 1. EXPERIMENTAL DETAILS

## 1.1. Materials.

The RAFT agent, 4-cyano-4-thiothiopropylsulfanylpentanoic acid (CTPPA), was synthesized as described elsewhere.<sup>1</sup> The fatty acid-modified iron oxide nanoparticles (hereafter denoted as FA@IONPs, commercial name: EMG1200) were purchased from Ferrotec. The monomers, 2-dimethylaminoethyl methacrylate (DMAEMA, 99%, Sigma-Aldrich), styrene (S, 99%, Acros Organics) and divinyl benzene (DVB, 80%, Sigma-Aldrich) were used as received. 4,4'-azobis(4-cyanopentanoic acid) (ACPA, 99%), 2,2'-azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride (ADIBA, 99%, Wako), sodium nitrate (NaNO<sub>3</sub>, 99%), 1,3,5-trioxane (>99%), 1,4-dioxane (puriss. p.a., >99.5%), dimethyl sulfoxide-d<sub>6</sub> (DMSO-d<sub>6</sub>, 99%), chloroform-d (CDCl<sub>3</sub>, 99%) and petroleum ether were all purchased from Sigma-Aldrich and used with no further purification. Tetrahydrofuran (THF, HPLC, stabilized/BHT, Sigma Aldrich) and dimethyl sulfoxide (DMSO, HPLC, Biosolve) were used for SEC analyses.

## 1.2. Methods

*Synthesis of the hydrophilic poly(2-dimethylaminoethyl methacrylate) (PDMAEMA) macroRAFT agent.* PDMAEMA carrying a reactivable trithiocarbonate end group (PDMAEMA-TTC) was synthesized via RAFT-mediated solution polymerization. Before synthesizing a large batch of PDMAEMA-TTC, a polymerization was carried out to follow the kinetics of the reaction (run MR1, Table SII and Figure SI1). 0.18 mmol of RAFT agent (CTPPA), 1.2 mmol of 1,3,5-trioxane, 14.5 mmol of DMAEMA and 0.036 mmol of ACPA were introduced in a round-bottom glass flask. The mixture was diluted with 12 mL of 1,4-dioxane and the flask was purged with nitrogen for 30 min and sealed with a septum. The flask was then immersed in an oil bath at 90 °C and the reaction was conducted during 6 h. Samples were taken during the polymerization to determine the evolution of conversion as a

function of time, and that of molar masses and molar mass distributions versus conversion. The monomer conversions were determined by  $^1\text{H}$  NMR spectroscopy in  $\text{DMSO-d}_6$  from the relative integration of the protons of 1,3,5-trioxane and the vinylic protons of DMAEMA. Theoretical number-average molar masses ( $M_{n,\text{th}}$ ) were obtained using the following equation:

$$M_{n,\text{th}} = \frac{X [\text{Mon}]_0 M_{\text{Mon}}}{[\text{RAFT}]_0} + M_{\text{RAFT}} \quad (1)$$

where  $M_{\text{Mon}}$ ,  $[\text{Mon}]_0$ ,  $M_{\text{RAFT}}$  and  $[\text{RAFT}]_0$  are the molar masses and the initial concentrations of the monomer and the RAFT agent, respectively, and X is the fractional monomer conversion determined by  $^1\text{H}$  NMR.

Then, MR1 was scaled up ten times (run MR2, Table SI1 and Figure SI1) and stopped at a moderate conversion, *i.e.* around 50%, to guarantee a high chain-end functionality and avoid irreversible termination reactions often observed at high conversions. The synthesized macroRAFT was purified by precipitation, at least 3 times, in a large volume of petroleum ether, and characterized by size exclusion chromatography (SEC) (Figure SI2).

**Table SI1** – Synthesis of PDMAEMA-TTC (MR1 and MR2) and PDMAEMA-*b*-PS-TTC (MR3) via RAFT polymerization in 1,4-dioxane using CTPPA as RAFT agent.

Exp.	[Mon] (mol L <sup>-1</sup> ) <sup>a</sup>	[Mon]/ [RAFT]	[RAFT]/ [Ini]	X (NMR) (%)	$M_{n,\text{th}}^d$ (g mol <sup>-1</sup> )	$M_{n,\text{exp}}$ (g mol <sup>-1</sup> )/ $\mathcal{D}$	
						THF-SEC <sup>e</sup>	DMF-SEC <sup>f</sup>
MR1	1.2 <sup>b</sup>	77	5	62	7800	7770/1.29	n.d.
MR2	1.2 <sup>b</sup>	80	5	56	7300	6950/1.36	5300/1.33
MR3	1.0 <sup>c</sup>	30	3	27	7950	n.d.	6850/1.24

<sup>a</sup>Based on 1,4-dioxane.

Monomers: <sup>b</sup>DMAEMA and <sup>c</sup>Styrene.

<sup>d</sup>Theoretical  $M_n$  calculated according to equation 1.

Experimental number-average molar mass and dispersity determined either by: <sup>e</sup>SEC in THF based on PDMAEMA calibration by using the MWHS equations 5 and 6, or by <sup>f</sup>SEC in DMF using PMMA calibration.

*Synthesis of the amphiphilic PDMAEMA-*b*-PS-TTC macroRAFT agent.* The reaction was carried out following a protocol similar to the one described above for the synthesis of PDMAEMA-TTC. RAFT polymerization of styrene was conducted in 1,4-dioxane at 80 °C in the presence of the previously synthesized PDMAEMA-TTC (run MR3, Table SI1). The synthesized amphiphilic macroRAFT was purified by precipitation in a large volume of petroleum ether, and characterized by SEC (Figure SI2) and <sup>1</sup>H NMR (Figure SI3). Theoretical molar masses were also obtained using equation 1, where  $M_{\text{RAFT}}$  and  $[\text{RAFT}]_0$  are respectively the molar mass and the initial concentration of the hydrophilic macroRAFT agent.

