Supporting information

*Julien Mahin, Christoph O. Franck, Luise Fanslau, Mick Mantle, Ljiljana Fruk, Laura Torrente-Murciano**

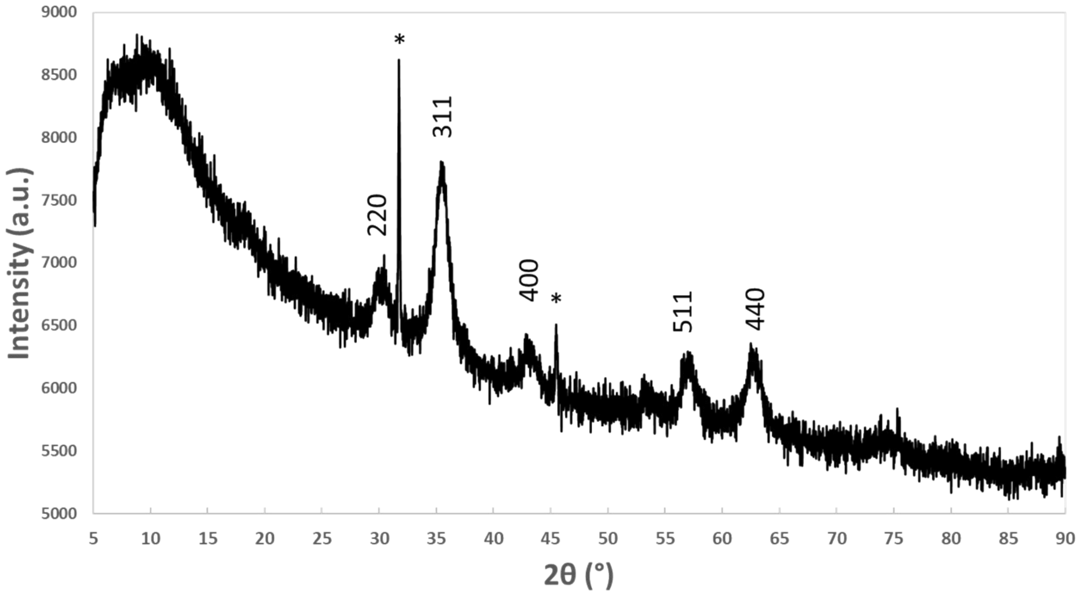

Figure S1: Powder X-ray diffractogram of the as-synthesised bare Fe_3O_4 nanoparticles, illustrating the typical inverse spinel reflections characteristic of magnetite/maghemite. The sharp reflections marked with an asterisk correspond to leftover NaCl used to flocculate and precipitate the nanoparticle suspension.

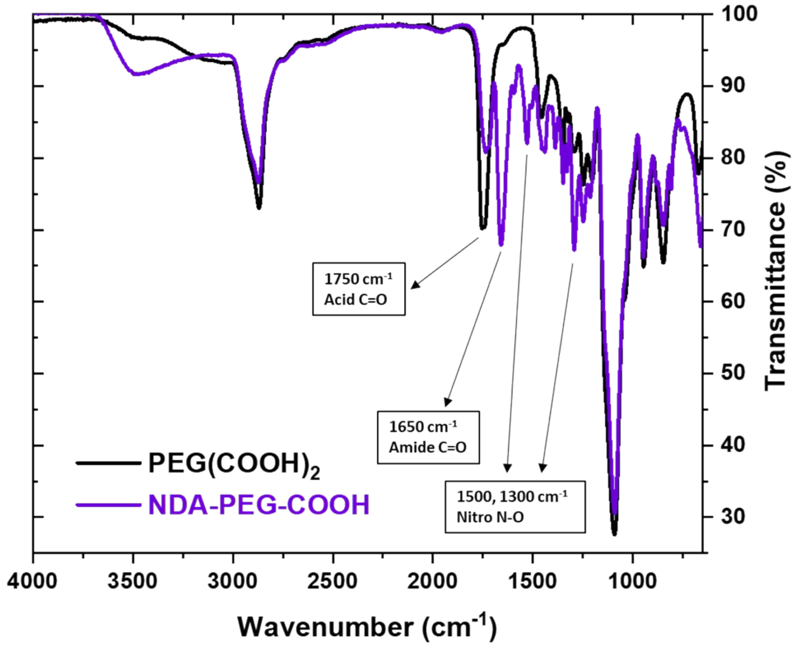

Figure S2: Fourier Transform Infrared (FTIR) spectroscopy of PEG(COOH)$_2$ (black line) and NDA-PEG-COOH (purple line). The appearance of characteristic vibration peaks of amide (1650 cm^{-1}) and nitro (1300, 1500 cm^{-1}), as well as decrease in the carboxylic acid peak (1750 cm^{-1}) indicates the target NDA-PEG-COOH was formed.

