

John E. Wong
Walter Richtering

Surface Modification of Thermoresponsive Microgels via Layer-by-Layer Assembly of Polyelectrolyte Multilayers

Abstract This study describes the layer-by-layer (LbL) assembly of polyelectrolyte multilayers of poly(diallyldimethylammonium chloride) (PDADMAC) and poly(styrenesulfonate) (PSS) on soft and porous supports as provided by the entangled mesh network of poly(*N*-isopropylacrylamide) (PNiPAM) microgels with varying thermoresponsive core and core-shell structures. Dynamic light scattering was used to follow the build-up of the PDADMAC/PSS multilayer assembly on thermoresponsive microgel particles and electrophoresis measurements were used to confirm charge reversal after each layer deposition. We demonstrate an “odd-

even” effect of the size of the coated microgel depending on the type of polyelectrolytes in the outermost layer. We also show that a priming layer of polyethyleneimine (PEI) causes drastic surface modification of the microgel, but that on subsequent adsorption of the next layer (PSS) the thermoresponsive behavior of the native microgel can be recovered. Similarities and differences to LbL assembly of polyelectrolyte multilayers on hard and rigid supports will be discussed.

Keywords Core-shell microgel · Layer-by-layer · PNiPAM · Polyelectrolytes · Thermoresponsive

John E. Wong (✉) · Walter Richtering
Institute of Physical Chemistry,
University of Aachen, Landoltweg 2,
52056 Aachen, Germany
e-mail: wong@pc.rwth-aachen.de

Introduction

In the early 1990s, Decher developed the layer-by-layer (LBL) assembly [1–3] of polyelectrolyte multilayers on charged substrates. LbL has become a versatile way of fabricating thin films with tailored architecture on substrates of virtually any size and shape [1–13]. A tremendous amount of research has been done on LBL assembly on rigid and planar substrates to study the physicochemical [14, 15] aspects of film formation and growth as influenced by the degree of charge of polyelectrolytes, pH, salt and ionic strength [16–24] from which the film is deposited from. It was once thought that electrostatic interactions are the main driving force for multilayer formation between two oppositely charged polyelectrolytes. However it has been recently demonstrated that secondary (non electrostatic) or cooperative interactions such as hydrogen-

bonding and hydrophobic interactions [25–29], could also play a substantial role as well. The polyelectrolyte conformation, its adsorbed layer structure, and the degree of charge reversal upon adsorption determine ultimately, not only the film formation behavior but also, the structure of the resulting multilayer films (thickness, porosity, permeability, etc.). Polyelectrolyte multilayers deposited on hard and rigid planar substrates have been shown to be extremely interdigitated [30, 31] but with nevertheless distinct regions within the film assembly [32, 33] depending on whether the layers are situated closest to the substrate (inner layers), or in the middle core, or furthest from the substrate (outermost layers).

The LbL technique was subsequently extended to solid and hard particles, substituting planar substrates with colloids as precursors to hollow capsules. In the late 1990s, Sukhorukov [4–6] and Caruso [7–9] systematically

studied the LbL of polyelectrolytes on sacrificial core particles, which were then dissolved to leave well-defined hollow capsules made up of only polyelectrolyte multilayers. The size of the hollow capsules was determined by the template diameter while the capsule wall thickness was controlled with nanoscale precision by the number of layers deposited on the particles. In this case as well the permeability of these capsule walls was additionally determined by the interdigitation of the multilayers, which confers the elastic properties of the capsules wall. Since then it has opened up a new era for the potential use of these hollow capsules for drug (or any other active agents) encapsulation (storage), transport, and delivery [10].

Recently, Caruso demonstrated the feasibility of LbL assembly of polyelectrolyte multilayers onto rigid but porous templates [11, 12]. Caruso exploited the electrostatic interactions between charged polymers (poly(acrylic acid), PAA and poly(allylamine hydrochloride), PAH) and mesoporous silicas to sequentially infiltrate and coat the inside of the pores. The mesoporous silica spheres used by Caruso possessed a bimodal pore structure; that is they possess small (2–3 nm) and large pores (10–40 nm), while the particles themselves have a diameter of 2–4 μm . Evidence of the successive deposition of polyelectrolytes within the pores was obtained by Fourier transform infrared experiments [11].

