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## Enhancing colloidal stability of anisotropic magnetic nanodiscs through mesoporous silica and P(NIPAM/MAA) copolymer coatings

P. Rafael Donnarumma, <sup>a,b</sup> Micaela A. Macchione, <sup>a,c</sup> Franziska Wasner,<sup>d</sup> Elif Kocar,<sup>d</sup> Vicente Durán Toro,<sup>d</sup> Santiago Marzini Irranca, <sup>e,f</sup> Eduart Gutiérrez Pineda, <sup>a</sup> Sunisa Thongsom, <sup>a</sup> Danijela Gregurec <sup>\*d</sup> and Sergio E. Moya <sup>\*a,g</sup>

Magnetic nanodiscs (MNDs), a class of anisotropic magnetite nanomaterials, have attracted considerable attention in smart actuation as they can generate heat through hysteretic losses and their discoidal shape can be tuned to exhibit vortex magnetization and generate mechanical stimuli. Despite near-zero net magnetization, at high concentrations, interparticle forces become dominant leading to MND aggregation. Here, we have optimized a previously reported synthetic approach based on the synthesis of hematite templates subsequently converted into a magnetite phase. We show that removal of oleic acid (OA) during the reduction step results in the same colloidal stability as in the presence of OA but avoids erosion of the MNDs associated with OA. We introduce a thin mesoporous silica coating on the surface of hematite, effectively diminishing aggregation during reduction while allowing complete conversion into magnetite. This silica layer facilitates subsequent silane chemistry and the grafting of poly(*N*-isopropylacrylamide-co-methacrylic acid) P(NIPAM/MMA) coatings with 80 : 20 and 50 : 50 ratios, yielding highly stable aqueous suspensions of MNDs, both in aqueous and cell culture media. These findings establish a versatile pathway toward colloidal stable MNDs, thereby broadening their applicability in biomedical research.

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## Introduction

Anisotropic Magnetic Materials (AMMs), such as nanodiscs, nanorods, and nanotubes, have recently gained considerable scientific attention due to their multiple possibilities as smart materials and their promising applications in biomedicine, particularly in areas like neuromodulation.<sup>1,2</sup> Magnetic materials can respond to external magnetic fields by generat-

ing heat through hysteretic losses in frequencies of hundreds of kilohertz. This heat has been applied to eradicate tumours in the so-called magnetic hyperthermia technique.<sup>3–6</sup> This property can also be exploited for wireless magnetothermal deep brain stimulation at optimal heat dissipation temperatures.<sup>7</sup> Furthermore, the anisotropic shape of AMMs allows them to trigger mechanical stimulation through torque on mechanosensory cells under slower, 1–10 Hz magnetic fields, when ground vortex magnetization in a specific geometric aspect ratio aligns in plane with the direction of the magnetic field.<sup>8</sup>

Among AMMs, magnetic nanodiscs (MNDs) are particularly suited for mechanical stimulation, as the piconewton scale torques demonstrated efficient modulation of the activity in mechanosensory cells.<sup>8</sup> Magnetomechanical activation of the mechanosensitive cation channel TRPV4, heterologously expressed in non-mechanosensitive HEK293 cells, confirmed that the stimulation is mediated through mechanosensitive ion channels.

Because magnetite has an inverse spinel lattice that favors isotropic growth, AMMs are typically obtained through the chemical reduction of non-magnetic hematite ( $\alpha\text{-Fe}_2\text{O}_3$ ) templates with a hexagonal lattice to magnetite ( $\text{Fe}_3\text{O}_4$ ).<sup>3,5,9</sup> The

<sup>a</sup>Soft Matter Nanotechnology Group, CIC biomaGUNE, Basque Research and Technological Alliance, San Sebastian, Spain. E-mail: smoya@cicbiomagune.es

<sup>b</sup>Departamento de Química Aplicada, Universidad del País Vasco UPV/EHU, Leioa, Bizkaia, Spain

<sup>c</sup>CONICET, Centro de Investigaciones y Transferencia de Villa María (CIT Villa María), Villa María X5900LQC, Argentina

<sup>d</sup>Biointerfaces Lab, Department of Chemistry and Pharmacy, Friedrich-Alexander Universität Erlangen-Nuremberg, Erlangen, Germany.

E-mail: danijela.gregurec@fau.de

<sup>e</sup>Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Ciudad Universitaria, Córdoba, Argentina

<sup>f</sup>Instituto de Investigación y Desarrollo en Ingeniería de Procesos y Química Aplicada (IPQA-CONICET), Córdoba, Argentina

<sup>g</sup>Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand



crystal structure of hematite allows for directional growth, leading to well-defined anisotropic morphologies.<sup>10</sup>

Hematite nanoparticles can be synthesized with diverse exposed facets, resulting in distinct morphologies such as rhombic cubes, hexagonal platelets or discs, and hexagonal bipyramids.<sup>11,12</sup> Due to the aggregation that may take place during synthesis and reduction to magnetite, further efforts are still required to develop synthesis strategies and surface functionalization towards enhancing their colloidal stability.

A well-established strategy to stabilize inorganic nanomaterials that otherwise form unstable colloidal dispersions in water is to coat them with silica.<sup>13</sup> Silica coatings are widely employed not only to enhance the colloidal stability of core materials but also because they can be readily functionalized *via* silanization with a broad range of molecules, including polymers that further improve stability and biocompatibility.<sup>14</sup>

In the case of magnetic nanomaterials, silica coatings additionally serve as barriers between individual nanoparticles, reducing their magnetic interactions. Besides deposition of a dense, hard silica shell on inorganic nanoparticles, it is also possible to grow a permeable mesoporous silica layer, which confers similar benefits to those of a hard shell while introducing pores and channels that prevent complete isolation of the core from its surrounding medium.<sup>15</sup>

This manuscript presents an optimized synthetic strategy for producing MNDs, as schematized in Fig. 1, focusing on modifications to the reduction process that preserve a uniform nanodisc morphology, minimize aggregation, and enhance colloidal stability with the ultimate goal of advancing their biomedical potential while maintaining their unique properties. We demonstrate that some functionalization steps commonly used in MND synthesis are not necessary for the stabilization of the MNDs in aqueous media and that the coating of hematite with mesoporous silica prevents aggregation of the nanoparticles during reduction, while the pores of the silica coating allow the reducing agents to reach the hematite core and carry out a 100% conversion of the hematite core to magnetite.<sup>16–18</sup> In addition, the silica coatings facilitate further functionalization of MNDs through silane chemistry, allowing the grafting of polymers around the MNDs that provide additional stability to the hybrid nanostructures.<sup>19</sup> Our results reveal that poly(*N*-isopropylacrylamide) (NIPAM) and methacrylic acid (MAA) coatings confer superior colloidal stability over time, both in water and in cell culture media.