^{1}H-NMR spectra of NDA-PEG-COOH was measured on a Bruker 400 MHz spectrometer in $CDCl_3$: δ 8 (s, 1H), 7.65 (s, 1H), 6.81 (s, 1H), 4.12 (s, 2H), 3.96 (s, 2H), 3.55-3.74 (m, 46H), 2.8 (t, J= 6.3 Hz, 2H). Conversion of PEG(COOH)$_2$ into NDA-PEG-COOH was estimated at 52% based on the ratio of acid/amide Hα peak area.

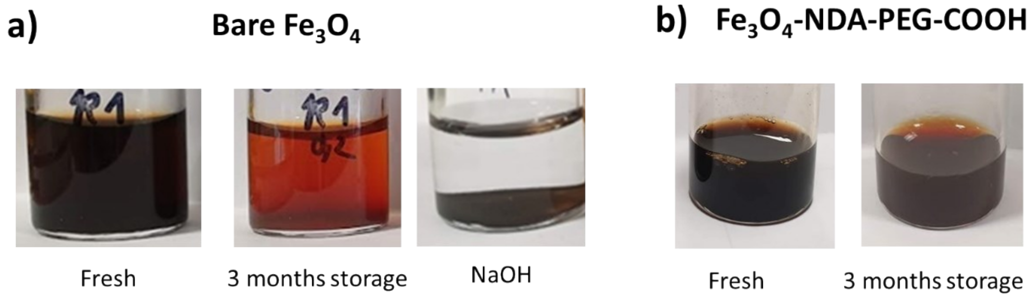

Figure S3: Pictures of suspensions of a) bare Fe_3O_4NP and b) Fe_3O_4NP-NDA-PEG-COOH, immediately after synthesis and after 3 months of storage in ambient conditions. Bare nanoparticles synthesised with NaOH as the base instead of NEt_4OH as the base remained fully aggregated.