This paper demonstrates the LbL assembly of polyelectrolyte multilayers onto soft and porous templates as provided by the entangled mesh network of a commonly studied microgel, Poly(*N*-isopropylacrylamide) (PNiPAM) [34–36]. PNiPAM is thermoresponsive with a lower critical solution temperature (LCST) of around 32 °C, which means that below the LCST PNiPAM is water-soluble with a hydrophilic coil and becomes water-insoluble with a hydrophobic globule above the LCST. Microgel particles have a very high surface area to volume ratio and usually contain between 80 and 99% water in the swollen state [35] making them suitable for dye or drug encapsulation and delivery as well as providing support for immobilization of functionalized monomer units (e.g. enzymes, proteins, DNA, etc.) within the particles or on the surface. Unlike hard and rigid templates, we are now dealing with soft and porous templates [13] whereby adsorbed polyelectrolyte layers can not only interdigitate among themselves, but also penetrate the templates, conferring novel surface modification and properties to soft and porous substrates. In an attempt to vary the LCST or the swelling and deswelling behavior of microgels, hydrophobic or hydrophilic components (with polyelectrolyte structures) have been widely employed to be chemically incorporated into the microgel as a copolymer. In contrast, this paper actually explores the LbL assembly of polyelectrolyte multilayers to coat microgels [13], and investigates the characterizations of both the substrate (microgel) and the multilayer coated microgel. The physicochemical behavior of the swelling and deswelling of the

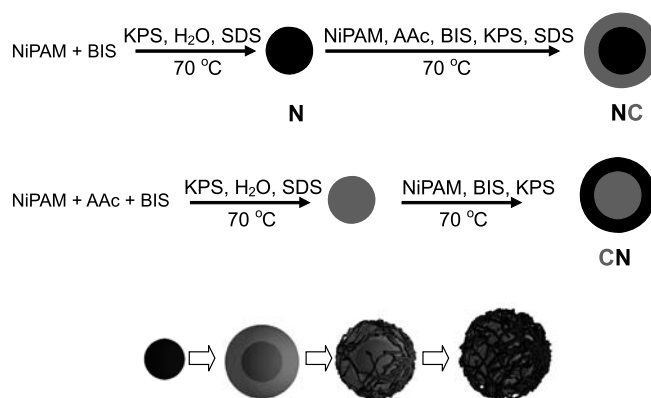
coated microgels as influenced by the presence of the polyelectrolytes “shell” is also assessed.

Experimental Section

Materials: Poly(diallyl dimethylammoniumchloride) (PDADMAC, $M_w = 100\,000$), Poly(styrene sulfonate) (PSS, $M_w = 70\,000$), and Polyethyleneimine (PEI, $M_w = 750\,000$) were purchased from Sigma–Aldrich. All chemicals from commercial origin were used without purification. The water used in all experiments (unless otherwise stated) was double-distilled Ultrapure water (Milli-Q-plus system, Millipore). The polyelectrolytes were dissolved in 0.5 M NaCl at a concentration of 1 mg mL^{-1} and used as such with no further adjustment of the pH.

Preparation of microgels: Three different types of building block were investigated: (a) a “neutral” core, constituted of poly(*N*-isopropylacrylamide) (PNiPAM), N; (b) a core-shell, wherein the shell is negatively charged (made up of a PNiPAM core and a poly(*N*-isopropylacrylamide-*co*-acrylic acid) (P(NiPAM-*co*-AA) shell), NC; and (c) a core-shell, wherein the core is negatively charged (made up of a P(NiPAM-*co*-AA) core and a PNiPAM shell), CN (inverse configuration of NC). The PNiPAM core microgel, N, was prepared via free radical polymerization [37, 38] while NC and CN were prepared by seed-and-feed polymerization of NiPAM/AAc onto a PNiPAM core [37–40] and NiPAM onto a PNiPAM/AAc core [41] respectively. The size of our building block varies between 140 nm for N, 200 nm for NC, and 250 nm for CN in the swollen state (at low temperatures) and 50 nm for N and 80 nm for NC and CN in the collapsed state (at high temperatures).

