

Supporting Information

Functional Responsive superparamagnetic core/shell Nanoparticles and their drug release properties

Z. Ferjaoui^{a,b}, R Schneider^c, A. Meftah^b, E. Gaffet^a, H. Alem^a

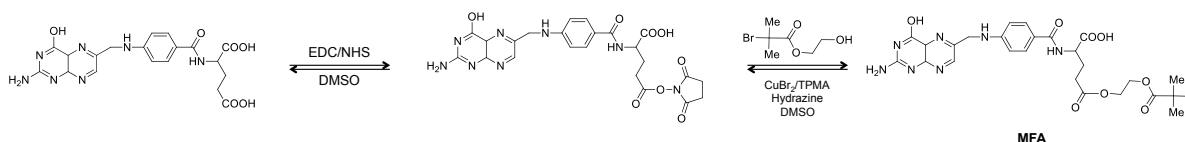
1. Synthesis of the modified Folic Acid

1.a Modification of the Folic Acid

The folic acid (FA: 2g, 4.53 mmol, 1 eq) was first dissolved in DMSO (20 mL) followed by the addition of N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (EDC:1.04g, 5.4 mmol, 1.2 eq) and N-Hydroxysuccinimide (NHS : 0.62g, 5.4 mmol, 1.2 eq). After stirring the mixture for 3 hours, the 2-Hydroxyethyl 2-bromoisobutyrate (0.71 mL, 4.53 mmol, 1 eq) was added to the mixture. After stirring for 24 hours, the modified FA (MFA) was precipitated in an excess of dichloromethane and the resulting orange solid was washed several times by dichloromethane and acetone and dried under vacuum. The structure of the MFA was confirmed by NMR ¹H. The Yield of the reaction was of 85%.

1.b Grafting of the Modified Folic acid to the polymer chain end

The same procedure was used for all the monomer composition. 50 mg of Fe₃O₄@P(MEO₂MA_x-OEGMA_y) were dissolved in Milli-Q water (200 mL). The MFA was added to the solution (2g, 2,15 mmol), and 200 μL of stock solution (in water) of CuBr₂/TPMA (0.884 μmol CuBr₂, 4,3 μmol) were added. The reaction mixture was degassed by three freeze-pump-thaw cycles. Subsequently 250 μL of a solution of hydrazine in DMSO (7.1 mg/mL) was added to the mixture. The NPs were maintained under stirring during 24 hours. Afterwards, the mixture was poured into hot Milli-Q water to precipitate the insoluble components. The materials were purified by washing with hot Milli-Q water by centrifugation until the supernatant was completely clear, to make sure that all the physisorbed MFA was completely removed from the NPs system. We could confirm the MFA grafting by FT-IR.



Scheme SI 1: reaction scheme for the synthesis of Hydroxyethyl 2-bromoisobutyrate modified folic acid (MFA).

Supplementary data

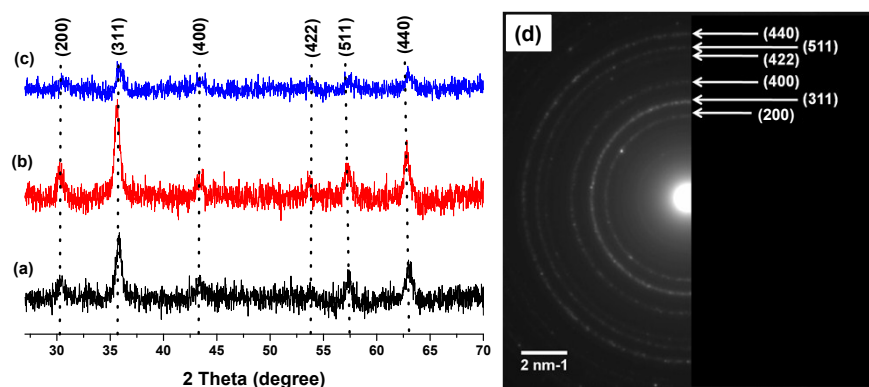


Figure SI 2. (a) Fe₃O₄ NPs, (b) Fe₃O₄@Silane NPs, (c) Fe₃O₄@MEO₂MA-co-OEGMA NPs, and (d) SAED pattern of SPION, with clear diffraction rings.

