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Design of responsive double-hydrophilic A-*b*-(B-*co*-C) diblock terpolymers with tunable thermosensitivity☆

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Abstract

Double-hydrophilic poly[(oligo(ethylene glycol) methacrylate)-*co*-methyl methacrylate]-*b*-poly(2-(diethylamino)ethyl methacrylate), P(EGMA-*co*-MMA)-*b*-PDEA, diblock terpolymers were designed and explored in aqueous media. Thanks to the thermosensitivity of the P(EGMA-*co*-MMA) statistical block and the pH sensitivity of the PDEA block, these terpolymers form two distinct micellar self-assemblies at different conditions of pH and temperature. The thermosensitivity of these terpolymers can be tuned by controlling the LCST of the statistical block through its monomer unit composition.

Keywords: Diblock terpolymers; Double-hydrophilic; Thermosensitivity

1. Introduction

Double-hydrophilic block copolymers (DHBCs) constitute a special category of water-soluble block copolymers [1] that undergo spontaneous self-organization upon switching an external stimulus, belonging therefore to the interesting class of responsive nanostructured materials [2].

In the case that both hydrophilic blocks are sensitive to the same or to different external stimulus e.g. pH, ionic strength or temperature, two types of micellar self-assemblies can be formed in which the different blocks interchange in the core/shell position. This behavior has been described by the term ‘‘schizophrenic’’ [3].

More recently, ABA double-hydrophilic triblock copolymers have appeared that exhibit two types of self-organization, i.e. micellization and/or gelation, responding to pH [4] or behaving as thermo-reversible gelators responding to temperature [5].

DHBCs that respond to pH and temperature have also been designed and explored in aqueous media [6]. In most cases the thermo-sensitive block exhibits a lower critical solution temperature (LCST) behaving as hydrophilic below LCST and as hydrophobic above LCST. For potential applications of this kind of DHBC, the LCST of the one block must be regulated. As it is known, the addition of salt induces LCST decrease (salting out effect). However, the ionic strength of the medium has to be kept low if applications are targeted to living organisms, such as drug delivery.

In a previous communication, novel double-hydrophilic diblock terpolymers of the type A-*b*-(B-*co*-C) bearing poly(oligo(ethylene glycol) methacrylate), PEGMA, as the thermo-sensitive block and poly{[(diethylamino)ethyl methacrylate]-*co*-(methacrylic acid)}, P(DEA-*co*-MAA), ampholytic statistical copolymer as the pH sensitive block was designed and explored in aqueous media. It was shown that these terpolymers can form three types of micelles with positive, negative and neutral corona at different environmental conditions. The achievement of this micellar diversity was due to the A-*b*-(B-*co*-C) diblock terpolymer architecture in which statistical polyampholytes with tunable isoelectric point were incorporated [8].

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In the present work, tailor-made pH–thermo responsive double-hydrophilic diblock terpolymers have been designed bearing thermo-sensitive blocks of tunable LCST. This was achieved by incorporating statistical copolymer building blocks, inspired by the A-*b*-(B-*co*-C) architecture. It is known that the LCST of the statistical copolymers depends on the nature and the composition of the monomers [9] and therefore can be tuned at will by macromolecular chemistry.

2. Experimental part

2.1. Materials

All reagents were purchased from Aldrich, Germany, except when stated otherwise. Three monomers were used for the synthesis of the polymers: methyl methacrylate (MMA, 99%), 2-(diethylamino)ethyl methacrylate (DEA, 98%), and methoxy-capped poly(ethylene glycol) methyl ether methacrylate (average M_n *ca.* 300 g/mol, i.e. methacrylate with 4/5 ethylene oxide units in the side chains, EGMA). All monomers were distilled over calcium hydride under vacuum, to remove the polymerization inhibitor and protic impurities. Then they were stirred overnight in the presence of calcium hydride in the freezer under a dry argon atmosphere and were distilled for a second time just before the polymerization.

The monofunctional initiator methyl trimethylsilyl dimethylketene acetal 95% (MTS) was also purchased from Aldrich. Tetrabutylammonium bibenzoate (TBABB) served as the catalyst of the group transfer polymerization. This was prepared by the reaction of tetrabutylammonium hydroxide (40% aqueous solution) with benzoic acid (99%) [10]. The resulting TBABB was stored under vacuum until use. MTS was vacuum-distilled and stored in the refrigerator under a dry argon atmosphere.

THF was the polymerization solvent, which was dried by distillation over Na-wire/benzophenone mixture twice prior to use.