Layer-by-Layer assembly: The LbL assembly of polyelectrolyte was done by slowly adding an aqueous solution of the microgel to a 0.5 M NaCl solution of the polycat-



Scheme 1 Reaction pathways to obtain various core, core-shell structure microgels as template for LbL assembly of polyelectrolyte multilayers

ion (step 1), PDADMAC (or PEI) in a volume ratio of 1 : 5 under constant stirring for 30 minutes. The excess polycation was removed by centrifugation at 40000 rpm for 20 minutes at 20 °C (step 2). The coated microgel was re-dispersed in water by vigorous shaking (step 3). Step 3 was repeated three times before adsorption of the next layer, which is the polyanion, PSS (step 4). Again the excess polyanion is removed (step 2) and re-dispersed in water three times (step 3). The whole sequence was repeated until the desired number of layers was obtained, after which time the coated microgel was re-dispersed in water overnight. Prior to characterizations, the coated microgel was filtered at least three times through a non-pyrogenic single-use 0.45 μm filter (Minisart from Sartorius) in a laminar-flow box.

Particle size determination: The particle size was measured by dynamic light scattering (DLS) as a function of temperature (ranging from 20 to 60 °C). Light scattering experiments were carried out on highly diluted samples (double-distilled Milli-Q water) with an ALV goniometer equipped with an avalanche photodiode. The samples were allowed to equilibrate for 20 minutes before a reading is done, 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 autocorrelator using an ALV Software version 5.3.2. Particle size was calculated by cumulant fits.

Electrophoretic measurements: The zeta potential and the electrophoretic mobility of the particles were measured with a Zetasizer 3000HSA (from Malvern Instruments, England) as a function of the number of layers and temperature (from 20 to 60 °C). Each point is the average of at least ten measurements. For temperature dependent measurements, the sample was allowed to equilibrate for 15–20 minutes to the set temperature before any recording was done.

Results and Discussion

DLS was used to monitor the stepwise deposition of each layer onto microgels by measuring the hydrodynamic radius, R_H , of the microgel. Figure 1 shows the thermoresponsive behaviors of various microgels coated with different number of layers as a function of temperature. The uncoated microgels differ not only in their architecture and size but also in their responsive behaviors: N undergoes a sharp LCST around 32 °C, Fig. 1a; CN presents a rather broad LCST around 35 °C, Fig. 1b while NC presents a timid two transitions at 33 (sharp) and 42 °C (broad), Fig. 1c; and swelling and deswelling are completely reversible for all the uncoated microgels. On adsorption of polyelectrolyte layers, the thermoresponsive behavior of