## Experimental section

### Materials

All chemicals used in this work were of analytical grade and utilized as received without further purification. 3-(Trimethoxysilyl) propyl methacrylate (MEMO) (>97%), isopropanol (99.5%), sodium dodecyl sulfate (SDS) (>99%), *N,N,N',N'*-tetramethylethylenediamine (TEMED) (>99%), ammonium persulfate (APS) (99%), *N*-isopropylacrylamide (NIPAM) (97%), methacrylic acid (MAA), FeCl<sub>3</sub>·6H<sub>2</sub>O (97%), tri-*n*-octylamine (TOA) (98%), oleic acid (OA) (90%), tetraethyl orthosilicate (TEOS) (98%), and hexadecyltrimethylammonium bromide (CTAB) (>99%) were purchased from Sigma-Aldrich. NH<sub>4</sub>OH solution (25% in water) and toluene (>99.7%) were purchased from Fisher. Anhydrous sodium acetate (>99.0%) was purchased from Merck. Absolute ethanol was purchased from Scharlau. RPMI 1640 solution was purchased from HyClone. H<sub>2</sub> (100%) was provided by Carbueros Metálicos.

### Methods

**Hematite and magnetite nanodisc synthesis.** Magnetite nanodiscs were produced using a two-step process in which hematite ( $\alpha$ -Fe<sub>2</sub>O<sub>3</sub>) nanodisc templates are hydrothermally fabricated and subsequently reduced *via* a hydrogen-wet reduction method.<sup>3,8</sup>

In the first step,  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> nanodiscs were synthesized by mixing 0.273 g of FeCl<sub>3</sub>·6H<sub>2</sub>O and 0.8 g of anhydrous sodium acetate in a solution of 10 mL of absolute ethanol and 1 mL of Milli-Q H<sub>2</sub>O inside a Teflon-lined steel vessel. The reaction mixture was homogenized through stirring. The Teflon-lined vessel was then heated to 180 °C for 18 h. The red  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> nanodiscs were cooled down to room temperature, centrifuged, and washed three times with deionized (DI) H<sub>2</sub>O and three times with ethanol to remove unreacted reagents; finally, they were left to air dry for further reduction.

In the second step,  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> nanodiscs were reduced to magnetite (Fe<sub>3</sub>O<sub>4</sub>) by dispersing the hematite in 20 mL of TOA and homogenized by ultrasound for 10 min. The mixture was placed in a three-neck flask with an overhead stirrer with Teflon palettes and fluxed at 360 °C in an atmosphere of H<sub>2</sub> (100%) for 30 min until it changed its color from red to black. Once cooled, the Fe<sub>3</sub>O<sub>4</sub> nanodiscs were washed several times with ethanol and then left to air dry.

**Mesoporous silica coated magnetite nanodiscs.** To obtain mesoporous silica coated magnetic nanodiscs, a mesoporous

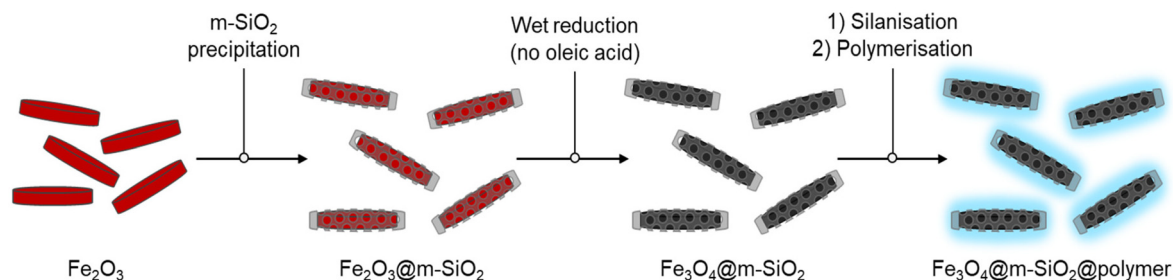


Fig. 1 Scheme of the fabrication of polymer/mesoporous silica-coated magnetite nanodisc hybrid nanostructures.



silica layer was deposited on  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> nanodiscs before the reduction step adapting a protocol from the literature.<sup>8</sup> Four different conditions were tested varying the TEOS amount and the isopropanol:water ratio, while keeping the CTAB and base concentrations constant. For this, 5 mg of  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> nanodiscs and 40 mg of CTAB were put in a mixture of isopropanol and DI H<sub>2</sub>O, and 0.125 mL of NH<sub>4</sub>OH 25% was added. This solution was sonicated in a bath for 5 min. The resultant dispersion was ultrasonicated with a tip-probe ultrasonicator for 10 min at room temperature, at 40% amplitude (VCX 500, 500 W). Parallely, 4  $\mu$ L of TEOS was pipetted into 1 mL of isopropanol.

Half of the TEOS solution was added to the  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> solution in a sonication bath. The mixture was ultrasonicated with the tip-probe ultrasonicator for 30 min in an ice bath to control the temperature. The rest of the TEOS solution was added and then the mixture was ultrasonicated for 30 min more. The  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub>@m-SiO<sub>2</sub> was centrifuged and washed twice with a washing solution (50% 0.5 M HCl, and 50% ethanol) and three times with ethanol; finally, it was left to air dry overnight. The reduction proceeded in the same way as for uncoated  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> to produce Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>.

**Surface modification of Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>.** The surface functionalization of the MNDs was carried out *via* silanization using MEMO. Briefly, 1 mg of Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub> was suspended in 10 mL of toluene and ultrasonicated in an ice bath for 10 min. Then, 2 mL of MEMO was added, and the resulting dispersion was ultrasonicated for 30 min at 70 °C. The reaction mixture was washed three times with isopropanol to remove unreacted species. Finally, the Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@MEMO particles were dried to obtain a powder.

**Synthesis of polymeric coatings on Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>.** The synthesis of polymeric coatings was carried out following a previously reported protocol, consisting of a free radical precipitation/dispersion polymerization assisted by ultrasonication, with some modification.<sup>20</sup> First, 0.1 mg of Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@MEMO were weighed and resuspended in 3 mL of water. In a separate vial, NIPAM was weighed and dissolved in 5 mL of water. The Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@MEMO suspension was ultrasonicated for 2 min, and the NIPAM solution was then added, followed by the addition of MAA, keeping the total monomer amount at 1 mmol; and SDS (0.6 mM) was subsequently added to the reaction flask. Finally, solutions of TEMED (0.075 mmol) and APS (0.015 mmol), used as the catalyst and initiator, respectively, were injected along with Milli-Q water to reach a final volume of 10.0 mL. The reaction mixture was then ultrasonicated at 70 °C using a tip-probe ultrasonicator for 15 min at 40% amplitude. The mixture was allowed to cool slightly and then subjected to 10 min of ultrasonication in an ice bath to achieve final stabilization of the system. Three different polymer compositions were produced by varying the monomer composition and ratios: pure PNIPAM (Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@P1), and copolymers of NIPAM and MAA (P(NIPAM-*co*-MAA)), at 80 : 20 (Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@P2) and 50 : 50 (Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@P3).