2.2. Polymer synthesis

All the polymerization reactions were carried out at room temperature under a dry argon atmosphere. The two monomers EGMA/MMA were vacuum-distilled sequentially in the same burette and afterwards they were shaken slowly several times until the mixture became homogeneous. A 250 mL three-neck round-bottom flask, containing 80 mL freshly distilled THF and a small amount (~10 mg) of TBABB catalyst, was fitted with two burettes (one containing the EGMA/MMA monomer mixture and the other the DEA monomer) and a rubber septum. To this flask a precalculated amount of initiator was added through the septum. The mixture of monomers was added dropwise under stirring into the flask and was left for 45 min to react to complete conversion. An aliquot of the resulting polymer was extracted for characterization. Sequentially the second monomer was added into the reactor in the same way and was left to react for another 45 min. The polymerization reaction was terminated with the addition of a small amount of methanol. All the polymers were recovered by precipitation in cold *n*-hexane and dried for three days under vacuum at room temperature.

Characterization of the precursors and the final polymers was performed by size exclusion chromatography (SEC), static light scattering (SLS) and ^{1}H NMR spectroscopy.

2.3. Size exclusion chromatography

Molecular weight distributions (M_w/M_n) were determined by SEC. The SEC equipment consisted of a Marathon II HPLC pump, Shodex RI-101 refractive index detector and two PLgel MiniMix columns "C" and "D". Calibration was carried out using PS standards. The eluent (THF containing 1% v/v triethylamine in order to prevent adsorption of the PDEA blocks onto the columns) was delivered at a flow rate of 0.5 mL/min.

2.4. ^{1}H NMR spectroscopy

The ^{1}H NMR spectra of polymer solutions in deuterated chloroform were recorded using a 400 MHz Avance Bruker spectrometer equipped with an Ultrashield magnet. The composition of the copolymers was determined from the ^{1}H NMR spectra by comparing the signals from the three methyl ester protons ($-COOCH_3$) of MMA at 3.6 ppm, the six methylene protons of DEA (adjacent to the N of the amine group, ($-CH_2N(CH_2-)_2$)) at 2.60 and 2.75 ppm and the three methyl protons of EGMA ($-OCH_3$) at 3.3 ppm.

2.5. Static light scattering

The weight-average molecular weights of the precursor and the micelles formed in aqueous solutions were determined by static light scattering (SLS) using a thermally regulated (±0.1 °C) spectrogoniometer model BI-200SM (Brookhaven) equipped with an He–Ne laser (632.8 nm). The intensity of the scattering light was measured in several angles for five solutions. By using the Zimm method, the weight-average molecular weight of the polymer was calculated.

2.6. Dynamic light scattering

Autocorrelation functions $g(q,t)$ were measured with a full multiple digital correlator (ALV-5000/FAST) equipped with 280 channels. The light source was an He–Ne laser operating at 632.8 nm. The correlation functions were analyzed by the constrained regularized CONTIN method [11] through CoVA-Jacek Gapinski 2001 software. The apparent diffusion coefficients, $D_{app} = \Gamma/q^2 (q = (4\pi n/\lambda)\sin(\theta/2)$, n is the refractive index of the solvent), were determined at the peak of the decay rate distributions and the apparent hydrodynamic radii via the Stokes–Einstein equation

$$R_{h,app} = k_B T/\left(6\pi\eta D_{app}\right) \quad (1)$$

where k_B is the Boltzmann constant and η is the viscosity of the solvent at absolute temperature T.

2.7. Turbidity measurements

A double beam HITACHI U-2001 UV/vis spectrometer was used for the turbidity measurements. The copolymer solution was placed in a 10 mm path-length quartz cuvette containing a small magnetic bar set in motion with the aid of a miniature magnetic stirrer. The temperature was controlled by a HAAKE K15 water-bath and could be adjusted from 5 to 90 °C with the help of a HAAKE DC1 controller. The optical density at 490 nm was monitored and the cloud point was determined at the intersection between the extrapolated straight lines below and above the abrupt change of the optical density.

2.8. Sample preparation

All the aqueous solutions were prepared by dissolving the appropriate amount of copolymer into distilled water and gently stirring overnight. Continuously the pH was fixed by the addition of small amounts of aqueous HCl or NaOH 1 N solutions. For the light scattering experiments all the solutions were filtered through a 0.45 μm PTFE hydrophilic millipore filter. In order to screen electrostatic interactions between the micelles, NaCl was added to the salt-free solutions to adjust the NaCl concentration to 0.05 N.

3. Results and discussions

Group transfer polymerization was used to prepare homo/statistical P(EGMA-*co*-MMA)-*b*-PDEA, diblock terpolymers (DTs) with different percentage of MMA content in the statistical block. The choice of the hydrophobic MMA comonomer of the statistical block was dictated from our aim to lower the LCST of the PEGMA homopolymer in order to approach the physiological temperature range (*ca.* 36–37 °C).

The synthetic route followed for preparing the diblock terpolymers has been applied recently to the synthesis of amphiphilic and/or double-hydrophilic DTs bearing polyampholyte sequences. This procedure allows block and statistical copolymerization in a one-pot reaction by sequential addition of monomers and/or monomer mixtures [8]. The partner homopolymer building block was chosen to be the weak cationic polyelectrolyte PDEA, which can be positively charged by protonation at low pH (hydrophilic state) but it turns hydrophobic in aqueous solutions with pH higher than 8. The molecular characteristics of the DTs were determined by size exclusion chromatography (SEC), static light scattering and ^{1}H NMR spectroscopy and are summarized in Table 1.

