Dual-stimuli responsive PNiPAM microgel achieved via layer-by-layer assembly: Magnetic and thermoresponsive

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We describe the synthesis, characterisation and surface-modification of magnetic nanoparticles and a poly(N-isopropylacrylamide) microgel, followed by the assembly and characterisation of magnetic nanoparticles on the microgel. To facilitate this deposition, the surface of the microgel is first modified via the layer-by-layer assembly of polyelectrolytes. One advantage of this concept is that it allows an independent optimization and fine tuning of the magnetic and thermoresponsive properties of individual components (nanoparticles and microgels) before assembling them so that the hybrid core–shell structure retains all the individual properties. The decisive parameter when exploiting the thermoresponsive and magnetic properties in such hybrid core–shell structures is the amount of heat transfer from the magnetic core onto the thermosensitive (loaded) microgel (for the subsequent heat-triggered release of drugs). Inductive heat study reveals that the heat generated by the magnetic nanoparticles is sufficient to cause the collapse of the microgel above its volume phase transition temperature. Successful confinement of positively and negatively charged magnetic nanoparticles between polyelectrolyte layers is achieved using the layer-by-layer deposition on the microgel. Dynamic light scattering measurements show (i) the presence of each layer successfully deposited, (ii) the preservation of thermoresponse in the coated microgel, and (iii) that the magnetic nanoparticles do not get detached during the phase transition of the microgel. Electrophoresis measurements confirm charge reversal at every stage of layering of the coated microgel, and (iii) that the magnetic nanoparticles do not get detached during the phase transition of the microgel. The decisive parameter when exploiting the thermoresponsive and magnetic properties in such hybrid core–shell structures is the amount of heat transfer from the magnetic core onto the thermosensitive (loaded) microgel (for the subsequent heat-triggered release of drugs).

1. Introduction

Much effort has been devoted to the synthesis of organic/inorganic nanocomposites [1–6] in an attempt to exploit new hybrid properties derived from the various components. Because of their small size, nanoparticles (NP) offer unique properties and magnetic nanoparticles (MNP) based on iron oxide composites or hybrid materials, essentially in the form of core–shell systems are finding great interest in the field of biomedical applications [7–12]. For in vivo applications of MNP, three basic prerequisites have to be met: (i) the surface has to be biocompatible, (ii) non-toxic, and (iii) the particles must be well-dispersed without forming aggregates. Ideally, surface modification should provide good colloidal stability [1,6], biocompatibility and chemical functionality for the potential attachment of biorecognisable ligands. From this has stemmed the idea of using a magnetic core encapsulated in a protective shell. One rational approach is to embed nanoparticles in silica since the latter can be readily functionalised to impart the protective shell [13,14]. We recently reported the in situ as well as the post-modification of MNP with polyelectrolytes, without the need for encapsulation in silica [15,16].

One of the numerous applications of MNP in medicine is cancer treatment [17,18]. Hyperthermia is a promising approach to cancer therapy [19–21]. MNP can be used to target specific tumor tissue, and cancer-specific hyperthermia may be achieved by applying an external alternating current (ac) magnetic field whereby causing MNP to generate heat by inductive heating and increase the temperature to 41–46 °C to kill tumor cells [19–21]. By combining the magnetic property of MNP with the thermoresponsive property of some polymers one can achieve dual-stimuli hybrid core–shell structures. Thermoresponsive magnetic polymer particles are particularly attractive for drug delivery [22–24]. Thermoresponsive microgels have the unique property of undergoing a reversible phase transition. Thermoresponsive microgels (i) have high surface-to-volume ratios, and hence high drug-loading capacities, and (ii) undergo fast, reversible structural changes from a swollen to a collapsed state by expulsing the solvent, therefore...
possess a release-trigger mechanism, making them potential candidates as remote-controlled drug delivery vehicles [22]. One of the most widely studied microgels is poly(N-isopropylacrylamide) (PNiPAM) [25]. It is non-hazardous, soluble in water, and possesses a volume phase transition temperature (VPTT) around 32°C, at which temperature it undergoes a transition from a swollen hydrophilic to a collapsed hydrophobic state. This means that above 32°C PNiPAM releases most of its water content so that a pronounced shrinking is simultaneously observed. This simultaneous shrinking and water release of PNiPAM could be exploited for drug storage, transport and release. If (drug-loaded) PNiPAM is to be used in vivo, one has to devise a means to remotely heat the microgel above its VPTT to release the drug. One way is to incorporate MNP in/on the microgel and use an external magnetic field as a “trigger” to inductively generate enough heat to cause the microgel to shrink [15].