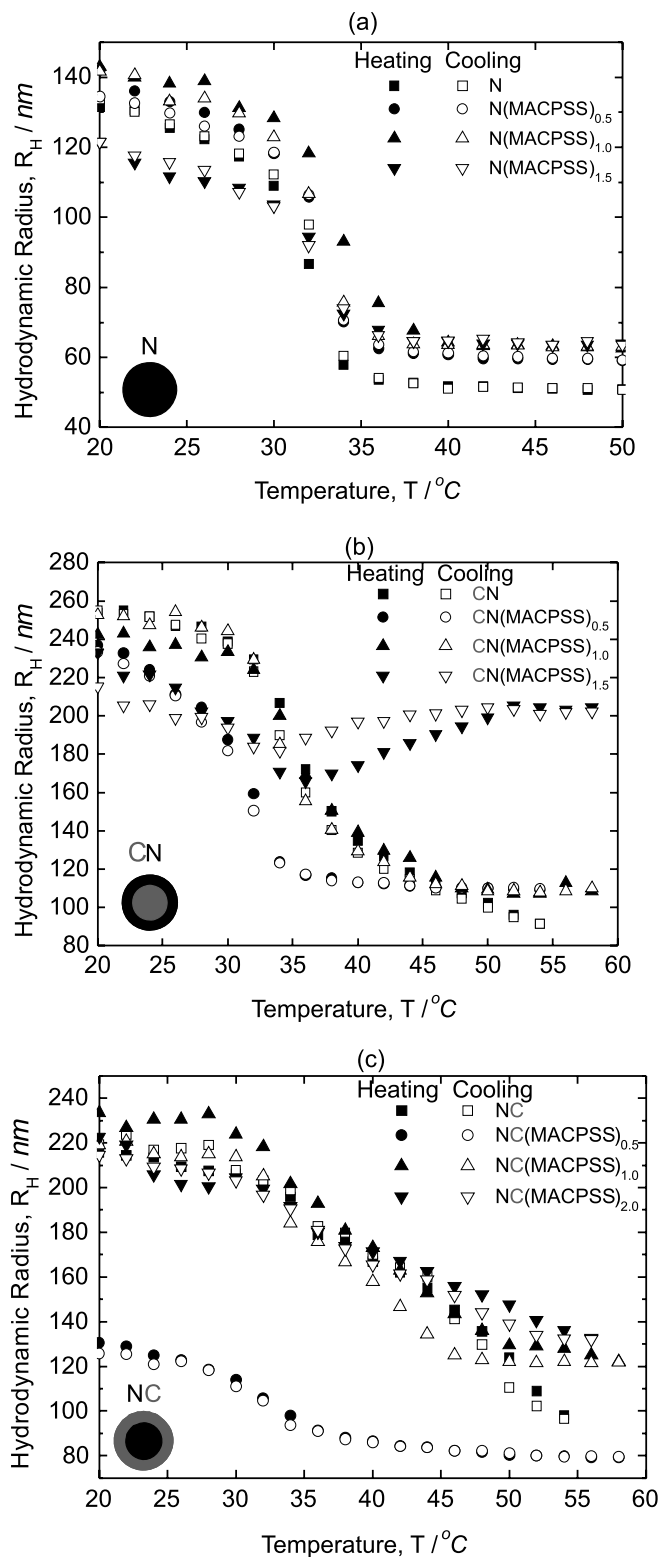


Fig. 1 Thermoresponsive behaviors of PDADMAC/PSS-coated **a** N, **b** CN and **c** NC

the coated microgels differs dramatically and can be seen to be template-dependent, or in other words, dependent on the location of charges in the uncoated microgel. LbL polyelectrolyte multilayer on a “neutral” microgel core does not affect the LCST of the microgel, Fig. 1a. In fact, N is not quite neutral since it still has some charges from the synthesis. However, there cannot be too many of them as confirmed by the zeta potential of N (data not shown) and the sharp LCST at around 32 °C. In the swollen state, the coated N shows an expected, but very minimal, increment in size when two layers (PDADMAC/PSS) are deposited but an additional layer of PDADMAC causes a collapse of the size (from 140 to 120 nm). In the collapsed state however all the coated N have about the same size (60 nm), which is, as expected, bigger than the uncoated N (50 nm). In the case of the CN system, Fig. 1b, the first layer (PDADMAC) has for effect to (i) decrease the size of the coated microgel in the swollen state, (ii) shift the LCST to lower temperature (32 °C), and (iii) make the transition from swollen to collapsed state a sharper one, as compared to the uncoated microgel. On addition of a second layer (PSS), the behavior of the uncoated microgel is recovered. A third layer (PDADMAC) again causes a collapse of the size of the coated microgel at low temperatures with an additional feature beyond the LCST, Fig. 1b. Above 34 °C, the three-layer coated CN microgel appears to exhibit a “reverse-effect” – starting to swell again before leveling off around 50 °C. The cooling curve shows some hysteresis, but taking into account conformational rearrangements, this additional feature is well present and can be fully reproduced.

In the case of NC system, Fig. 1c, we notice an “odd-even” effect on the size of the particle depending on the type of polyelectrolytes in the outermost layer. Deposition of the first layer (PDADMAC) anneals the native two-transition behavior of NC. NCMAC is drastically smaller (125 nm) in the swollen state than the uncoated NC (220 nm) – a situation analogous to [11]. Caruso found that the first layer deposited (PAA) on mesoporous silicas dramatically decreased the surface area by nearly 50%, and the author explained this decrease by the high PAA loading and blocking of some of the mesopores. Here it is unlikely that the pores are blocked since we are dealing with deformable substrates with “transient” pores. It could be due to a combination of two main effects. It could be that in the swollen state of NCMAC, PDADMAC chains are able to penetrate the microgel particle interior. The increase in “contact points” due to electrostatic interactions between the microgel and the polyelectrolyte restricts the extent of swelling of the ensemble. The deposition of this first layer forms like a network structure around the microgel [39]. The deposition of the second layer (PSS) now causes the coated microgel to expand (225 nm) in the swollen state. It was not possible to run any heating/cooling cycle during the DLS measurement on NC coated with 3 layers as the particles start to bridge and aggregate as the tempera-