Due to the synthetic strategy, the statistical blocks could be isolated by taking samples prior to the addition of the DEA. Both, the final DTs and their statistical block precursors exhibit narrow molecular weight distributions as expected from the 'living' character of the synthetic method [12].

3.1. Effect of composition on cloud point

Table 1
Molecular characteristics of the diblock terpolymers

Molecular formula	M_w	M_w/M_n [c]	EGMA:MMA:DEA (wt%)
P(EGMA$_{49}$-*co*-MMA$_{24}$)	17 150 [a]	1.09	86:14:0
P(EGMA$_{49}$-*co*-MMA$_{24}$)-*b*-PDEA$_{116}$	38 650 [b]	1.14	38.1:6.2:55.7
P(EGMA$_{61}$-*co*-MMA$_{54}$)	23 700 [a]	1.05	77:23:0
P(EGMA$_{61}$-*co*-MMA$_{54}$)-*b*-PDEA$_{59}$	34 700 [b]	1.04	52.7:15.6:31.7

[a] By SLS.

[b] From M_w of the P(EGMA$_{49}$-*co*-MMA$_{24}$) block and the polymer composition obtained by ^{1}H NMR.

[c] By SEC chromatography.

Before exploring the association behavior of the two diblocks P(EGMA-*co*-MMA)-*b*-PDEA in aqueous solutions, the phase behavior of each block should be mentioned. PDEA is protonated at low pH; it behaves as a cationic weak polyelectrolyte and therefore becomes water soluble at pH < 6.5 [13], while it precipitates from aqueous solutions when it is in its unprotonated form. It is known that the PEGMA homopolymer exhibits a lower critical solution temperature (LCST), which depends on the number of ethylene oxide side units [14] and the ionic strength of the solution. Turbidity measurements were carried out firstly in order to determine the cloud point (cp) of the PEGMA homopolymer (with similar M_w of the corresponding P(EGMA-*co*-MMA) block) in salt-free solution. PEGMA had a cloud point in salt-free solution at 65 °C, as can be observed by the abrupt increase of the optical density in Fig. 1. The cloud point was shifted to lower temperatures by copolymerizing EGMA with the hydrophobic MMA. Moreover, cloud point was lowered by increasing the MMA content in the statistical block. In particular the P(EGMA$_{49}$-*co*-MMA$_{24}$) copolymer (14 wt% or 33% mol MMA content) exhibited a cloud point at 58 °C, while the P(EGMA$_{61}$-*co*-MMA$_{54}$) copolymer (33 wt% or 47% mol MMA content) at 44 °C. Apparently, the cloud point of the copolymer in salt-free aqueous solutions can be tuned by adjusting the comonomer feed ratio. The cloud point of

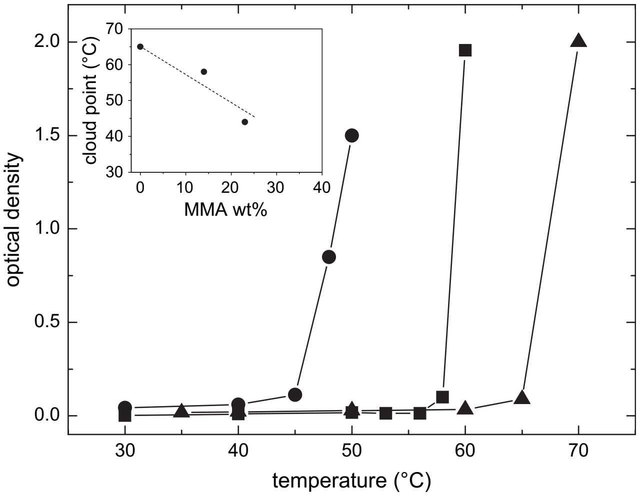

Fig. 1. Optical density at 490 nm of 0.4 wt% polymer in salt-free aqueous solutions as a function of temperature for PEGMA (▲) and P(EGMA-*co*-MMA) with different MMA content: 14 wt% (■) and 23 wt% (●). Inset: cp versus MMA wt%. Lines are provided to guide the reader.

a P(EGMA-*co*-MMA) copolymer could be regulated at even lower temperatures by further increasing the MMA content (Fig. 1, inset) rendering the copolymer applicable for any potential biological applications. However, the physiological saline exhibits an ionic strength of 0.15 M which affects the LCST and this has to be taken into account in polymer design.