To realise such a core–shell structure, one can employ the layer-by-layer (LbL) assembly devised by Decher et al. in the early 1990s [26,27]. The LbL is a very simple, versatile and elegant technique which involves the sequential adsorption of polycations and polyanions on any charged surface, irrespective of shape and size. Polyelectrolyte multilayers (PEM) as well as NP have been used without purification. Water was ion-exchanged to a specific resistance of $\rho \geq 18$ MΩ cm (Milli-Q) and then double-distilled. The polyelectrolytes were dissolved in water at a concentration of 1 g L$^{-1}$ and used as such with no further adjustment of the pH.

To give a stable ferrofluid. This unmodified MNP is positively charged.

MNP were prepared according to a co-precipitation technique [34] previously described with a slight modification [15]. Briefly, a Fe$^{3+}$ solution was prepared by dissolving 4.86 g FeCl$_3$·6H$_2$O in 30 ml distilled water and a Fe$^{2+}$ solution was prepared by dissolving 2.98 g FeCl$_2$·4H$_2$O in a mixture of 10 ml water and 1.5 ml 37% HCl. Both solutions were placed in an ultrasonic bath for 5 min to homogenize the mixture. The Fe$^{3+}$ and Fe$^{2+}$ solutions were then mixed and allowed to stand in the ultrasonic bath for a short time (about 2 min) just before the precipitation step. To precipitate the iron oxide, the resulting mixture of Fe$^{3+}$ and Fe$^{2+}$ was added drop-wise to a flask containing 240 ml water and 60 ml of 25% NH$_3$ under vigorous stirring (500 rpm). A black suspension was formed immediately and MNP formation was allowed to proceed for 30 min at room temperature with constant stirring to produce a stable, water-based suspension. Aggregates were first separated from the reaction mixture using a strong magnet, and then washed three times with 0.3 M NH$_3$ solution. The washed precipitate was then washed with 60 ml of 2 M HNO$_3$ solution.

Scheme 1. Simplistic representation of the LbL assembly of polyelectrolytes, unmodified and modified magnetic nanoparticles on microgels.
2.3. Synthesis of PSS-modified MNP

Briefly the same procedure was followed with 0.81 g FeCl$_3$·6H$_2$O in 5 ml distilled water and 0.49 g FeCl$_3$·4H$_2$O in a mixture of 1 ml water and 0.25 ml 37% HCl. However to precipitate the iron oxide, the mixture of Fe$^{3+}$ and Fe$^{2+}$ was added drop-wise to a three-necked round bottom flask now containing a mixture of 0.1 g of PSS in 40 ml of water and 10 ml of 25% NH$_4$H$_2$O solution under vigorous stirring (500 rpm) condition. Purification stages were similar (as described above) except that now three cycles of centrifugation at 10000 rpm for 10 min were used and the precipitate dispersed in 20 ml of double-distilled water to get a stable ferrofluid. This PSS-modified MNP, denoted in the text as (PSS-MNP), is negatively charged.