**In vitro cytotoxicity studies.** The normal human fibroblast WI-38 cell line and normal HEK-293T (American Type Culture Collection (ATCC), Manassas, WV, USA) were used to test the

biocompatibility of Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub> and Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@P3. HEK-293T cells were cultured in high glucose Dulbecco's Modified Eagle's Medium (DMEM), and WI-38 were cultured in Minimum Essential Medium (MEM); both media were supplemented with GlutaMAX™ (Gibco/Thermo Fisher Scientific, Waltham, MA, USA), with 10% fetal bovine serum (FBS, Gibco), 1% penicillin/streptomycin solution (Gibco) and incubated in a humidified incubator at 37 °C with 5% CO<sub>2</sub>. Cells were seeded at a density of 1 × 10<sup>4</sup> cells per well in 96-well plates (total 100  $\mu$ L per well) overnight. Cells were subsequently treated with various concentrations of Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub> and Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@P3 (0–200  $\mu$ g mL<sup>-1</sup>) for 24 and 48 h (total 200  $\mu$ L per well) and finally cell viability was determined using the MTS assay. In short, before detection, 40  $\mu$ L of MTS solution was added to the well (CellTiter 96® Aqueous One Solution Cell Proliferation Assay, Promega #G3580), incubated in a CO<sub>2</sub> incubator for 3 hours, and its optical density was measured at 490 nm. Cell viability was calculated using the following equation:

$$\text{Cell viability (\%)} = \frac{\text{OD}_{490 \text{ treatment}}}{\text{OD}_{490 \text{ control}}} \times 100$$

where OD<sub>490</sub> stands for the optical density at 490 nm for treated samples (with Fe<sub>3</sub>O<sub>4</sub> nanodiscs) and control (without nanodiscs).

**Characterization.** Transmission electron microscopy (TEM) micrographs were obtained on a Zeiss LEO912 microscope at an 80 keV acceleration voltage. Samples were prepared by drop casting 1  $\mu$ L of a diluted dispersion of the nanoparticles in ethanol on a 400 mesh copper carbon support film. For the observation of the mesoporous structure of the silica coating, ultrathin C films on lacey carbon grids were used. The size distribution and thicknesses were determined from populations of around 300 particles by using ImageJ software.

Scanning electron microscopy (SEM) images were obtained with a field-emission scanning electron microscope (FE-SEM; JSM-IT800HL, JEOL, Tokyo, Japan) in combination with an EDX detector (Oxford INCA). Samples were prepared the same way as for TEM.

Atomic force microscopy (AFM) was used to analyse the sample's morphology in a Multimode 8HR (Bruker). Samples were resuspended in a water:methanol solution and spin-coated (20  $\mu$ L) onto a freshly cleaved mica surface and allowed to dry. Images were captured using a conventional tapping mode with a TESP-V2 probe (Bruker). The data were processed with Nanoscope 2.0 software (Bruker).

X-ray diffraction (XRD) was performed between 10 and 80 (2 $\theta$ ) degrees using a Bruker D8 Advance diffractometer equipped with a Lynxeye XE-T detector using Cu K $\alpha$  radiation (1.5406 Å). Phase identification was done by comparing the diffraction pattern to the simulated diffractions of Fe<sub>2</sub>O<sub>3</sub> and Fe<sub>3</sub>O<sub>4</sub>. Infrared spectra were obtained using a Bruker Invenio-X Fourier transform infrared (FTIR) spectrometer by the accumulation of 64 scans over the 400–4000 cm<sup>-1</sup> range with a resolution of 4 cm<sup>-1</sup>. Samples were suspended in ethanol and deposited onto a diamond crystal. The ethanol was allowed to evaporate before measuring.



X-ray photoelectron spectra (XPS) were recorded using an XPS VersaProbe III energy spectrometer. Al-K $\alpha$  radiation of 1486 eV was used. Gaussian–Lorentzian functions were used to adjust data after baseline correction.

The hydrodynamic diameter ( $D_h$ ) and zeta potential of particles were determined by dynamic light scattering (DLS) using a Zetasizer Advance Ultra (Red Label) from Malvern Panalytical equipped with a He–Ne laser (633 nm, nominal maximal power of 10 mW) as the light source. The scattered light was measured at an angle of 90° and collected using an autocorrelator. Samples were dispersed in the corresponding solvent at a concentration of 0.01 mg mL<sup>-1</sup> and dispersed using ultrasound for 10 minutes before measuring at 25 °C. Measurements were carried out after allowing 5 min for sample equilibration, with three successive runs on each sample.

Room temperature hysteresis curves, which quantify magnetization saturation and coercivity, were generated using a superconducting quantum interference device SQUID magnetometer MPMS3 (Quantum Design) in a vibrating sample magnetometry (VSM) mode.

## Results and discussion

### Optimization of MNDs synthesis

We improved the synthesis of MNDs by streamlining the procedure to eliminate steps that may promote aggregation or induce detrimental morphology changes, thereby enhancing particle stability and ensuring uniform morphological distribution throughout the synthesis. We followed and adapted the two-step procedure for the synthesis of MNDs originally reported by Yang *et al.*<sup>3</sup> with size optimization of vortex MNDs as described by Gregurec *et al.*<sup>8</sup> Typically,  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> is hydrother-

mally produced in the presence of sodium acetate and ethanol to precipitate into disc-shaped nanoparticles. These templates are then converted into the Fe<sub>3</sub>O<sub>4</sub> phase by a wet hydrogen reduction process at 60 °C using tri-*n*-octylamine (TOA) as solvent and oleic acid (OA) as a surfactant added to prevent nanoparticle coalescence during the reaction. Water, acetate and ethanol have been shown in the literature to be necessary to produce the anisotropic shape of the  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> templates, and the associated synthetic conditions and mechanisms have been duly studied.<sup>21</sup> By contrast, the role of the OA in the reduction step as an efficient stabilising agent for preventing coalescence or aggregation of MNDs in TOA has not been fully investigated. Moreover, it has been indicated that an unfavorable ratio of oleic acid to nanoparticles could lead to material degradation as the harsh conditions in the presence of OA erode the MNDs resulting in smaller magnetic particles.<sup>3</sup>

With the aim of simplifying the reduction reaction and avoiding damage to the anisotropic shape of the Fe<sub>3</sub>O<sub>4</sub>, we studied the reduction process in the absence of OA. For this purpose, two samples were fabricated, with and without OA, labelled Fe<sub>3</sub>O<sub>4</sub>@OA and Fe<sub>3</sub>O<sub>4</sub> bare, respectively.

The interaction between carboxylate groups of OA and the surface of spherical magnetite nanoparticles has been previously studied by FTIR and XPS, revealing either adsorption or chemisorption of OA on the magnetite surface with a chelating effect, depending on the surface characteristics and morphology of the particles.<sup>22</sup> In the present study, FTIR spectra of samples with and without OA revealed that no significant differences were observed. Only weak bands corresponding to the symmetric and asymmetric stretching of coordinated carboxylate groups of oleic acid in Fe<sub>3</sub>O<sub>4</sub>@OA, were detected at 1407 cm<sup>-1</sup> and 1554 cm<sup>-1</sup>, respectively (Fig. 2a).<sup>23</sup> These results indicate a limited presence of OA on the particle surface.