3.2. Association phenomena: effect of ionic strength

The P(EGMA-*co*-MMA)-*b*-PDEA diblock terpolymer was explored for possible association above the cloud point of the P(EGMA-*co*-MMA) block at low pH (double-hydrophilic state) and at different ionic strengths by using static light scattering. The light scattering intensity at 90° (I_{90}) of 0.1 wt% P(EGMA$_{61}$-*co*-MMA$_{54}$)-*b*-PDEA$_{59}$ aqueous solutions was measured at different temperatures and NaCl contents and at a constant pH of 3. In Fig. 2, I_{90} is presented as a function of temperature for three solutions, one salt-free and two containing different amounts of NaCl, 0.15 M and 0.30 M, respectively. An abrupt enhancement of I_{90} can be observed which is correlated with a critical micelle temperature (CMT). The CMT coincides with the cloud point of the P(EGMA-*co*-MMA) statistical block precursor, implying that the driving force for the observed association phenomena is the temperature-induced hydrophobicity of the P(EGMA-*co*-MMA) blocks.

The CMT decreases with increasing salt concentration as is depicted in Fig. 2. Taking into account that the association is driven by the attractive hydrophobic forces between P(EGMA-*co*-MMA) blocks, and the fact that these forces appear only above the cloud point, it seems that by increasing the salt concentration of the solution, the cloud point of the P(EGMA-*co*-MMA) block is further reduced with respect to the salt-free values due to the well-known salting out effect [7].

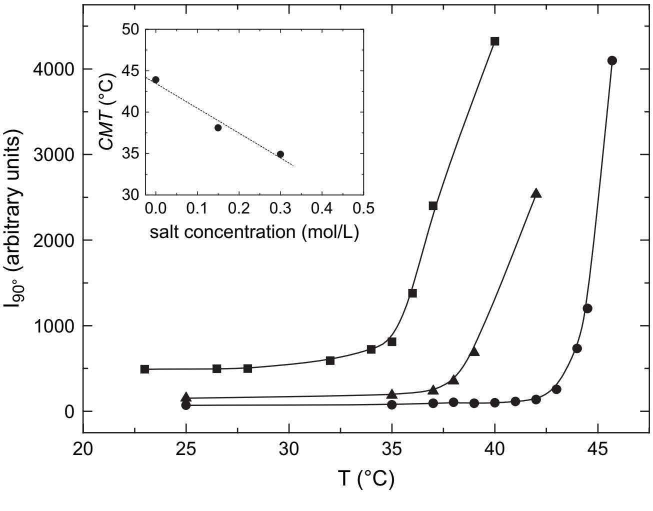

Fig. 2. Temperature dependence of the light scattering intensity at 90° of P(EGMA$_{61}$-*co*-MMA$_{54}$)-*b*-PDEA$_{59}$ in aqueous solutions at pH 3 and various ionic strengths: salt-free (●), 0.15 M NaCl (▲), 0.30 M NaCl (■). Inset: CMT versus salt concentration. Lines are provided to guide the reader.

3.3. Effect of pH

The third variable that induces the micellization of these DTs (apart from the temperature and the ionic strength) is the solution pH. As mentioned above, the PDEA block behaves as a responsive weak cationic polyelectrolyte due to the (de)protonation of the pendant amine group depending on the solution pH. The PDEA homopolymer dissolves in water at pH < 6.6 and precipitates when the solution pH exceeds the pK_a of 7.3 because the average degree of protonation (ionization) drops below a critical value [13].

In Fig. 3, I_{90} of P(EGMA-*co*-MMA)-*b*-PDEA aqueous solutions is presented as a function of pH for both terpolymers at 25 °C. The light scattering intensity increases with pH reaching a maximum value at about pH 8 and smoothly decreasing at higher pH. This behavior is due to the progressive deprotonation of the PDEA block, which eventually becomes entirely hydrophobic, driving the system to self-assemble producing PDEA-core micelles while the P(EGMA-*co*-MMA) blocks remain soluble at the temperature of 25 °C (T < LCST). In the transition region (6.5 < pH < 8) although the PDEA block is partially ionized (effective pK_a 6.9 in diblock copolymers) non-equilibrium micelles are formed with hydrated PDEA cores [14].

3.4. Self-assemblies at various conditions

From the above results it was deduced that at low pH and ambient temperature the terpolymers were molecularly dissolved. At low temperatures, pH-induced self-organization took place while at low pH temperature-induced self-organization occurred.