*Thermoresponsive properties.* The cloud point temperature of PDMAEMA-TTC was determined via UV-visible spectroscopy. A macroRAFT solution (20 g L<sup>-1</sup>) was first prepared and the pH was then adjusted by addition of 0.1 M HCl or 0.1 M NaOH solutions. After pH correction, water was added to fix the final concentration of macroRAFT at 10 g L<sup>-1</sup>. The polymer solution was transferred in a 1 cm path length quartz-cell, and the transmittance at 650 nm was monitored as a function of temperature (from 15 to 90 °C with a heating ramp of 0.5 °C min<sup>-1</sup>) using an Evolution 220 UV-visible spectrophotometer (Thermo Scientific) coupled with a Peltier thermocontroller PCCU1 (Thermo Scientific). The cloud point temperature of the PDMAEMA-TTC macroRAFT agent was defined as the temperature corresponding to 50% transmittance (T50%).

*Iron oxide cluster formation.* The strategy developed for the formation of iron oxide clusters is based on the emulsification/solvent evaporation technique reported by Paquet *et al.*<sup>2, 3</sup> Initially, the commercial fatty acid-modified iron oxide nanoparticles (EMG1200 from Ferrotec<sup>©</sup>) were dispersed in toluene at a concentration of 100 g L<sup>-1</sup> leading to the formation

of an organic ferrofluid. Using an Ultrasonic 750 W processor with a 12 mm probe, 24.0 g of the toluene ferrofluid was mixed with 95 g of PDMAEMA-*b*-PS-TTC aqueous solution ( $2.5 \times 10^{-4}$  M, pH = 4) during 240 s with an output power of 150 W. Toluene was then extracted by rotary evaporation under vacuum conditions at a maximum temperature of 45 °C to prevent any degradation of the RAFT-moiety present on the macroRAFT agent. Water was added intermittently in the round-bottom flask to maintain a constant volume. The resulting cluster dispersions were filtered on a 200-mesh grid to remove aggregates and then characterized by DLS ( $Z_{av} = 180$  nm and PDI = 0.05) and gravimetric analysis to determine their solids content ( $SC_{exp}$ ) and the yield of cluster formation ( $f$ ) as follows:

$$f (\%) = SC_{exp} \times 100 / SC_{theo} \quad (2)$$

where  $SC_{theo}$  is the theoretical solids content considering the water evaporation resulting in a yield of 86%.

The free macroRAFT was removed from the cluster dispersion by magnetic separation. In a typical experiment, 30 g of iron oxide cluster dispersion was exposed to an external magnetic field (NdFeB, Neodymium Iron Boron, 50.8 x 50.8 mm) during 10 min. After separation, the supernatant containing the free macroRAFT was removed and the collected clusters were redispersed in a buffer solution (37 mM NaCl at pH = 4).

*Seeded emulsion polymerization.* Surfactant-free emulsion polymerization of styrene was carried out using iron oxide clusters as seeds (Table SI2). In a typical experiment 15 g of the cluster dispersion was introduced in a 50 mL double-jacket round-bottom glass reactor equipped with a condenser, a nitrogen inlet and a mechanical stirrer. Then the initiator (ADIBA, 0.085 g) and styrene (0.79 g, 5 wt% based on overall mass) were introduced in the reactor. The dispersion was deoxygenated under nitrogen for 30 min while heating to 60 °C. The polymerization reactions were conducted during 6 h. Samples were periodically

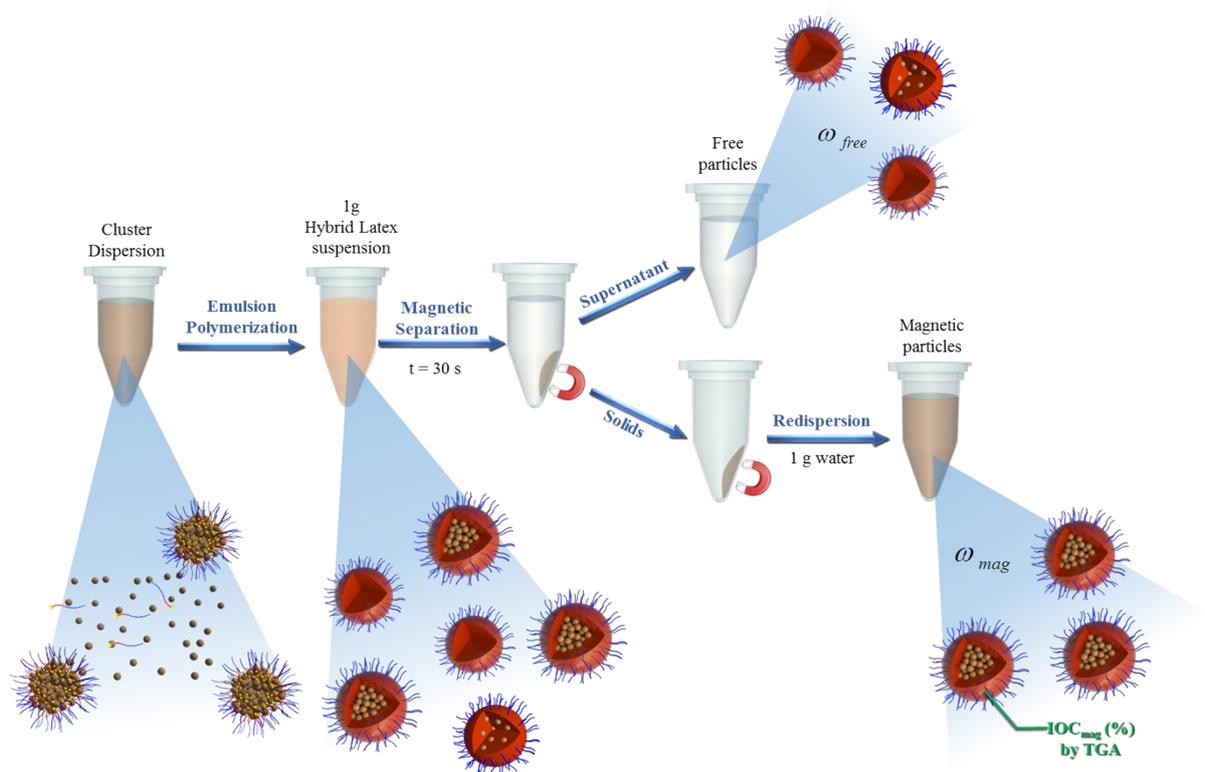
withdrawn to follow monomer conversion as a function of time and particle size as a function of conversion.