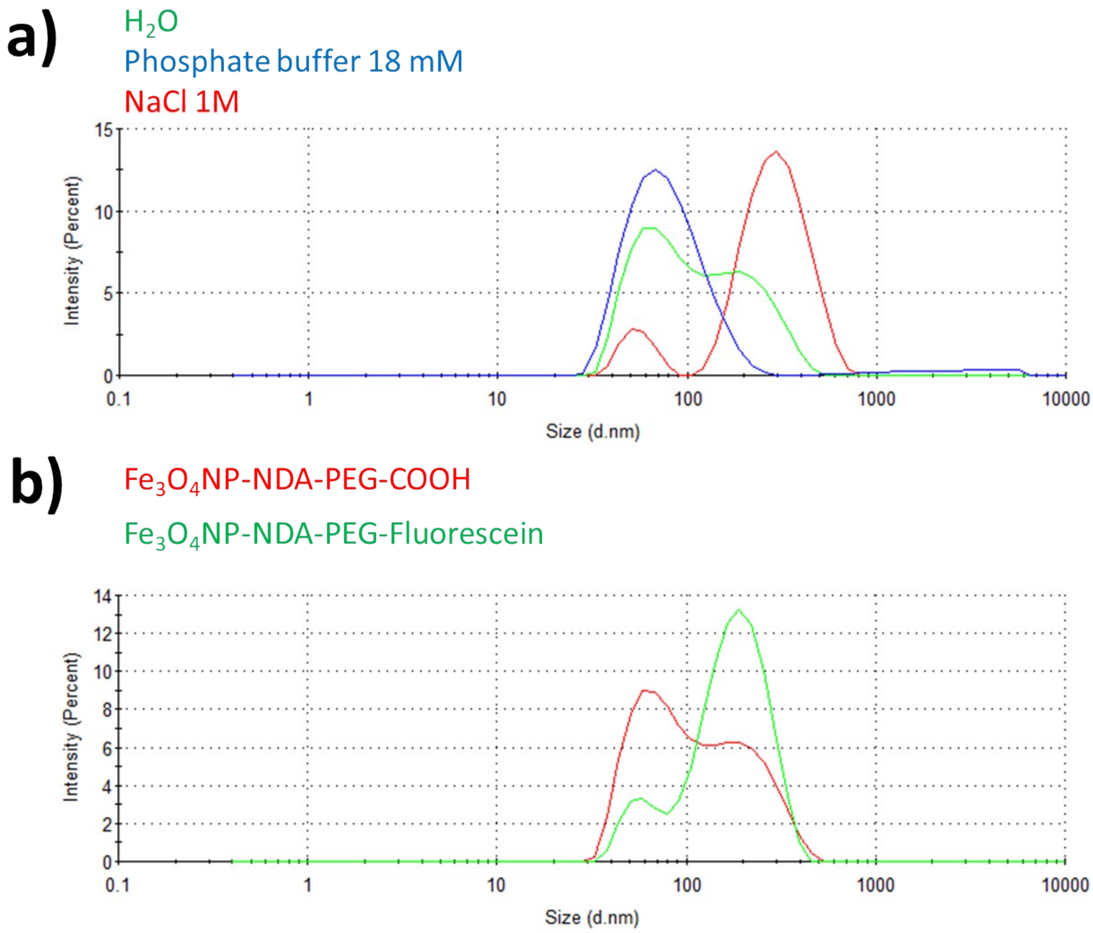

Figure S4: Particle size distributions measured by dynamic light scattering weighed by intensity of functionalized Fe_3O_4NP-NDA-PEG-COOH nanoparticles a) in various media b) before and after derivatization with aminofluorescein.

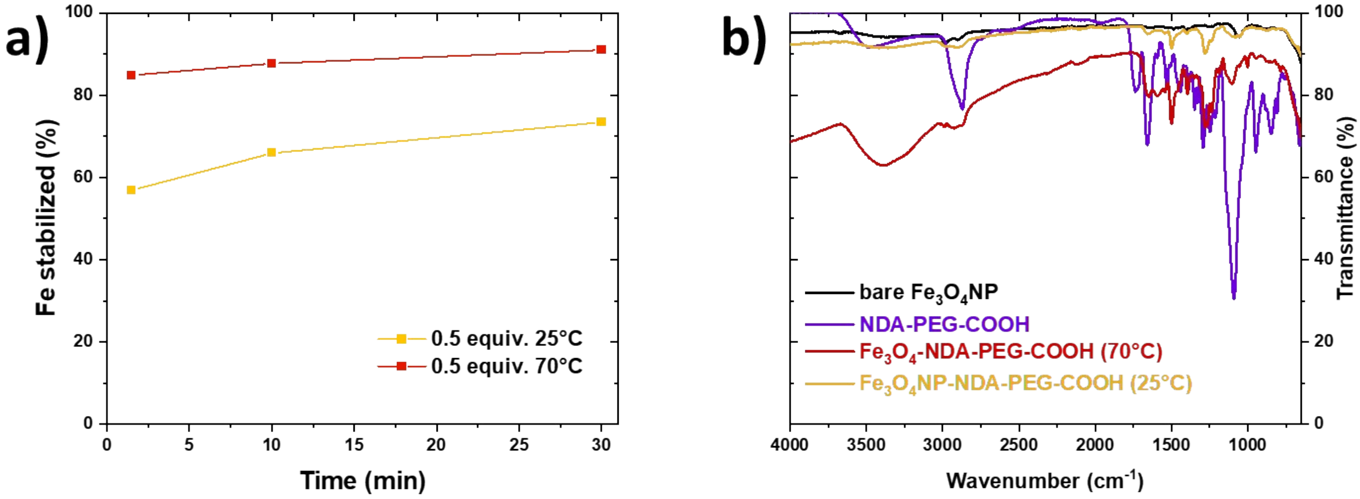

Figure S5: a) Evolution of the amount of iron oxide nanoparticle stabilized as a function of reaction time for 0.5 equiv. of NDA-PEG-COOH stabilizer added at different temperatures, after quenching the functionalization by adjusting the pH to 7. B) FTIR spectra for bare Fe_3O_4NP, NDA-PEG-COOH and Fe_3O_4NP-NDA-PEG-COOH functionalized in continuous flow at 25 and 70°C.