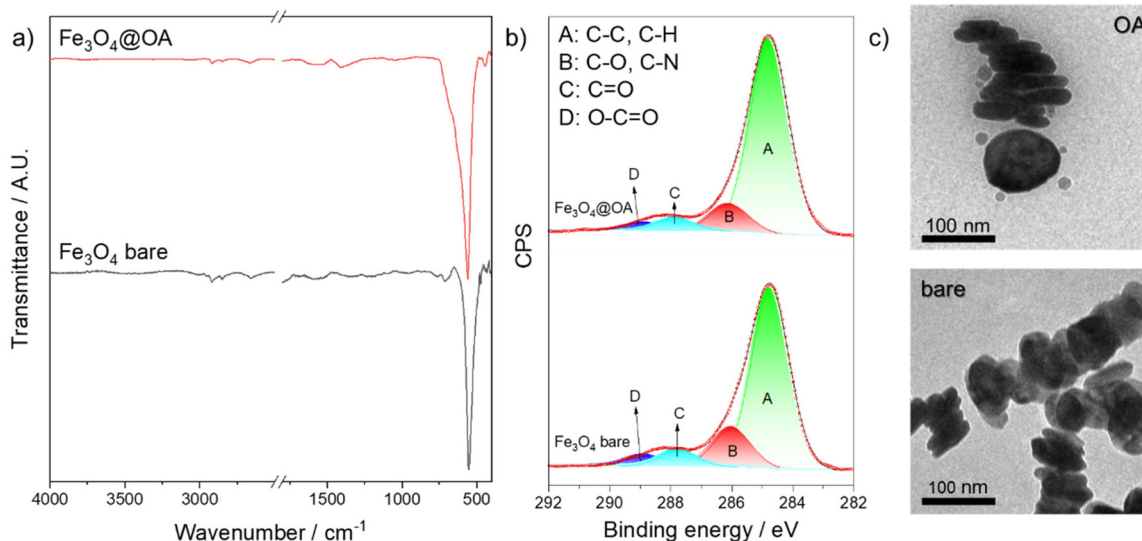


Fig. 2 Characterization of Fe<sub>3</sub>O<sub>4</sub>@OA and bare Fe<sub>3</sub>O<sub>4</sub> by (a) FTIR, (b) XPS corresponding to the C 1s region, and (c) TEM (top: Fe<sub>3</sub>O<sub>4</sub>@OA; bottom: bare Fe<sub>3</sub>O<sub>4</sub>).



XPS analysis also shows no detectable differences between the spectra of the two samples that would indicate the presence of surface OA. The C 1s signal intensity is of the same order of magnitude in both cases, despite the longer carbon chain in OA compared to acetate (Fig. 2b), providing further evidence that only acetates are present in the OA-treated sample. DLS was employed to probe the colloidal stability of the suspensions in the presence and absence of OA. Although DLS analysis assumes spherical geometry, while the particles studied here are anisotropic, this remains a reasonable approach to study their behavior in suspension, including colloidal stability and aggregation. Measurements of MNDs in both organic media (ethanol) and water confirm that neither sample exhibits solvent preference, as shown by both intensity and number distributions (Table S1 and Fig. S1). Bare Fe<sub>3</sub>O<sub>4</sub> shows hydrodynamic diameters of 524 ± 59 nm in ethanol and 538 ± 24 nm in water, whereas Fe<sub>3</sub>O<sub>4</sub>@OA exhibits 548 ± 52 nm in ethanol and 507 ± 14 nm in water.

Finally, TEM imaging reveals that after reduction in the presence of OA, smaller spheres are formed in addition to MNDs (Fig. 2c). In contrast, bare Fe<sub>3</sub>O<sub>4</sub> maintains the desired MND morphology, without evidence of small spherical particle formation.

### Mesoporous silica coating

DLS measurements show that the hematite nanodiscs in ethanol exhibit an average hydrodynamic diameter of 199 ± 2 nm, with a polydispersity index (PDI) of 0.12, whereas MNDs in the same solvent exhibit a significantly larger average diameter of 524 ± 59 nm and a PDI of 0.38 (Table S1). A similar trend is observed in water, indicating that hematite nanodiscs are better dispersed in both media than their magnetite counterparts, most likely due to the absence of magnetic interactions among them.

To mitigate these interactions during the reduction of hematite to magnetite, a mesoporous silica layer was grown on the hematite templates to act as a physical barrier, thereby reducing the interparticle magnetic coupling during the reduction process, when hematite is converted into magnetite. Mesoporous silica was selected over a hard (dense) silica shell because its interconnected pore network permits the diffusion of solvents and H<sub>2</sub> molecules through the pores. The α-Fe<sub>2</sub>O<sub>3</sub> templates were treated with hexadecyltrimethylammonium bromide (CTAB) as a shape-directing agent and dispersant in a mixture of different ratios of water and isopropanol, in the presence of NH<sub>4</sub>OH as a basic hydrolysing agent. The hematite templates (Fig. S2, a diameter of 107 ± 14 nm; a width of 26 ± 7 nm) were well dispersed with an ultrasound tip, after which half of the TEOS was added to initiate SiO<sub>2</sub> deposition, followed by ultrasonication for 30 min to allow SiO<sub>2</sub> formation. The remaining TEOS was then added, and the suspension was ultrasonicated for an additional 30 min to complete the growth of the SiO<sub>2</sub> shell. Four different conditions were tested for silica shell growth by varying the TEOS concentration and the isopropanol:water ratio, while maintaining the CTAB and base concentrations constant. Under three conditions, the TEOS amount was kept constant while the isopropanol:water

**Table 1** Tested conditions for m-SiO<sub>2</sub> growth. All coatings were prepared with the same α-Fe<sub>2</sub>O<sub>3</sub> concentration (1 mg mL<sup>-1</sup>), and NH<sub>4</sub>OH (25%) was kept at 0.025 mL mL<sup>-1</sup> solution

Condition	Water : isopropanol	TEOS (μL mL <sup>-1</sup> sol)
1	0 : 5	8
2	0.2 : 4.8	8
3	2.5 : 2.5	8
4	2.5 : 2.5	0.8

ratio was varied (Table 1), while under the fourth condition, the TEOS concentration was diluted tenfold with the isopropanol:water ratio set at 1 : 1. The resulting mesoporous SiO<sub>2</sub> (m-SiO<sub>2</sub>) coatings were characterized by TEM (Fig. S3). As reported in the literature, an increased water content accelerates TEOS hydrolysis, producing a thicker m-SiO<sub>2</sub> layer.<sup>24</sup> In contrast, when the water content was very low (less than 10% of the total volume), the silica layer was too thin to be resolved by TEM (conditions 1 and 2). Conversely, at high water fractions, excess TEOS led to the formation of thick m-SiO<sub>2</sub> layers encapsulating multiple nanodiscs (condition 3). Optimal conditions for coating of individual nanodiscs were achieved with an excess of water and reduced TEOS concentration (condition 4), yielding uniform m-SiO<sub>2</sub> coating of 6 ± 1 nm, determined by ImageJ analysis.