**Table SI2** – Results for seeded emulsion polymerization of styrene using PDMAEMA-*b*-PS-stabilized clusters as seeds.

Ref.	Cluster	PC (%)	IO <sub>0</sub> (%) <sup>a</sup>	X (%) / t (h) <sup>b</sup>	Z <sub>av</sub> (nm) / Poly <sup>c</sup>	ω <sub>mag</sub> (%) <sup>d</sup>	ω <sub>free</sub> (%) <sup>e</sup>	IOC <sup>TGA</sup> (%) <sup>f</sup>	Coag. (%) <sup>g</sup>
<b>Exp 1</b>	No purification	10	13	100/5	355/0.21	36	64	22	none
<b>Exp 2</b>	Purified by magnetic wash for 10 min	5.0	27	63/6	382/0.22	69	31	32	0.47
<b>Exp 3</b>		2.5	55	66/7	-	88	12	47	0.02
<b>Exp 4</b>		2.5	55	63/7	290/0.17	94	6	47	0.21

*SC = 12%; Temperature = 60 °C; cluster suspension = 15 g; Mon: Styrene, except for Exp 4 Sty/DVB: 77/23 wt/wt, ADIBA = 0.5 wt% based on total monomer. <sup>a</sup>Iron oxide content based on overall monomer mass; <sup>b</sup>Monomer conversion/reaction time; <sup>c</sup>Determined by DLS; <sup>d</sup>Determined using Equation 3 and <sup>e</sup>Equation 4 after 30 s of magnetic separation; <sup>f</sup>IO content in the magnetic fraction determined by TGA; <sup>g</sup>Coagulum content based on overall latex mass determined after latex filtration on a 160 mesh grid.*

*Determination of the fraction of magnetic particles and the iron oxide content.* The obtained hybrid latexes were characterized to determine the fraction of magnetic latex particles and the fraction of free (non-magnetic) latex particles (formed by secondary nucleation or containing a low amount of IO) as schematically represented in Scheme SI1.



**Scheme S11** – Scheme illustrating the overall procedure used to determine the fractions of magnetic particles ( $\omega_{mag}$ , wt%) and of free (non-magnetic) particles ( $\omega_{free}$ , wt%) composing the hybrid latex suspension, through magnetic separation.

Firstly, the hybrid latexes were exposed to a magnetic field using a permanent magnet (Dynamag – 2 from ThermoFisher Scientific) during 30 s to separate the magnetic fraction from the non-magnetic one (which may contain both free polymer particles and hybrid particles with a very low amount of iron oxide nanoparticles). The supernatant was collected and the solids content was determined gravimetrically ( $SC_{free}$ ). The magnetic fraction was redispersed in water while maintaining the same volume as the initial sample and the solids content was also determined gravimetrically ( $SC_{mag}$ ). The fractions of magnetic particles ( $\omega_{mag}$ , wt%) and of free (non-magnetic) particles ( $\omega_{free}$ , wt%) were then determined using equations 3 and 4, respectively where  $SC_{\text{hybrid latex}}$  is the experimental solids content of the hybrid latex before separation. At last, the magnetic fraction was dried and characterized by thermogravimetric analysis (TGA) in order to determine its iron oxide content ( $IOC_{mag}$ , wt%).

$$\omega_{mag} \text{ (wt\%)} = \frac{SC_{mag}}{SC_{hybrid\ latex}} \cdot 100 \quad (3)$$

$$\omega_{free} \text{ (wt\%)} = \frac{SC_{free}}{SC_{hybrid\ latex}} \cdot 100 \quad (4)$$

### 1.3. Characterizations

<sup>1</sup>H NMR analysis was performed in DMSO-d<sub>6</sub> at room temperature (Bruker DRX 300).