ture is increased. However, at 20 °C, NC(MACPSS)_{1,5} has a R_H of about 145 nm (data not shown), which means that every time PDADMAC is deposited there is a decrease in the particle size in the swollen state and on addition of each PSS layer the particle size increases again. To the best of our knowledge it is the first time that an “odd-even” effect is shown on LbL assembly of polyelectrolytes on soft and porous building blocks.

Particle swelling is entropy driven and is dependent on the hydrogen-bonding between the microgel segments and water. An increase in temperature causes rupture of these H-bonds causing the microgel to deswell and collapse as water is excluded from the microgel. Above the LCST, inter- and intra-chain hydrogen bonding and hydrophobic interactions are dominant. However, due to the polyelectrolyte coating, attractive electrostatic interactions between the polyelectrolyte layer and the microgel offer some opposition to this deswelling, which results in somewhat larger particles size for the coated microgel in the collapsed state as compared to the uncoated one. On cooling, previously buried, trapped, entangled segments become accessible to the continuous phase and become mobile and have the possibility to reorient, restructure, and reorganize as more water flows in the microgel, thence explaining the different hydrodynamic radii observed, and the hysteresis imparted to the microgel. This hysteresis can be exploited to tune novel surface properties conferred to coated microgel particles.

By substituting the first PDADMAC layer by a priming layer of PEI, a highly branched high molecular weight polyelectrolyte known for its high surface charge density and excellent anchoring properties, we cause a drastic change in the thermoresponsive behavior of the coated microgel. Figure 2 shows the hydrodynamic radius, R_H , of the coated microgel particles (NPEI) as a function of temperature. Due to the high branching and high molecular weight, PEI is assumed impenetrable in N, and this is translated as an increase in the particle size (from 140 to 150 nm) in the swollen state. As the temperature is in-

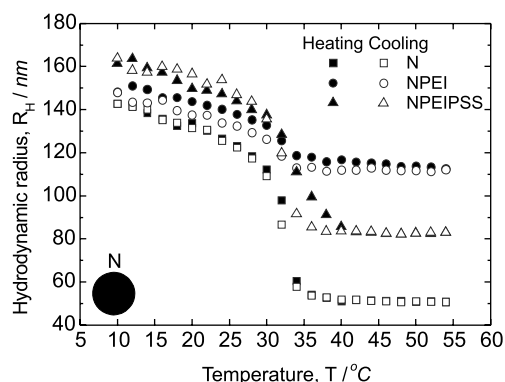


Fig. 2 Thermoresponsive behavior of N coated with a priming layer of PEI

creased the N core tendency to collapse is restricted by the electrostatic interaction of the PEI layer with N, resulting in a higher particle size, even around the LCST of N – which is also slightly shifted towards higher temperature by about 2 °C. Beyond the LCST, the coated microgel (NPEI) undergoes an abrupt and rapid transition to reach the collapsed state with a size particle of about 120 nm, which is about twice the size of the uncoated N in the collapsed state. The flow of water out of PEI-coated N is drastically impeded by the branched network around N and also the elastic properties conferred by the interactions between N and PEI chains allow the entire particle to expand further than the uncoated N. Deposition of a PSS layer on the PEI-coated N amazingly recovers partially the native thermoresponsive sensitivity of N. The LCST of NPEIPSS is shifted by about 5 °C to higher temperatures, and the particle size in the collapsed state is now surprisingly lower than NPEI but, as expected, higher than N. The positive charges inherent to PEI is now “shared” between interactions with N and this new layer of PSS layer; in other words, we have simultaneously a reinforcement of interactions between polyelectrolyte multilayers (PEI and PSS) and a diminishment of interactions between polyelectrolyte (PEI) and the microgel (N), resulting in the microgel to collapse more – bearing in mind, that it is, after all, the microgel which is thermosensitive.