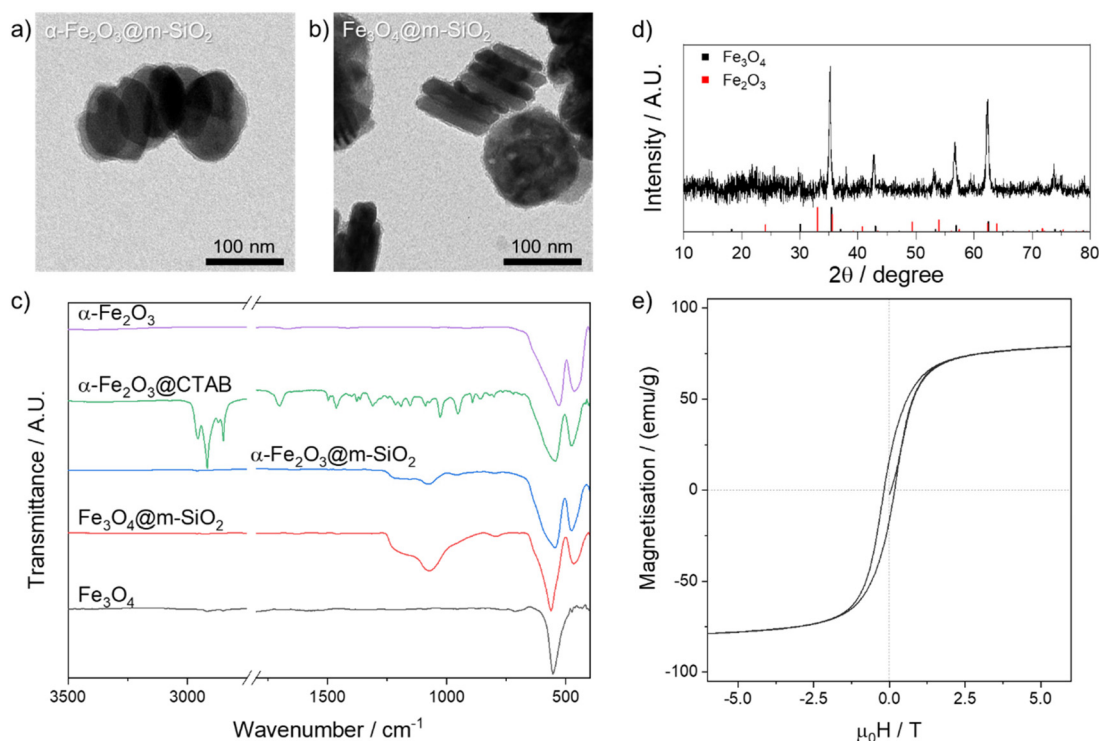
No difference in reduction time was observed between α-Fe<sub>2</sub>O<sub>3</sub> and α-Fe<sub>2</sub>O<sub>3</sub>@m-SiO<sub>2</sub>, with both samples being completely reduced after 30 min under a continuous flow of H<sub>2</sub> (100%) at 360 °C.

TEM images confirm that the m-SiO<sub>2</sub> shell remains structurally preserved after reduction, although the layer thickness decreases slightly to 4 ± 1 nm for Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>. In both α-Fe<sub>2</sub>O<sub>3</sub> and Fe<sub>3</sub>O<sub>4</sub>, the mesoporous nature of the silica shell is evident in the TEM images, with surfaces appearing rough and non-uniform, rather than smooth (Fig. 3a and b), consistent with the expected and the highly porous structure (Fig. S4).<sup>25</sup> Energy-dispersive X-ray spectroscopy (EDX) mapping performed at multiple positions across the nanodiscs further confirms that the m-SiO<sub>2</sub> layer is evenly distributed across both the α-Fe<sub>2</sub>O<sub>3</sub> and Fe<sub>3</sub>O<sub>4</sub> surfaces (Fig. S5 and S6).

Tapping-mode atomic force microscopy (AFM) was used to characterize the surface topography of Fe<sub>3</sub>O<sub>4</sub> and Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub> nanodiscs, with representative images and surface roughness profiles shown in Fig. S7. AFM analysis revealed that silica-coated MNDs exhibit increased density of valleys and ridges with a lower root-mean-square surface roughness (RMS) of 0.191 ± 0.030 nm compared to bare MNDs, with an RMS of 0.582 ± 0.105 nm. Moreover, Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub> nanodiscs exhibit a well-ordered surface geometry characterized by a hexagonal platelet arrangement resembling a pore array, absent in uncoated MNDs, indicating successful coating with mesoporous silica.<sup>26–28</sup>

X-ray diffraction (XRD) analysis further confirms the full reduction of α-Fe<sub>2</sub>O<sub>3</sub>@m-SiO<sub>2</sub> to the Fe<sub>3</sub>O<sub>4</sub> phase. Five strong diffraction peaks are observed in the spectrum at 35.4°, 43.0°, 44.7°, 50.3° and 56.6°.





**Fig. 3** TEM images (a) of  $\alpha\text{-Fe}_2\text{O}_3@m\text{-SiO}_2$  and (b)  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$ . (c) XRD of  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  with the diffraction lines indicating the  $\alpha\text{-Fe}_2\text{O}_3$  and  $\text{Fe}_3\text{O}_4$  phases. (d) FTIR spectra of different stages of the sample before and after reduction.  $\text{Fe}_3\text{O}_4$  is added as the reference. (e) Room temperature magnetization curves of  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$ .

53.4°, 56.9°, and 62.5°, corresponding to the (311), (400), (422), (511), and (440) crystalline planes attributed to the  $\text{Fe}_3\text{O}_4$  phase (Fig. 3c). XPS quantitative analysis of  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  reveals a low total atomic percentage of iron, at 1.76%, consistent with the shallow XPS probing depth of  $\sim 5$  nm. Nonetheless, the Fe 3p and Fe 2p<sub>3/2</sub> signals are clearly detectable (Fig. S8).<sup>29</sup> The Fe 3p component at 55.5 eV is assigned to the Fe–Si bond, while the O 1s spectrum shows a component at 530.2 eV attributable to the Fe–O–Si interfacial bonds.<sup>30</sup> A second component at 532.9 eV is assigned to the SiO<sub>2</sub> environment, in agreement with the Si 2p<sub>3/2</sub> core peak at 103.7 eV.

FTIR spectroscopy (Fig. 3d) provides further evidence of successful shell formation and reduction. Prior to silica coating,  $\alpha\text{-Fe}_2\text{O}_3$  exhibits characteristic stretching vibrations at 463 and 530  $\text{cm}^{-1}$  (purple line).<sup>31</sup> After complexation with CTAB and before the ethanol/water washing, additional bands appear that can be attributed to trapped surfactant and unreacted reactants within the pores of  $\alpha\text{-Fe}_2\text{O}_3@m\text{-SiO}_2$  (green line). These bands fully disappear after the ethanol/water washing, while the Fe–O stretching bands shift to 476 and 547  $\text{cm}^{-1}$  (blue line). These bands are shifted to higher wavenumbers because of the vibration modes of SiO<sub>2</sub>. The shift at 476 nm is linked to the asymmetric stretching of Si–O,<sup>32</sup> while the band at 547  $\text{cm}^{-1}$  is affected by the Fe–O–Si bending vibration. Additional Si–O bands are observed at 794, 977, 1073, and 1195  $\text{cm}^{-1}$ .<sup>32</sup> Finally, the characteristic Fe–O stretching of  $\text{Fe}_3\text{O}_4$  is slightly shifted in  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$ , from

551  $\text{cm}^{-1}$  to 561  $\text{cm}^{-1}$ , also due to the contribution of Fe–O–Si.<sup>33</sup> A band near  $\sim 475$   $\text{cm}^{-1}$  is also present, corresponding to the Si–O–Si bending vibration.<sup>34</sup>

The size distribution from TEM micrographs shows that  $\alpha\text{-Fe}_2\text{O}_3@m\text{-SiO}_2$  nanodiscs have an average diameter of around  $112 \pm 11$  nm (Fig. S9), while the average diameter for the  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  nanodiscs is  $110 \pm 14$  nm (Fig. S10).