*Size exclusion chromatography (SEC).* All polymers were analyzed at a concentration of 4 mg mL<sup>-1</sup> after filtration through a 0.45 μm pore size membrane. SEC analyses in DMF (SEC-DMF / with LiBr, 0.01 mol L<sup>-1</sup>) were performed at 70 °C with a flow rate of 1.0 mL min<sup>-1</sup> using an Eco-SEC semi-micro SEC system from Tosoh. The separation was carried out using two PSS GRAM columns (7 μm, 300 × 7.5 mm). The setup was equipped with a dual flow refractive index (RI) detector and a UV detector. The average molar masses (number-average molar mass,  $M_n$  and weight-average molar mass,  $M_w$ ) and the molar mass dispersity ( $D = M_w/M_n$ ) were derived from the RI signal using a calibration curve based on poly(methyl methacrylate) (PMMA) standards from Polymer Laboratories. SEC measurements in THF (THF-SEC) were carried out at 50 °C with a flow rate of 1 mL min<sup>-1</sup>. Separation was carried out on three columns from PSS Instruments [PSS SDV analytical (8x300 mm)]. The device (Viscotek TDA305) was equipped with a RI detector ( $\lambda = 670$  nm). To determine  $M_n$ ,  $M_w$  and  $D$ , the RI signal was derived from a PDMAEMA calibration curve obtained using the Mark-Houwink-Sakurada (MHWS) equations:

$$[\eta] = K \cdot M^\alpha \quad (5)$$

$$K_1 \cdot M_1^{1+\alpha_1} = K_2 \cdot M_2^{1+\alpha_2} \quad (6)$$

where  $K$  and  $\alpha$  are the MHWS parameters and  $M$  the molar mass for polymer 1 and 2. To do so, a conventional calibration curve based on PMMA standards was first plotted. By using equation 6 with known molar masses of PMMA standards and MHWS parameters for PMMA ( $K = 1.28 \cdot 10^{-4}$  and  $\alpha = 0.69$ ; THF; 30 °C)<sup>4</sup> and PDMAEMA ( $K = 4.98 \cdot 10^{-5}$  and  $\alpha = 0.73$ ; THF; 30 °C),<sup>5</sup> a new calibration curve was plotted based on PDMAEMA polymers.

*Dynamic Light Scattering (DLS).* Z-average diameters ( $Z_{av.}$ ) were measured by DLS using the Zetasizer NanoZS instrument from Malvern. The data were collected at 173° scattering angle using the fully automatic mode of the Zetasizer system and the cumulants fit analysis was used. The broadness of the distribution was given by a dimensionless number called *PDI* (the higher this value, the broader the size distribution).

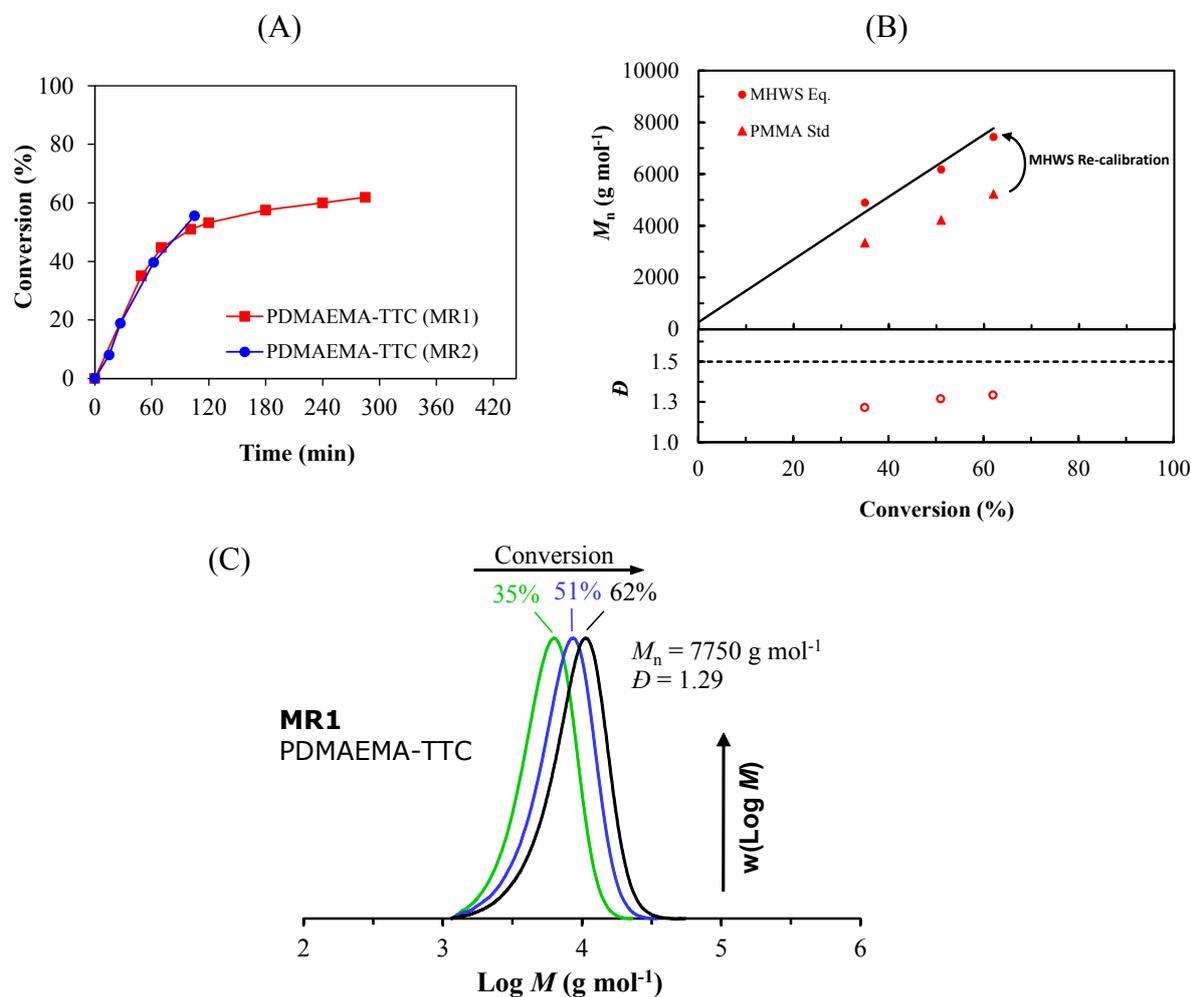
*ζ-potential measurements.* Zeta potential measurements were performed with the Zetasizer Nano ZS instrument from Malvern. The measurements were performed after dilution (1/10000) of the cluster suspension in a  $10^{-3}$  mol L<sup>-1</sup> KCl aqueous solution. The pH was adjusted within the range of pH = 4 to pH = 10 by using  $10^{-3}$  mol L<sup>-1</sup> HCl or NaOH aqueous solutions.