2.4. Synthesis of PNiPAM microgel

The synthesis of PNiPAM microgel via free radical dispersion polymerisation has been reported elsewhere [35,36]. Briefly, 68.86 g N-isopropyl-acrylamide (NiPAM), 1.313 g N,N’-methylenebis(acrylamide) (BIS), and 1.313 g sodium dodecyl sulfate (SDS) were dissolved in 4000 ml water at 72°C under an inert atmosphere of nitrogen at 300 rpm. 3.5 g potassium persulphate (KPS) was dissolved in 50 ml of water and added to the reaction vessel to start the reaction. The reaction was continued for another 5 h under nitrogen. The reaction mixture was passed through glass wool in order to remove particulate matter and further purified by three centrifugation cycles (30, 20, and 15 min) using a Sorvall Discovery™ 90SE ultracentrifuge, with removal of the supernatant and redispersion between each cycle. The microgel was finally collected, redispersed in water overnight, and filtered through a 1.2 μm filter.

2.5. LbL of PEM on PNiPAM microgel

The surface modification of the PNiPAM was carried out using the LbL technique to deposit PEM [28,30,32] (see Scheme 1). PNiPAM (MG) is negatively charged, and consequently, the first coating is accomplished by the deposition of a PDADMAC layer. Briefly, 10 ml of a 1:100 diluted dispersion of microgel were added to 20 ml of an aqueous solution of 1 mg ml$^{-1}$ PDADMAC solution and mixed for 24 h. The excess polyelectrolyte was removed by ultracentrifugation at 50 000 rpm for 30 min at 25°C, and the PDADMAC-coated microgel (MG/PDADMAC) washed by redispersion in water. The washing, redispersion and centrifugation steps were repeated three times to ensure removal of loosely bound PDADMAC. The MG/PDADMAC obtained was finally redispersed in water overnight and filtered through a 1.2 μm filter. MG/PDADMAC constitutes the main precursor for further build-up of either PEM or (PSS-MNP). In order to deposit positively charged MNP, a negatively charged surface is needed, and this is achieved by depositing a layer of polyanion such as PSS to obtain MG/PDADMAC/PSS. To add a layer of PSS on MG/PDADMAC, the above-mentioned procedure is employed.

2.6. LbL of MNP on surface-modified PNiPAM

Positively charged MNP were added to PSS-terminated surface-modified microgel, MG/PDADMAC/PSS while negatively charged (PSS-MNP) were added to PDADMAC-terminated surface-modified microgel, MG/PDADMAC [15], as illustrated in Scheme 1. Briefly, to deposit the MNP on the polyelectrolyte-coated microgel, a solution of the oppositely charged surface-modified microgel was added slowly to a dilute solution of MNP in a volume ratio of 1:5 and mixed for 24 h. The microgel coated with MNP was separated from excess MNP by magnetic separation. We observed that MNP are very stable and do not form agglomeration in the presence of a magnetic field. However, when microgels coated with (PSS-MNP) are exposed to a magnetic field, these particles are then attracted to the magnet very fast due to the higher magnetic dipole interaction between the MNP present on the microgel. The MNP-coated microgels, MG/PDADMAC/PSS/MNP and MG/PDADMAC/(PSS-MNP), were then washed 3 times with water by using the above-mentioned procedure at 25°C, and finally redispersed in water overnight. To confine the MNP onto the microgel, one or two layers of polyelectrolyte were deposited on the MNP-coated microgel using the procedure mentioned above.

