Electronic Supplementary Material (ESI) for Materials Chemistry Frontiers.

Direct Correlation of PNIPAM Thermal Transition on Magnetic Resonance Relaxation of Iron Oxide Nanoparticles

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Supporting Information

Experimental Section

Reagents and Materials**:** All chemicals were purchased from Sigma-Aldrich unless otherwise stated: benzyl ether (99%), iron (III) acetylacetonate ($Fe(acac)_3$; 97%), oleic acid (BDH, 92%), oleylamine (70%), Pluronic® F-108, carboxy terminated poly (*N*-isopropyl acrylamide) (PNIPAM-COOH; M_n 3500, M_w 12,300), and 1,2-tetradecanediol (90%) were used as received. Poly(glycidyl methacrylate) (PGMA; M_w 360,920 g mol^{-1}) was kindly provided by Dr Marck Norret of The University of Western Australia.

Preparation of Iron Oxide Nanoparticles: Fe_3O_4 was synthesized by the organic decomposition of $Fe(acac)_3$ in benzyl ether at 300°C, in the presence of oleic acid, oleylamine, and 1,2-tetradecanediol, as previously described.[1] In brief, $Fe(acac)_3$ (508 mg), 1,2-tetradecandiol (2304 mg), oleic acid (1.69 g) and oleylamine (1.61 g) were added to benzyl ether (10 mL). Moisture was removed by heating the solution to 100°C under constant stirring. The mixture was heated to 200°C for 2 hr and then heated to reflux (~300 °C) under an atmosphere of nitrogen for 1 hr. After cooling, the reaction mixture was precipitated in ethanol (40 mL) and centrifuged at 3000*g* for 15 minutes to collect the black precipitate. The precipitate was resuspended in hexane (7.5 mL) and centrifuged again under identical conditions. The supernatant containing magnetite nanoparticles was stored under an atmosphere of argon in dark before further use.

Synthesis of PNIPAM-g-PGMA*:* Poly(glycidyl methacrylate) (PGMA) (50 mg) dissolved in 1.2 mL methyl ethyl ketone (MEK) was added dropwise to carboxy terminated poly (*N*-isopropyl acrylamide) (100 mg). Polymerization was carried out in thermostatic oil bath at 80°C for 24 hours. The mixture was precipitated into diethyl ether from MEK. The final white powder product was obtained after vacuum drying for 24 h (32 g, yield: 64%).[2] ^1H NMR (600 MHz, $CDCl_3$, δ in ppm): 0.80-1.24 ($C\boldsymbol{H}_3$-), 1.63-1.89 (-$C\boldsymbol{H}_2C\boldsymbol{H}$-), 2.65, 2.83 (-$CHC\boldsymbol{H}_2O$-), 3.22 (-$CH_2C\boldsymbol{H}(CH_2)O$-), 4.00 (-$NHC\boldsymbol{H}$-), 3.80, 4.29 (-

OC***H***$_2$CH-) (Figure S1).

Polymer Nanoparticles Preparation: Nanoparticles were prepared using a non-spontaneous emulsification route. The organic phase was prepared by dispersing iron oxide nanoparticles (20 mg) and dissolving PNIPAM-*g*-PGMA (75 mg) or PGMA (75 mg) in a 1:3 ratios of $CHCl_3$ and MEK (6 mL). The organic phase was added dropwise, with rapid stirring, to an aqueous solution of Pluronic® F-108 (1.25% w/v, 30 mL). The resulting emulsion was homogenized with a probe-type ultrasonicator at low power for 1 minute to form the nanoparticles. The organic solvents were allowed to evaporate overnight under the flow of N_2. Excess polymer and large aggregated magnetite were removed by centrifugation at 3000*g* for 45 minutes. The magnetic polymeric nanoparticles were collected on a magnetic separation column (LS, Miltenyl Biotec), washed and eluted using Pluronic® F-108 before further use.

Characterization

Transmission electron microscopy was performed on samples using the JEOL 2100 electron microscope operated at 120 kV. PNIPAM-PGMA-NPs and PGMA-NPs suspensions were pipetted onto a continuous 200-mesh carbon-coated copper grid and left to dry in air for a few hours before commencing the measurements. The polymer nanoparticles were further characterized with ATR-FTIR (Perkin Elmer Spectrum One FT-IR spectrometer) and ^{1}H NMR (Bruker Avance 600MHz spectrometer).