*Transmission Electron Microscopy (TEM).* Samples for TEM analyses were dropped on a carbon-coated copper grid and dried under air. The TEM images were recorded using a Philips CM120 transmission electron microscope at an accelerating voltage of 120 kV (Centre Technologique des Microstructures (CTμ), platform of Université Claude Bernard Lyon 1, Villeurbanne, France).

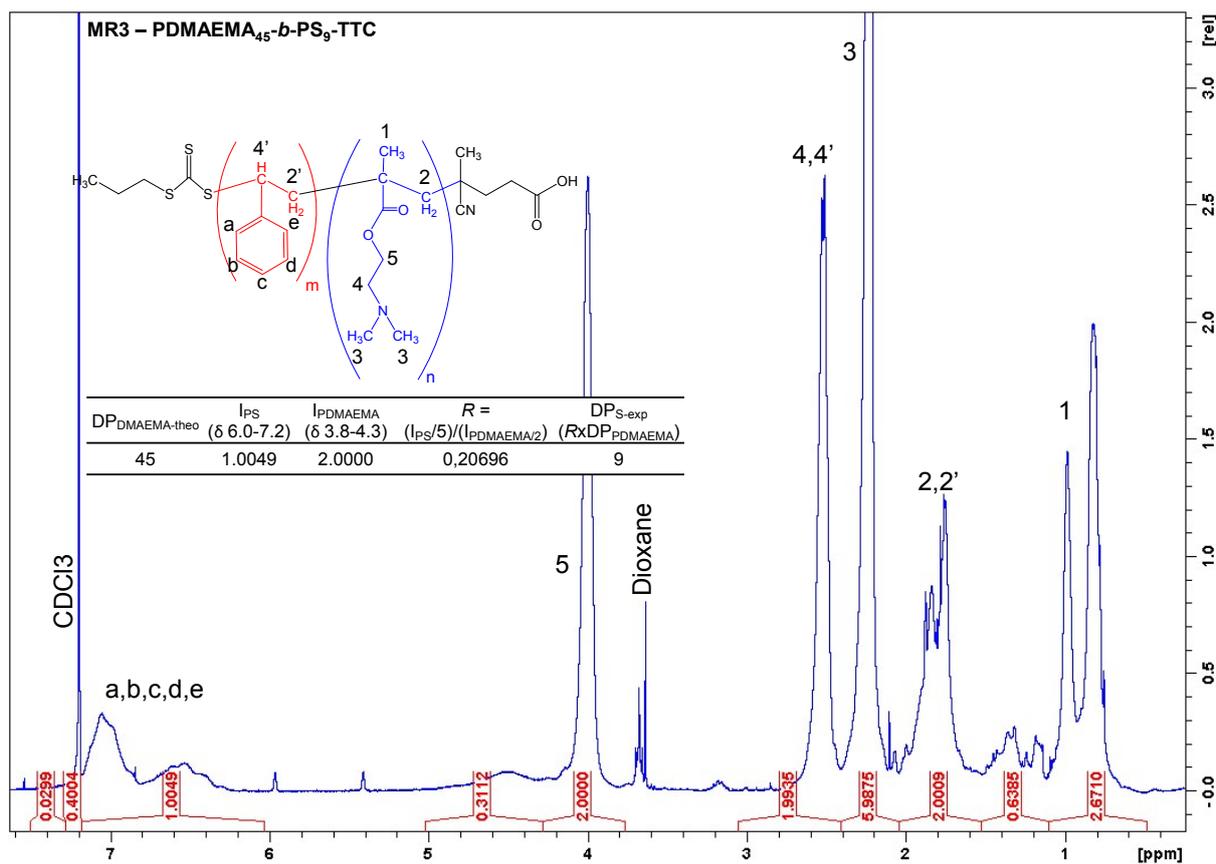
*Superconducting quantum interference device (SQUID) analysis.* Magnetic measurements were made with a SQUID MPMS-XL5 (Quantum Design) equipped with an integrated helium liquefier magnetometer. The analysis was performed with the kind support of Ruben Checa from the Laboratoire des Multimatériaux et Interfaces, UMR CNRS 5615, Claude Bernard University.