2.7. Characterisation

X-ray diffraction (XRD) of the MNP was performed on a Philips X’pert Diffractometer, PW 3040/60 system using CuK$_\alpha$ radiation ($\lambda$ = 0.1541 nm). XRD graphics were compared to the JCPDS standard data in order to deduce the crystal structure of the product. The crystallite size was determined from the X-ray line broadening using Scherrer’s formula. Thermogravimetric analysis (TGA) was carried out on the dried samples with a heating rate of 10°C min$^{-1}$ (from 20 to 600°C), using a DuPont 9900 thermogravimetric analyser in a nitrogen atmosphere. Fourier transform infrared (FTIR) spectra were recorded on a Nicolet Magna 550 spectrometer within the wave range of 4000–400 cm$^{-1}$. For FTIR analysis, an aqueous solution of the MNP was dried in an oven at 80°C and the powder samples were peltalized with dried KBr. Magnetic properties of the particles were measured by Vibrating Sample Magnetometer (VSM) (Lake Shore, Model 7410) while zero-field cooled (ZFC) and field-cooled (FC) magnetisation data (in the range of 5–300 K) were obtained from a SQUID magnetometer (MPMS-5s, Quantum Design, San Diego, USA). Transmission Electron Microscope (TEM) images of particles directly deposited on a carbon-coated grid were taken on a Philips, CM200 microscope working at 200 kV. Inductive heating was performed using a generator–oscillator-combination (TIG 5/300, Hüttinger, Freiburg, Germany) operated at maximum output: power 5.2 kW; current 26.5 A and a frequency of 200 kHz. Under these conditions a maximum magnetic field amplitude of 3.8 kA m$^{-1}$ was calculated at the centre of the coil. A Varian SpectraAA-50B Atomic Absorption Spectrometer was used to determine the iron concentration. Dynamic light scattering (DLS) experiments were carried out on highly diluted samples with an ALV goniometer equipped with an avalanche photodiode and a temperature-controlled cell compartment to determine the hydrodynamic diameter, $D_h$. The samples were allowed to equilibrate for 20 min before a reading was taken, and three sets of recordings were measured at each temperature. Temperature was varied from 20 to 60°C, in steps of 2°C, in both directions, so that one complete cycle consists of a heating curve followed by a cooling curve. Scattered light was detected at 60° with an integration of 120 s and computed with a digital ALV 5000E auto-correlator using an ALV Software version 5.3.2. Particles size was calculated by cumulant fits. The zeta potential ($\zeta$-potential) and the electrophoretic mobility ($\mu$) were determined using a Zetasizer 3000HSA (from Malvern Instruments, England) as a function of the number of layers. Each point is the average of at least ten consistent measurements.

3. Results and discussion

3.1. MNP characterisation

Fig. 1a shows the XRD analysis carried out on both the native MNP and the modified one, (PSS-MNP). The same characteristic peaks of magnetite or maghemite ($2\theta \sim 34.9°, 41.2°, 50.3°, 67.1°$ and $74.3°$), marked, respectively, by their indices ($\{220\}$, $\{311\}$,
The study. The increase in $D_h$ of (PSS-MNP) as compared to MNP is consistent with the presence of the polyelectrolyte which can form tails and loops around the MNP core.

Further evidence of the presence of the polyelectrolyte bound to the MNP is provided by FTIR spectra as shown for MNP and (PSS-MNP) in Fig. 2. For as prepared MNP, the broad absorption band 

$\delta=3000$ and $3600 \text{ cm}^{-1}$ (with peak at around 3404 cm$^{-1}$) and the band at 1620 cm$^{-1}$ are associated with the fundamental valence stretching vibrations of the H$_2$O; the band at 1385 cm$^{-1}$ is due to bending modes of O–C–H, C–C–H, and C–O–H angles of carbonate present on the surface of the MNP (as reaction was done in ambient conditions); and bands at 568 and 644 cm$^{-1}$ are due to the stretching vibration of Fe–O at the tetrahedral site [9]. Confirmation of the attachment of PSS onto the MNP was obtained by observing the following peaks in the spectra of (PSS-MNP): (a) an increase in intensities of bands between 3000 and 3700 cm$^{-1}$ (stretching vibration of water) and 1620 cm$^{-1}$ (O–H bending vibrations of water) in agreement with the increase in the water content in the polymeric network; (b) presence of absorption bands at 2930 and 2854 cm$^{-1}$ supports the presence of PSS on (PSS-MNP) particles.

Fig. 2. FTIR spectra of positively charged MNP and negatively charged (PSS-MNP) provide evidence of the polyelectrolyte bound to the MNP. Additional peaks at 2930 and 2854 cm$^{-1}$, and decrease in intensity at 588, 680 and 1380 cm$^{-1}$ supports the presence of PSS on (PSS-MNP) particles.

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Fig. 3. TGA curves of positively charged MNP and negatively charged (PSS-MNP). The initial weight loss in MNP is due to evaporation of residual water, while the two-step weight loss in (PSS-MNP) is due to an initial loss of residual water followed by degradation of PSS.