In Fig. 2, we can see new features in the behavior of NPEIPSS: some form of hysteresis between the heating and cooling curves. Figure 3 shows the thermoresponsive response of NPEIPSS after different periods of time. In between experiments the samples were stored at room temperature. We previously reported [13] hysteresis on a two-layer coated NC where we found that the first heating cycle results in major alteration of the particle, and that extended time periods under harsher conditions leads only to small changes. In the case of NPEIPSS the highly branched positively charged PEI causes fast and permanent alteration, Fig. 3. The only difference after 1 month was that,

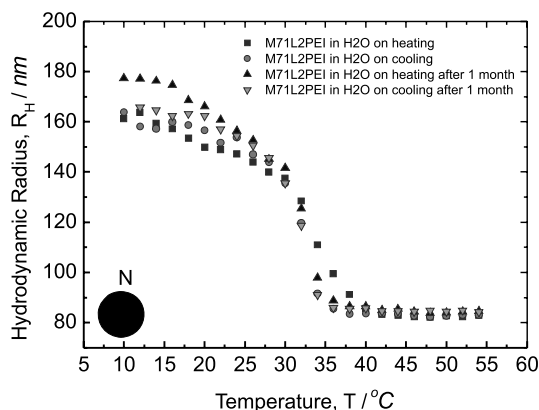


Fig. 3 Hysteresis behavior of NPEIPSS over different periods of time

in the swollen state (below the LCST), the particles size was bigger than that originally prepared. However on the cooling curve, the original behavior of NPEIPSS was restored. Above the LCST, swelling and deswelling were completely reversible.

Because of the expansion and contraction of the soft template during adsorption of polycations and polyanions on microgels (NC and CN), it is difficult to obtain a direct measurement of the increment in film thickness upon deposition of the polyelectrolyte at each adsorption step. Therefore, evidence of the successive deposition of polyelectrolytes on the microgels was obtained qualitatively by electrophoretic measurements as a function of temperature. Figure 4 shows the zeta potentials and electrophoretic mobility of the coated microgel as a function of the number of layers, here only shown for NC measured at 20 °C. Figure 4 clearly indicates that the surface charge of the microgel is reversed with each additional adsorption step, suggesting that polyelectrolytes are adsorbed in discrete layers. The result is consistent with electrophoretic measurements of polyelectrolyte multilayers adsorbed on rigid particles. Of particular interest is the value of the zeta potential after deposition of each PDADMAC layer. It is well-documented that the zeta potential of PDADMAC/PSS system on rigid particles alternates between +40 and -40 mV upon addition of every PDADMAC and PSS layer respectively. However for assembly on soft and porous supports, we find that we reach -40 mV whenever we deposit PSS, but hardly reach +40 mV when PDADMAC is deposited. Similarly, for N (data not shown), after deposition of the first (PDADMAC) and second (PSS) layer, the zeta potential alternates between +40 and -40 mV but on addition of the third (PDADMAC) layer, only -5 mV is reached, indicating that no charge reversal occurs. In the case of NC, this low positive surface potential is a possible cause for particles bridging observed during the heating cycle of the DLS measurements. In this respect, polyelectrolyte multilayer assembly on soft and porous supports differs from that on

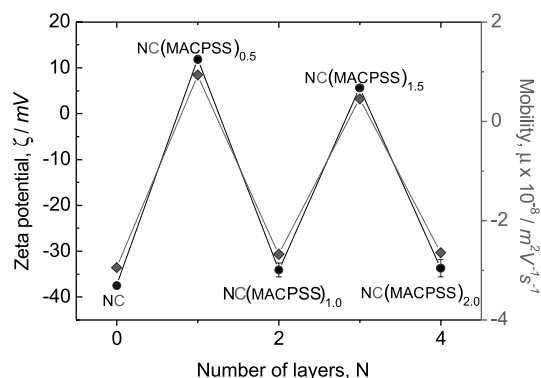


Fig. 4 Electrophoretic measurements as a function of number of layers coated on NC

rigid and solid substrates – it is support-dependent. The nature of the soft and porous template (core or core-shell system) dictates whether we have (i) complete or partial coverage of the surface, (ii) penetration of the polyelectrolyte in the interior of the support or not, and/or (iii) secondary cooperative interactions coming into play during the LbL assembly.