In the following micellar self-assemblies of the P(EGMA-*co*-MMA)-*b*-PDEA terpolymers formed at two different external conditions will be presented: (i) at ambient temperature and pH 8 (above the pK of the PDEA block) and (ii) at pH

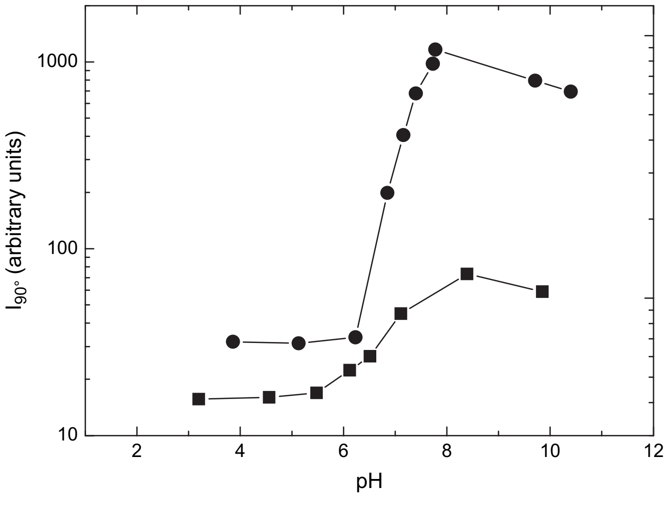

Fig. 3. pH dependence of the light scattering intensity at 90° of P(EGMA$_{61}$-*co*-MMA$_{54}$)-*b*-PDEA$_{59}$ (●) and P(EGMA$_{49}$-*co*-MMA$_{24}$)-*b*-PDEA$_{116}$ (■) terpolymers at 25 °C. Lines are provided to guide the reader.

3 and at a temperature above the corresponding cloud point of the P(EGMA-*co*-MMA) statistical blocks.

At pH > 8 and 25 °C, the P(EGMA-*co*-MMA)-*b*-PDEA terpolymer becomes amphiphilic since the PDEA block is deprotonated and hence hydrophobic, whereas the P(EGMA-*co*-MMA) block is hydrophilic. Micellar self-assemblies are expected with PDEA cores and P(EGMA-*co*-MMA) soluble coronas as first observed by ^{1}H NMR spectroscopy. Fig. 4 represents the ^{1}H NMR spectra of P(EGMA$_{61}$-*co*-MMA$_{54}$)-*b*-PDEA$_{59}$ in D_2O at low and high pH. It is clear that the signals due to the PDEA block, δ 1.35, 3.25 and 4.40 are suppressed at high pH, indicating dehydration of this block, whereas signals due to the MMA units at δ 3.5 and EGMA units at δ 3.7–3.9 are still prominent in agreement with recent findings [13].

On the other hand at low pH and at temperatures above the cloud point of P(EGMA-*co*-MMA) block, micellar self-assemblies were organized with these statistical blocks (hydrophobic) in the core and the positively charged PDEA blocks located in the corona. The ^{1}H NMR signals corresponding to the EGMA and MMA repeating units were partially attenuated, as also observed previously for PEGMA homopolymers [15], suggesting loose hydrated micellar cores.

DLS measurements were conducted to confirm the formation of micelles for both copolymers in water under different conditions. Aqueous P(EGMA$_{61}$-*co*-MMA$_{54}$)-*b*-PDEA$_{59}$ copolymer solutions of 0.06 wt% concentration were measured at 90° angle. In order to avoid electrostatic interactions between the charged PDEA blocks, NaCl (0.05 M) was added to the terpolymer solutions.

In Fig. 5, autocorrelation functions together with the relaxation time distributions, after CONTIN analysis, of the P(EGMA$_{61}$-*co*-MMA$_{54}$)-*b*-PDEA$_{59}$ aqueous solutions at either pH 3 and 47 °C (Fig. 5a) or pH 8 and 25 °C (Fig. 5b) are depicted. Under both conditions monomodal and narrow distributions of relaxation times were obtained revealing the formation of narrow distributed micelles with polydispersity indices (regarding R_H), as low as 0.03 at pH 3, 47 °C and 0.13 at pH 8, 25 °C, respectively. The apparent hydrodynamic radii of the micelles were determined using the Stokes–Einstein equation at 116 nm for pH 3, 47 °C and 17 nm for pH 8, 25 °C, respectively.

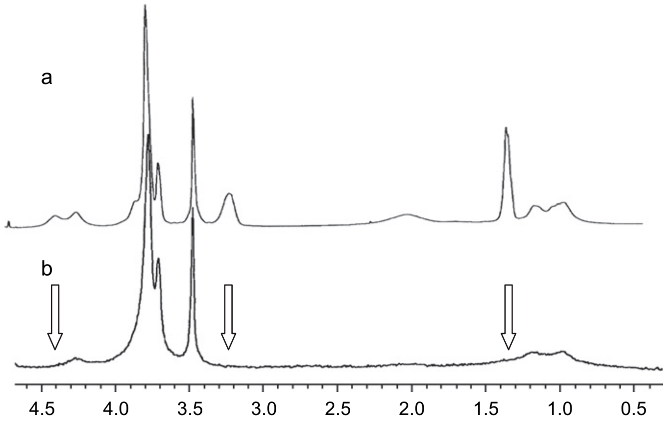

Fig. 4. ^{1}H NMR spectra of P(EGMA$_{61}$-*co*-MMA$_{54}$)-*b*-PDEA$_{59}$ terpolymer in D_2O: unimers at pH 3 (a) and PDEA-core micelles at pH 12 (b).