Table S1: Chemical cost breakdown of the batch synthesis of nitrodopamine (NDA) on a 5 g scale, estimated at 4.22 £/g. A reaction yield of 60% was considered. The prices per gram of the precursors are derived from considering the cheapest option on common chemical supplier websites.

Chemical	mol	MM (g/mol)	Mass (g)	Supplier	Quantity (g)	Unit price (£)	Mass cost (£/g)	Cost per batch (£)
Dopamine	0.0264	189.64	5	Sigma Aldrich	100	260	2.60	13.00
$NaNO_2$	0.0913	69	6.3	Alfa Aesar	1000	19.7	0.02	0.12
H_2SO_4	0.0939	98	9.2	Fischer scientific	4410	45.11	0.01	0.09

Table S2: Chemical cost breakdown of the batch synthesis of NDA-PEG-COOH on a 3 mmol scale, estimated at 3.46 £/g based on the previously derived chemical cost of NDA. A reaction yield of 80% was considered. The prices per gram of the precursors are derived from considering the cheapest option on common chemical supplier websites.

Chemical	mol	MM (g/mol)	Mass (g)	Supplier	Quantity (g)	Unit price (£)	Mass cost (£/g)	Cost per batch (£)
$PEG(COOH)_2$	0.003	574	1.722	Sigma Aldrich	296	84.4	0.29	0.49
EDC	0.003	155.25	0.46575	TCI	100	480	4.80	2.24
NHS	0.003	115.05	0.34515	TCI	500	165	0.33	0.11
NDA	0.003	198	0.594	-	-	-	4.22	2.51
DMF	0.194	73	14.16	Fischer scientific	2360	49.23	0.02	0.30
DCM	0.469	85	39.9	Fischer scientific	6650	53.55	0.01	0.32
LiCl	0.05	42.4	2.12	Alfa Aesar	1000	139	0.14	0.29

Table S3: Chemical cost breakdown of the continuous flow synthesis of Fe_3O_4NP-NDA-PEG-COOH estimated at 61 £/g without workup and 430 £/g including the workup, on a 0.4 mmol scale using the previously derived chemical cost of NDA-PEG-COOH. A yield of 50% was considered. The prices per gram of the precursors are derived from considering the cheapest option on common chemical supplier websites.

Chemical	mol	MM (g/mol)	Mass (g)	Supplier	Quantity (g)	Unit price (£)	Mass cost (£/g)	Cost per run (£
$FeCl_2$	6.67E-05	198.81	0.013254	Alfa aesar	250	24.9	0.001	0.10
$FeCl_3$	1.33E-04	270.3	0.03604	Alfa aesar	500	38.5	0.003	0.08
NEt_4OH	1.20E-03	147.26	0.176712	Sigma Aldrich	1000	480	0.085	0.48
MES	2.00E-03	195.2	0.3904	Alfa aesar	500	150	0.117	0.30
HCl	1.00E-04	37	0.0037	Fischer scientific	148	128	0.003	0.86
NDA-PEG-COOH	1.00E-04	754	0.0754	-	-	-	0.261	3.46
EtOH	8.23E-01	46	37.872	Fischer scientific	1972.5	74.37	1.428	0.04
hexane	3.66E-01	86	31.44	Fischer scientific	1637.5	73.59	1.413	0.04

Table S4: Cost breakdown of the different components of the continuous flow reaction setup for flow rates of 0.2 and 10 mL/min. The length of tubing must be increased as the flow rate *is increased to maintain the same residence time. The larger operating volumes necessitate more expensive pumps (such as microannular gear pumps) which can operate with larger volumes of reactant solutions.*

Flow rate (mL/min)	0.2		10	
Component	**Price (£)**	**Cost per run (£)**	**Price (£)**	**Cost per run (£)**
Fittings	122	0.24	122	0.24
Tubing	13.3	0.03	665	1.33
Syringes	0.1	0.4	0	0
Pumps	3600	7.2	25000	50
Glassware	100	0.2	100	0.2
Total	**3835**	**8.07**	**25785**	**51.77**

Table S5: Cost breakdown for the labour and energy required to run the continuous flow reaction setup. A standard run consisted of an 8h work shift and the energy-demanding equipment was assumed to be on for 7h during this run.

	Hourly cost (£/h)	**Cost per run (£)**
Energy	0.14	0.98
Labour	37.5	300