The modification by PSS can be quantified by TGA as shown from the TGA curves of MNP and (PSS-MNP) in Fig. 3. As expected, the TGA curve for MNP shows no significant weight loss; the initial weight loss (at around 100–120 °C) is simply due to the evaporation of residual water. For (PSS-MNP), the initial weight loss up to about 200 °C is due to the loss of residual water in the sample and the pronounced weight loss above 200 and up to 370 °C is due to the degradation of PSS [15]. There is a minor weight loss between 370 and 600 °C, which could possibly be attributed to release of entrapped gases formed during the decomposition process. The result confirms that PSS is bound to the MNP. Fig. 3 shows pronounced weight loss (about 9%) for (PSS-MNP) and the approximate polymer content in (PSS-MNP) is estimated to be about 7–8%.

Fig. 4a shows the room temperature magnetisation loops of MNP and (PSS-MNP) in a 2 T field at 310 K. In both cases, the magnetisation curves exhibit zero coercivity and remanence indicating the superparamagnetic properties of both particles. The saturation magnetisation values of MNP and (PSS-MNP) are about 46 and 42 emu g⁻¹, respectively. The latter value is about twice that obtained by Flesch et al. [38] or Kamruzzaman Selim et al. [39] who reported values of 22 and 27 emu g⁻¹ for poly(ε-caprolactone)- and lactobionic acid-modified MNP, respectively. (PSS-MNP) shows a (~9%) decrease in the mass magnetisation compared to the native MNP, consistent with the non-magnetic polyelectrolytes coating bound to the MNP as determined previously by TGA [15,16]. Zero-field-cooled (ZFC) and field-cooled (FC) magnetisation data (obtained from SQUID) in the temperature range of 5–300 K are shown in Fig. 4b. In the ZFC experiment, the field was set to zero and the sample was cooled down to 5 K, then the magnetisation was measured with a field of 100 Oe between 5 and 300 K. In the FC experiment, a field of 100 Oe was applied as the sample was cooled down and the magnetisation was measured when the sample was heated from 5 to 300 K in a field of 100 Oe. The ZFC curve shows a maximum $T_{\text{max}}$ at 126 K and collapses into the FC curve before the two curves separate at 250 K, which is the blocking temperature, $T_B$. Such behaviour is characteristic of superparamagnetism and is due to the progressive blocking of the magnetic moment of nanoparticles with decreasing temperature. The relatively large difference in the value of $T_B - T_{\text{max}}$ and the broad maximum suggest a broad distribution of the anisotropy energy barriers for reorientation of the magnetic moments due to the broad distribution size.

Fig. 5 depicts the time-dependent temperature curves of MNP and (PSS-MNP) in a 200 kHz and 3.8 kA m⁻¹ ac magnetic field. Under the selected field parameters, sufficient heat is produced which leads to a substantial temperature increase within a short time frame, even at low concentrations.
on the frequency of the external field as well as the nature of the particles such as magnetism and surface modification [15,40]. The specific absorption rate (SAR) was calculated using the formula
\[
\text{SAR} = \frac{C \times \Delta T \times 1}{\Delta t \times m_{\text{ferro}}}
\]
where \(\Delta T / \Delta t\) is the initial slope of the curve, \(m_{\text{ferro}}\) is the mass of ferrite and \(C\) is the specific heat capacity of the solution. Here, \(C = 0.937 \text{ J/(g K)}\) for ferrofluids and \(C = 4.18 \text{ J/(g K)}\) for water. The SAR values of MNP and (PSS-MNP) were calculated to be around 16 and 29 W/g. The SAR value of (PSS-MNP) is almost twice that of MNP most probably because of the absorption of heat by the polymer coating which is bound to the magnetic core [15,16]. The decisive parameter when exploiting the inductive heating in combination with the thermosensitive principle is the effectiveness of heat transfer from the magnetic core (unmodified or modified by PSS) onto the thermoresponsive (loaded) microgel and the subsequent heat-triggered drug-release. The inductive heating reveals the advantages of having a polymeric coating or polymer-modified MNP surface by polyanions and polycations. The increase in polymeric content enhances the amount of heat generated by the MNP. Under the above-mentioned experimental conditions, MNP or (PSS-MNP) generate enough heat to raise the temperature above 40 °C within a few minutes—a property exploitable in association with thermoresponsive microgels with VPTT below that temperature.