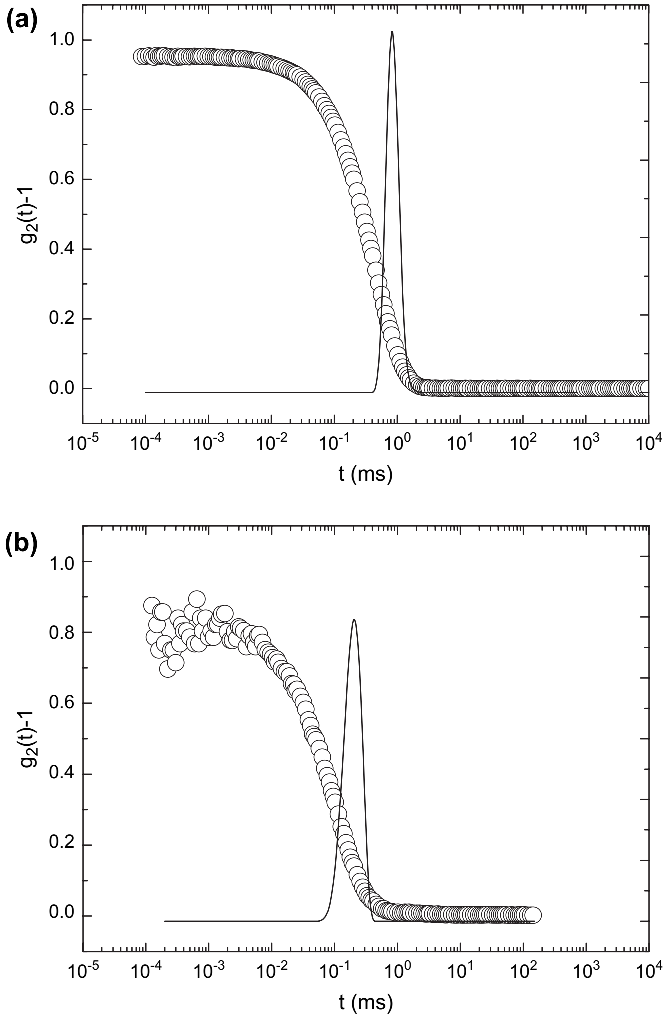

Fig. 5. Autocorrelation functions (at 90°) and distribution of relaxation times (after CONTIN analysis) of 0.06 wt% P(EGMA$_{61}$-*co*-MMA$_{54}$)-*b*-PDEA$_{59}$ aqueous solutions at various conditions: pH 3, 47 °C (a) and pH 8, 25 °C (b).

At pH 3, 47 °C the hydrophobic/hydrophilic balance is shifted to hydrophobic as the P(EGMA-*co*-MMA) block (almost 2/3 in moles of the polymer chain) becomes hydrophobic above its cloud point. Under these conditions the hydrodynamic radius exceeds the fully extending chains and large micelles (or aggregates) with loose hydrated cores and positively charged coronas were formed.

DLS experiments were performed also for the second terpolymer under similar conditions. The autocorrelation functions and time relaxation distributions after CONTIN analysis at pH 3, 60 °C (Fig. 6a) and pH 8, 25 °C (Fig. 6b) of 0.06 wt% P(EGMA$_{49}$-*co*-MMA$_{24}$)-*b*-PDEA$_{116}$ aqueous solutions are presented in Fig. 6. The distributions are bimodal revealing two populations of aggregates with apparent R_H 17 and 88 nm at pH 3, 60 °C, as well as 12 and 103 nm at pH 8, 25 °C, respectively.

Since CONTIN analysis reports intensity-weighted distributions, the proportion of the large particles is strongly exaggerated, as the scattering intensity is strongly dependent on the