Figure 5 shows the electrophoretic measurements as a function of temperature for NC coated with different number of layers. One striking feature is that every time the outermost layer is PSS, the absolute zeta potential either slightly decreases (NC(MACPSS)_{1,0}) with temperature or remains roughly constant (NC(MACPSS)_{2,0}), while the absolute value of the electrophoretic mobility increases smoothly with temperature. However, when NC is PDADMAC-terminated (NC(MACPSS)_{0,5} and NC(MACPSS)_{1,5}) the absolute value of both zeta potential and electrophoretic mobility are roughly constant below the LCST and increase abruptly above it. At this point it is not clear why we observe such differences in behavior, but it is nevertheless obvious from these results that polyelectrolyte adsorption strongly influence the thermoresponsive behavior of microgels. Hysteresis between the heating and cooling cycle, Fig. 5, is particularly noticeable after the very first layer adsorption (NC(MACPSS)_{0,5}). On cooling, there are drastic reorganization of the interdigitation and interpenetration of polyelectrolyte and microgel.

Conclusions

The results presented in this work demonstrate the feasibility of layer-by-layer polyelectrolyte multilayer assembly on soft and porous building block as provided by the entangled mesh network of various core/core-shell microgels. Charge reversal was achieved and indicated successful deposition of polyanions and polycations, although there are indications that build-up could be incomplete or assisted by cooperative interactions. Polyelectrolyte coated microgels possess new thermoresponsive behaviors through new surface properties. We demonstrated for the first time an “odd-even” effect in the size of the coated microgel depending on the type of polyelectrolyte in the outermost layer. We also showed that a priming layer of PEI drastically modifies the surface properties of the microgel, but that the native thermoresponsive sensitivity of the microgel

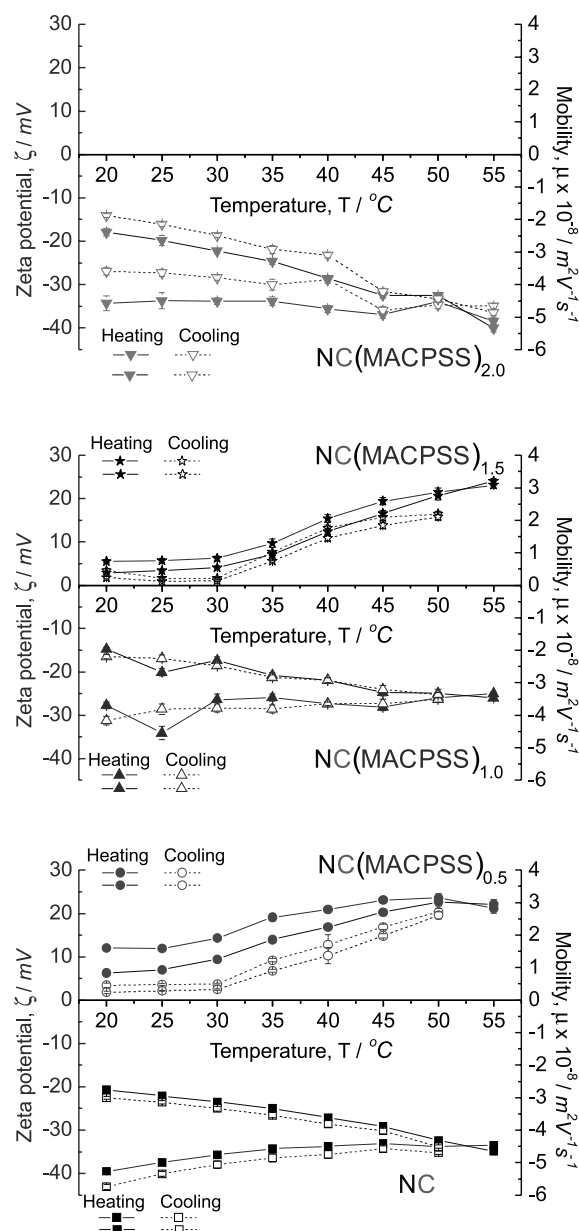


Fig. 5 Temperature dependence of the electrophoretic measurements for coated NC

could be recovered on subsequent layer deposition on the PEI layer.

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