3.2. Microgel-MNP characterisation

MNP were assembled on thermoresponsive PNIPAM microgel (MG) via the LbL assembly in an attempt to confer magnetic properties to the resulting hybrid core–shell structure [15]. The LbL assembly of PEM [28,30,32] and MNP [15] on the microgel was monitored by DLS and electrophoretic measurements. While DLS measures the hydrodynamic diameter, \(D_h\), of the hybrid core–shell structures, the sign of the mobility, \(\mu\), confirms charge reversal indicating successful LbL assembly after the deposition of each layer. Fig. 6a shows the dependence of \(D_h\) of MG and subsequent LbL assembly of polyelectrolytes and positively charged MNP on MG as a function of temperature [28,30,32]. In this example, we first coated MG with PDADMAC (MG/PDADMAC), then with PSS (MG/PDADMAC/PSS), followed by positively charged MNP (MG/PDADMAC/PSS/MNP), and finally with a last layer of PSS to confine the MNP (MG/PDADMAC/PSS/MNP/PSS). MG has a \(D_h\) of around 380 nm and 200 nm in the swollen and collapsed state respectively, with a VPTT around 32 °C. On addition of the first layer of PDADMAC, there is a slight increase in the size of MG/PDADMAC in the swollen state (around 420 nm). However in the collapsed state, the size of MG/PDADMAC is about 360 nm. The collapse of the microgel is hindered by the strong electrostatic interactions between the positively charged PDADMAC and the negatively charged MG, thus preventing the complete collapse of the microgel [15,28,30,32]. Upon addition of the second polyelectrolyte, the thermoresponsivity of MG/PDADMAC/PSS is comparable to that of the native microgel, but with a collapsed state at around 260 nm. On addition of the positively charged MNP in the third layer, DLS curve of MG/PDADMAC/PSS/MNP shows no significant change, with a \(D_h\) of around 400 nm in the swollen state. To confine the MNP in this hybrid core–shell structure, a fourth layer of the negatively charged PSS is assembled to give the final structure MG/PDADMAC/PSS/MNP/PSS, which surprisingly has a \(D_h\) of 320 nm and 240 nm in the swollen and collapsed state respectively [41]. It has been shown that the size of polyelectrolyte-coated microgels depends on the number of layers as well as the nature of the polyelectrolyte [30], but how MNP affect the size, hence thermostresponsive behaviour, is still not fully understood. The aim of this work is to show that one could successfully confine MNP between PEM at various positions on the microgel.

Fig. 6b shows the dependence of \(D_h\) of MG and subsequent LbL assembly of polyelectrolytes and negatively charged (PSS-MNP) on MG as a function of temperature. In this case, we coated MG/PDADMAC with the negatively charged (PSS-MNP) (MG/ PDADMAC/[PSS-MNP]), followed by a layer of PDADMAC to confine the MNP (MG/PDADMAC/[PSS-MNP]/PDADMAC). In the swollen state, the hydrodynamic diameter of MG/PDADMAC/[PSS-MNP] is almost identical to the size of the native MG (around 370 nm). However, careful analysis of the DLS curves at temperatures above the VPTT reveals that MG/PDADMAC/[PSS-MNP] is bigger than MG/PDADMAC. This indicates the presence and successful assembly of (PSS-MNP) onto the PDADMAC layer [15,28,30,32]. The final hybrid core–shell structure MG/PDADMAC/[PSS-MNP]/PDADMAC has a \(D_h\) of 440 nm and 260 nm in the swollen and collapsed state, respectively.