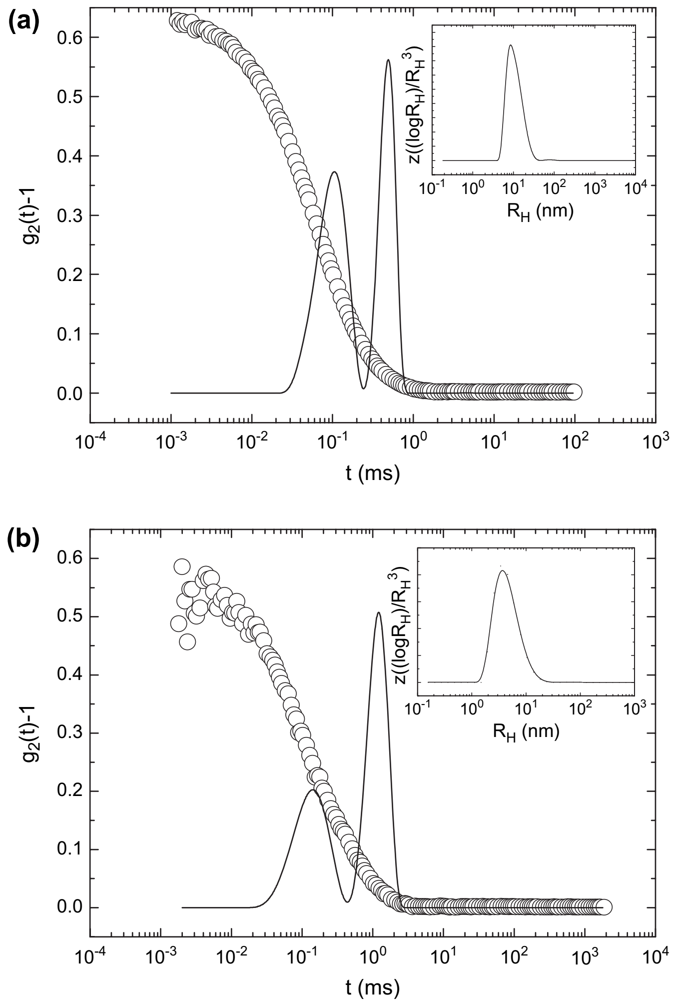

Fig. 6. Autocorrelation functions (at 90°) and distribution of relaxation times (after CONTIN analysis) of 0.06 wt% P(EGMA$_{49}$-*co*-MMA$_{24}$)-*b*-PDEA$_{116}$ aqueous solutions at pH 3, 60 °C (a) and pH 8, 25 °C (b). Insets: hydrodynamic radius mass distribution.

radius of the particles ($\sim R^3$ for spherical particles) [6b]. Thus, the weight fraction of the larger aggregates is actually rather small. Indeed in a corresponding mass distribution plot, $w(\log R_\mathrm{H}) \sim z((\log R_\mathrm{H})/R_\mathrm{H}^3)$, the peak of the larger aggregates disappears (insets of Fig. 6). Again at pH 3, 60 °C and pH 8, 25 °C micelles with P(EGMA-*co*-MMA) and PDEA cores are formed, respectively.

Therefore the terpolymers under investigation exhibit a rich responsive behavior as described schematically in Fig. 7. They are molecularly dissolved in aqueous solutions under acidic conditions (low pH) and room temperature, while they self-assemble responding to pH and/or temperature changes. They form two types of micelles in which the different blocks interchange in the core, exhibiting "schizophrenic" behavior.

The dimensions of the various micellar self-assemblies are summarized in Table 1. Well-defined core/shell micelles are formed either for the P(EGMA$_{49}$-*co*-MMA$_{24}$)-PDEA$_{116}$ at pH 3 [P(EGMA$_{49}$-*co*-MMA$_{24}$)-core] or for the P(EGMA$_{61}$-*co*-MMA$_{54}$)-PDEA$_{59}$ at pH 8 (PDEA core). In both cases, the core/corona molar ratio of the associated chains is lower than unity (0.62 and 0.51, respectively) which implies that star-like micelles are formed.

On the other hand the core/corona molar ratio is higher than unity (e.g. 1.95 and 1.59) and the hydrophobic content predominates in the case of micelles at pH 3 for P(EGMA$_{61}$-*co*-MMA$_{54}$)-PDEA$_{59}$ and pH 8 for P(EGMA$_{49}$-*co*-MNA$_{24}$)-PDEA$_{116}$. In the former case, the apparent hydrodynamic radius exceeds considerably the contour length of the associated macromolecular chains implying that the morphology is not a compact sphere as observed for the latter case, probably because it is more hydrophobic (higher core/corona ratio).

It is also interesting to compare the micellar characteristics of the PDEA-core micelles formed at pH 8 from the different terpolymers. The P(EGMA$_{61}$-*co*-MMA$_{54}$)-PDEA$_{59}$ micelles scatter the light significantly more intensively than those

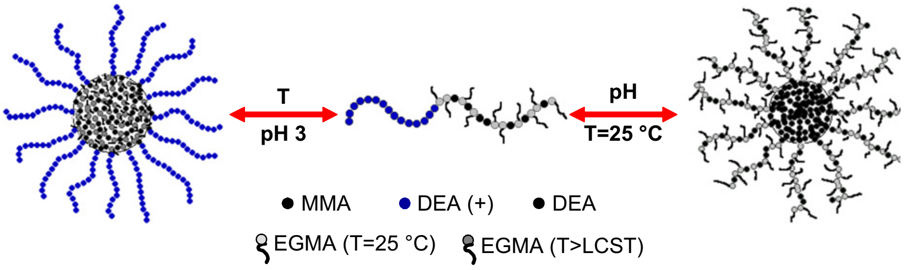

Fig. 7. Schematic representation of reverse micelle formation from the P(EGMA-*co*-MMA)-*b*-PDEA diblock terpolymer by switching the solution pH and/or temperature. At pH > 8 PDEA becomes hydrophobic and it is represented by black dot.