The intensity-weighted DLS size distribution of  $\alpha\text{-Fe}_2\text{O}_3$  templates dispersed in ethanol exhibits a cumulant hydrodynamic diameter (z-average) of  $\sim 199$  nm, exceeding the dimensions determined by electron microscopy. This discrepancy reflects the partial particle aggregation in suspension. Following the growth of the mesoporous silica, the average hydrodynamic diameter increases to 230 nm. After reduction,  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  exhibits further increase with a hydrodynamic average diameter of 451 nm, accompanied by increased PDI (0.42 vs. 0.11 for  $\alpha\text{-Fe}_2\text{O}_3@m\text{-SiO}_2$ ). While  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  nanodiscs exhibit a larger hydrodynamic diameter ( $\sim 451$  nm) relative to uncoated MNDs ( $\sim 100$  nm), this increase is consistent with small aggregates of approximately three to four discs, suggesting limited aggregation rather than extensive clustering. Importantly, the mesoporous silica shell provides improved colloidal stability over time, as will be discussed below.

In addition to stabilising the dispersions, the silica shell does not compromise the intrinsic magnetic properties of the nanodiscs. Hysteresis curves recorded at room temperature



(Fig. 3e) show that  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  retains a saturation magnetization ( $M_s$ ) of  $83.96 \text{ emu g}^{-1}$  (Fig. 3e), corresponding to 97.6% of the bulk  $\text{Fe}_3\text{O}_4$  value ( $86 \text{ emu g}^{-1}$  at 300 K),<sup>35</sup> and higher than previously reported values for  $\sim 100 \text{ nm}$   $\text{Fe}_3\text{O}_4$  nanodiscs with  $M_s \approx 80 \text{ emu g}^{-1}$ .<sup>3</sup> These findings demonstrate that the mesoporous silica coating improves colloidal stability without significantly diminishing magnetic performance.

### Surface modification via polymer grafting

Considering potential biomedical applications of the MNDs, we employed a synthetic strategy designed to grow a polymeric shell through covalent bonding between the inorganic cores and a polymer matrix. This covalent approach was chosen over physical interactions to ensure chemically stable attachment, minimizing the risk of detachment of the nanoparticle coating in complex biological environments and preserving colloidal stability. The synthetic route involves two main steps: first,  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  nanoparticles were functionalized with a silane bearing a terminal vinyl group (MEMO). Subsequently, a free-radical precipitation/dispersion polymerization was carried out under ultrasonication using an SDS as a stabilizing agent and an APS/TEMED system to initiate the polymerization. The silanization reaction was optimized to proceed under continuous ultrasonication in toluene at  $70 \text{ }^\circ\text{C}$  for 30 min. Polymer coatings were then grafted using NIPAM and MAA in three different compositions: pure PNIPAM ( $\text{Fe}_3\text{O}_4@m\text{-SiO}_2@P1$ ), and copolymers of NIPAM and MAA (P(NIPAM-co-MAA)), with monomer ratios of 80:20 ( $\text{Fe}_3\text{O}_4@m\text{-SiO}_2@P2$ ) and 50:50 ( $\text{Fe}_3\text{O}_4@m\text{-SiO}_2@P3$ ).

TEM micrographs (Fig. 4a–c) revealed that the polymer shell around MNDs exhibits a smoother appearance, with no clear contrast between silica and the organic material, suggesting that the polymer could have grown within the mesoporous structure of the silica. Gaussian fitting of the shell thickness (Fig. 4d and e) gives values of  $6.1 \pm 1.4 \text{ nm}$ ,  $7.3 \pm 1.5 \text{ nm}$ , and  $7.5 \pm 1.7 \text{ nm}$  for  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2@P1$ , P2, and P3, respectively, while  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  shows a thickness of  $3.4 \pm 0.8 \text{ nm}$ . Statistical analysis using one-way ANOVA followed by Dunnett's multiple comparison test confirms a significant increase in thickness for polymer-coated samples compared to the bare  $m\text{-SiO}_2$  layer ( $P < 0.0001$ ) (Table S2).

AFM analysis further highlights morphological changes of the mesoporous silica-coated magnetite nanodiscs after polymer functionalization (Fig. S6 and S11). The hexagonal platelet topography of  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  is replaced by large, densely packed plateaus on the surface of polymer-coated nanodiscs. Phase contrast imaging suggests that while silica-coated MNDs exhibit rigid, homogeneous surfaces, polymer-coated MNDs exhibit smoother profiles with increased apparent height and heterogeneous phase responses, indicative of viscoelastic dissipation.

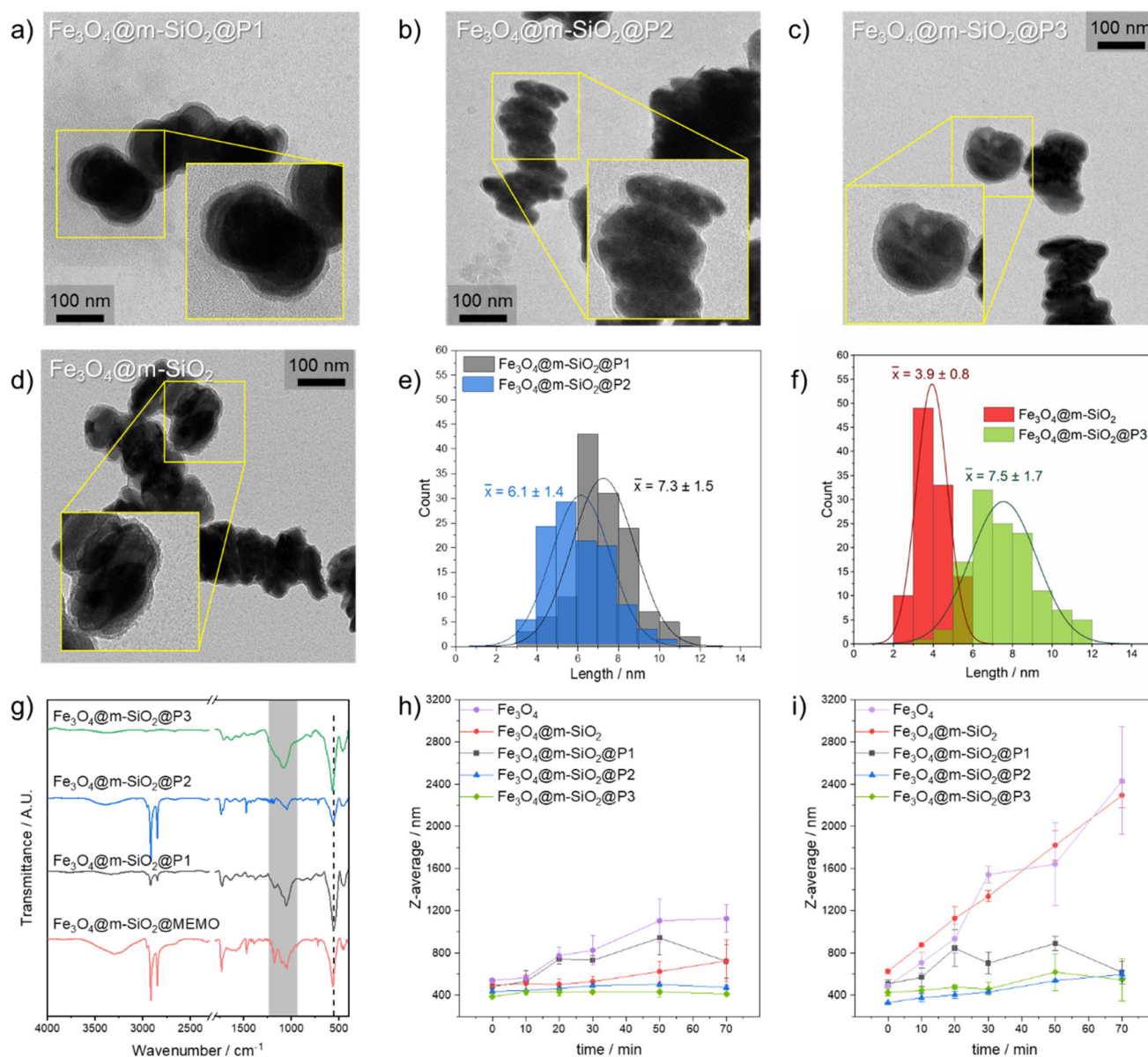
The successful anchoring of the silane was confirmed by FTIR spectroscopy through the appearance of a characteristic carbonyl stretching vibration at around  $1720 \text{ cm}^{-1}$ . Additionally, the presence of the polymer shell was verified by the appearance of the amide I (mainly due to the C=O stretch-