The hydrodynamic diameter and zeta potential of the dispersions were measured at different temperatures using dynamic light scattering (Zetasizer Nano, Malvern Instruments). Samples were transferred into clear disposable zeta cells at a concentration of approximately 10 µg/mL and data for each sample was averaged for 10 measurements. Measurements were taken using a 4 mW, solid-state He-Ne laser operating at 633 nm with scattering angle of 173°. The refractive index (1.330) and viscosity (0.8872 cPa) of water at 25 °C were used.

The proton transverse relaxation rates of the magnetic nanoparticles suspension were measured at different temperatures using a Bruker Mq60 Minispec NMR analyzer. The instrument has a magnetic field strength of 1.4 T with measuring frequency of 60 MHz. This field strength corresponds to a proton Larmor frequency of 60 MHz. Proton transverse relaxation times (T_2) were obtained from fitting a monoexponential decay curve to signal data generated by a Carr-Purcell-Meiboom-Gill (CPMG)[3, 4] spin-echo pulse sequence with an echo spacing of 1 ms and a repetition time of 5 s. The echo spacing was 0.5 ms for the short echo (T_2) time measurements (2000 echoes) with a repetition time of 5 s. Longitudinal relaxation times (T_1) were obtained from fitting a monoexponential recovery curve to signal data generated with an inversion recovery (IR) pulse sequence using 10 logarithmically spaced inversion times between 50 ms and 10000 ms. Each sample (500 μL) was transferred into a 7.5-mm NMR tube, sealed with an airtight cap and vortexed. Samples were prepared by diluting to specific concentration between 0.1 and 0.01 wt%. Samples were briefly equilibrated in an external water bath for at least 15 minutes at 25 °C to eliminate temperature differences between sample and the relaxometer.

The magnetic measurement used throughout this work was performed on Quantum Design MPMS SQUID VSM. Samples were prepared by compressing 10 mg of lyophilized magnetite and polymer nanoparticles into in a gel capsule. Samples were mounted within a brass holder and connected to one end of a sample rod that is inserted into the dewar. The other end is attached to a stepper motor that is used to position the sample within the center of the SQUID pickup coils. The Zero-Field-Cool/Field Cool (ZFC/FC) experiment measures how the magnetization of a system changes with increasing temperature. This experiment has two parts. The first part is the measurement of the ZFC curve, while the second part is the measurement of the FC curve.

For the ZFC measurements, the sample was cooled from room temperature to 5 K in the absence of a magnetic field. A magnetic field of 100 Oe was then applied to create a potential that preferentially favours magnetic moments in the direction parallel to the applied field. Then, the temperature was increased in increments of a few Kelvin and the magnetic moment of the samples were measured at each incremental level.

Meanwhile, FC measurements were made after cooling down the sample with an applied field of few Oe. In this way, the magnetic moments were partially aligned in the field direction. Then, similar to the ZFC curve, a 100 Oe field was applied and the magnetization was measured while increasing the temperature. As happened in the ZFC curve, the magnetization decreases due to thermal activation.

The hysteresis loop is a signature of a magnetic material and can be used to determine the magnetic properties of a nanoparticle in the presence of an applied magnetic field at a particular temperature.

This experiment involves measuring the magnetization, *M* of the sample as the function of the applied magnetic field, *H*. It is often referred to as the *M*-*H* loop.

The samples were cooled from room temperature to 5 K in zero-field. Hysteresis loops were subsequently measured at 5 K by sweeping the field to -70 kOe and back to +70 kOe. The field spacing was 1 kOe on these sweeps. Hysteresis loops were measured at higher temperatures by warming at the completion of the lower temperature loop. Saturation magnetization values reported here are based on the magnetization of the sample in a field of 70 kOe at 5 K.