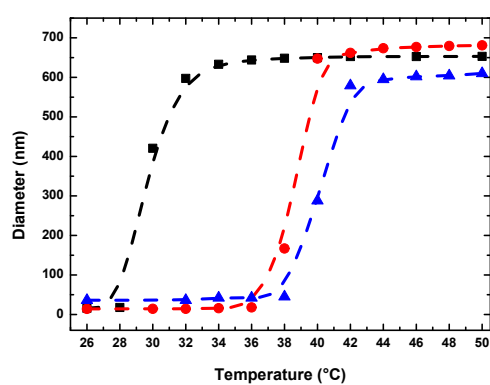


Figure SI 3. (A) Evolution of Fe₃O₄@P(MEO₂MA₈₀-OEGMA₂₀) (black), Fe₃O₄@P(MEO₂MA₆₅-OEGMA₃₅) (red) and Fe₃O₄@P(MEO₂MA₆₀-OEGMA₄₀) (blue) diameter and aggregation with temperature.

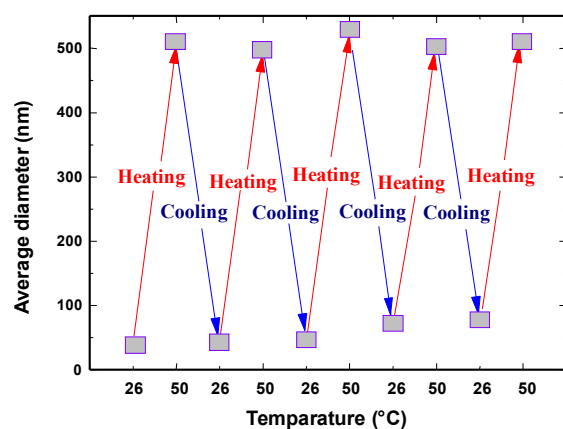


Figure SI 4. Reversibility of the core-shell NPs hydrodynamic diameter study with temperature

in water of $\text{Fe}_3\text{O}_4@\text{P}(\text{MEO}_2\text{MA}_{80}\text{-OEGMA}_{20})$. The same curves were obtained for all the samples.

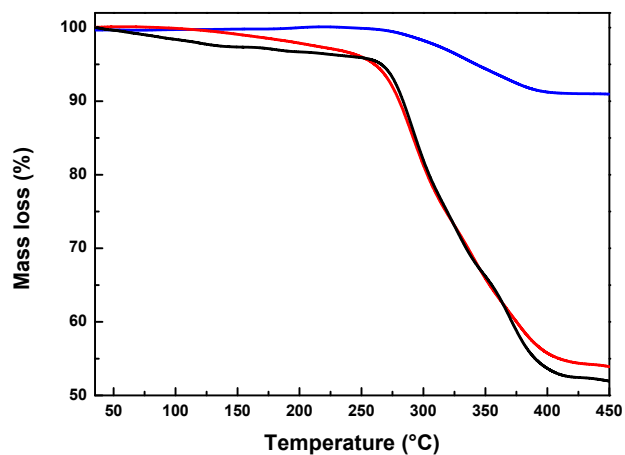


Figure SI5. (a) TGA curves of $\text{Fe}_3\text{O}_4@\text{Silane}$ (blue), $\text{Fe}_3\text{O}_4@\text{P}(\text{MEO}_2\text{MA}_{60}\text{-OEGMA}_{40})$ (black) and $\text{Fe}_3\text{O}_4@\text{MEO}_2\text{MA}_{65}\text{-co-OEGMA}_{35}\text{-FA}$ (red) samples

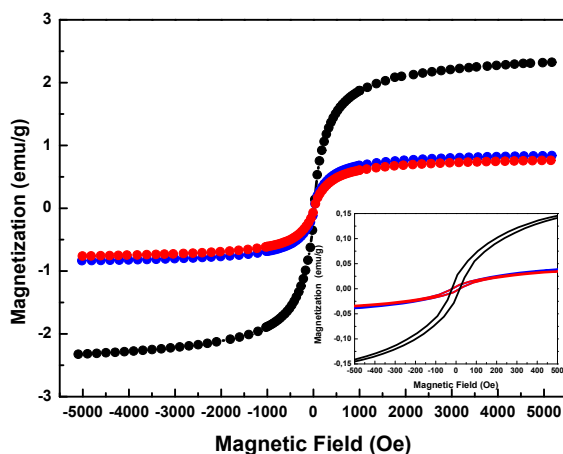


Figure SI 6. Magnetization curves of the $\text{Fe}_3\text{O}_4@\text{MEO}_2\text{MA}_{80}\text{-co-OEGMA}_{20}$ (black), $\text{Fe}_3\text{O}_4@\text{MEO}_2\text{MA}_{65}\text{-co-OEGMA}_{35}$ (red) and $\text{Fe}_3\text{O}_4@\text{MEO}_2\text{MA}_{60}\text{-co-OEGMA}_{40}$ (blue) nanoparticles