## 2. SUPPLEMENTARY DATA

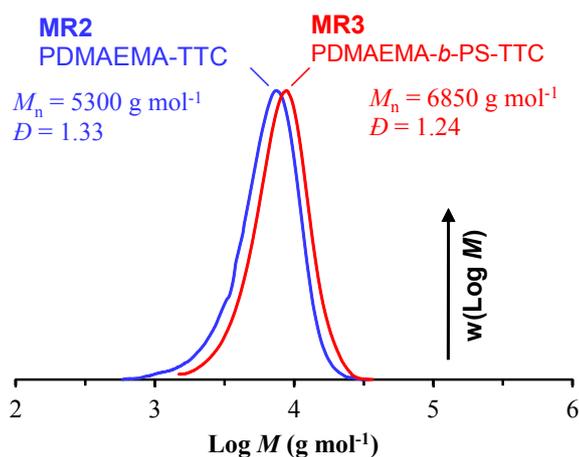
### 2.1. Synthesis of PDMAEMA and PDMAEMA-*b*-PS macroRAFT agents



**Figure S11** – RAFT polymerization of DMAEMA in 1,4-dioxane using CTPPA as RAFT agent (MR1 and MR2). Evolutions of (A) monomer conversion versus time and (B)  $M_n$  and  $D$  versus conversion (MR1). The straight line corresponds to the theoretical evolution of  $M_n$  with conversion. The triangles (◻) correspond to  $M_n$  calculated from PMMA calibration and the circles to  $M_n$  (●) and  $D$  (○) from PDMAEMA calibration using the MWS parameters. (C) SEC-traces for PDMAEMA-TTC (run MR1) in THF using PDMAEMA calibration recalculated using the MWS equations.

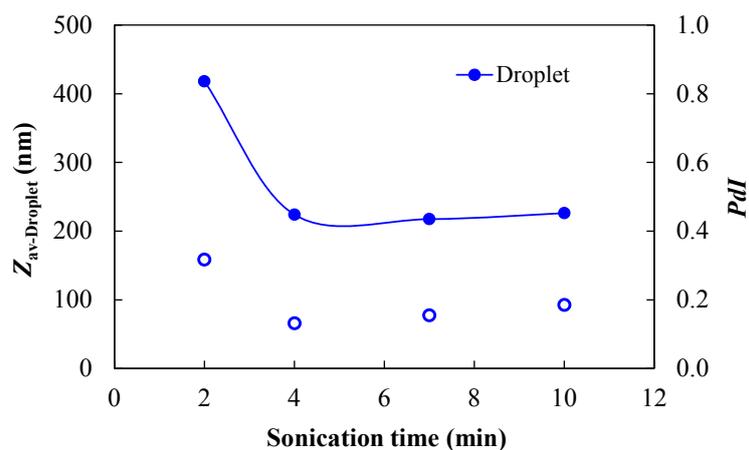


**Figure S12** – <sup>1</sup>H NMR spectrum of PDMAEMA<sub>45</sub>-*b*-PS<sub>9</sub>-TTC (MR3). Determination of the degree of polymerization of styrene via the relative integration of the PDMAEMA characteristic peak (5) and the aromatic peaks from PS (a, b, c, d, e).

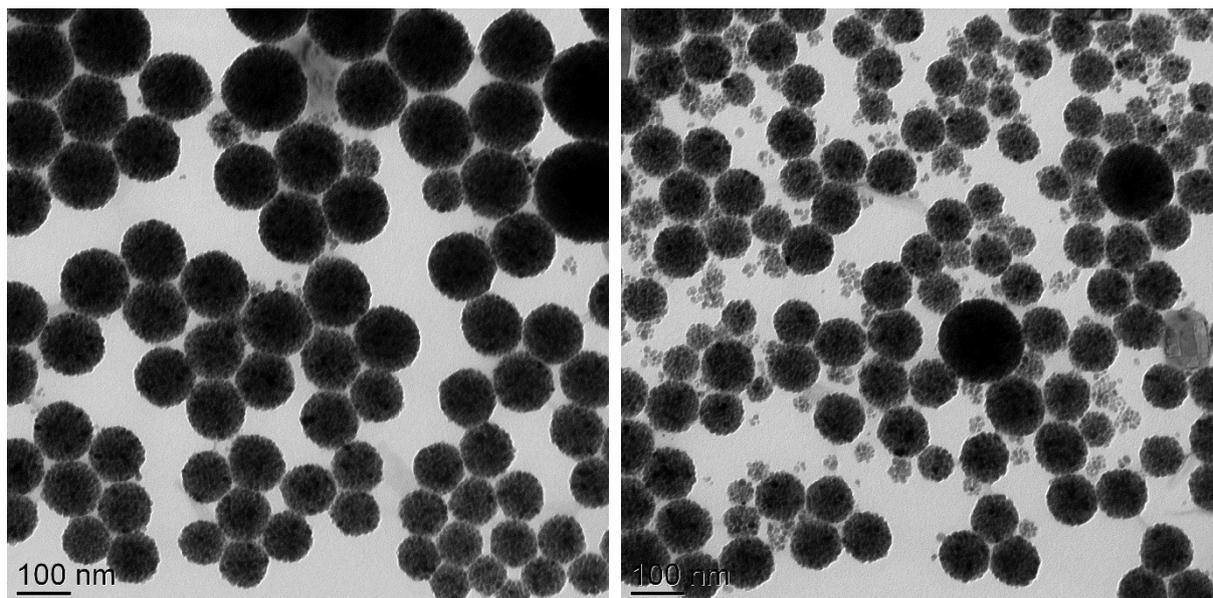


**Figure S13** – SEC-DMF traces for PDMAEMA-TTC (MR2, Table S11) and PDMAEMA-*b*-PS-TTC (MR3, Table S11) using conventional PMMA calibration.