From Fig. 6 it can be seen that swelling and deswelling of the hybrid core–shell structure is completely reversible and reproducible as revealed by the heating and cooling cycles during the DLS measurements. In the case of MG/PDADMAC/PSS/MNP/PSS microgel and MG/PDADMAC/[PSS-MNP]/PDADMAC microgel two heating and cooling cycles were run back-to-back. The DLS curve from the second cycle (data not shown) matched that from the first cycle revealing that MNP do not get detached after the phase...
transition of MG during the first cycle and that the resulting hybrid core–shell systems are thermosensitive and magnetic.

The time-dependent temperature curve for MG/PDADMAC/(PSS-MNP)/PDADMAC microgel under a 200 kHz and 3.8 kAm

\[ T = \text{Temperature, } C \]

\[ t = \text{Time, } \text{s} \]

\[ \mu = \text{Electrophoretic mobility, } \text{m}^2 \text{V}^{-1} \text{s}^{-1} \]

\[ N = \text{Number of layers} \]

The \( \mu \) alternates between negative and positive values corresponding to the sequential adsorption of cationic and anionic species, respectively, and thereby revealing charge overcompensation necessary for charge reversal for further build up of multilayers [15, 28, 30]. One would expect a drastic charge reversal during the deposition of MNP (either positively or negatively charged) since a large amount of MNP would be required to overcompensate the charges of the underlying layer, but this is not the case. It could be that, due to strong electrostatic attractions, some of the deposited MNP find themselves buried deeper in the interdigitated layers underneath, with the result that less MNP actually contribute to the net surface charge of the ensemble. It is also interesting to point out that confining the positive MNP with a layer of negatively charged PSS leads to significant charge reversal, Fig. 8a. If this is the result of the surface behaving now like a rigid one due to the deposition of the hard MNP in the layer underneath, then one would expect also a drastic charge reversal when a PDADMAC layer is deposited on the negatively charged (PSS-MNP). However, as shown in Fig. 8b, this is not the case. It is still not clear why this sudden increase in \( \mu \) (in magnitude) is observed when MNP is confined with a single layer of PSS and not when (PSS-MNP) is confined with a single layer of PDADMAC. However, if an additional layer of PSS is added to the latter system [i.e. (PSS-MNP) are confined by two outer layers of polyelectrolytes instead of one] to obtain a final hybrid core–shell structure: MG/PDADMAC/(PSS-MNP)/PDADMAC/PSS (last point in Fig. 7b where \( N = 4 \)) a \( \mu \) of around \(-4.1 \times 10^{-8} \text{m}^2 \text{V}^{-1} \text{s}^{-1}\) is reached. This could be an indication that the deposition of PSS leads to a better surface coverage than that of PDADMAC as we previously reported [30].

**4. Conclusion**

We demonstrate the feasibility of independently tuning the magnetic and thermoresponsive properties of individual components, namely of magnetic nanoparticles and PNiPAM microgel, respectively, before assembling them into hybrid core–shell structures with dual-stimuli properties. We describe the synthesis and characterisation of the PNiPAM microgel, and of both positively and negatively charged magnetic nanoparticles. The layer-by-layer technique proves to be very versatile firstly in the surface modification of the PNiPAM microgel using polyelectrolytes (polyelectrolytes on microgel), secondly in the deposition of magnetic nanoparticles (nanoparticles on polyelectrolytes), and thirdly in confining these magnetic nanoparticles with another layer on polyelectrolyte (polyelectrolytes on nanoparticles). Dynamic light scattering studies show that at every stage of polyelectrolyte layering, the resulting core–shell structure retains its thermoresponsivity, and more
importantly, that upon deposition of magnetic nanoparticles, the resulting hybrid core–shell structure retains both thermoresponsive and magnetic properties and the nanoparticles do not get detached after the phase transition. Electrophoretic measurements show charge reversal after each layer is deposited which is a clear indication of successful deposition. Inductive heat study reveals that the heat generated by the magnetic nanoparticles is high enough to cause the collapse of the microgel above its volume phase transition temperature. These hybrid core–shell microgels possess a unique combination of thermoresponsivity and magnetism with high specific absorption rate which could open up novel prospects for remotely controlled drug carriers.

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