ing vibration) and amide II (a combination of the N–H bending vibration and C–N) bands of PNIPAM, typically observed around  $1650 \text{ cm}^{-1}$  and  $1540 \text{ cm}^{-1}$ , respectively.

The colloidal stability of the hybrid nanostructures with different polymers (varying monomer ratios in the P(NIPAM-MAA) copolymer) in water was evaluated by monitoring the average hydrodynamic diameter over time *via* DLS (Fig. 4h). The bare  $\text{Fe}_3\text{O}_4$  (magenta) initially exhibits an average size of  $538 \pm 24 \text{ nm}$  which increases after 70 min to  $1130 \pm 131 \text{ nm}$  (109% increase), indicating particle aggregation over time.  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  shows improved stability, increasing from  $490 \pm 20 \text{ nm}$  up to  $725 \pm 200 \text{ nm}$  (48% increase) after the same time period.  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2@P1$  nanostructures exhibit an initial average size of  $480 \pm 13 \text{ nm}$ , which increases over time to reach  $942 \text{ nm}$  at 50 min, and then decreases to  $719 \pm 157 \text{ nm}$  after 70 min (corresponding to an overall increase of  $\sim 50\%$ ).  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2@P2$  and P3 composed of the copolymer P(NIPAM-co-MAA) in a ratio of 80:20 and 50:50, respectively, consistently show smaller hydrodynamic diameters across all time points compared with P1 (PNIPAM alone) and the inorganic nanostructures. The hydrodynamic diameter varies from  $436 \pm 11 \text{ nm}$  to  $472 \pm 24 \text{ nm}$  for  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2@P2$ , and  $386 \pm 23 \text{ nm}$  to  $410 \pm 17 \text{ nm}$  for  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2@P3$ . Furthermore, the size variation between the initial measurement and the final time point (70 min) for P2 is only around  $36 \text{ nm}$  (8% increase), and for P3 is around  $24 \text{ nm}$  (6% increase), highlighting their improved colloidal stability. This behavior is attributed to the negatively charged MAA units, as evidenced by the negative Zeta potential values (Table S1), which enhance electrostatic repulsion and thereby more effectively prevent nanoparticle aggregation in water.

The stability of the MNDs with different coatings was evaluated in RPMI 1640 medium (Roswell Park Memorial Institute 1640), used here as a model of physiological conditions (Fig. 4i). Both  $\text{Fe}_3\text{O}_4$  and  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  show a high degree of aggregation over 70 min, with hydrodynamic diameters increasing from  $489 \pm 1 \text{ nm}$  to  $2430 \pm 511 \text{ nm}$  (397%), and  $652 \pm 20 \text{ nm}$  to  $2290 \pm 115 \text{ nm}$  (251%), respectively, indicating that the silica coating alone is insufficient to prevent agglomeration in biological media.  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2@P1$  behaves similarly to its behavior in water (Fig. 4e), increasing from  $507 \pm 35 \text{ nm}$  to  $614 \pm 109 \text{ nm}$  (21% increase), even reaching values up to  $891 \pm 68 \text{ nm}$ . This demonstrates that PNIPAM, a neutral polymer, provides limited protection against aggregation, although better than  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$ . In contrast,  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  coated with P2 and P3 maintain improved colloidal stability than P1 in RPMI medium, with hydrodynamic diameter increasing from  $330 \pm 5 \text{ nm}$  to  $595 \pm 34 \text{ nm}$  (80% increase), and from  $424 \pm 33 \text{ nm}$  to  $545 \pm 198 \text{ nm}$  (29% increase), respectively, over the same time period. Notably, P2 exhibits lower hydrodynamic diameters in RPMI than P3 in water, highlighting its enhanced ability to prevent aggregation under physiological conditions. Moreover, hybrid P2-coated nanostructures consistently show lower PDI values in RPMI medium throughout the entire measurement period, remaining below 0.45 (Fig. S12).





**Fig. 4** TEM images of (a) Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@P1, (b) Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@P2, (c) Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@P3 and (d) Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub> including magnification of selected nanodiscs. Width distribution of the coatings measured from multiple TEM images for (e) Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@P1 and Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@P2, and (f) Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@P3 and Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>. (g) FTIR spectra showing the silane functionalization, followed by polymerization and purification for the different polymer compositions: P1 corresponds to PNIPAM, P2 to P(NIPAM-co-MAA) 80 : 20, and P3 to P(NIPAM-co-MAA) 50 : 50. Temporal evolution of particle size measured by DLS, showing the average hydrodynamic diameter of the nanomaterials at different time points in (h) water and (i) RPMI.

### Cytotoxicity assay

Since nanodiscs are intended for biological applications, their cytotoxicity was evaluated. *In vitro* cytotoxicity of Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub> and Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@P3 was assessed using WI-38 fibroblasts and HEK-293T (Fig. S13). Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@P3 was selected because these nanodiscs showed the highest stability both in water and in cell medium. Non-toxicity is considered as higher than 80% cell viability, according to ISO 10993-5, while 80%–60% is weak, 60%–40% is moderate, and below 40% is strong cytotoxicity.<sup>36</sup> Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub>@P3 showed no signs of cytotoxicity as cell viability remained above the 80%

threshold at all evaluated time points and concentrations for both HEK-293T and WI-38. Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub> without polymer coating<sub>2</sub> exhibits cytotoxicity in HEK-293T at concentrations of 25 μg mL<sup>-1</sup> and higher. In contrast, no toxicity is shown for Fe<sub>3</sub>O<sub>4</sub>@m-SiO<sub>2</sub> to WI-38 cells.