## 2.2. Clusters formation

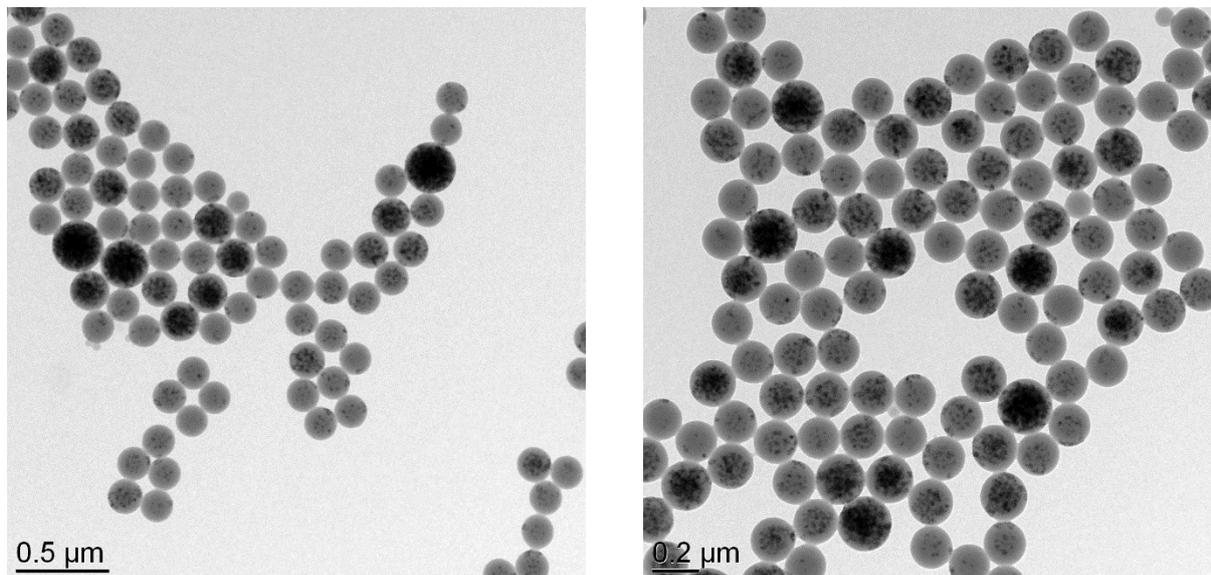


**Figure SI4** – Effect of sonication time on the evolution of  $Z_{av}$  (full symbols) and  $PDI$  (open symbols) of toluene droplets loaded with iron oxide nanoparticles before solvent evaporation using PDMAEMA<sub>45</sub>-*b*-PS<sub>9</sub>-TTC (MR3, Table SI1) as stabilizer at fixed sonication power of 75 W.

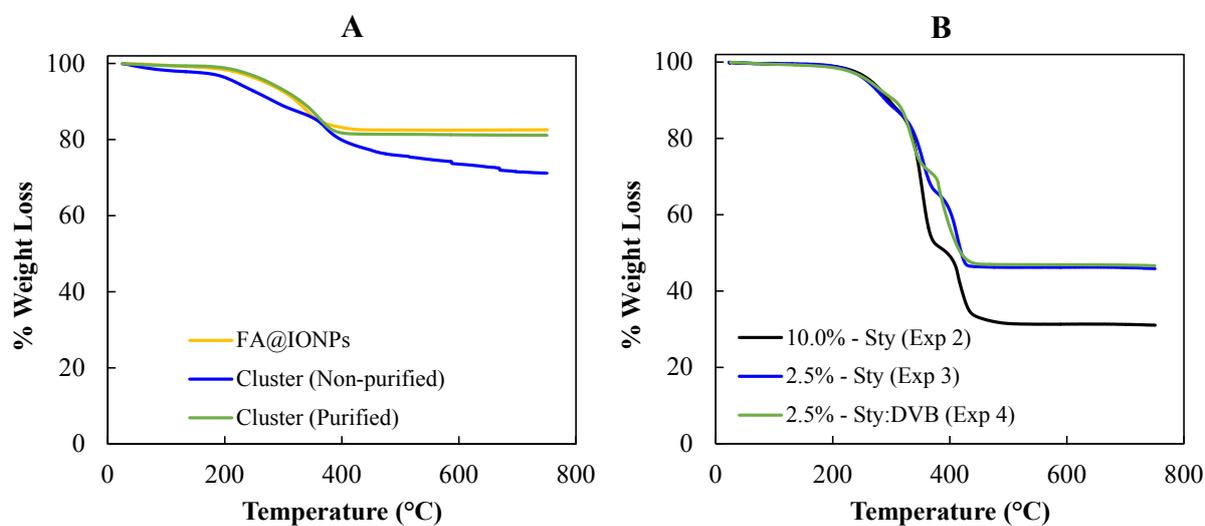


**Figure SI5** – Additional TEM images of iron oxide clusters. Scale-up experiment prepared with a PDMAEMA-*b*-PS-TTC concentration of  $2.5 \cdot 10^{-4}$  M.