Table 2
Micellar characteristics of P(EGMA-*co*-MMA)-*b*-PDEA at various conditions

Sample	MMA (%) statistical block	P(EGMA-*co*-MMA)-core micelles pH 3, $T >$ LCST		PDEA-core micelles pH 8, $T = 25$ °C		
		R_H (nm)	Core/corona[a]	R_H (nm)	Core/corona[a]	N_agg[b]
P(EGMA$_{49}$-*co*-MMA$_{24}$)-*b*-PDEA$_{116}$	33	17 (88)	0.62	12 (103)	1.59	30
P(EGMA$_{61}$-*co*-MMA$_{54}$)-*b*-PDEA$_{59}$	47	116	1.95	17	0.51	86

[a] Molar ratio of the block repeating units in the core/corona.

[b] By SLS (Zimm plot) $N_\mathrm{agg} = M_\mathrm{w,mic.}/M_\mathrm{w,unim}$.

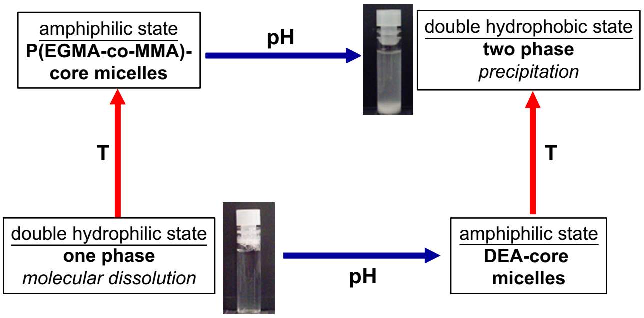

Fig. 8. The four states of the P(EGMA-*co*-MMA)-*b*-PDEA diblock terpolymer in aqueous media.

micelles formed by the P(EGMA$_{49}$-*co*-MMA$_{24}$)-PDEA$_{116}$ although the PDEA length is much shorter (see Fig. 3). The determination of the apparent aggregation numbers through SLS showed indeed that the less hydrophobic terpolymer has the higher N_{agg} (Table 2). This effect should be attributed to the higher hydrophobic content of the corona chains that is responsible for the micelle stabilization. The MMA molar percentages of the stabilizing statistical block of the P(EGMA$_{61}$-*co*-MMA$_{54}$)-PDEA$_{59}$ reaches 47% inducing higher N_{agg}. Therefore the copolymer composition not only controls the cloud point (and/or LCST) of the statistical block but also its hydrophobicity. This in turn significantly affects the observed association phenomena and the characteristics of the micellar self-assemblies.

3.5. The double-hydrophobic state

Another interesting aspect of these double-hydrophilic terpolymers is their double-hydrophobic state in which two phases coexist (precipitation). This state can be reached following two main routes as depicted in Fig. 8, i.e. by increasing temperature and sequentially pH or the opposite. In both cases, the terpolymers pass through the amphiphilic state where micelles are spontaneously formed. This procedure could be used to remove chemical species from water that can be entrapped within the cores of the micelles formed in the amphiphilic state. The choice of the precipitation route is dictated by the chemical affinity between the solutes and the core-chains (advantage of the ‘‘schizophrenic’’ character). After precipitation of the micelles by switching pH (or temperature) the solutes can be removed by filtration.

4. Conclusions

Novel double-hydrophilic diblock terpolymers of the A-*b*-(B-*co*-C) type were designed and explored in aqueous media. The main target of this work was to show that the incorporation of statistical copolymers with tunable LCST as building blocks for block copolymers results in interesting responsive polymeric materials.

More precisely, P(EGMA-*co*-MMA)-*b*-PDEA diblock terpolymers exhibit a rich phase behavior due to their pH, temperature and ionic strength sensitivity. At low pH and room temperature they are molecularly dissolved (double-hydrophilic state). Two stimuli can impose transformation of the terpolymers to their amphiphilic form (i.e. temperature and pH) inducing spontaneous self-organization that leads to two distinct micellar self-assemblies (‘‘schizophrenic’’ behavior). This rich phase behavior could be considered as potential applications for separation procedures.

A more general impact of the present study is that although the polymerization method chosen here was group transfer polymerization, other controlled/living polymerization methods such as ATRP or RAFT, can be applied for the preparation of such block copolymers bearing statistical copolymer segments. The difference between the classical block copolymers (constituted of homopolymer blocks) and the homo/statistical copolymers is that in the latter case the statistical building blocks exhibit combined tunable properties (e.g. polyampholytes with tunable isoelectric point [8], thermoresponsive with tunable LCST) that cannot be afforded by any single monomeric unit. Therefore the use of statistical copolymer segments in macromolecular engineering of block copolymers opens up new routes towards ‘‘smart’’ polymeric materials with unique properties.

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