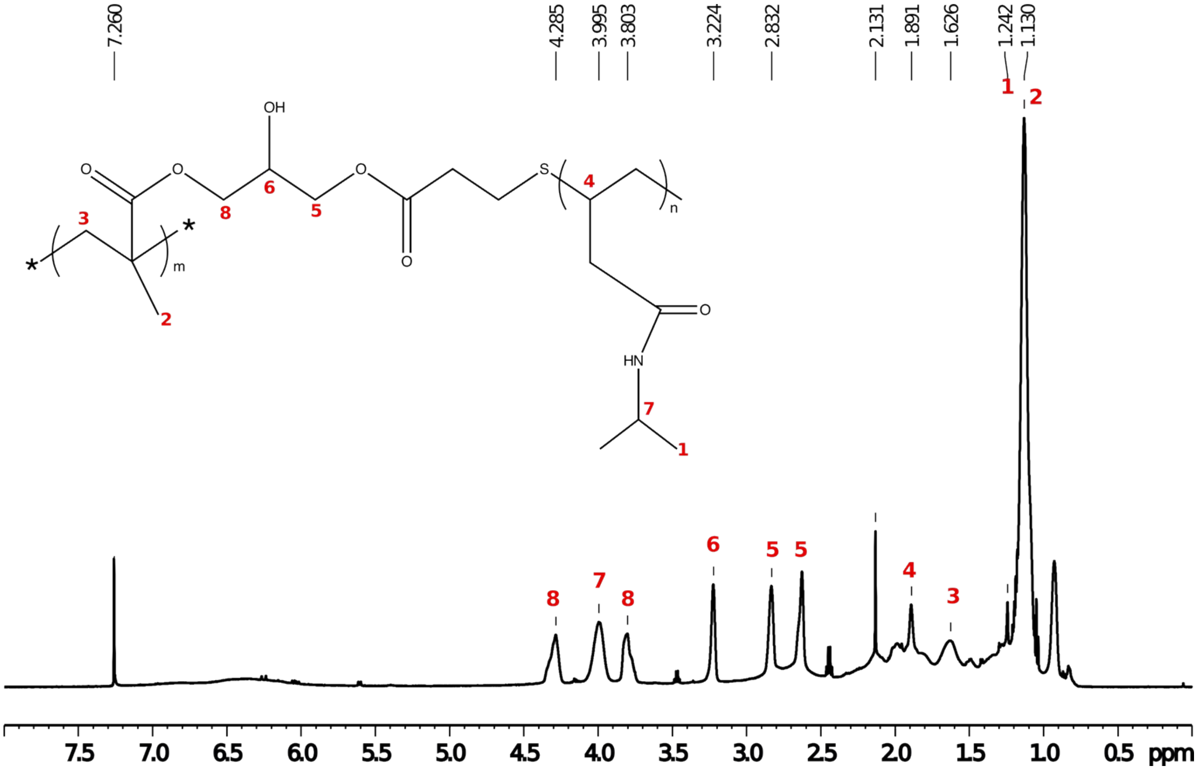

Figure S1. ^{1}H NMR spectra of polymer PNIPAM-*g*-PGMA in CDCl$_3$.

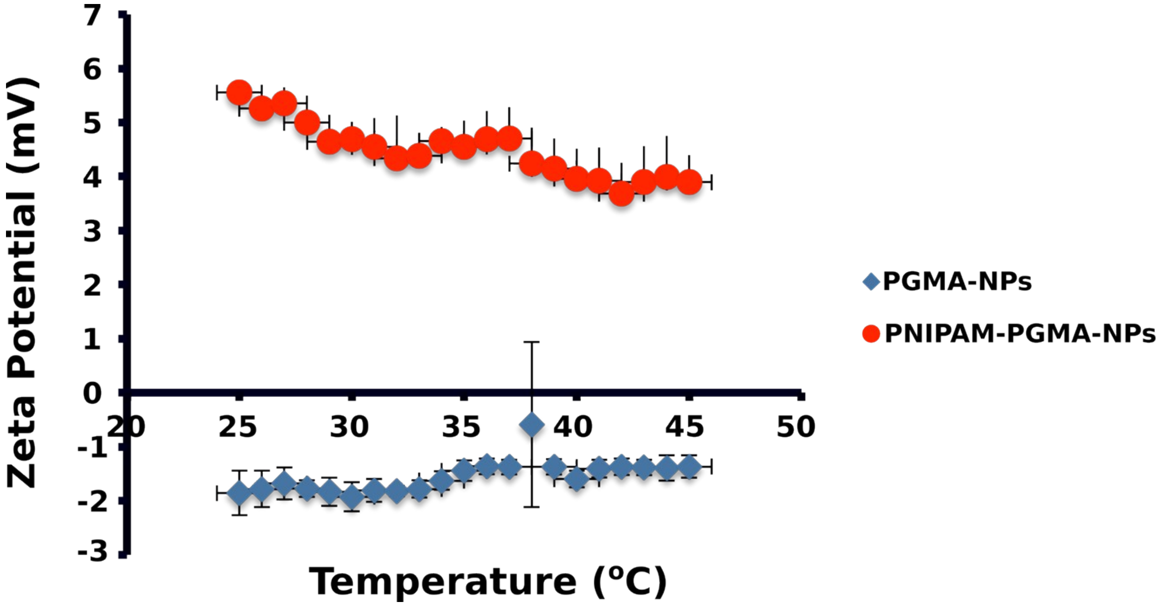

Figure S2. Zeta potential of PNIPAM-PGMA-NPs and PGMA-NPs at different temperatures.

References:

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