### 2.3. Magnetic latex particles

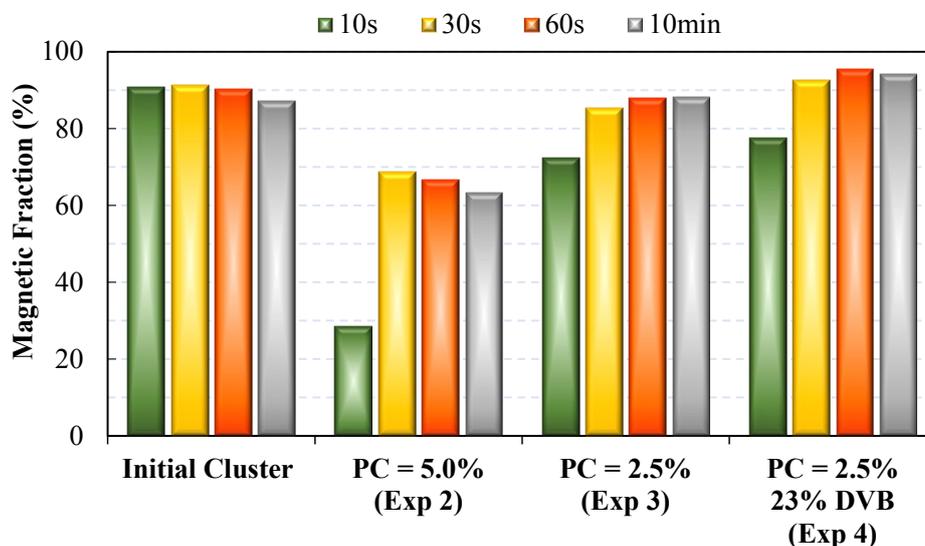


**Figure SI6** – TEM images of crude (non-separated) magnetic latex particles prepared via seeded emulsion polymerization using the purified iron oxide clusters as seed (Exp 1 in Table SI2).

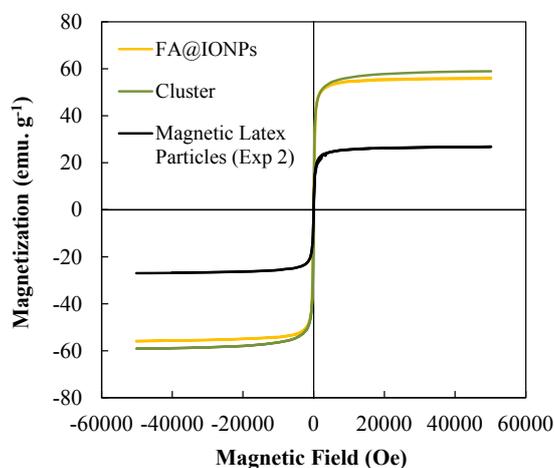


**Figure SI7** – Thermogravimetric analysis (TGA) of (A) commercial fatty acid-modified iron oxide nanoparticles (FA@IONPs) and cluster before (non-purified) and after magnetic wash (purified). (B) TGA of magnetic latex particles with different polymer contents and monomer compositions (Exp 2-4, Table SI2).

## 2.4. Magnetic properties of FA@IONP, clusters and hybrid particles



**Figure SI8** – Magnetic fractions ( $\omega_{\text{mag}}$ ) obtained after different times of magnetic separation of the clusters and magnetic latex particles prepared via seeded emulsion polymerization in the presence of clusters as seeds for different polymer contents (PC) (Exp 2-Exp 4, Table SI2).

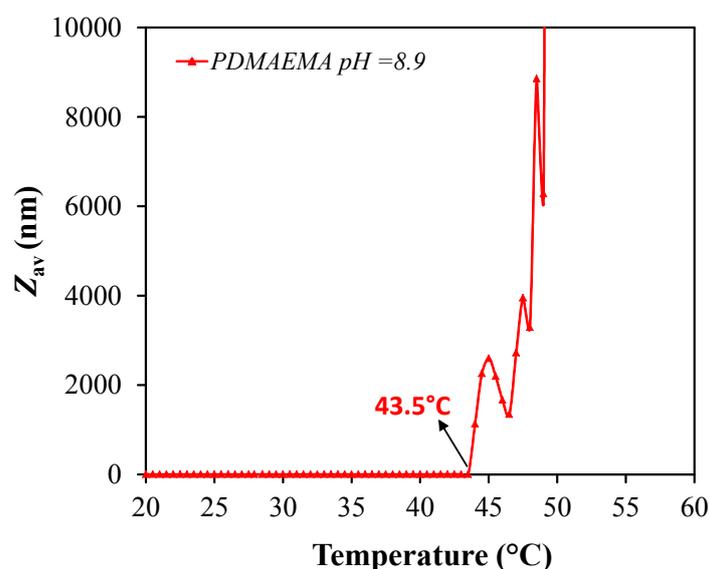


**Figure SI9** – Superconducting quantum interference device (SQUID) analysis of the commercial fatty acid-modified iron oxide nanoparticles (FA@IONPs), the clusters after magnetic wash and the isolated magnetic latex particles (Exp 2, Table SI2).

*Further explanation on the similar magnetization at saturation for the commercial IO nanoparticles and the magnetic clusters*

As discussed in the main text, TGA of FA@IONPs (Fig. SI7) indicates that the commercial nanoparticles contain only 17 wt% of organic ligand (identified by Ferrotec<sup>®</sup> as “fatty acid”) resulting in a high magnetization at saturation (56 emu g<sup>-1</sup>, Fig. SI9). After cluster formation and purification, the organic content of the obtained clusters was almost the same as that of the FA@IONPs (19 wt%, Fig. SI7) resulting in a similar magnetization at saturation (59 emu g<sup>-1</sup>, Fig. SI9). This is at first sight surprising, as the organic content should increase (and hence the saturation magnetization decrease) due to the presence of the macroRAFT. Besides, TGA analysis of the clusters before and after magnetic wash shows that the organic content of the purified clusters decreased by 10 wt% (Figure SI7), which is higher than the amount of macroRAFT initially introduced (i.e., 5.8 wt%). Together, these results suggest that the magnetic wash also removed part of the fatty acid, which was not attached to the iron oxide nanoparticles, resulting in an almost constant magnetic response.

## 2.5. Thermo-responsive properties of PDMAEMA-TTC



**Figure SI10** – Cloud point temperature of PDMAEMA-TTC at pH = 8.9 (MR2 in Table SI1) determined by DLS.

### 3. REFERENCES

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