### Discussion

During the reduction of hematite, aggregation is likely to take place upon conversion to magnetite as dipole-dipole inter-



actions of closely packed MNDs become prevalent over vortex magnetization, which is detrimental for applications in biological environments. Here, we have explored strategies to improve the colloidal stability of MNDs, particularly under physiological conditions.

First, oleic acid (OA) was evaluated as a stabilizing agent during reduction. TEM analysis revealed the erosion of the material, showing small spheres alongside the MNDs, attributed to successive cycles of dissolution and reprecipitation of iron oxide from the discs under harsh reaction conditions.<sup>37,38</sup> DLS measurements both in water and ethanol showed no significant differences between the MNDs reduced in the presence or absence of OA. XPS and FTIR spectra further confirmed minimal OA adsorption. These results suggest that OA is inefficiently adsorbed on the MNDs during the reduction process, possibly due to surface-bound acetate ions that block binding.

To mitigate aggregation, applying a silica coating on the  $\text{Fe}_3\text{O}_4$  surface should provide a physical barrier preventing direct contact between MNDs and reducing magnetic dipole interactions that dominate after reduction. As evidenced by the DLS size distribution analysis, hematite exhibits a lower tendency to aggregate than magnetite; therefore, silica coating was applied to the hematite template prior to reduction. A mesoporous layer of silica is preferable over a hard silica coating because the large pore area available in the mesoporous layer enables  $\text{H}_2$  to freely flow through the silica layer reaching the hematite template for reduction. The successful mesoporous shell formation was confirmed by TEM, XPS, FTIR and AFM analyses and the efficient reduction within 30 min to the  $\text{Fe}_3\text{O}_4$  phase was demonstrated by the saturation magnetization and XRD spectrum showing the presence of a pure magnetite crystalline phase with high  $M_s$  values.

The silica layer remains chemically and morphologically stable after the reduction step, with a slight decrease in thickness from 6 nm in hematite to 4 nm in magnetite as evidenced by FTIR, XPS and TEM analyses. DLS measurements show that  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  nanodiscs exhibit significantly less aggregation in water than uncoated MNDs over time. While uncoated  $\text{Fe}_3\text{O}_4$  suffered an increment in hydrodynamic diameter of 109% (538 nm to 1130 nm) over 70 min, the mesoporous silica-coated material,  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$ , showed a much higher degree of stabilization, with only a 48% increase in hydrodynamic diameter (490 nm to 725 nm). However, in RPMI medium, both  $\text{Fe}_3\text{O}_4$  and  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  show increments in size of 397% (489 nm to 2430 nm) and 266% (625 nm to 2290 nm) over 70 min, respectively, in agreement with the reported behavior of silica nanoparticles in this medium.<sup>39</sup>

The mesoporous silica coating also offers great versatility for surface functionalization. Its surface can be readily modified with silane groups, and the mesoporous structure increases the surface area available for covalent attachment of these molecules. Using this approach, we grafted NIPAM/MAA copolymers onto the porous silica coating.

MNDs@m-SiO<sub>2</sub> with PNIPAM coating exhibited larger hydrodynamic diameters over time compared to  $\text{Fe}_3\text{O}_4@m$ -

SiO<sub>2</sub> alone. Nonetheless, this polymer grafting leads to a higher degree of stabilization in RPMI medium compared to both uncoated MND and the m-SiO<sub>2</sub> coated MNDs. Polymer coatings P2 and P3 (containing 20% and 50% MAA, respectively) showed improved stability up to 70 min in both water and cell media, with increases in hydrodynamic diameter of 8% (436 nm to 472 nm) and 6% (386 nm to 410 nm) in water and 80% (330 nm to 595 nm) and 29% (424 nm to 545 nm) in RPMI medium.

Although the colloidal stability of P2 and P3 coated MNDs is better in water than in RPMI media, these hybrids exhibit lower size distribution in both environments compared with the MNDs and MNDs@m-SiO<sub>2</sub>. Hybrid nanostructures with P2 coating show an increase in hydrodynamic diameter of approximately threefold smaller than that of bare inorganic MNDs in water and about fivefold smaller in cell culture media. These results demonstrate that negatively charged MAA monomers effectively prevent aggregation under physiological conditions.

Finally, cytotoxicity evaluation of  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  and  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2@P3$  was performed with WI-38 fibroblasts and HEK-293T cells.  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2@P3$  showed no cytotoxicity at any of the tested concentrations, even at 200  $\mu\text{g mL}^{-1}$ , for both cell lines.  $\text{Fe}_3\text{O}_4@m\text{-SiO}_2$  was only observed to be cytotoxic (cell viability lower than 80%) for HEK-293T cells at concentrations higher than 12.5  $\mu\text{g mL}^{-1}$ . These results hint at a positive effect of the polymer coating on decreasing toxicity, which may be related to a lower cellular uptake of the polymer coated nanodiscs. Further studies on cell uptake and the intracellular fate of nanodiscs are on the way.

Overall, applying a mesoporous silica shell to hematite templates allows complete reduction to magnetite while physically reducing aggregation, and subsequent silanization and polymer grafting significantly improve colloidal stability in both aqueous and biologically relevant environments.

## Conclusions

We have improved the synthesis of MNDs by removing the unnecessary and potentially detrimental addition of OA from the wet-reduction process. Hematite templates were successfully coated with a thin mesoporous silica shell, which reduced aggregation while allowing efficient reduction to magnetite, yielding nanodiscs with magnetic properties comparable to those of uncoated magnetite. The mesoporous silica coating alone improved colloidal stability in water when contrasted with uncoated MNDs but was insufficient to prevent aggregation in cell culture media. Subsequent functionalization of the mesoporous silica shell with negatively charged NIPAM/MAA copolymers (P2 and P3) further enhanced colloidal stability in cell culture media. Over 70 min, the size increase of hybrid nanostructures with P2 coating is approximately threefold smaller than that of bare inorganic MNDs in water and about fivefold smaller in cell culture media.



## Author contributions

P. R. D.: investigation, data curation, methodology, conceptualization, writing – original draft, and writing – review & editing. M. A. M.: investigation, data curation, supervision, and writing – review & editing. E. K.: investigation. F. W.: investigation. V. D. T.: investigation and supervision. S. M. I.: investigation. E. G. P.: investigation and data curation. S. T.: investigation. D. G.: funding acquisition, conceptualization, supervision, and writing – review & editing. S. E. M.: funding acquisition, conceptualization, supervision, writing – original draft, and writing – review & editing.

## Conflicts of interest

There are no conflicts of interest to declare.

## Data availability

Data for this article are available at Zenodo, <https://zenodo.org/uploads/17090464>.

Supplementary information (SI) is available. Supplementary information includes additional characterization of magnetic nanodiscs and coatings: DLS, TEM, XPS, AFM, EDX data; and the toxicity evaluation of MNDs in two cell lines. See DOI: <https://doi.org/10.1039/d5nr03822g>.

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